Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Clinical Evaluation of etafilcon A with Ketotifen

Protocol CR-5930

Version: v3.0, Amendment 2.0

Date: 31 October 2017

Investigational Products: etafilcon A with 0.019 mg ketotifen (K-Lens)

Key Words: etafilcon A, etafilcon A with ketotifen, 1-DAY ACUVUE® Brand Contact Lenses, Daily Disposable, Dispensing, logMAR visual acuity, K-Lens, Placebo, Wearing Time, CLUE™ Handling, daily wear.

Statement of Compliance to protocol, GCP and applicable regulatory guidelines:
This trial will be conducted in compliance with the protocol, ISO 14155,[1] the International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP),[2] the Declaration of Helsinki,[3] and all applicable regulatory requirements.

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION

Title: Clinical Evaluation of etafilcon A with Ketotifen
Protocol Number: CR-5930
Version: 3.0, Amendment 2.0
Date: 31 October 2017

SPONSOR NAME AND ADDRESS

Johnson & Johnson Vision Care, Inc.
7500 Centurion Parkway,
Jacksonville, FL 32256

MEDICAL MONITOR

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Title: Principal Research Optometrist
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The Medical Monitor must be notified by the clinical institution/site by e-mail or telephone within 24 hours of learning of a Serious Adverse Event. The Medical Monitor may be contacted during business hours for adverse event questions. General study related questions should be directed towards your assigned clinical research associate.

The Medical Monitoring Plan is maintained as a separate document and included in the Trial Master File.

AUTHORIZED SIGNATURES

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations,[4] ICH guidelines,[2] ISO 14155,[1] and the Declaration of Helsinki.[3]

Author	See Electronic Signature Report Brian Pall Senior Principal Research Optometrist	Date
Clinical Operations Manager	See Electronic Signature Report [redacted]	Date
Biostatistician	See Electronic Signature Report [redacted]	Date
Data Management	See Electronic Signature Report [redacted]	Date
Reviewer	See Electronic Signature Report [redacted]	Date
Approver	See Electronic Signature Report [redacted]	Date

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
1.0	Brian Pall	Original Protocol	10 August 2017
2.0	Brian Pall	Section 2.2 – updated Secondary Endpoint to "clinically significant (Grade 3 or 4) slit lamp findings." Section 6.4 – updated lens packaging information. Section 14.2 – updated reference information and changed Table 1 to Table 4. Updated TOC. Section 14.6 – Added section number for Secondary Analysis and updated to "Secondary endpoints will be summarized descriptively using all available data including data from unscheduled visits." Updated protocol version and date throughout.	19 September 2017
3.0	Brian Pall	Figure 1 – updated study flowchart to clarify lens modification procedures Section 7.2 – Updated Visit 1 instructions on Step 1.13 and 1.16 to clarify lens modification procedures. Updated protocol version and date throughout Section 5.2 - Removed the specific randomization letter codes New medical monitor assigned to the study Appendix C – Added package insert	31 October 2017

SYNOPSIS

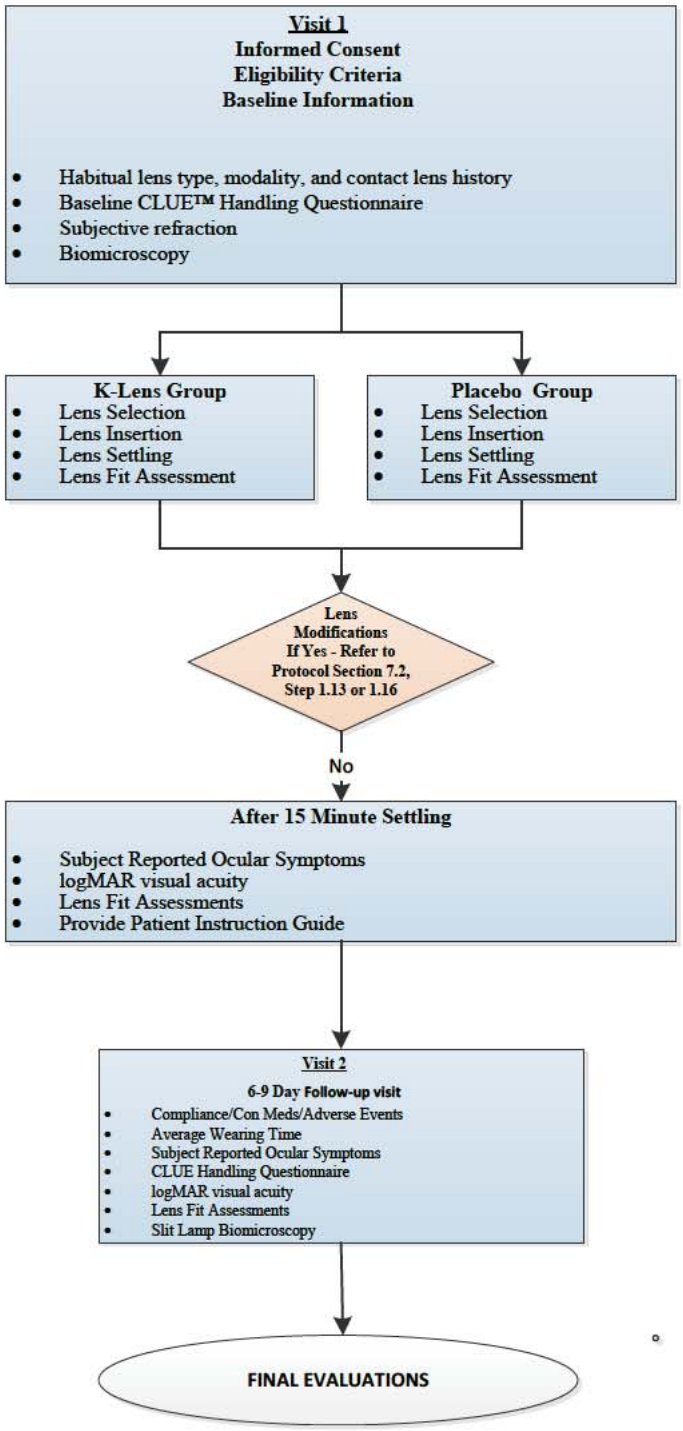
Protocol Title	Clinical Evaluation of etafilcon A with ketotifen
Sponsor	Johnson & Johnson Vision Care, Inc., 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Developmental phase: Phase 2
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor
Test Article(s)	Investigational Products: K-Lens: etafilcon A with 0.019 mg ketotifen Placebo: 1·Day ACUVUE® Brand Contact Lens
Wear and Replacement Schedules	Wear Schedule: Daily Disposable Replacement Schedule: Daily
Objectives	The purpose of this study is to evaluate the clinical performance of K-Lens produced on the new J&J Vision Care, Inc. manufacturing line in Limerick, Ireland.
Study Endpoints	The primary endpoint is monocular contact lens best-corrected distance visual acuity on logMAR scale. This will be evaluated under high luminance and high contrast conditions at 4 meters from ETDRS charts at 1-Week Follow-up Visit. The secondary endpoints are: • Proportion of eyes with significant (Grade 3 or 4) slit lamp findings • Proportion of eyes with unacceptable lens fitting Adverse events, subject reported ocular symptoms, subjective assessment of lens handling, number and reasons for discontinuation, number and reasons for unscheduled lens replacement including lens damage will be monitored and summarized.
Study Design	This is a randomized, double-masked, bilateral, controlled, two-arm parallel group, multi-site, 1-Week dispensing study. Subjects are scheduled for 2 study visits: • Visit 1: Initial screening, baseline evaluation, lens assignment, lens dispensing and clinical assessments • Visit 2: Follow-up visit 6 to 9 days after the initial visit with clinical assessments and exit procedures. See the flowchart at the end of the synopsis for the schematic of the study visits and procedures of main observations.

Sample Size	This study will target to enroll approximately 132 subjects with a target completion of 80 subjects in the K-Lens arm and 40 in the Placebo arm.
Study Duration	The study duration will be approximately 8 weeks
Anticipated Study Population	The study populations will be healthy normal habitual contact lens wearers that are at least 18 years old and less than 40 years.
Eligibility Criteria	Potential subjects must satisfy all of the following criteria to be enrolled in the study 1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol 3. Between 18 and 39 (inclusive) years of age at the time of baseline visit 4. The subject must be a habitual lens wearer for a least 6 days/week and for a minimum of 8 hours per day over the last month. 5. The subject's contact lens correction must be in the range of -1.00 D to -6.00 D (inclusive) in each eye. 6. The subject's refractive cylinder must be 1.00 D or less in each eye 7. Have a spherocylindrical best corrected visual acuity of 20/30 or better in each eye (Snellen Visual Acuity) Potential subjects who meet any of the following criteria will be excluded from participating in the study: 1. Currently pregnant or lactating 2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study 3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear 4. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion

	5. Any corneal distortion resulting from previous hard or rigid gas permeable contact lens wear, history of strabismus, or current monovision, multi-focal, or toric contact lens correction. 6. Any current use of rewetting drops or ocular medication 7. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.) 8. Any grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA Biomicroscopy Scale 9. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear 10. Any known hypersensitivity or allergic reaction to ketotifen 11. Participation in any eye drop, contact lens or lens care product clinical trial within 14 days prior to study enrollment 12. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician)
Disallowed Medications/Interventions	No ocular medications (Rx or OTC) or any systemic medications that (e.g., chronic steroid use) are known to interfere with contact lens wear
Measurements and Procedures	Monocular contact lens best-corrected distance visual acuity (measured via logMAR visual acuity charts)
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	None

Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
logMAR	Logarithm of Minimal Angle of Resolution
MOP	Manual of Procedures
NIH	National Institutes of Health
OD	Right Eye
OS	Left Eye
OTC	Over the Counter
OU	Both Eyes
PD	Protocol Deviation
PI	Principal Investigator
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRO	Patient Reported Outcome
QA	Quality Assurance
QC	Quality Control
Rx	Prescription
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan

SAS	Statistical Analysis System
SD	Standard Deviation
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VA	Visual Acuity

1. INTRODUCTION AND BACKGROUND

The etafilcon A with ketotifen contact lens is being developed as a novel drug/device combination product that incorporates the anti-allergy agent ketotifen with the same material as the 1•DAY ACUVUE® Brand disposable contact lens (etafilcon A daily disposable contact lens). This new product will be referred to hereafter as K-Lens. The control 1•DAY ACUVUE® Brand disposable contact lens will be referred to hereafter as Placebo. Ocular allergy, and the discomfort associated with its signs and symptoms, is a common cause of contact lens intolerance and of seasonal exacerbation of eye allergy symptoms in contact lens wearers.[5,6] The creation of a concomitant system of an anti-allergy agent and a contact lens will offer significant advantages over existing therapies in that it allows contact lens users to continue wearing their lenses during the allergy season while preventing ocular itching associated with allergic conjunctivitis.

Ketotifen fumarate, a benzocycloheptathiophene derivative, is an approved noncompetitive H_1 receptor antagonist that stabilizes mast cells and prevents eosinophil accumulation, thus providing multiaction therapy. Ketotifen fumarate ophthalmic solution is an effective, safe, and well-tolerated therapy for the management of ocular allergy with a duration of action of up to 12 hours as demonstrated in the conjunctival allergen challenge mode.[7, 8]

K-Lens has been evaluated for safety, tolerability, and efficacy (prevention of ocular itching) in previous studies.[9-20] The results of these studies have shown it to be safe, tolerable and efficacious. Two (2) pivotal Phase 3 studies have shown that K-Lens was effective in the prevention of ocular itching associated with allergic conjunctivitis at 15 minutes and 12 hours following lens insertion.[16, 17] The goal of this study is to evaluate the clinical performance of K-Lens produced on the new J&J Vision Care, Inc. manufacturing line in Limerick, Ireland, in a population of normal, healthy, habitual contact lens wearers.

1.1. Name and Descriptions of Investigational Products

The K-Lens is a combination product consisting of an etafilcon A soft hydrophilic contact lens with 0.019 mg ketotifen. Additional information pertaining to the device and drug components is listed below:

Device component – The device component is an etafilcon A soft contact lens equivalent to 1-DAY ACUVUE® Brand Contact Lenses. This product is currently cleared by Food & Drug Administration (FDA) under 510(k) K013973. The predicate device in this 510(k) was ACUVUE® (etafilcon A) Brand Contact Lenses, approved by FDA under PMA N18-033.

The etafilcon A soft hydrophilic contact lenses have an extensive history on the United States (US) market and are indicated for the correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00 D or less of astigmatism. Lenses are to be worn as a daily wear contact lens (periods of less than 24 hours while awake) and disposed of after removal.

Drug component – The drug component, ketotifen, is the active ingredient in the currently marketed eye drop, ZADITOR® (ketotifen fumarate ophthalmic solution, 0.035%)

manufactured by Alcon Pharmaceuticals. ZADITOR® was originally approved under NDA 21-0166 in 1999 as a prescription drug for the prevention of ocular itching associated with allergic conjunctivitis (selective H_1 antihistamine/mast cell stabilizer) and switched to over-the-counter in 2006 (NDA 21-066/S011). The drug component may use the Reference Listed Drug under NDA 021066 (ZADITOR® [ketotifen fumarate ophthalmic solution, 0.035%]).

1.2. Intended Use of Investigational Products

The proposed intended use of K-Lens, a daily disposable contact lens, is to provide vision correction while preventing ocular itching associated with allergic conjunctivitis. The prevention of itch has been demonstrated to last through 12 hours in clinical studies; however, the contact lens may be worn for longer than 12 hours for vision correction.

The intended users are phakic or aphakic patients who are suitable for contact lens wear and experience ocular allergic itch due to allergic conjunctivitis and who do not have red eye(s) or more than 1.00 D of astigmatism.

1.3. Summary of Findings from Nonclinical Studies

K-Lens was shown to be biocompatible and tolerable on eye. Specifically, K-Lens extracts were shown to be non-cytotoxic, non-ocular irritating and non-sensitizing. The extracts of K Lens in a packing solution were not mutagenic. K-Lens placed on rabbit eyes has been shown to be non-irritating and non-toxic to the eye, and without systemic toxicity following a minimum seven hours of daily lens wear for up to 6 months.[21]

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans.

For the most comprehensive nonclinical information regarding K-Lens, refer to the latest version of the Investigator's Brochure.[21]

1.4. Summary of Known Risks and Benefits to Human Subjects

K-Lens has been evaluated for safety, tolerability, and efficacy (prevention of ocular itching) in previous studies.[9-20]

The results from the Phase 3 safety trials for K-Lens have shown that the risks to wearing K-Lens are not substantially increased as compared to other non-medicated contact lenses worn in a daily disposable modality or the use of ketotifen fumarate ophthalmic drops. The ocular adverse events with the highest reported incidence from the Phase 3 safety trials were instillation site irritation (3.7%), dry eye (0.9%), eye irritation (0.8%). All non-ocular adverse events from the two Phase 3 safety trials were assessed by the Investigators as not related to study medication.

The benefits of K-Lens include the correction of refractive error and the prevention of itch associated with allergic conjunctivitis.

For the most comprehensive clinical information regarding K-Lens refer to the latest version of the Investigator's Brochure.[21]

1.5. Relevant Literature References and Prior Clinical Data Relevant to Proposed Clinical Study

K-Lens is an investigational drug/device combination product and the clinical results have yet to be published. Additionally, there are no known publications reporting clinical data with a contact lens containing an anti-allergy medication.

K-Lens has been evaluated in previous studies.[9-20] for safety, tolerability, and efficacy (prevention of ocular itching). Additionally, in the previous K-Lens studies, visual acuity was assessed using Snellen visual acuity charts which are commonly used in clinical practice. The proposed clinical study will assess visual acuity using logMAR (ETDRS) charts which are more commonly used in clinical research studies. By collecting data from both types of visual acuity charts, a more comprehensive assessment of visual acuity with K-Lens will be obtained.

