Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Evaluating Soft Contact Lens Prototypes for Myopia Control

Protocol CR-5959

Version: 3.0, Amendment 2

Date: 11 September 2018

Investigational Products:
Test Lenses: Daily disposable soft contact lenses made in senofilcon A material with three different types of optical designs for myopia control.

- EMO-114
- EMO-116
- EMO-118

Control Lens:

- EMO-117

Key Words: Myopia control, Soft contact lens, Dispensing, Daily Wear, Daily disposable, Senofilcon A, Axial length, Cycloplegic auto refraction, Pediatric population

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.

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PROTOCOL TITLE, NUMBER, VERSION

Title: Evaluating Soft Contact Lens Prototypes for Myopia Control

Protocol Number: CR- 5959
Version: 3.0, Amendment 2
Date: 11 September 2018

SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

The Medical Monitor must be notified by the clinical institution/site by e-mail, fax, 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] ISO 14155,[1] ICH guidelines,[2] and the Declaration of Helsinki.[3]

Author	**See Electronic Signature Report** [redacted]	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
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	[redacted]	Original Protocol	09 Oct 2017
2.0	[redacted]	1. Updated the protocol to the latest Clinical Study Protocol Template [redacted] 2. Added "Soft contact lens" and "Pediatric population" as key words 3. Added "by the Sponsor" under Trial Registration in the Synopsis and Section 21 4. Repeated the targeted age distribution of subjects in the Synopsis and Section 3.1 per that specified in Section 5.1 5. Corrected an error in the estimated lens quantity in Section 6.1 6. Updated the sample images of lens packing and labeling and carton size in Section 6.4 7. Updated the reference number of [redacted] in Section 6.7 per the Protocol Template v 7.0 8. Specified that should Visit 1 be completed in two separate days, up to 21 days is allowed between the two days in Section 7.2. 9. Added "be read to" in the detailed procedure for children's assent in Section 7.2 to be consistent with that specified in Inclusion Criteria 10. Corrected the Final Evaluation slit lamp classification scale to be per ISO 11980 in Section 7.2 11. Added references of [redacted] in Section 13.5; [redacted] in Appendix D 12. Specified statistical analysis will be performed by the Sponsor in Section 14.1 13. Added the Canada privacy law (PIPEDA) in Section 18.5 14. Corrected a typographical error in the instruction of PRO questionnaires in Appendix A 15. General formatting, punctuation, and spelling corrections throughout	12 Dec 2017

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
3.0	[redacted]	1. Allowed axial length to be measured with "a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor" in Synopsis and Sections 2.2 and 7.2. 2. Added IOLMaster work aid in Appendix D	11 Sep 2018

SYNOPSIS

Protocol Title	Evaluating Soft Contact Lens Prototypes for Myopia Control
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Development phase, Phase 1
Trial Registration	The study will be registered on clinicaltrial.gov by the Sponsor based on the following: This is an interventional clinical trial for evaluating safety and effectiveness of novel soft contact lenses for controlling myopia progression in pediatric populations.
Test Article(s)	Daily disposable soft contact lenses (SCL) made in senofilcon A material with four different types of optical designs. Test Lenses: • EMO-114 • EMO-116 • EMO-118 Control Lens: • EMO-117
Wear and Replacement Schedules	Wear Schedule: Daily wear Replacement Schedule: Daily disposable Subjects will be randomly assigned to receive one of the four test articles.
Objectives	The objective of the study is to evaluate the safety and effectiveness of three soft contact lens prototypes for controlling myopia progression by comparing to a control soft contact lens.
Study Endpoints	Primary endpoints: 1. Change of Axial Length (AL) at 6-month from baseline 2. Change of Spherical Equivalent Cycloplegic Auto Refraction (SECAR) at 6-month from baseline Secondary endpoint: • Serious and significant ocular adverse events Other observations: 1. Non-significant AEs and non-ocular AEs 2. Slit lamp findings per the ISO 11980 grading scale 3. Subject-reported ocular symptoms 4. Corneal radius of curvature measured by an autorefractor 5. Over-the-lens near visual acuity