For additional clinical information regarding K-Lens, refer to the latest version of the Investigator's Brochure.[21]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

The purpose of this study is to evaluate the clinical performance of K-Lens produced on the new J&J Vision Care, Inc. manufacturing line in Limerick, Ireland.

2.2. Endpoints

Primary Endpoint

The primary endpoint is monocular contact lens-corrected distance visual acuity using a logMAR visual acuity scale. This will be evaluated under high luminance and high contrast conditions at 4 meters from ETDRS charts at the 1-week follow-up visit.

Secondary Endpoint(s)

- Proportion of eyes with clinically significant (Grade 3 or 4) slit lamp findings.
- Proportion of eyes with unacceptable lens fitting.

Other Endpoints

Average daily wear time (in Hours):
Average daily wear time will be calculated as the number of hours between subjects reported time of insertion and time of removal of the study lenses, on an average day, at 1-Week Follow-up evaluation.

Subjective assessment of lens handling:
Lens handling will be assessed using Contact Lens User Experience™ (CLUE) questionnaire at 1-Week Follow-up evaluation. CLUE™ is a validated patient reported outcomes (PRO) questionnaire to assess patient-experience attributes of soft contact lenses (comfort, vision, handling, and packaging) in a contact-lens wearing population in the US, ages 18-65. Derived CLUE™ scores using Item Response Theory (IRT) follow a normal distribution with a population average score of 60 (SD 20), where higher scores indicate a more favorable/positive response with a range of 0-120. A 5-point increase in an average CLUE™ score translates into 10% shift in the distribution of scores for population of soft contact lens wearers.[22]

Slit-lamp findings:
Frequency and severity by eye of slit lamp findings (SLFs) including conjunctival injection, corneal edema, corneal neovascularization, corneal staining, tarsal abnormalities or any other complications. SLFs will be evaluated at fitting and post-fitting evaluation visits including unscheduled visits.

Subject's Reported Ocular Symptoms:
Frequency and severity by eye of subject's reported ocular symptoms and problems with the study lens at fitting and post-fitting evaluation visits including unscheduled visits.

Lens fitting characteristics:
Frequency by eye of mechanical lens fitting characteristics including lens centration and lens movement and overall lens fitting acceptability at fitting and 1-Week Follow-up evaluations.

Adverse events, number and reasons for discontinuation, number and reasons for unscheduled lens replacement including lens damage will be monitored and descriptively evaluated.

2.3. Hypotheses

Primary Hypotheses

The K-Lens will be non-inferior to the Placebo lens with respect to monocular distance contact lens-corrected visual acuity. A non-inferiority margin of 0.1 logMAR (one line) units will be used.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

The study populations will be healthy normal habitual contact lens wearers that are at least 18 years old and less than 40 years old.

3.2. Inclusion Criteria

Potential subjects must satisfy all of the following criteria to be enrolled in the study:

1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form

2. Appear able and willing to adhere to the instructions set forth in this clinical protocol
3. Between 18 and 39 (inclusive) years of age at the time of baseline visit
4. The subject must be a habitual lens wearer for a least 6 days/week and for a minimum of 8 hours per day over the last month.
5. The subject's contact lens correction must be in the range of -1.00 D to -6.00 D (inclusive) in each eye.
6. The subject's refractive cylinder must be 1.00 D or less in each eye
7. Have a spherocylindrical best corrected visual acuity of 20/30 or better in each eye (Snellen Visual Acuity)

3.3. Exclusion Criteria

Potential subjects who meet any of the following criteria will be excluded from participating in the study:

1. Currently pregnant or lactating
2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study
3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear
4. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion
5. Any corneal distortion resulting from previous hard or rigid gas permeable contact lens wear, history of strabismus, or current monovision, multi-focal, or toric contact lens correction.
6. Any current use of rewetting drops or ocular medication
7. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.)
8. Any Grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA Biomicroscopy Scale
9. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear
10. Any known hypersensitivity or allergic reaction to ketotifen
11. Participation in any eye drop, contact lens or lens care product clinical trial within 14 days prior to study enrollment
12. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician)

3.4. Enrollment Strategy

Study subjects will be recruited from the Institution/clinical site's subject database and/or utilizing Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approved materials.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is a randomized, double masked, bilateral, controlled, two-arm parallel group, multi-site, 1-week dispensing study. Approximately 132 subjects will be screened and randomly assigned to either K-Lens or Placebo using 2:1 ratio (i.e. 2/3 of subjects on the K-Lens arm and 1/3 on the Placebo arm). The goal is for a sample size of 120 (80 subjects in K-lens and 40 subjects in Placebo) after subjects who withdraw or are lost-to-follow-up.

The study begins with an Initial Visit (Visit 1). If a subject is found to meet all eligibility criteria (see Section 34.), they will be randomized and fit with either the K-Lens or Placebo lens in both eyes based on the randomization scheme provided to the investigators; otherwise, the subject will be deemed ineligible for this study.

Successfully dispensed subjects at the initial visit will be scheduled for a follow-up visit (Visit 2). The follow-up visit will occur approximately 6 to 9 days after the Initial Visit. Unscheduled follow-up visits may occur during the study. Subjects will be advised to wear the study lenses at least 8 hours a day for a minimum of 6 days.

Both study lenses will be worn as a daily disposable modality. J&J Vision will provide the investigational sites with sufficient quantities of study lenses and supplies to complete the study.

The Investigator is responsible for ensuring that all subjects entering the study conform to subject selection criteria. The number of subjects targeted for randomization and completion are as follows:

Table 1: Target number of subjects by arm and site

	K-Lens	Placebo	Total
Randomization	88	44	132
Completion	80	40	120
Number of sites	6	6	6
Subjects/site (Min-Max)	12-16	5-9	20-24

4.2. Study Design Rationale

Randomized, double masked, controlled designs are the gold standard to perform scientifically sound evaluations of the intervention by reducing bias associated with the conduct and interpretation of a clinical trial and avoiding confounding from other factors. The unequal

assignment using 2:1 K-Lens versus Placebo ratio was considered to gain additional information on the K-Lens produced on the new JJVC manufacturing line in Limerick, Ireland.

4.3. Enrollment Target and Study Duration

- This study will target to enroll approximately 132 subjects (88 subjects in K-lens arm and 44 in Placebo arm) with a minimum of 120 subjects to complete (80 subjects in K-lens arm and 40 in Placebo arm).
- Subjects will be considered enrolled in this trial only after they have reviewed and signed the informed consent.
- The study duration will be approximately 8 weeks and there will be a total of 2 visits

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

Subjects will be randomly assigned to either K-Lens or Placebo arm based on a computer-generated randomization schedule prepared before the start of the study. The randomization will be stratified by investigational site and randomly permuted blocks of 3 assignments will be used to achieve 2:1 K-Lens versus Placebo ratio within each study site.

Randomization must be performed at the initial visit. The following must have occurred prior to randomization:

- Informed consent has been obtained
- It has been determined that the subject meets all the inclusion / exclusion criteria
- Subject history and baseline information has been collected

When the trial fitting assessment is ready to be conducted, the following steps should be followed:

1. Investigator or designee (documented on the Delegation Log) will consult the randomization scheme to obtain the study test article assignment for that subject prior to dispensing.
2. Investigator or designee will record the subject's number on the appropriate line of the randomization scheme.
3. Investigator or designee will pull the appropriate test articles from the study supply. All test articles that were opened, whether dispensed or not, must be recorded on the Test Article Accountability Log in the "Lenses Dispensed" section.

5.2. Masking

This is a double-masked study where subjects, investigators are masked to the identity of the study lenses during the study period. Every attempt will be made to keep the other clinical trial personnel involved in the study (e.g. Data management, Biostatistician and Clinical Operations) unaware of the identity of the study lenses. The identity of the study lenses will be masked by over labeling the blister packs with a label containing the study number, lot number, sphere power, expiration date and the randomization codes. Only the personnel involved in the over labeling and the Statistician generating the randomization scheme will

have access to the decode information translating the randomization codes into K-Lens and Placebo arms. The medical monitor will also have access to the decode information in case breaking the mask is necessary for the urgent medical treatment of a subject.

5.3. Procedures for Maintaining and Breaking Randomization Codes

Under normal circumstances, the mask should not be broken until all subjects have completed the study and the database is finalized. Otherwise, the mask should be broken only if specific emergency treatment/course of action would be dictated by knowing the treatment status of the subject. In such cases, the Investigator may, in an emergency, contact the medical monitor. In the event the mask is broken; the Sponsor must be informed as soon as possible. The date, time, and reason for the unmasking must be documented in the subject record. The Investigator is also advised not to reveal the study treatment assignment to the clinical site or Sponsor personnel.

Subjects who have had their treatment assignment unmasked are expected to return for all remaining scheduled evaluations.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 2: Test Articles

	Test	Placebo
Name	etafilcon A with 0.019 mg ketotifen	1·DAY ACUVUE® Brand Contact Lens
Other Name	K-Lens	Placebo
Manufacturer	J&J Vision	J&J Vision
[redacted]	[redacted]	[redacted]
Lens Material	etafilcon A with 0.019 mg ketotifen	etafilcon A
Nominal Base Curve @ 22°C	8.5	8.5
Nominal Diameter @ 22°C	14.2	14.2
Nominal Distance Powers (D)	-1.00 to -6.00 D in 0.25 D steps	-1.00 to -6.00 D in 0.25 D steps
Nominal Oxygen Permeability (Dk)	25.5	25.5
Modality in Current Study	Daily Disposable	Daily Disposable
Replacement Frequency	Daily	Daily
Packaging Form (vial, blister, etc.)	Blister pack	Blister pack
Concentration of ketotifen per lens	0.019 mg	0 mg

Given the daily disposable modality and the one week duration, approximately 6-9 lenses per eye per subject will be needed for each lens type.

6.2. Ancillary Supplies/Products

None allowed.

6.3. Administration of Test Articles

Test articles will be dispensed to subject meeting all eligibility requirements, including any dispensing requirements set forth in this clinical protocol. Subjects will be dispensed an adequate supply of test articles to complete the study. Lost or damaged test articles may be replaced at the discretion of the Investigator and/or the Sponsor.

6.4. Packaging and Labeling

The test articles will be packaged in blisters as the primary packaging. The test article will be over-labeled to mask the subject/Investigators to the identity of the lens. The test articles will be in investigational cartons sealed with a tamper evident seal.
Storage Conditions

Test articles will be maintained at controlled room temperature. Controlled room temperature is the temperature maintained thermostatically that encompasses at the usual and customary working environment of 20°–25°C (68°–77°F).

Excursions between 15° and 30°C (59° and 86°F) are allowed and transient spikes up to 40°C are permitted as long as they do not exceed 24 hours.

Temperatures above 30°C that exceed 24 hours and any temperature spikes above 40°C will require a non-conformance investigation. The investigation will be conducted by the J&J Vision, R&D Quality Systems Stability Group. As part of the investigation conclusions, a final disposition of the lots involved with the temperature excursion will be required.

Test articles should remain in their closed secondary cartons during storage to minimize light exposure.

Test articles must be kept under secure conditions.

6.5. Collection and Storage of Samples

When possible, any lens or test article associated with an Adverse Events and/or a Product Quality Complaint must be retained and stored in a glass vial with moderate solution pending directions from the sponsor for potential return back to J&J Vision.

6.6. Accountability of Test Articles

J&J Vision Care, Inc. will provide the Investigator with sufficient quantities of study articles and supplies to complete the investigation. The Investigator is asked to retain all lens shipment documentation for the test article accountability records.

Test article must be kept in a locked storage cabinet, accessible only to those assigned by the Investigator for dispensing. The Investigator may delegate this activity to authorized study site personnel listed on the Site Delegation Log. All test articles must be accounted. This includes:

1. What was dispensed for the subject for trial fitting, to wear out of the office, or issued for the subject to replace appropriately between visits
2. What was returned to the Investigator unused
3. The number and reason for unplanned replacements.

The Investigator will collect all unused test articles from the subjects at the end of the subject's participation. Subject returned unused test articles must be separated from the clinical study inventory of un-dispensed test articles, and must be labeled with the subject number and date of return. Following final reconciliation of test articles by the monitor, the Investigator or monitor will package and return all unused test articles to JJVC.

If there is a discrepancy between the shipment documents and the contents, contact the study monitor immediately.

[redacted] Site Instructions for Test Article Receipt and Test Article Accountability for additional information.

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Information	Visit 1 Screening, Baseline, Randomization, Lens Dispensing, Initial Clinical Assessments	Visit 2 1-Week Follow-up, Final Evaluation
Time Point	Day 1	Day 6-9
Estimated Visit Duration	2.0 hours	1.5 hours
Statement of Informed Consent	x	
Demographics	x	
Medical History/Concomitant Medications	x	x
Inclusion/Exclusion Criteria	x	
Habitual Contact Lens Information	x	
Compliance and Subject Reported Ocular Symptoms and Adverse Event Review	x	x
Entrance Snellen Distance Visual Acuity	x	x
Subjective Sphero-Cylindrical Refraction and visual acuities	x	x
Subjective Best Sphere Refraction and visual acuities	x	
Slit Lamp Classification Scale	x	x
Lens Assignment	x	

Visit Information	Visit 1 Screening, Baseline, Randomization, Lens Dispensing, Initial Clinical Assessments	Visit 2 1-Week Follow-up, Final Evaluation
Time Point	Day 1	Day 6-9
Estimated Visit Duration	2.0 hours	1.5 hours
Lens Insertion & Settling	x	
Visual Acuity and Over Refraction	x	
Monocular logMAR Visual Performance (High Contrast, High Illumination)	x	x
Lens Fit Assessment	x	x
Reported Average Wearing Time		x
CLUE Handling	x	x
Exit Snellen Distance Visual Acuity	x	x
Dispense Patient Instruction Guide	x	
Dispense Test Article	x	
Study Completion		x

7.2. Detailed Study Procedures

VISIT 1

The subject must present to Visit 1 wearing their habitual contact lenses on the day of the visit.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note**: The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's date of birth, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.4	Habitual Lenses	Questions regarding the subject's habitual lens type and parameters.	
1.5	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be	

		answered "no" for the subject to be considered eligible.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.6	Baseline Questionnaire	The subject will respond to the CLUE™ Baseline Handling Questionnaire (Appendix A)	
1.7	Entrance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual contact lens correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.8	Subjective Sphero-cylindrical Refraction	Complete subjective spherocylindrical refraction and record the resultant distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
1.9	Subjective Best Sphere Refraction	Perform subjective best sphere refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity (OD, OS, OU) to the nearest letter. **Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leave the red chart sharper.	[redacted]
1.10	Slit Lamp Findings	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are Grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to determine eligibility. If discontinued a final examination must be completed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]

1.11	Eligibility after Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.12	Lens Selection	Assign the study lens based on the randomization scheme. Select the contact lens power based on subjective best sphere refraction.	
1.13	Lens Insertion	The Investigator or the subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable. Note: If a damaged lens needs to be replaced, the subject will have to return no sooner than the following day, since subjects are not allowed to wear more than one lens per eye per day. When a subject returns for another lens, new baseline information must be recorded (starting with step 1.7), and then proceed per protocol through the remaining Visit 1 steps.	
1.14	Lens Settling	Allow the study lenses to settle for a minimum of 15 minutes.	
1.15	Subjective Best Sphere Over Refraction	Perform subjective best sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU). **Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leave the red chart sharper.	[redacted]

1.16	Lens Power Modification (if applicable)	Adjust the lens power if the subject's best sphere over-refraction is not plano. One power modification is allowed. If the subject's best sphere over-refraction is not plano, the subject will have to return no sooner than the following day, since subjects are not allowed to wear more than one lens per eye per day. When a subject returns for another lens, new baseline information must be recorded (starting with step 1.7), and then proceed per protocol through the remaining Visit 1 steps.	
1.17	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.18	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement; • edge lift; • excessive movement in primary and up gaze; or • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push up test. **Note**: if lens fit is unacceptable subject will be discontinued from the study.	[redacted]
1.19	Distance ETDRS LogMAR Visual Acuity	Perform monocular distance ETDRS LogMAR visual acuity test at a 4-meter distance over the test eye only under the following condition: • bright illumination (e.g., >400 lux), high luminance, with high contrast charts (HLHC); The Precision Vision 4-meter high contrast ETDRS charts (Chart 1 and Chart 2) will be used. One measurement will be recorded per eye.	[redacted]

1.20	Exit Snellen VA	Record subjects' distance visual acuity, OD, OS and OU to the nearest letter.	[redacted]
1.21	Continuance	For the subject to continue in the study, they must meet all three of the following criteria: • Visual acuity is 20/30 or better OD and OS • The lens fit is acceptable OD and OS • Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject.	
1.22	Dispense	The lenses will be dispensed for a 6-9 day wearing period. During this time, they will be instructed to wear the lenses at least 6 days and at least 8 hours per day that they are worn. • Dispense enough lenses to last the subject to their scheduled follow-up visit. Do not dispense extras*. • The lenses will be worn as daily wear/daily disposable only. • Rewetting drops are not permitted • A patient instruction booklet will be provided. • Subjects will be scheduled for their 1-week follow-up visit, * **Note:** In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.	

VISIT 2

The subject must present to Visit 2 wearing test article on the day of the visit.

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
2.1.	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
2.2.	Wearing Time	Record the average wearing time and comfortable wearing time.	
2.3.	Compliance	Confirm compliance with the prescribed wear schedule.	
2.4.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.5.	Visual Acuity	Record the distance Snellen visual acuity with the contact lenses (OD, OS, and OU) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
2.6.	Follow-Up Questionnaire	The subject will respond to the CLUE Handling Questionnaire (Appendix A)	
2.7.	Distance ETDRS LogMAR Visual Acuity	Perform monocular distance ETDRS LogMAR visual acuity test at a 4-meter distance over the test eye only under the following condition: • bright illumination (e.g., >400 lux), high luminance, with high contrast charts (HLHC); The Precision Vision 4-meter high contrast ETDRS charts (Chart 1 and Chart 2) will be used. One measurement will be recorded per eye.	[redacted]
2.8.	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement; • edge lift;	[redacted]

		• excessive movement in primary and up gaze; or • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push up test. **Note**: if lens fit is unacceptable subject will be discontinued from the study.	
2.9.	Slit Lamp Findings	FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" grade for all observations listed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]

FINAL EVALUATION

The final evaluation will ordinarily take place immediately following the last scheduled follow-up visit per the study protocol. It may also take place at any point the subject discontinues the study or is terminated from the study.

Final Evaluation			
Step	Procedure	Details	[redacted]
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study indicate the reason.	[redacted]
F.2	Subjective spherocylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU). [redacted]	

7.3. Unscheduled Visits

If, during the investigation, a subject requires an unscheduled visit to the clinical site, the following information will be collected at a minimum:

- Chief complaint prompting the visit. If the reason is an adverse event, the applicable eCRF for the adverse event must be completed and subject record completed as appropriate
- Date and time of the visit and all procedures completed at the unscheduled visit
- Review of adverse event and concomitant medications
- Documentation of any test article dispensed or collected from the subject, if applicable
- Slit lamp findings (using the Slit Lamp Classification Scale)

If the Investigator withdraws a subject from the study, the final study visit case report forms must be completed indicating the reason(s) why the subject was withdrawn. The subject record must be completed documenting the date and primary reason for withdrawal and the study CRA notified.

Any ocular and non-ocular adverse events that are ongoing at the time of the study visit will be followed by the Investigator, within licensure, until they have resolved, returned to pre-treatment status, stabilized, or been satisfactorily explained. If further treatment i.e., beyond licensure is required, the subject will be referred to the appropriate health care provider.

The following information will be collected during an unscheduled visit.

Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit	
U.2	Change of Medical History and Concomitant Medications	Questions regarding the change of subjects' medical history and concomitant medications.	
U.3	VA	Record the distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
U.4	Subjective Sphero-cylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU).	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" grade for all observations listed. After the slit lamp examination, at the discretion of the Investigator, rinse the subject's eyes thoroughly with preservative-free saline.	
U.6	Dispensing	Based on the specific reason for the unscheduled visit, additional study lenses may be dispensed according to the randomization scheme.	
U.7	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

7.4. Laboratory Procedures

Not Applicable

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent;
- they are eligible;
- have not withdrawn/discontinued from the study for any reason described in Section 8.2
- completed all visits through the final visit 2

8.2. Withdrawal/Discontinuation from the Study

A subject will be withdrawn from the study for any of the following reasons:

- Subject death during the study period
- Subject withdrawal of consent
- Subject not compliant to protocol
- Subject lost to follow-up
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant)
- Subject develops significant or serious adverse events causing discontinuation of study lens wear. Greater than 2 consecutive days of missed lens wear will lead to discontinuation.
- Subjects who have experienced a Corneal Infiltrative Event (CIE)
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment)
- Subject missed any study visits
- Subject not compliant with study lens wear schedule
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit

For discontinued subjects, the Investigator will:

- Complete the current visit (scheduled or unscheduled)
- Complete the Final Evaluation, indicating the reason that the subject was discontinued from the study
- Record the spherocylindrical refraction with best corrected distance visual acuity
- Collect used test article(s) (worn or brought to the visit) from the subject and discard them, unless otherwise stated in Section 7.2.
- Collect all unused test article(s) from the subject

An additional subject will not be enrolled if a subject discontinues from the study prematurely.

In cases where a subject is lost to follow-up, every possible effort must be made to contact the subject and determine the reason for discontinuation/withdrawal. The measures taken to follow up must be documented including two written attempts and a certified letter (or equivalent) as the final attempt.

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications or any concomitant therapies that are disallowed for this study include: Any ocular medications or any systemic medications that (e.g., chronic steroid use) that are known to interfere with contact lens wear.

10. DEVIATIONS FROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. Major protocol deviations must be reported to the sponsor within 24 hours after discovery of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked and corrective actions implemented as appropriate.

If it becomes necessary for the Investigator to implement a deviation in order to eliminate an immediate hazard to the trial subject, the Investigator may implement the deviation immediately without notification to the sponsor. Within 24 hours after the implemented deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, the IEC/IRB.

Any protocol deviation that could impact the primary endpoints will result in the subject being excluded from the Per-Protocol analysis population.

11. STUDY TERMINATION

The occurrence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be ruled out, may result in stopping further dispensing of test article. In the event of a USADE or SAE, the Sponsor may unmask the treatment regimen for the subject(s) and will discuss this with the Investigator before any further subjects are enrolled.

The Sponsor will determine when a study will be stopped. The Principal Investigator always has the discretion to initiate stopping the study based on patient safety or if information indicates the study's results are compromised.

JJVC reserves the right to terminate the study at any time for any reason. Additionally, the IEC/IRB reserves the right to terminate the study if an unreasonable risk is determined. The study can be terminated by the Principal Investigator at the individual clinical site due to specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

JJVC (and the IEC/IRB and DMC, if applicable) will evaluate all adverse events. If it is determined that an adverse event presents an unreasonable risk, the investigation, or that part of the investigation presenting the risk, will be terminated, as soon as possible.

Should the study be terminated (either prematurely or as scheduled), the Investigator will notify the IEC/IRB and Regulatory Authority as required by local regulatory requirements.

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

A Product Quality Complaint (PQC) refers to any written, electronic, or oral communication that alleges deficiencies related to the identity, quality, durability, reliability, safety, effectiveness or performance of test articles after they have been released for clinical trial use.

Potential complaints may come from a variety of sources including but not limited to subjects, clinical research associates (CRA), clinical operations managers (COM), medical monitors, and site personnel, etc. The following are not considered product quality complaints:

- Subject satisfaction inquiries reported via "Subjective Questionnaires" and "Patient Reported Outcomes (PRO)".
- Clinical test articles that are stored improperly or damaged after receipt at the investigational site.
- Lens replacements that occur due to drops/fall-outs.
- Damage deemed by clinicians or clinical staff to be caused by handling by the user, and not indicative of a quality deficiency (i.e. tears, rips, etc.), only in situations where there is no deficiency alleged by the subject.

Within 24 hours of site personnel becoming aware that a PQC has occurred, the PQC must be recorded in the EDC system, which will trigger an automatic email notification to the appropriate COM/CRA and Clinical QA representative. In cases where the EDC system in use is not configured to send automatic notifications or when an EDC system is not used, the COM/CRA is responsible for notifying Clinical QA upon discovery that a PQC has occurred.

Upon receipt of the EDC notification, the COM/CRA will contact the study site to collect additional information which will include:

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness)
- Who received the complaint
- Study number
- Clinical site information (contact name, site ID, telephone number)
- Lot number(s)
- Unique Subject Identifier(s)
- Indication of who first observed complaint (site personnel or subject)
- OD/OS indication, along with whether or not the lens was inserted
- Any related AE number if applicable
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.)

- Eye Care Provider objective (slit lamp) findings if applicable
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return (Refer to Form Control No. VCT-0152 for test article return instructions)

Once a complaint is received, it will be assessed by the COM, CRA, or trained site personnel to determine if it is an Adverse Event/Serious Adverse Event (AE/SAE). If the complaint results in an AE/SAE, the COM/CRA, or trained site personnel will follow Section 13 of this protocol. If the AE/SAE was potentially the result of a product quality related deficiency, these procedures also applies and will be executed in parallel.

In some cases, a PQC form may be generated in EDC by the site in error. In this event, the PQC forms will be marked "Intentionally Left Blank" or "ILB". Justification for ILB must be documented.

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.
Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.
Note 2 to entry: This definition includes events related to the procedures involved.
Note 3 to entry: For users or other persons, this definition is restricted to events related to investigational medical devices."[1]

An AE includes any condition (including a pre-existing condition) that:

1. Was not present prior to the study, but appeared or reappeared following initiation of the study
2. Was present prior to the study, but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event

Serious Adverse Event (SAE) – An SAE is any untoward medical occurrence that:

- Results in death
- Is life threatening
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (e.g., a sight threatening event, a significant persistent or permanent change, impairment, damage, or disruption to the subject's body)
- Is a congenital anomaly/birth defect, or

- Requires intervention to prevent permanent damage (the use of the test article resulting in a condition which requires medical or surgical intervention to preclude permanent impairment of the body structure or a body function). Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition

Diagnoses and conditions that are considered Ocular Serious Adverse Events include, but not limited to:

- Microbial Keratitis (MK)
- Iritis (including cells in the anterior chamber)
- Permanent decrease in best spectacle corrected visual acuity equivalent to 2 acuity lines or greater
- Central Corneal Opacity
- Central Corneal Neovascularization
- Uveitis
- Endophthalmitis
- Hypopyon
- Hyphemia
- Penetration of Bowman's Membrane
- Persistent Epithelial Defect
- Limbal cell Damage leading to Conjunctivalization

Significant Adverse Events – Those events that are usually symptomatic and warrant discontinuation (temporary or permanent) of the test article (excluding Serious Adverse Events).

Diagnoses and conditions that are considered Ocular Significant Adverse Events include, but not limited to the following:

- Contact Lens Induced Peripheral Ulcer (CLPU)
- Significant Infiltrative Events (SIE)
- Superior Epithelial Arcuate Lesions (SEALs)
- Any Temporary Loss of >2 Lines of BSCVA
- Other grade 3 or higher corneal findings, such as abrasions or edema
- Non-contact lens related corneal events - e.g. Epidemic Keratoconjunctivitis (EKC)
- Asymptomatic Corneal Scar
- Any corneal event which necessitates temporary lens discontinuation >2 weeks

Non-Significant Adverse Events – Those conditions that are usually asymptomatic and usually do not warrant discontinuation (temporary or permanent) of the test article. However, the Investigator may choose to treat as a precautionary measure.

Diagnoses and conditions that are considered Ocular Non-Significant Adverse Events include, but not limited to the following:

- Non-significant Infiltrative Event (NSIE)
- Contact Lens Papillary Conjunctivitis (CLPC)
- Superficial Punctate Keratitis (SPK)
- Conjunctivitis: Bacterial, Viral, Allergic
- Blepharitis
- Meibomianitis
- Contact Dermatitis
- Localized Allergic Reactions
- Any corneal event not explicitly defined as serious or significant adverse event, which necessitates temporary lens discontinuation <2 weeks

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device.
Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Note 2 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device." [1]

Unanticipated Adverse Device Effect (UADE) – Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the test article, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, Investigator's Brochure or protocol, or any other unanticipated serious problem associated with the test article that relates to the rights, safety and welfare of subjects.

13.2. Assessing Adverse Events

In conjunction with the medical monitor, the Investigator will evaluate adverse events to ensure the events are categorized correctly. Elements of categorization will include:

- Seriousness/Classifications (see definition in Section 13.1)
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; unlikely related; possibly related; related - see definition in Section 13.2.1)
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild; moderate; severe for all events - see definition in Section 13.2.2)
- Outcome – not recovered or not resolved; recovering or resolving; recovered or resolved with sequelae; recovered or resolved; death related to adverse event; unknown
- Actions Taken – none; temporarily discontinued; permanently discontinued; other

13.2.1 Causality Assessment

Causality Assessment – A determination of the relationship between an adverse event and the test article, study treatment, or study procedure. The test article, study treatment or study procedure relationship for each adverse event shall be determined by the Investigator using these explanations:

- Not Related- An adverse event that is not related to the use of the test article, study treatment or study procedures.
- Unlikely Related – An adverse event for which an alternative explanation is more likely, e.g. concomitant treatment, concomitant disease(s), or the relationship of time suggests that a causal relationship is not likely.
- Possibly Related – An adverse event that might be due to the use of the test article, or to the study treatment or study procedures. An alternative explanation, e.g. concomitant treatment, concomitant disease(s), is inconclusive. The relationship in time is reasonable. Therefore, the causal relationship cannot be excluded.
- Related – An adverse event that is listed as a possible adverse effect (device) or adverse reaction (drug) and cannot be reasonably explained by an alternative explanation, e.g. concomitant treatment of concomitant disease(s). The relationship in time is very suggestive, e.g. it is confirmed by de-challenge and re-challenge.

13.2.2 Severity Assessment

Severity Assessment – A qualitative assessment of the degree of intensity of an adverse event as determined by the Investigator or reported to him/her by the subject. The assessment of severity is made irrespective of test article, study treatment or study procedure relationship or seriousness of the event and should be evaluated according to the following scale:

- Mild – Event is noticeable to the subject, but is easily tolerated and does not interfere with the subject's daily activities
- Moderate – Event is bothersome, possible requiring additional therapy, and may interfere with the subject's daily activities
- Severe – Event is intolerable, necessitates additional therapy or alteration of therapy and interferes with the subject's daily activities

13.3. Documentation and Follow-Up of Adverse Events

The recording and documenting of adverse events (ocular and non-ocular) begins when the subjects are exposed to the test article, study treatment or study procedure. Adverse events reported before the use of test article, start of study treatment, or study procedures will be recorded as medical history. However, if the condition deteriorates at any time during the study it will be recorded and reported as an AE. Untoward medical events reported after the subject's exit from the study will be recorded as adverse events at the discretion of the Investigator.

Upon finding an adverse event, the Principal Investigator will document the condition in the subject record and in the eCRFs. He/she will complete the Adverse Event /eCRF.

Complete descriptions of all adverse events must be available in the subject record. All Adverse Events including local and systemic reactions not meeting the criteria for "serious adverse events" shall be captured on the appropriate case report form or electronic data system. All adverse events occurring while the subject is enrolled in the study must be documented appropriately regardless of relationship.