	6. Subjective best-sphere over-refraction 7. Number of power modification per each prescription update 8. Number of prescription update during the study 9. Lens fit characteristics 10. Distance logMAR visual acuity under High Luminance High Contrast (HLHC) conditions 11. Subjective vision, comfort, and handling scores based on the Pediatric Contact Lens User Experience (pCLUE) questionnaire. 12. Lens wear time compliance 13. Number of visits for contact lens insertion/removal training
Study Design	This is a multi-site, prospective, randomized, controlled, double-masked, four-arm-parallel-group, dispensing study. Each subject will be bilaterally fitted with one of the four types of test articles and wear lenses of the assigned lens type during the entire course of the study. Test articles will be worn a minimum 8 hours per day and 5 days per week (subjects will be encouraged to wear study contact lenses 10 hours or more per day and 7 days per week) in a daily disposable modality for a minimum of 6 months and up to 1 year*. There will be a total of 7 scheduled visits. Visit 1: Screening, baseline evaluation, Visit 2: Baseline, randomization, lens fit and dispensing Visit 3: 1-week follow-up Visit 4: 1-month follow-up Visit 5: 3-month follow-up Visit 6: 6-month follow-up Visit 7: 1-year follow-up (optional) * The study will complete after all subjects have completed the 6-month follow-up (Visit 6). Considering the extensive enrollment period (e.g., approximately 8 months), while waiting for the last enrolled subjects to complete the 6-months follow-up, the study allows subjects enrolled at the beginning of the enrollment period to continue wearing study lenses for up to 1 year and complete the 1-year follow-up (Visit 7) before completing the final evaluation and exiting the study. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	Approximately 240 subjects will be enrolled in the study with a minimum of 160 subjects (40/arm) targeted to complete the 6-month follow-up.
Study Duration	The total duration of the study is estimated to be about 18 months, including approximately 8 months of enrollment period.

Anticipated Study Population	Healthy male and female children between 7 and 12 years of age (inclusive) with best sphere refraction between -0.75D and -4.50D (inclusive), 1.00D or less astigmatism. Potential subjects can be spectacle lens wearers, current soft lens wearers, or symptomatic myopes (e.g., with complaints of blurry vision) but currently with no correction. Study sites will aim to enroll at least 50% of subjects in the age group of 7 – 9 years as well as subjects with 0.50D or more myopia progression in the past 12 months (documented or by self-report) to their best effort.
Eligibility Criteria	Potential subjects must satisfy all following criteria to be enrolled in the study: Inclusion Criteria after Screening: 1. The subject must read (or be read to), understand, and sign the Statement of Information and Assent and receive a fully executed copy of the form. 2. The subject's parent(s) or legal guardian(s) must read, understand and sign the Statement of Informed Consent and receive a fully executed copy of the form. 3. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 4. Between 7 and 12 years of age (inclusive). 5. Have normal eyes (ie, no ocular medications or infections of any type). Inclusion Criteria after Baseline 1: 6. Distance subjective best-sphere refraction must be between -0.75D and -4.50D (inclusive) in each eye. 7. Cylindrical refraction must be 1.00D or less in each eye, by subjective sphero-cylindrical refraction. 8. Have sphero-cylindrical best-corrected visual acuity of 20/25 (ie, 0.8 in decimal convention or 0.10 logMAR) or better in each eye. Inclusion Criteria after Baseline 2: 9. Cycloplegic objective sphero-cylindrical refraction (by auto refraction) must be between -0.75D and -4.50D in sphere and is 1.00D or less in cylinder in each eye (based on the average of 5 repeated sphero-cylindrical refraction measures). 10. The difference in spherical equivalent power between the two eyes must be less than 1.50D (based on the average of 5 repeated sphero-cylindrical refraction measures). Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria after Screening: 1. Currently pregnant or lactating.