It is the Investigator's responsibility to maintain documentation of each reported adverse event. All adverse events will be followed in accordance with applicable licensing requirements. Such documentation will include the following:

- Adverse event (diagnosis not symptom)
- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.)
- Date the clinical site was notified
- Date and time of onset
- Date and time of resolution
- Adverse event classification, severity, and relationship to test articles, as applicable
- Treatment regimen instituted, including concomitant medications prescribed, in accordance with applicable licensing requirements
- Any referral to another health care provider if needed
- Outcome, ocular damage (if any)
- Likely etiology
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event

In addition, if an infiltrate(s) is present, he/she will complete the Corneal Infiltrate Assessment eCRF. Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. If cultures are collected, the date of culture collection and laboratory utilized will be recorded.

Changes in the severity of an AE shall be documented to allow an assessment of the duration of the event at each level of intensity to be performed. Adverse events characterized as intermittent require documentation of the onset and duration of each episode. Changes in the assessment of relationship to the Test Article shall also be clearly documented.

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether or not a subject reporting with an adverse event will continue in the study. If a subject is discontinued from the study, it will be the responsibility of the Investigator to record the reason for discontinuation. The Investigator will also document the adverse event appropriately and complete the Adverse Event eCRF. Any subjects with ongoing adverse events related to the test article, study treatment or study procedures, as of the final study visit date, should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator. Non-ocular adverse events that are not related to the test article, study treatment, or study procedures may be recorded as "ongoing" without further follow-up.

13.4. Reporting Adverse Events

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant

adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to their requirements (Section 13.4.2). The report will comment whether or not the adverse event was considered to be related to the test article, study treatment or study procedures.

13.4.1 Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events
The Investigator will inform the sponsor of all serious/significant adverse events occurring during the study period as soon as possible by e-mail, fax, or telephone, but no later than 24 hours following discovery of the event. The Investigator is obligated to pursue and obtain information requested by the Sponsor in addition to that information reported on the eCRF. All subjects experiencing a serious/significant adverse event must be followed up and all outcomes must be reported.

When medically necessary, the Investigator may break the randomization code to determine the identity of the treatment that the subject received. The Sponsor and study monitor should be notified prior to unmasking the test articles.

In the event of a serious/significant adverse event, the Investigator must:

- Notify the Sponsor immediately
- Obtain and maintain in the subject's records all pertinent medical information and medical judgment for colleagues who assisted in the treatment and follow-up of the subject
- Provide the Sponsor with a complete case history which includes a statement as to whether the event was or was not related to the use of the test article
- Notify the IEC/IRB as required by the IEC/IRB reporting procedure according to national regulations

Unanticipated (Serious) Adverse Device Effect (UADE)
In the event of an Unanticipated (Serious) Adverse Device Effect (UADE), the Investigator will submit a report of the UADE to the Sponsor and IEC/IRB as soon as possible, but no later than 24 hours after the Investigator first learns of the effect. This report is in addition to the immediate notification mentioned above.

The Sponsor must conduct an evaluation of the UADE and must report the results of the evaluation to FDA, the IEC/IRB and participating Investigators within 10 working days after the Sponsor first receives notification of the effect.

Non-Serious Adverse Events
All non-serious adverse events, including non-serious adverse device effects, will be reported to the sponsor by the Investigator no later than 2 days from discovery.

13.4.2 Reporting Adverse Events to the Responsible IEC/IRB and Health Authorities

Adverse events that meet the IEC/IRB requirements for reporting must be reported within the IEC/IRB's written guidelines. Each clinical site will refer to and follow any guidelines set forth

by their Approving IEC/IRB. Each clinical site will refer to and follow any guidelines set forth by their local governing Health Authorities.

The Sponsor will report applicable Adverse Events to the local health authorities according the written guidelines, including reporting timelines.

13.4.3 Event of Special Interest

None

13.5. Reporting of Pregnancy

Subjects reporting pregnancy (by self-report) during the course of the study will be discontinued after the event is recorded as an Adverse Event. Once discontinued, pregnant participants and their fetuses will not be monitored for study related purposes. At the Investigator's discretion, the study participant may be followed by the Investigator through delivery. However, this data will not be collected as part of the clinical study database. Pregnant participants are not discontinued from contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below. For more details, refer to the stand-alone Statistical Analysis Plan (SAP).

All data summaries and statistical analyses will be performed using the SAS software version 9.4 or higher (SAS Institute, Cary, NC). Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation (SD), median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

14.2. Sample Size Justification

The study is designed to evaluate the clinical performance of K-Lens produced on the new JJVC manufacturing line in Limerick, Ireland with the primary objective to show that the K-Lens is non-inferior to the Placebo lens with respect to best-corrected distance visual acuity. The plan is to enroll 132 eligible subjects with a target completion of 120 subjects (80 subjects in K-Lens and 40 subjects in Placebo).

The sample size of 120 subjects is considered sufficiently large to test for non-inferiority with a minimum statistical power of 85% and two-sided type I error of 0.05. Assuming a perfect correlation between left eye visual acuity and the right eye visual acuity (worst case scenario), the total sample size (n) required to achieve 85% power with two-sided type I error of 0.05 was calculated for different scenarios of mean difference (Δ = K-Lens – Placebo) and common standard deviation (σ) in the two arms. The results are summarized in the Table below:

Table 4: Sample size for different scenarios of mean Δ and σ

Δ	σ	n
0	0.05	15
0	0.01	45
0.04	0.05	33
0.04	0.1	117

The sample size calculation was conducted using the PROC POWER Procedure (SAS/STAT 14.1, SAS Institute, 2015) for two-sample means with allocation weight of 2:1.

Justification of Non-inferiority margin:
The non-inferiority margin of one line loss on best-corrected distance visual acuity was considered based on the work done by Jane E. Lovie-Kitchin and Brian Brown on evaluating the repeatability and intercorrelations of five standard vision tests in subjects with normal vision. The authors concluded that one line change is, on average, a useful criterion to adopt on clinical decision making[23].

14.3. Analysis Populations

Per-Protocol Population:
All subjects who have successfully completed all visits and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock. Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

Safety Population:
All subjects who were administered any test article excluding subjects who drop out prior to administering any test article. At least one observation should be recorded.

The primary analyses will be performed on per-protocol population. Additional sensitivity analyses may be conducted on the safety population.

14.4. Level of Statistical Significance

All planned analysis will be conducted with an overall type I error rate of 5%. Unless otherwise specified, all statistical tests will be 2-sided.

14.5. Primary Analysis

Contact lens monocular distance best-corrected visual acuity on logMAR scale will be analyzed using a linear mixed effects model to test for non-inferiority of K-Lens relative to Placebo. Lens group will be included as fixed effects in the model; and investigator site as random effect. The covariance matrix between the left eye visual acuity and right eye visual acuity will be selected based on the finite-sample Corrected Akaike's Information Criterion.[24] Covariance structures considered include Compound Symmetry (CS) and Unstructured (UN). The covariance structure that returns the lowest AICC will be selected as the structure that best fit the data. Heterogeneous covariance structures across study lens groups will be considered

when appropriate. The log-likelihood ratio test will be used to test for the homogeneity between the residual covariance structures. The Kenward and Roger method will be used to calculate the denominator degree of freedom.[25]

The null and alternative hypotheses for non-inferiority of K-Lens relative to Placebo are as follows:

$$H_0: \Delta \geq 0.1$$
$$H_A: \Delta < 0.1,$$

where Δ is the mean difference in visual acuity between K-Lens and Placebo (K-Lens minus Placebo). The non-inferiority test will be based on the least-square mean difference (K-Lens minus Placebo) and corresponding 95% confidence interval calculated using the final selected model. The upper bound of the 95% confidence interval will be compared to the non-inferiority margin of 0.1 LogMAR. If the upper bound is less than 0.1, K-Lens will be considered non-inferior to Placebo with respect to visual Acuity.

14.6. Secondary Analysis

Secondary endpoints will be summarized descriptively using all available data including data from unscheduled visits.

14.7. Other Exploratory Analyses

No exploratory analysis is planned for this study. Further analysis may be conducted at the discretion of the study responsible clinician at the end of the study.

14.8. Interim Analysis

There will not be an interim analysis performed for this study.

14.9. Procedure for Handling Missing Data and Drop-Outs

Missing or spurious values will not be imputed as the number of missing values is expected to be low. The count of missing values will be included in the summary tables and listings.

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, a sensitivity analysis will be conducted using multiple imputation methods if the proportion of subject dropout is greater than 15%.

14.10. Procedure for Reporting Deviations from Statistical Plan

The analysis will be conducted according to that specified in above sections. There are no known reasons for which it is planned to deviate from these analysis methods. If for any reason a change is made, the change will be documented in the study report along with a justification for the change.

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

The data for this study will be captured on electronic case report forms (eCRFs) using the Bioclinica system. An authorized data originator will enter study data into the eCRFs using the Bioclinica system. Data collected on equipment that is not captured in Bioclinica will be formatted to the specification of the JJVC database manager and sent to JJVC for analysis.

External Date Sources for this study include: Not Applicable

The clinical data will be recorded on dedicated eCRFs specifically designed to match the study procedures for each visit. Once completed, the eCRFs will be reviewed for accuracy and completeness and signed by the Investigator. The sponsor or sponsor's representatives will be authorized to gain access to the subject recordation for the purposes of monitoring and auditing the study.

Edit checks, electronic queries, and audit trails are built into the system to ensure accurate and complete data collection. Data will be transmitted from the clinical site to a secure central database as forms are completed or updated, ensuring information accuracy, security, and confidentiality. After the final database lock, the Investigator will be provided with Individual Patient Profiles (IPP) including the full audit trail on electronic media in PDF format for all of the study data. The IPP must be retained in the study files as a certified copy of the source data for the study.

The content and structure of the eCRFs are compliant with ISO14155:2011.

15.2. Subject Record

At a minimum, subject record should be available for the following:

- subject identification
- eligibility
- study identification
- study discussion
- provision of and date of informed consent
- visit dates
- results of safety and efficacy parameters as required by the protocol
- a record of all adverse events
- follow-up of adverse events
- medical history and concomitant medication
- test article receipt/dispensing/return records
- date of study completion
- reason for early discontinuation of test article or withdrawal from the study, if applicable

The subject record is the eCRF or an external record. The author of an entry in the subject record must be identifiable. The first point of entry is considered to be the source record.

Adverse event notes must be reviewed and initialed by the Investigator.

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

The Investigator/Institution will permit trial-related monitoring, audits, IEC/IRB review and regulatory inspection(s) by providing direct access to source data/documents. Should the clinical site be contacted for an audit by an IEC/IRB or regulatory authority, JJVC must be contacted and notified in writing within 24 hours.

16.2. Confidentiality of Information

Information concerning the investigational product and patent application processes, scientific data or other pertinent information is confidential and remains the property of JJVC. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJVC will use information developed in this clinical study in connection with the development of the investigational product and therefore may disclose it as required to other clinical investigators and to regulatory agencies. In order to allow the use of the information derived from this clinical study, the Investigator understands that he/she has an obligation to provide complete test results and all data developed during this study to the Sponsor.

16.3. Data Quality Assurance

Steps will be taken to ensure the accuracy and reliability of data, include the selection of qualified investigators and appropriate clinical sites and review of protocol procedures with the Principal Investigator. The Principal Investigator, in turn, must ensure that all Sub-Investigators and clinical site personnel are familiar with the protocol and all study-specific procedures and have appropriate knowledge of the study article.

Training on case report form completion will be provided to clinical site personnel before the start of the study. The Sponsor will review case report forms for accuracy and completeness remotely during the conduct of the study, during monitoring visits, and after transmission to data management. Any data discrepancies will be resolved with the Investigator or designee, as appropriate.

Quality Assurance representatives from JJVC may visit clinical sites to review data produced during the study and to access compliance with applicable regulations pertaining to the conduct of clinical trials. The clinical sites will provide direct access to study-related source data/documents and reports for the purpose of monitoring and auditing by JJVC and for inspection by local and regulatory authorities.

17. MONITORING

The study monitors will maintain close contact with the Principal Investigator and the Investigator's designated clinical site personnel. The monitor's responsibilities will include:

- Ensuring that the investigation is being conducted according to the protocol, any subsequent amendments, and regulatory requirements are maintained
- Ensuring the rights and wellbeing of subjects are protected
- Ensuring adequate resources, including facilities, laboratories, equipment, and qualified clinical site personnel
- Ensuring that protocol deviations are documented with corrective action plans, as applicable
- Ensuring that the clinical site has sufficient test article and supplies
- Clarifying questions regarding the study
- Resolving study issues or problems that may arise
- Reviewing of study records and source documentation verification in accordance with the monitoring plan

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

Potential subjects will be fully informed of the risks and requirements of the study and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only subjects who are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP), and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013 and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP), and applicable regulatory requirements.

18.3. Independent Ethics Committee or Institutional Review Board (IEC/IRB)

Before the start of the study, the Investigator (or Sponsor when applicable) will provide the IEC/IRB with current and complete copies of the following documents (where applicable):

- Final protocol and, if applicable, amendments
- Sponsor-approved informed consent form (and any other written materials to be provided to the subjects)
- Investigator's Brochure (or equivalent information) and amendments
- Sponsor-approved subject recruitment materials

- Information on compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's curriculum vitae, clinical licenses, or equivalent information (unless not required, as documented by IEC/IRB)
- Information regarding funding, name of the Sponsor, institutional affiliations, other potential conflicts of interest, and incentives for subjects
- Any other documents that the IEC/IRB requests to fulfill its obligation

This study will be undertaken only after IEC/IRB has given full approval of the final protocol, amendments (if any), the informed consent form, applicable recruiting materials, and subject compensation programs, and the Sponsor has received a copy of this approval. This approval letter must be dated and must clearly identify the documents being approved.

During the study, the Investigator (or Sponsor when applicable) will send the following documents to the IEC/IRB for their review and approval, where appropriate:

- Protocol amendments
- Revision(s) to informed consent form and any other written materials to be provided to subjects
- If applicable, new or revised subject recruitment materials approved by the Sponsor
- Revisions to compensation for study-related injuries or payment to subjects for participation in the study
- Investigator's Brochure amendments or new edition(s)
- Summaries of the status of the study (at least annually or at intervals stipulated in guidelines of the IEC/IRB)
- Reports of adverse events that are serious, unanticipated, and associated with the test articles, according to the IRB's requirements
- New information that may adversely affect the safety of the subjects or the conduct of the study
- Major protocol deviations as required by the IEC/IRB
- Report of deaths of subjects under the Investigator's care
- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

For protocol amendments that increase subject risk, the amendment and applicable informed consent form revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).

At least once a year, the IEC/IRB will review and reapprove this clinical study. This request should be documented in writing.

At the end of the study, the Investigator (or Sponsor where required) will notify the IEC/IRB about the study completion. Documentation of this notification must be retained at the clinical site and a copy provided to the CRO or Sponsor as applicable.

18.4. Informed Consent

Each subject must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and ISO 14155[1] guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential subject the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects will be informed that their participation is voluntary and that they may withdraw consent to participate at any time.

The subject will be given sufficient time to read the informed consent form and the opportunity to ask questions. After this explanation and before entry into the study, consent should be appropriately recorded by means of the subject's dated signature. After having obtained the consent, a copy of the informed consent form must be given to the subject.

If involving vulnerable population, provide description of specific informed consent process. Below is an example for study involving children as subjects:

Each subject for this study will complete an assent and a parent or legal guardian must give written informed consent according to local requirements after the nature of the study has been fully explained. The assent and consent forms must be signed before performance of any study-related activity. The assent and consent forms that are used must be approved by both the Sponsor and by the reviewing IEC/IRB. The assent and informed consent forms should be in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and GCP guidelines, applicable regulatory requirements, and Sponsor policy. Before entry into the study or pre-screening, the Investigator or an authorized member of the clinical site personnel must explain to the potential subject and parent and/or legal guardian the aims, methods, reasonably anticipated benefits, and potential hazards of the study or pre-screening, and any discomfort it may entail. Subjects and parent and/or legal guardian will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the subject will receive. Finally, they will be told that the Investigator will maintain a subject identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized Sponsor personnel without violating the confidentiality of the subject, to the extent permitted by the applicable law(s) or regulations. By signing the assent and informed consent form, the subject is authorizing such access and agrees to be contacted after study completion by health authorities and authorized Sponsor personnel for the purpose of obtaining consent for additional safety evaluations if needed.