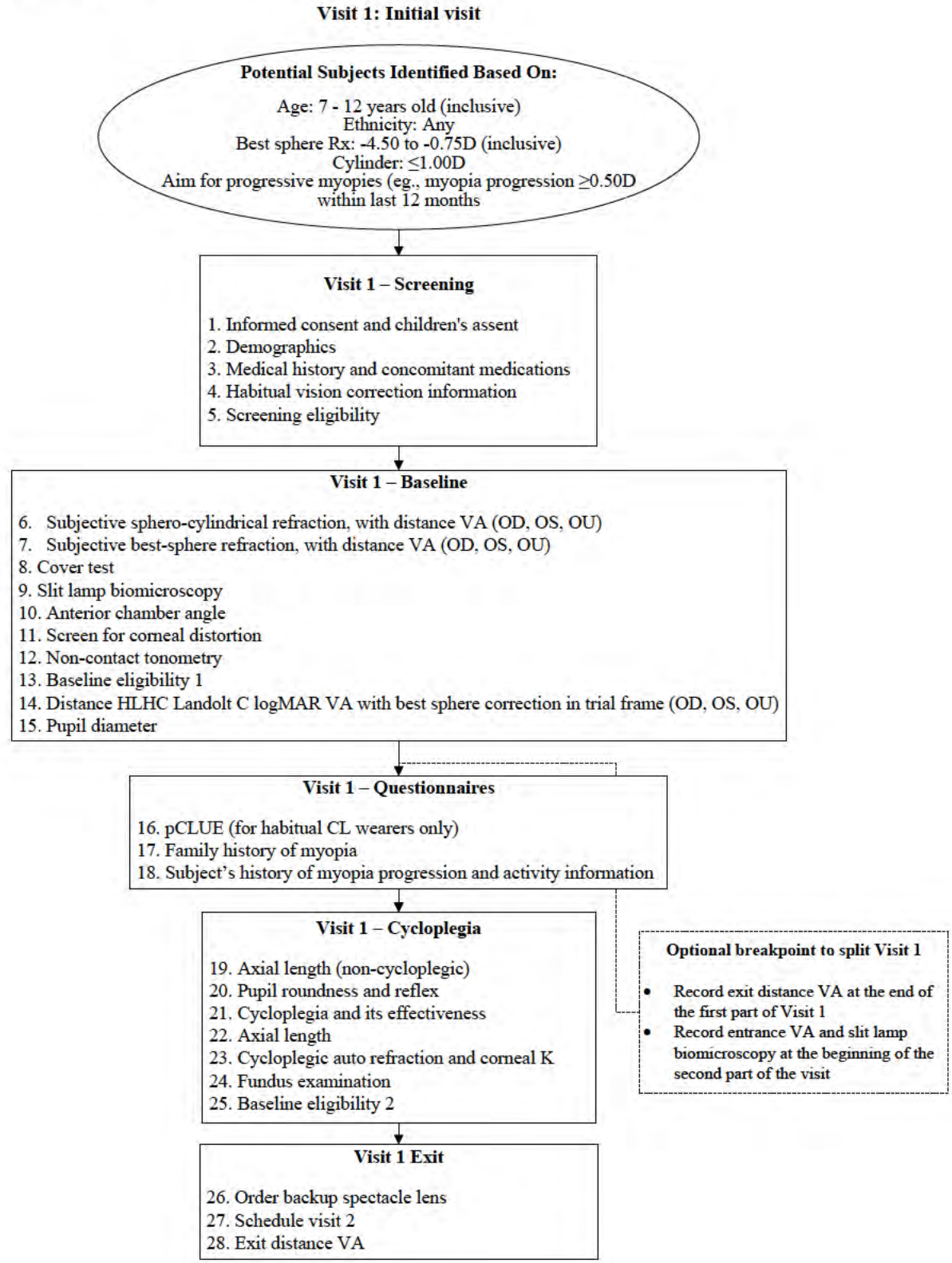
	2. Any systemic allergies, infectious disease (e.g., hepatitis, tuberculosis), autoimmune disease (e.g., rheumatoid arthritis), or other systemic diseases (e.g., diabetes), by the parent or legal guardian's report, which are known to interfere with contact lens wear and/or participation in the study. 3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear. 4. Any current use of ocular topical medication. 5. Any previous or planned ocular or intraocular surgery, including refractive surgery. 6. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment. 7. Participation in any prior myopia control clinical study in the test group. 8. Current or recent (within 30 days from enrollment) rigid lens wearers. 9. History of orthokeratology treatment or use of other ophthalmic devices (e.g., bifocal, multifocal contact or spectacle lenses) or drugs (e.g., atropine or pirenzepine) for the purpose of controlling myopia progression. 10. Any known hypersensitivity or allergic reaction to EyeCept® (or sponsor approved equivalent) Rewetting Drop Solution. 11. Relatives of employee of investigational clinic (e.g., Investigator, Coordinator, Technician). Exclusion Criteria after Baseline: 12. 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, aphakia, uveitis, ocular hypertension, glaucoma, severe keratoconjunctivitis sicca, history of recurrent corneal erosions, keratoconus, keratoconus suspect, pellucid marginal degeneration, entropion, ectropion, extrusions, chalazia, and recurrent styes. 13. Grade 3 or greater palpebral conjunctival observations or any other Grade 2 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, conjunctival injection) on the ISO 11980 classification scale. 14. 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 may contraindicate contact lens wear. 15. Any central corneal scar 16. Any corneal distortion resulting from ocular diseases or previous hard or rigid gas permeable contact lens wear.