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) in the United States[26] and other applicable personal data protection and security laws and regulations[27]. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

All information obtained during the course of the investigation will be regarded as confidential. All personal data gathered in this trial will be treated in strictest confidence by Investigators, monitors, Sponsor's personnel and IEC/IRB. No data will be disclosed to any third party without the express permission of the subject concerned, with the exception of Sponsor personnel (monitor, auditor), IEC/IRB and regulatory organizations in the context of their investigation related activities that, as part of the investigation will have access to the CRFs and subject records.

The collection and processing of personal data from subjects enrolled in this study will be limited to those data that are necessary to investigate the efficacy, safety, quality, and utility of the investigational product(s) used in this study.

These data must be collected and processed with adequate precautions to ensure confidentiality and compliance with applicable data privacy protection laws and regulations.
The Sponsor ensures that the personal data will be:

- processed fairly and lawfully
- collected for specified, explicit, and legitimate purposes and not further processed in a way incompatible with these purposes
- adequate, relevant, and not excessive in relation to said purposes
- accurate and, where necessary, kept current

Explicit consent for the processing of personal data will be obtained from the participating subject before collection of data. Such consent should also address the transfer of the data to other entities and to other countries.

The subject has the right to request through the Investigator access to his personal data and the right to request rectification of any data that are not correct or complete. Reasonable steps should be taken to respond to such a request, taking into consideration the nature of the request, the conditions of the study, and the applicable laws and regulations.

Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of study subjects confidential.

19. STUDY RECORD RETENTION

In compliance with the ICH/GCP guidelines,[2] the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH/GCP[2] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

Essential documents must be retained until at least two (2) years after the last approval of a marketing application in an ICH region and until there are no pending or contemplated marketing applications in an ICH region or until at least two (2) years have elapsed since the formal discontinuation of clinical development of the investigational product. These documents will be retained for a longer period if required by the applicable regulatory requirements or instructed by the Sponsor. It is the responsibility of the Sponsor to inform the Investigator/Institution as to when these documents no longer need to be retained.

If the responsible Investigator retires, relocates, or for other reasons withdraws from the responsibility of keeping the study records, custody must be transferred to a person who will accept the responsibility. The Sponsor must be notified in writing of the name and address of the new custodian. Under no circumstance shall the Investigator relocate or dispose of any study documents before having obtained written approval from the Sponsor.

If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the Investigator must permit access to such reports.

If the Investigator has a question regarding retention of study records, he/she should contact JJVC.

20. FINANCIAL CONSIDERATIONS

Remuneration for study services and expenses will be set forth in detail in the Clinical Research Agreement. The Research Agreement will be signed by the Principal Investigator and a JJVC management representative prior to study initiation.

JJVC reserves the right to withhold remuneration for costs associated with protocol violations such as:

- Continuing an ineligible subject in the study
- Scheduling a study visit outside the subject's acceptable visit range

JJVC reserves the right to withhold final remuneration until all study related activities have been completed, such as:

- Query resolution
- Case Report Form signature
- Completion of any follow-up action items

21. PUBLICATION

This study will be registered on ClinicalTrials.gov by the Sponsor.

22. REFERENCES

1. ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at: https://www.iso.org/standard/45557.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at: http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
4. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
5. Kumar, P., et al., Allergic rhinoconjunctivitis and contact lens intolerance. Clao j, 1991. 17(1): p. 31-4.
6. Pritchard, N., D. Fonn, and D. Brazeau, Discontinuation of contact lens wear: a survey. Int Contact Lens Clin, 1999. 26(6): p. 157-162.
7. Abelson, M.B., Conjunctival Allergen Challenge. Archives of Ophthalmology, 1990. 108(1): p. 84.
8. Abelson, M.B., L. Smith, and M. Chapin, Ocular Allergic Disease: Mechanisms, Disease Sub-types, Treatment. The Ocular Surface, 2003. 1(3): p. 127-149.
9. [redacted]

22. Wirth, R.J., et al., Development of the Contact Lens User Experience: CLUE Scales. Optom Vis Sci, 2016. 93(8): p. 801-8.
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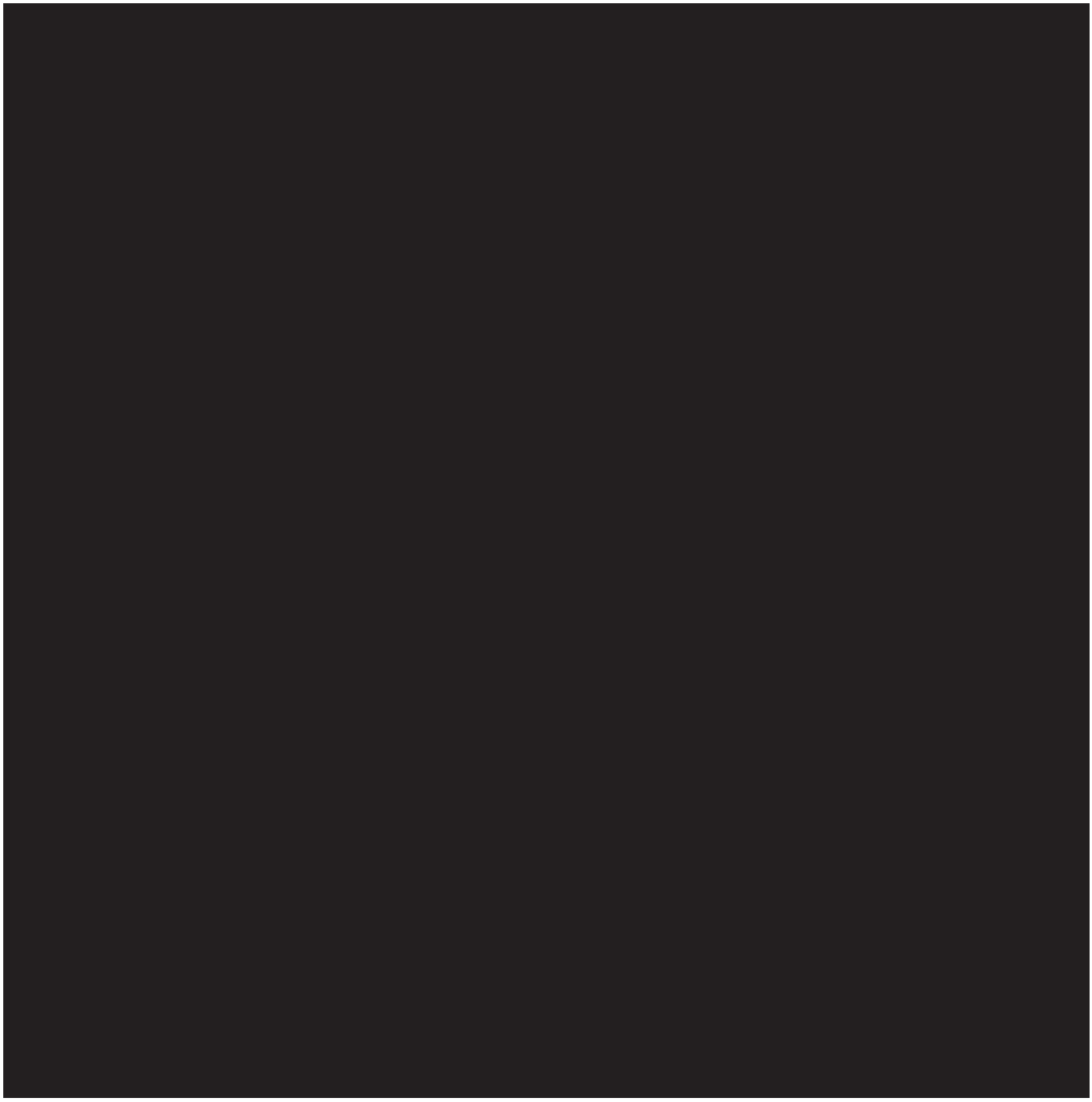
24. Keselman, H., et al., A comparison of two approaches for selecting covariance structures in the analysis of repeated measurement. Communications in Statistics, 1998. Simulation & Computation(27): p. 591-604.
25. Kenward, M.G. and J.H. Roger, Small Sample Inference for Fixed Effects from Restricted Maximum Likelihood. Biometrics 1997. 53(3): p. 983-997.
26. Health Information Portability and Accountability Act (HIPAA). https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
27. Data Protection Act. http://www.legislation.gov.uk/ukpga/1998/29/contents

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)



APPENDIX B: PATIENT INSTRUCTION GUIDE

Patient Instruction Guide will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

1·DAY ACUVUE®

WARNING:
Do not store lenses or rinse lens cases with water or any non-sterile solution. Only fresh multi-purpose solution should be used to prevent contamination of the lenses or lens case. Use of non-sterile solution can lead to severe infection, vision loss, or blindness.

PRECAUTIONS

Special Precautions for Eye Care Professionals:

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

  The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing Eye Care Professional.

- Patients who wear these lenses to correct presbyopia using monovision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.

- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.

- Eye Care Professionals should instruct the patient to remove the lenses immediately if the eyes become red or irritated.

For Extended Wear:

It is recommended that the contact lens wearer first be evaluated on a daily wear schedule. If successful, then a gradual introduction of extended wear can be followed as determined by the prescribing Eye Care Professional. The Eye Care Professional should examine the patient during the early stages of extended wear.

These lenses have been approved for extended wear from 1 to 7 days / 6 nights of continuous wear. Not all patients can achieve the maximum wear time.

REPLACEMENT SCHEDULE

For Lenses Prescribed for Frequent Replacement:

When prescribed for daily wear (frequent replacement), it is recommended that the lenses be discarded and replaced with a new lens every 2 weeks. However, the Eye Care Professional is encouraged to determine an appropriate replacement schedule based upon the response of the patient.

When these lenses are replaced at intervals ranging from 1 day to 2 weeks, the risk of developing giant papillary conjunctivitis may be reduced.[4]

[4] The CLAO Journal, July, 1999, Volume 25, Number 3

For Lenses Prescribed for Disposable Wear:

When prescribed for disposable wear, lenses should be discarded after the prescribed wearing schedule.

Once removed, it is recommended that the lens remain out of the eye for a period of rest of overnight or longer and discarded in accordance with the prescribed wearing schedule.

CR-5930, v3.0 Amendment 2.0

Eye Care Professionals should carefully instruct patients about the following care regimen and safety precautions:

Handling Precautions:

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove the lenses or should have someone else available who can remove the lenses for him or her.
- **DO NOT** use if the sterile blister package is opened or damaged.
- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup. Water-based cosmetics are less likely to damage lenses than oil-based products.
- **DO NOT** touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, cleaning, disinfecting, storing, and wearing instructions in the "Patient Instruction Guide" for the prescribed wearing schedule and those prescribed by the Eye Care Professional.
- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.

Lens Wearing Precautions:

- If the lens sticks (stops moving) on the eye, follow the recommended directions in "Care for a Sticking (Non-Moving) Lens." The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. They have been prescribed to fit their eyes and to cor vision to the degree necessary. Sharing lenses greatly increas chance of eye infections.
- If aerosol products, such as hair spray, are used while wearin exercise caution and keep eyes closed until the spray has se
- Avoid all harmful or irritating vapors and fumes while wearing
- Always discard lenses worn as prescribed by the Eye Care P

Lens Care Precautions:

- Different solutions cannot always be used together and not al are safe for use with all lenses. Use only recommended soluti
- Never use solutions recommended for conventional hard con only.
- Chemical disinfection solutions should not be used with heat cifically indicated on product labeling for use in both heat and disinfection.
- Always use fresh, unexpired lens care solutions and lenses.
- Do not change solution without consulting with the Eye Care sional.
- Always follow directions in the package insert for the use of c solutions.
- Use only a chemical (not heat) lens care system. Use of a hea care system can damage the contact lenses.
- Sterile unpreserved solutions, when used, should be discarde time specified in the directions.
- Do not use saliva or anything other than the recommended s lubricating or wetting lenses.
- Always keep the lenses completely immersed in the recomm storage solution when the lenses are not being worn (stored). periods of drying will reduce the ability of the lens surface to r wettable state. Follow the lens care directions in "Care for A D (Dried Out) Lens" if lens surface does become dried out.

LENS CARE DIRECTIONS

When lenses are dispensed, the Eye Care Professional should provide the patient with appropriate and adequate warnings and instructions in accordance with the individual patient's lens type and wearing schedule. The Eye Care Professional should recommend an appropriate care system tailored to the patient's individual requirements.

For complete information concerning contact lens handling, care, cleaning, disinfecting, and storage, refer to the "Patient Instruction Guide" for the prescribed wearing schedule. Copies are available for download at www.acuvue.com.

For Contact Lenses Prescribed for Frequent Replacement Wear:

The Eye Care Professional should review with the patient, the lens care directions for cleaning, disinfecting, and storing, including both basic lens care information and specific instructions on the lens care regimen recommended for the patient.

For Contact Lenses Prescribed for Disposable Wear:

The Eye Care Professional should review with the patient that no cleaning or disinfection is needed with disposable lenses. Patients should always dispose of lenses when they are removed and have spare lenses or spectacles available. Lenses should only be cleaned, rinsed, and disinfected on an emergency basis when replacement lenses or spectacles are not available.

Care for a Dried Out (Dehydrated) Lens

If the frequent replacement lens is off the eye and exposed to air from 30 minutes to 1 hour or more, its surface will become dry and gradually become non-wetting. If this should occur, discard the lens and use a new one.

Care for Sticking (Non-Moving) Lenses

If the lens sticks (stops moving), the patient should be instructed to apply a few drops of the recommended lubricating or rewetting solution directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement of the lens continues after a few minutes, the patient should **immediately** contact the Eye Care Professional.

EMERGENCIES

The patient should be informed that if chemicals of any kind (ho products, gardening solutions, laboratory chemicals, etc.) are s into the eyes, the patient should: FLUSH EYES IMMEDIATELY WATER AND IMMEDIATELY CONTACT THE EYE CARE PROF OR VISIT A HOSPITAL EMERGENCY ROOM WITHOUT DELA

HOW SUPPLIED

ACUVUE®, ACUVUE® 2, ACUVUE® BIFOCAL, 1-DAY ACU SUREVUE™ Contact Lenses:

Each sterile lens is supplied in a foil-sealed plastic package co buffered saline solution. The plastic package is marked with ba diopter power, diameter, lot number, and expiration date.

1-DAY ACUVUE® for ASTIGMATISM Contact Lenses:

Each sterile lens is supplied in a foil-sealed plastic package co buffered saline solution. The plastic package is marked with ba diopter power, axis, cylinder, diameter, lot number, and expirati

ACUVUE® 2 COLOURS Contact Lenses:

Each sterile lens is supplied in a foil-sealed plastic package co buffered saline solution. The plastic package is marked with ba diopter power, diameter, lens color, lot number, and expiration

SYMBOLS KEY

The following symbols may appear on the label or carton:

SYMBOL	DEFINITION
	Consult Instructions for Use
	Manufactured by or in
	Date of Manufacture
	Use By Date (expiration date)
LOT	Batch Code
STERILE	Sterile Using Steam or Dry Heat
DIA	Diameter
BC	Base Curve
D	Diopter (lens power)
CYL	Cylinder
AXIS	Axis
CE 0086	Quality System Certification Symbol
	UV-Blocking
	Fee Paid for Waste Management
Rx Only	CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner
	Lens Orientation Correct
	Lens Orientation Incorrect (Lens Inside Out)
E-AQU	Enhancer Aqua
E-BLU	Enhancer Blue
E-GRN	Enhancer Green
O-GRY	Opaque Gray
O-GRN	Opaque Green
O-HNY	Opaque Honey
O-CHN	Opaque Chestnut
O-SPH	Opaque Sapphire
O-BLU	Opaque Blue
O-HZL	Opaque Hazel

WARNING: UV absorbing contact lenses are NOT substitutes for protective UV absorbing eyewear, such as UV absorbing goggles or sunglasses because they do not completely cover the eye and surrounding area. The patient should continue to use UV absorbing eyewear as directed.

ACTIONS

In its hydrated state, the contact lens, when placed on the cornea, acts as a refracting medium to focus light rays onto the retina.

The UV blocking averages for these contact lenses are as follows:

	UVA in the range of 316 nm to 380 nm	UVB in the range of 280 nm to 315 nm
ACUVUE®	82%	97%
ACUVUE® BIFOCAL	86%	98%
ACUVUE® 2	88%	99%
ACUVUE® 2 COLOURS	81%	97%
1-DAY ACUVUE®	82%	97%
1-DAY ACUVUE® for ASTIGMATISM	82%	97%
SUREVUE™	87%	99%

NOTE: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-Blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-Blocking contact lenses reduces the risk of developing cataracts or other eye disorders. The Eye Care Professional should be consulted for more information.

DESCRIPTION

The ACUVUE® Brand, ACUVUE® 2 Brand, ACUVUE® 2 COLOURS Brand, 1-DAY ACUVUE® Brand, and SUREVUE™ Brand soft (hydrophilic) contact lenses are available as spherical lenses. The ACUVUE® Brand BIFOCAL soft (hydrophilic) contact lenses are available as spherical bifocal lenses. The 1-DAY ACUVUE® Brand for ASTIGMATISM soft (hydrophilic) contact lenses are available as toric lenses.

The lens material (etafilcon A) is a copolymer of 2-hydroxyethyl methacrylate and methacrylic acid cross-linked with 1,1,1-trimethylol propane trimethacrylate and ethylene glycol dimethacrylate.

The lenses are tinted blue using Reactive Blue Dye #4 to make the lenses more visible for handling. The ACUVUE® 2 COLOURS Brand Contact Lenses contain a pigmented area that will mask or enhance the color of the natural iris. The lens is colored with one or more of the following color additives: iron oxides, titanium dioxide, phthalocyaninato (2-) copper, phytalocyanine green, vat orange 1, and Reactive Blue Dye #4. The ACUVUE® 2 COLOURS Brand Contact Lenses are available in the following opaque colors: Blue, Gray, Green, Honey, Chestnut, Hazel, and Sapphire. They are also available in the following enhancer colors: Blue, Green, and Aqua.

A benzotriazole UV absorbing monomer is used to block UV radiation. The UV-Blocking averages:

	UVA in the range of 316 nm to 380 nm	UVB in the range of 280 nm to 315 nm
ACUVUE®	82%	97%
ACUVUE® BIFOCAL	86%	98%
ACUVUE® 2	88%	99%
ACUVUE® 2 COLOURS	81%	97%
1-DAY ACUVUE®	82%	97%
1-DAY ACUVUE® for ASTIGMATISM	82%	97%
SUREVUE™	87%	99%

INDICATIONS (USES)

The indications are described by brand name below. The definitions of daily wear and extended wear within these indications follow:

- **EXTENDED WEAR: 1 to 7 days/6 nights of continuous wear including while asleep.**
- **DAILY WEAR: Periods of less than 1 day while awake.**

The ACUVUE® and ACUVUE® 2 Brand Contact Lenses are indicated for daily and extended wear for the correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

The ACUVUE® Brand Contact Lens BIFOCAL is indicated for daily and extended wear for the correction of distance and near vision in presbyopic phakic or aphakic persons with non-diseased eyes who may have 0.75D or less of astigmatism.

The SUREVUE™ Brand Contact Lens is indicated for daily wear for the correction of refractive ametropia (myopia and hyperopia) in phakic and aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

The 1-DAY ACUVUE® Brand Contact Lens is indicated for daily disposable wear for the correction of refractive ametropia (myopia and hyperopia) in phakic and aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

The 1-DAY ACUVUE® Brand Contact Lens for ASTIGMATISM is indicated for daily disposable wear for the correction of visual acuity in phakic or aphakic persons with non-diseased eyes who are hyperopic or myopic and may have 0.50D to 2.50D of astigmatism.

The ACUVUE® 2 COLOURS Brand Contact Lens is indicated for daily and extended wear to enhance or alter the apparent color of the eye and/or for the correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

Lens Properties:

The physical/optical properties of the lens are:

- Specific Gravity (calculated):

  ACUVUE®, ACUVUE® BIFOCAL, ACUVUE® 2, 1-DAY ACUVUE®, 1-DAY ACUVUE® for ASTIGMATISM, and SUREVUE™: 0.98 – 1.12

  ACUVUE® 2 COLOURS: 0.98 – 1.13
- Refractive Index: 1.40
- Visible Light Transmission: 85% minimum, visibili 95% minimum, clear greater than 70%, co
- Surface Character: Hydrophilic
- Water Content: 58%
- Oxygen Permeability:

VALUE	METHOD
28.0 x 10^{-11} (cm^2/sec) (ml O_2/ml x mm Hg) at 35°C	Fatt (boundary correc edge corrected)
21.4 x 10^{-11} (cm^2/sec) (ml O_2/ml x mm Hg) at 35°C	Fatt (boundary correc corrected)

Lens Parameters:

These lenses are hemispherical or hemitoric shells of the follow dimensions:

- Diameter Range: 12.0 mm to 15.0 mm
- Center Thickness: varies with power
- Base Curve Range: 7.85 mm to 10.00 mm
- Spherical Power Range: Daily Wear: -20.00D to +20 Extended Wear: -20.00D to

These contact lenses contain a UV Blocker to help protect aga mission of harmful UV radiation to the cornea and into the eye.

Frequent Wear Replacement:
When prescribed for frequent/planned replacement wear (see " ment Schedule"), the contact lenses are to be cleaned, rinsed, disinfected each time the lens is removed. The contact lens is t carded after the recommended wearing period prescribed by t Professional. When prescribed for frequent/planned replacemen contact lens may be disinfected using a chemical disinfection s

Disposable Wear:
When prescribed for disposable wear (see "Replacement Sche contact lenses are to be discarded after each removal.

CONTRAINDICATIONS (REASONS NOT TO

DO NOT USE these contact lenses when any of the follo conditions exist:

- Acute or subacute inflammation or infection of the anterior ch the eye.
- Any eye disease, injury or abnormality that affects the cornea or eyelids.
- Severe insufficiency of lacrimal secretion (dry eye).
- Corneal hypoesthesia (reduced corneal sensitivity).
- Any systemic disease that may affect the eye or be exaggera wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa that may be in exaggerated by wearing contact lenses or use of contact lens
- Ocular irritation due to allergic reactions which may be cause use of contact lens solutions (i.e., cleaning and disinfecting so rewetting drops, etc.) that contain chemicals or preservatives mercury, Thimerosal, etc.) to which some people may develo response.
- Any active corneal infection (bacterial, fungal, protozoal or vir
- If eyes become red or irritated.

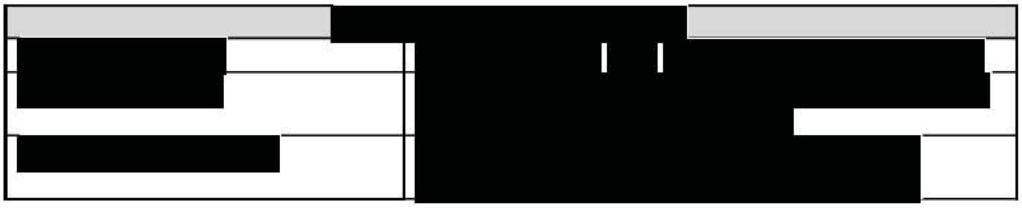
APPENDIX D: CLINICAL TECHNICAL PROCEDURES [redacted]

[redacted] Lens Fitting Characteristics
[redacted] Subject Reported Ocular Symptoms/Problems
[redacted] Determination of Distance Spherocylindrical Refractions
[redacted] Biomicroscopy Scale
[redacted] Distance and Near Visual Acuity Evaluation
[redacted] Distance logMAR Visual Acuity Measurement Procedure

[redacted] LENS FITTING CHARACTERISTICS

[redacted] **Lens Fitting Characteristics**

[redacted]



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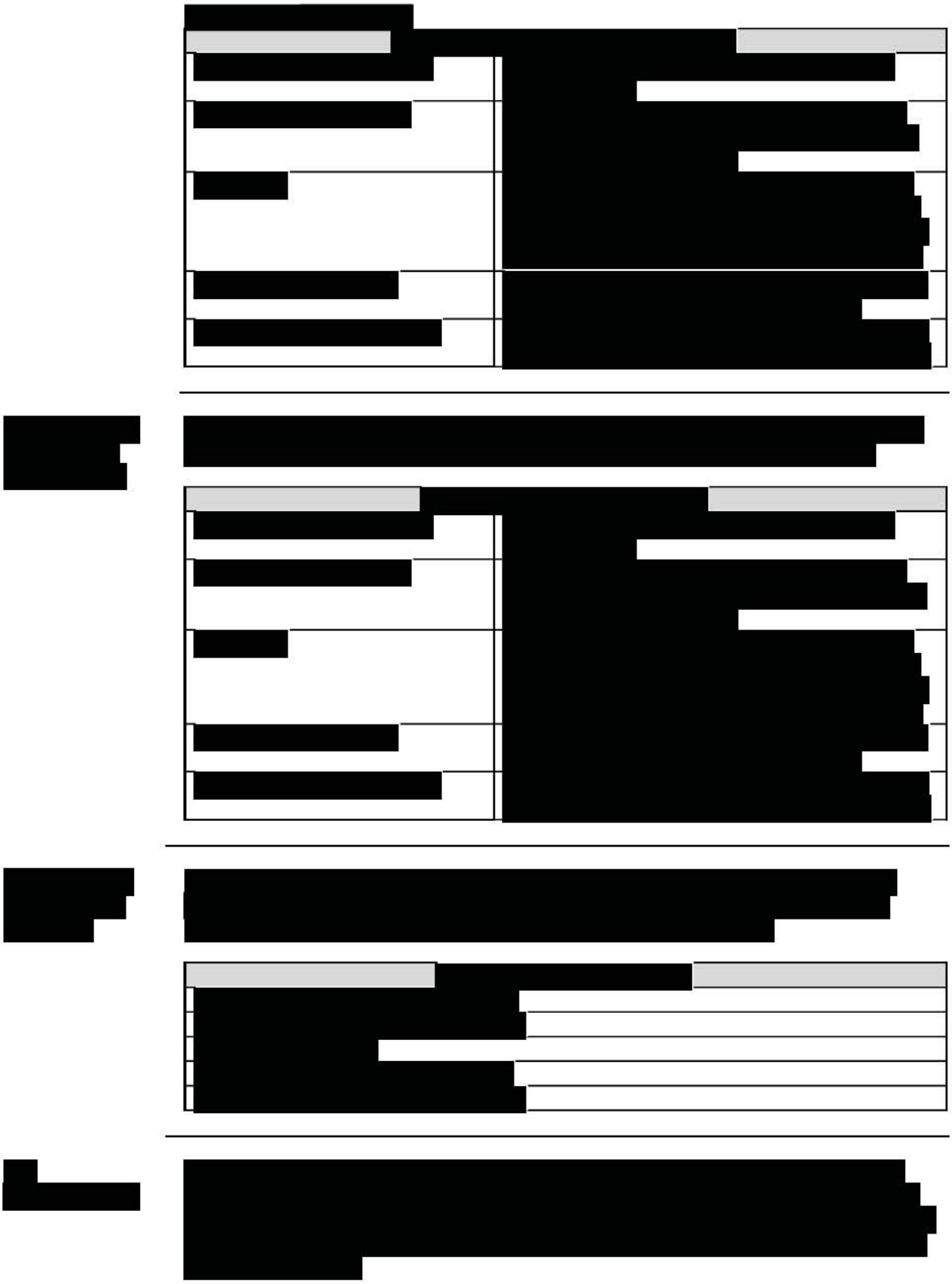