	17. Binocular vision abnormality, intermittent strabismus or strabismus. 18. Anterior chamber angle is Grade 2 or narrower in either eye. 19. IOP is 21 mmHg or higher in either eye.
Disallowed Medications/ Interventions	Disallowed medications for this study included the following: 1. Any chronic (3 months or more) or seasonal (30 days or more) use of topical ophthalmic medication except for artificial tears or contact lens rewetting drops. This includes but is not be limited to, topical ophthalmic anti-histamine, topical ophthalmic mast cell stabilizers, topical ophthalmic antibiotics, topical ophthalmic vasoconstricting agents, and topical decongestants, including nasal decongestants (naphazoline, tetrahydrozoline, and phenylephrine), etc. Short-term use of above listed topical ophthalmic medication may be allowed, but must be completed at least 7 days prior to any scheduled study visit. 2. Any outside the study use of topical agents with anti-muscarinic properties for more than 3 consecutive days (i.e., other than for diagnostic use), or repeated single use of these agents for more than 3 doses within the last 6 months. This includes but is not limited to atropine, scopolamine, pirenzepine, tropicamide, cyclopentolate and homatropine. Occasional use of these agents (i.e., three doses or less during the last 6 months) must be completed 21 days prior any scheduled study visit. 3. Any chronic use of oral agents with anti-muscarinic properties. This includes, but is not limited to 1) Any GI anti-spasmodic medicine containing atropine, hyoscyamine, and dicyclomine 2) Over-the-counter cold & allergy preparations and sleeping agents that contain first generation anti-histamines (diphenhydramine, chlorpheniramine) 3) Tricyclic anti-depressant (amitriptyline, imipramine, nortriptyline) 4) Anti-psychotics agents (chlorpromazine, thioridazine) 5) Anti-nausea/anti-cough medication containing promethazine, prochlorperazine, meclizine and scopolamine 6) Anti-anxiety agent (hydroxyzine) 7) Ipratropium bromide Short-term use of above listed oral agents with anti-muscarinic properties may be allowed but must be completed at least 7 days prior to any scheduled study visit. 4. Any chronic use of human growth hormone products containing somatropin, eg, Genotropin, Nutropin, Saizen, etc. Short-term use of these medications may be allowed but must be completed at least 30 days prior to any scheduled study visit.