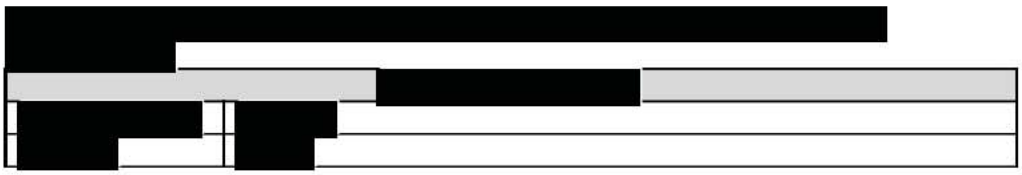

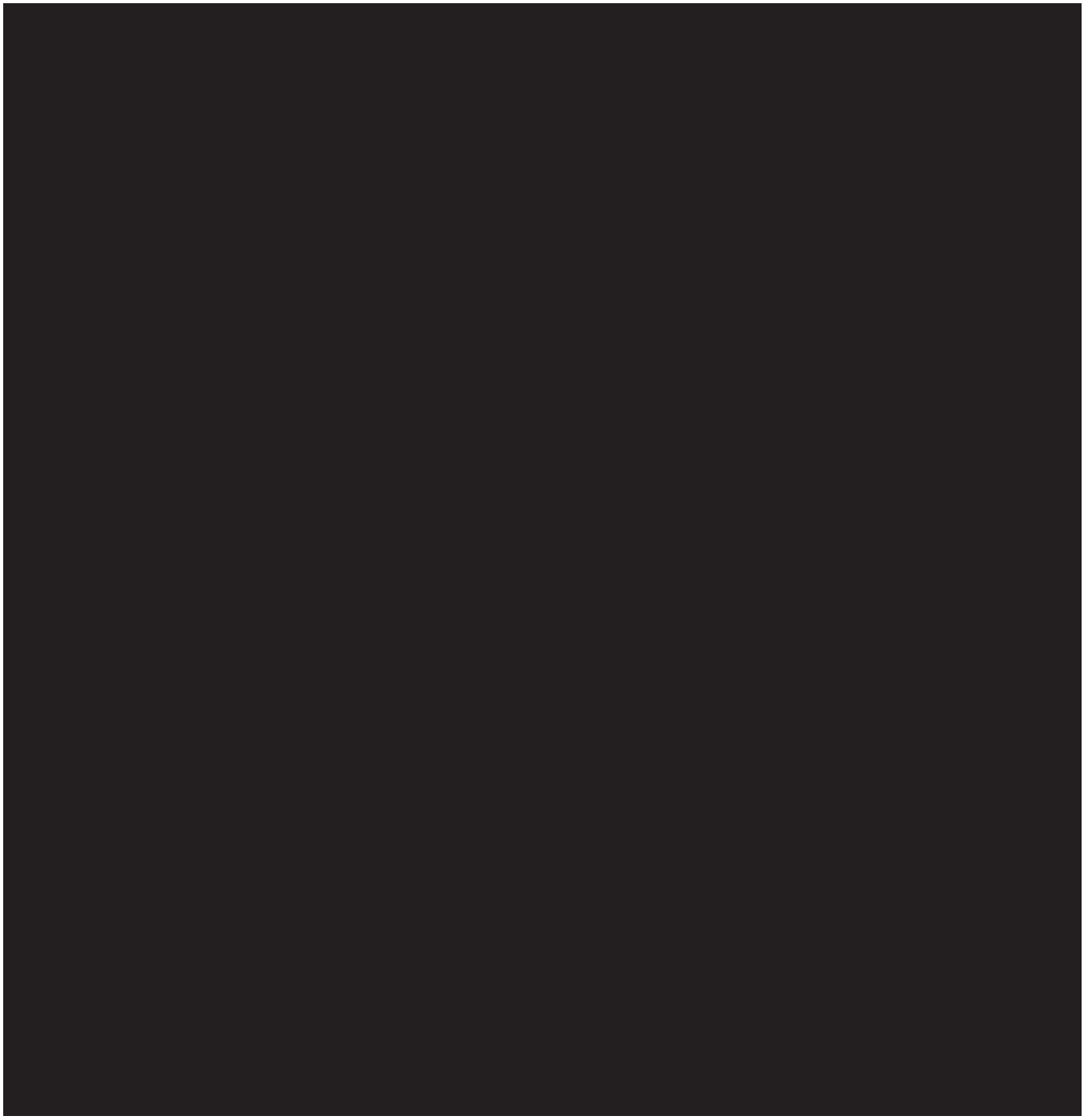

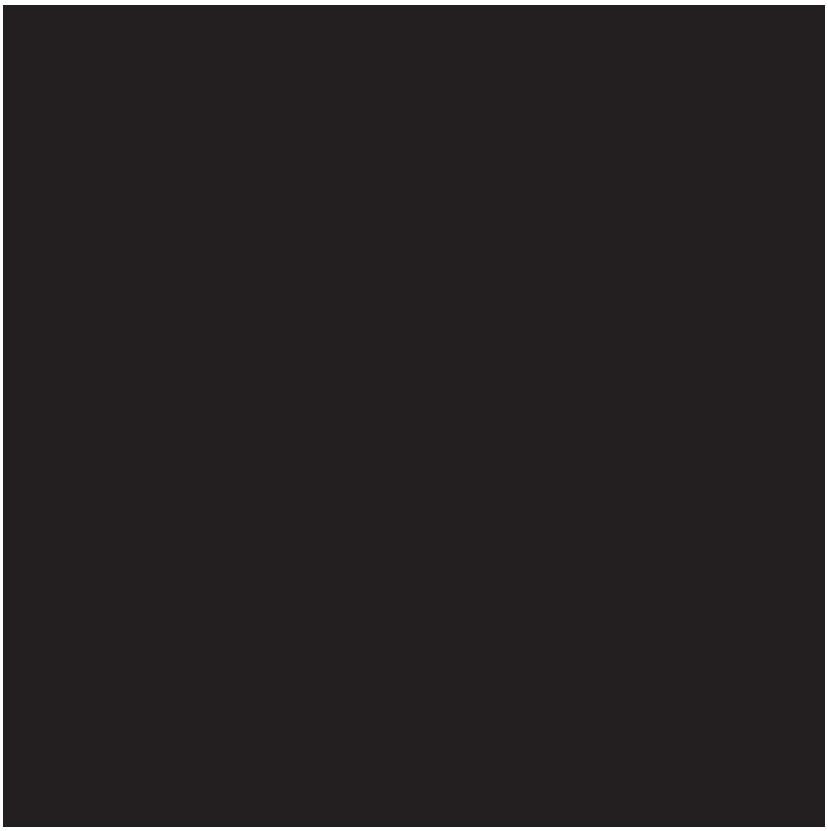

[redacted] SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS

[redacted] **Subject Reported Ocular Symptoms/Problems**

[redacted]

[redacted]

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[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

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Determination of Distance Spherocylindrical Refractions

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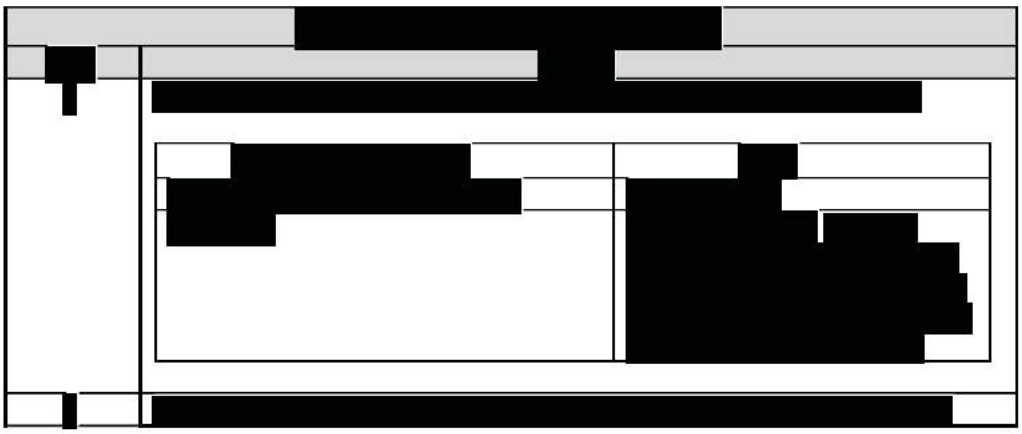

[redacted] BIOMICROSCOPY SCALE

[redacted] **Biomicroscopy Scale**

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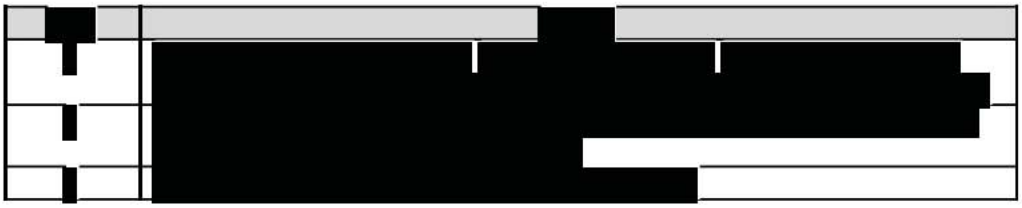
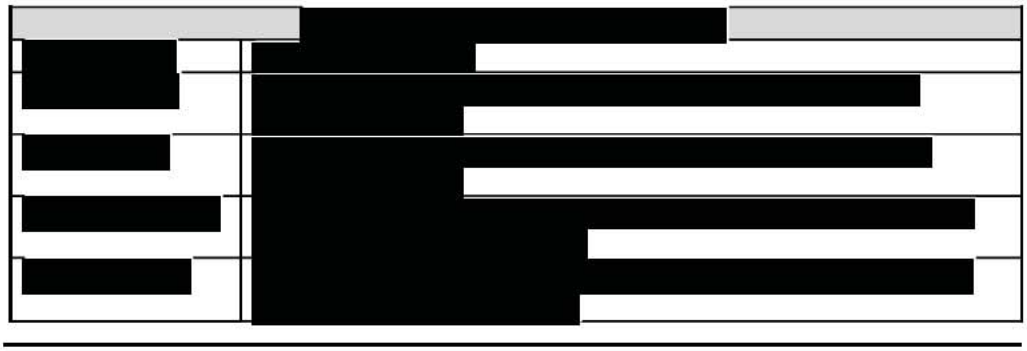
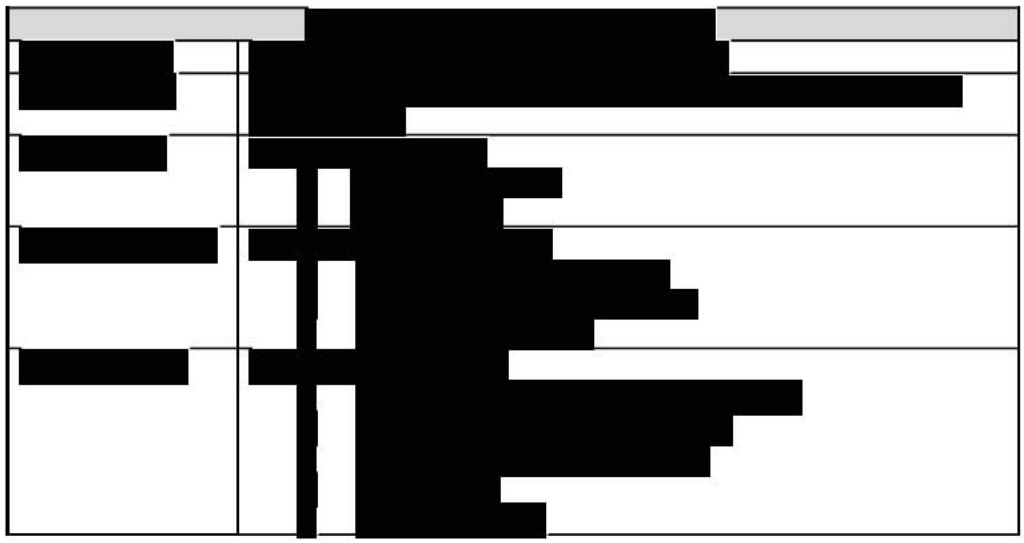
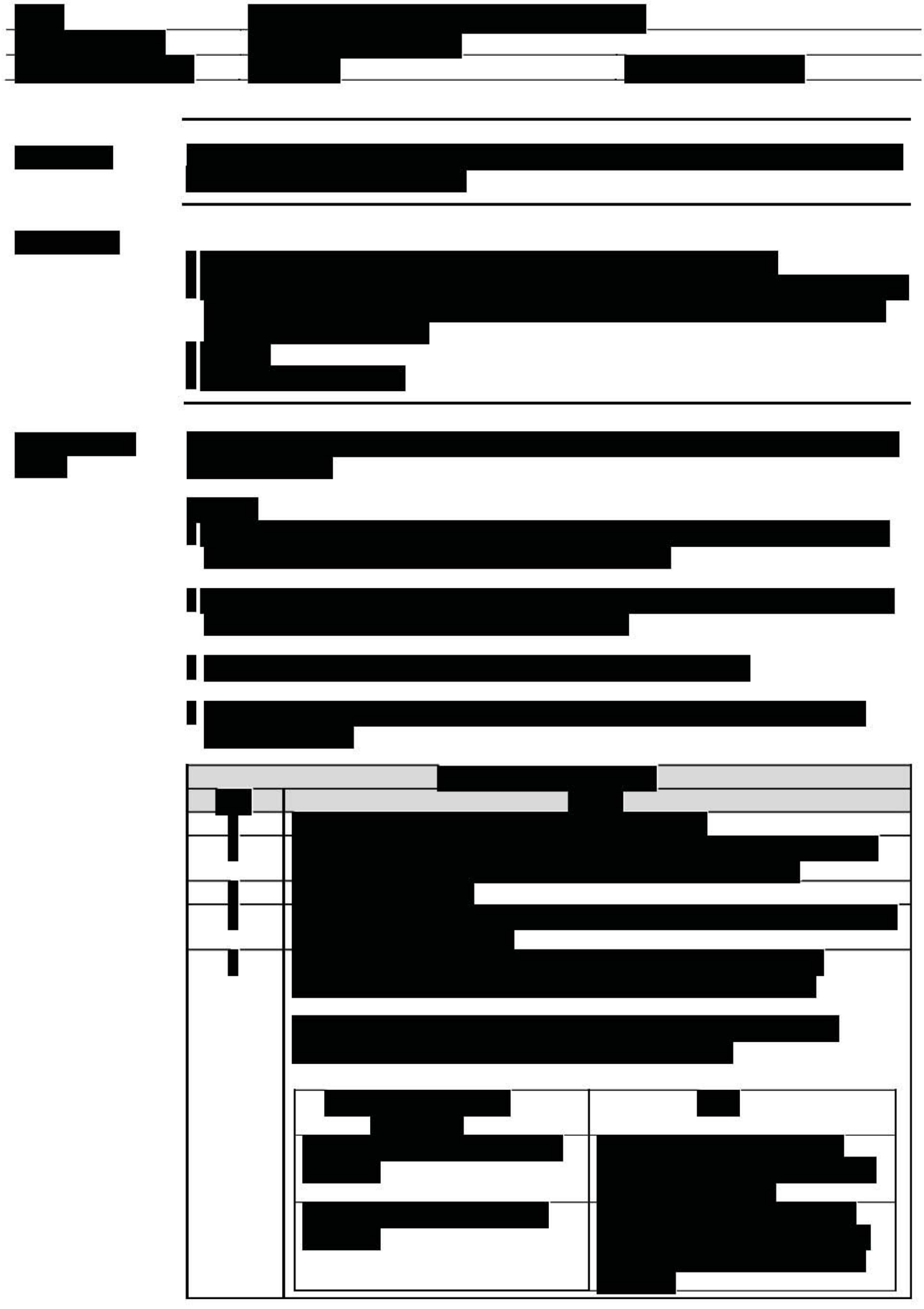
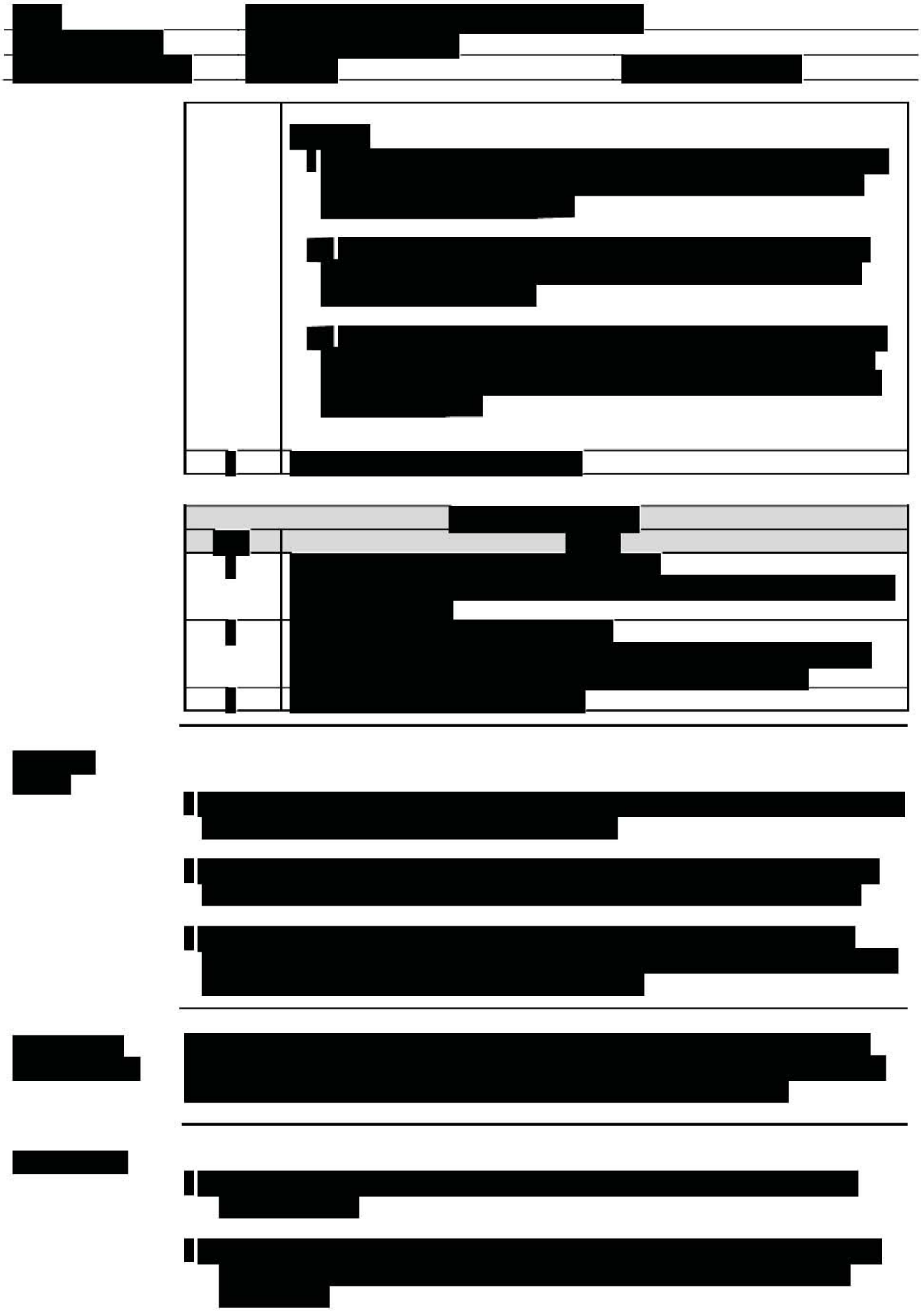


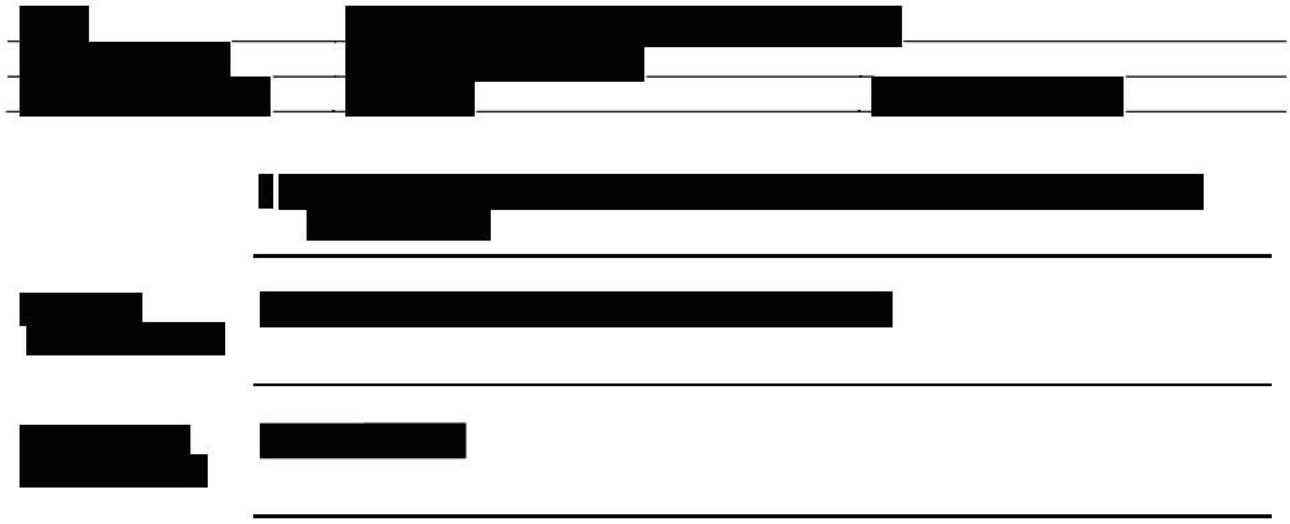


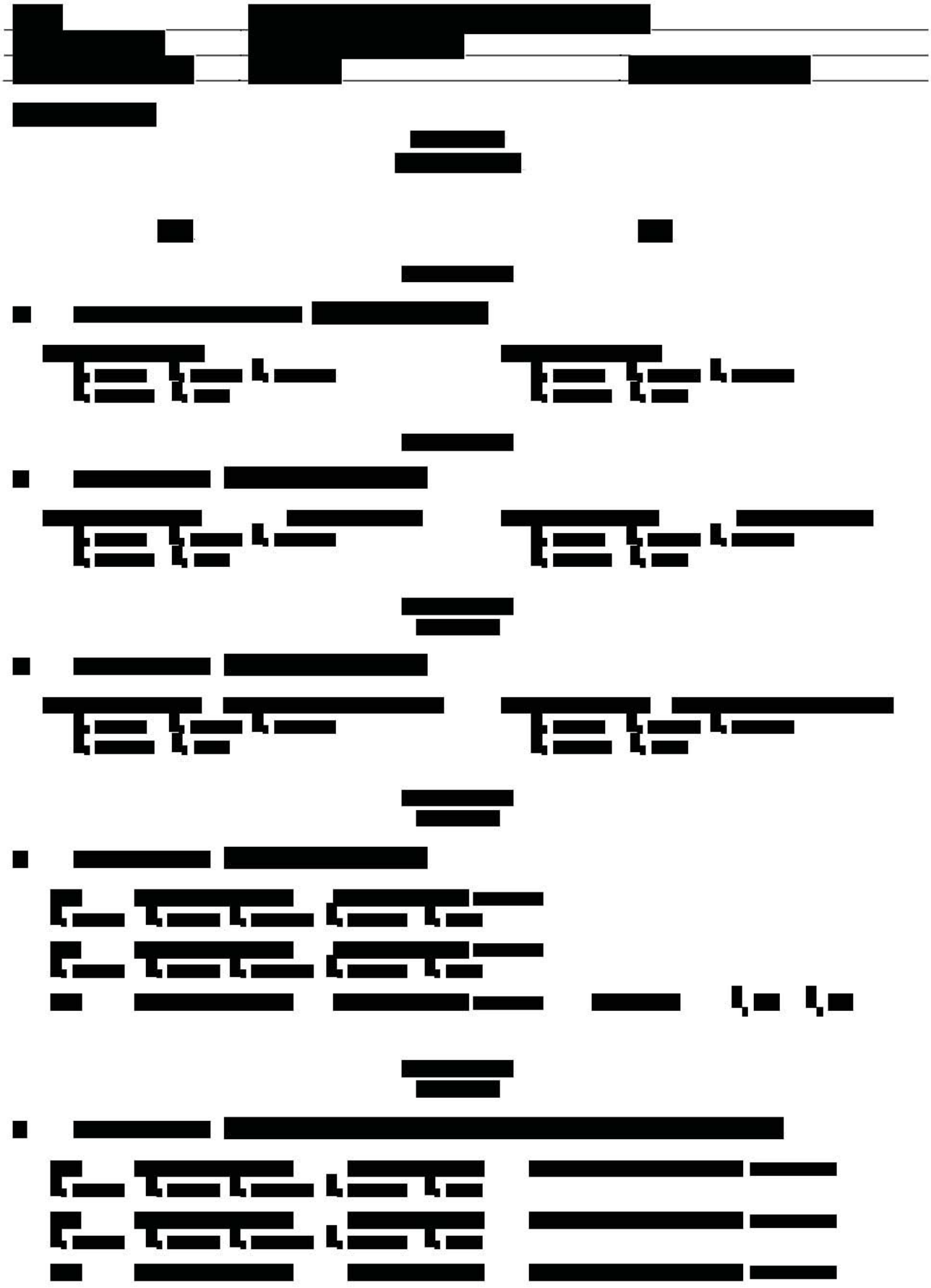


[redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION

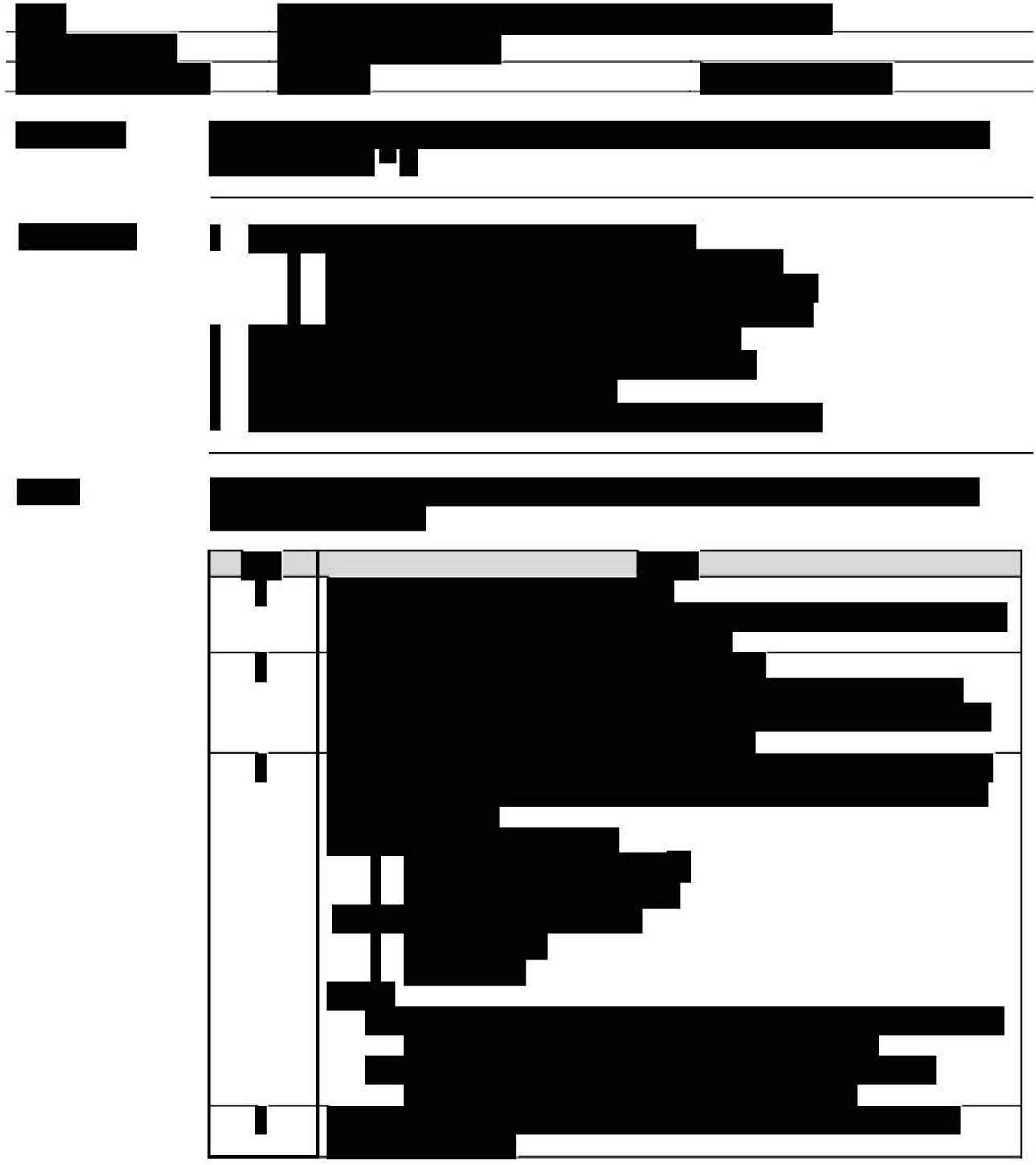








[redacted] DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE



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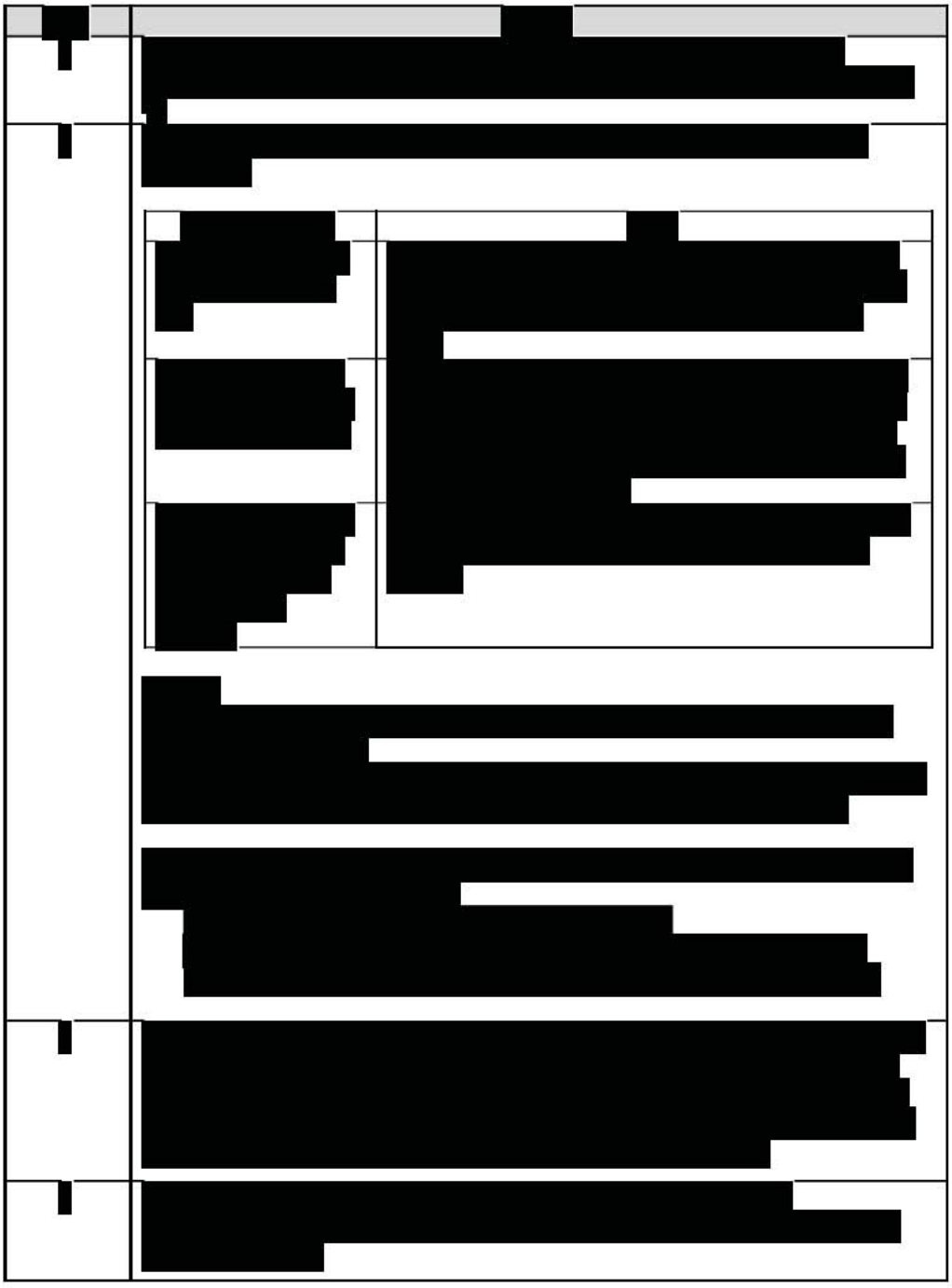

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-5930 Clinical Evaluation of etafilcon A with Ketotifen

Version and Date: v3.0, Amendment 2.0 31 October 2017

I have read and understand the protocol specified above and agree on its content.

I agree to conduct this study according to ISO 14155,[1] GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] United States (US) Code of Federal Regulations (CFR),[4] and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. The Principal Investigator is responsible for ensuring that all clinical site personnel, including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

I will assure that no deviation from, or changes to the protocol will take place without prior agreement from the Sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants.

I am responsible for ensuring that all clinical site personnel including Sub-Investigators adhere to all ICH [2] regulations and GCP guidelines regarding clinical trials during and after study completion.

All clinical site personnel involved in the conduct of this study have completed Human Subjects Protection Training.

I agree to ensure that all clinical site personnel involved in the conduct of this study are informed about their obligations in meeting the above commitments.

I shall not disclose the information contained in this protocol or any results obtained from this study without written authorization.

Principal Investigator:

_____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site:

_____

Institution/Site Name

_____

Institution/Site Address

Electronic Signature Report

Job Name: VIS-CR-005930/A-R&D Clinical Study
Revision: VIS-CSPR-005767/3-Clinical Protocol
Title: VIS Clinical Study Protocol Approval
Status: Approved
System: Vision Care R&D Knowledge Management
Generated By: Cook, Kara
Generated On: 2017-11-03 10:34:26

Signoff Details

Function/Role	Approval Details			
	Participant	WWID	Decision	Decision Date
Biostatistician Approval	Toubouti, Moulay Youssef	373334	Approved	2017-11-03T09:38:08

Function/Role	Approval Details			
	Participant	WWID	Decision	Decision Date
Clinician Approval	Pall, Brian	176727	Approved	2017-11-01T21:52:13

Function/Role	Approval Details			
	Participant	WWID	Decision	Decision Date
Clinical Research Manager Approval	Anderson, Annette	6558	Approved	2017-11-01T16:26:50

Function/Role	Approval Details			
	Participant	WWID	Decision	Decision Date
Other Approval	Paulk, Randall	375676	Approved	2017-11-03T09:47:57
	Moody, Kurt	358947	Approved	2017-11-01T15:52:46
	Dalton, Joseph	372536	Approved	2017-11-01T16:15:48