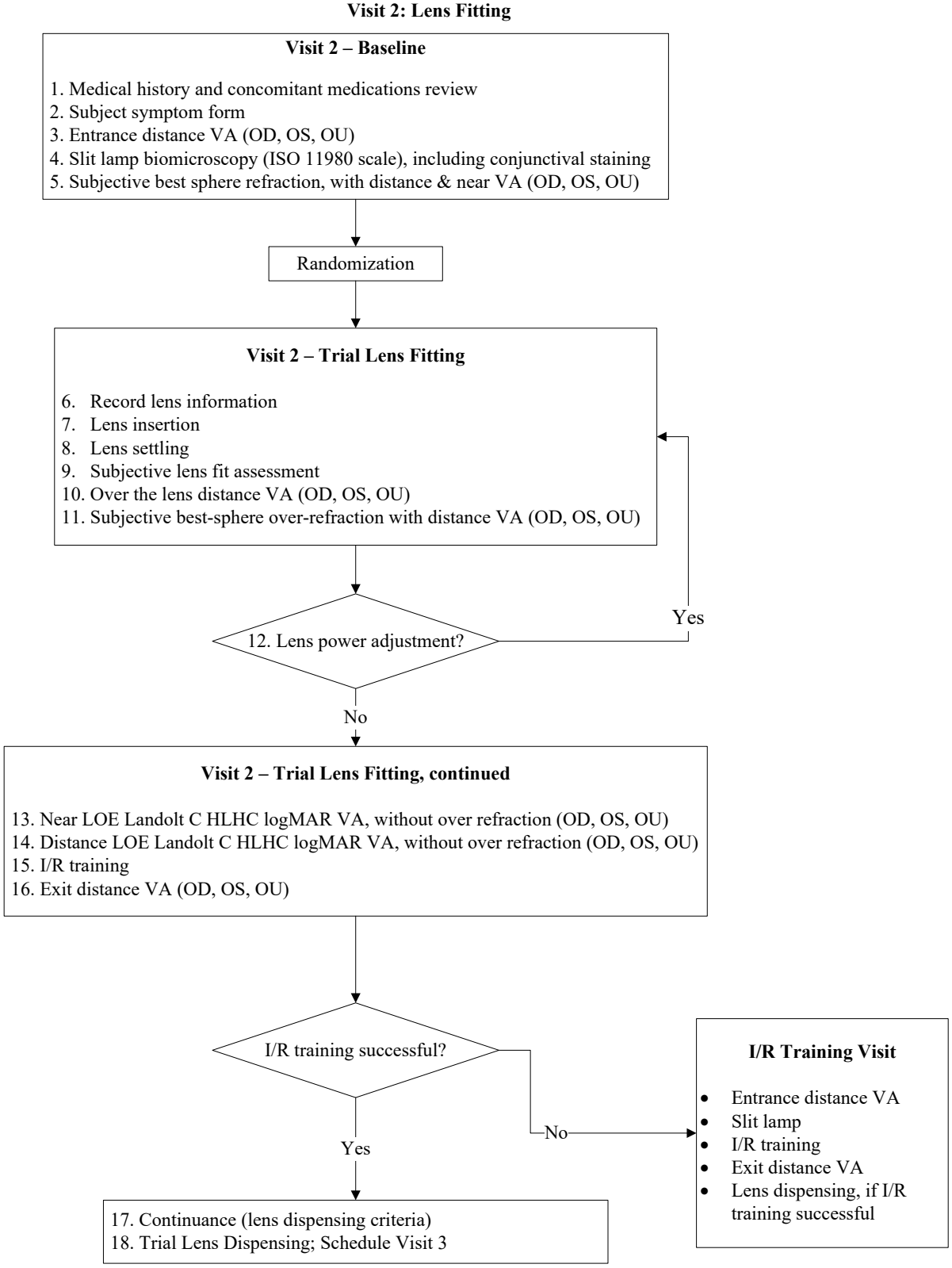
	5. Any chronic use of oral beta-blocker. Short-term use of oral beta-blockers may be allowed but must be completed at least 7 days prior to any scheduled study visit. 6. Any chronic use of anti-psychotic and neurological. This includes but is not limited to, 1) ADHD medications containing methylphenidates, amphetamines and its derivatives (Ritalin, Concerta, Adderall, and Strattera, etc.) 2) Anti-psychotic agents phenothiazines (chlorpromazine, thioridazine) Short-term use of above listed medications may be allowed, but must be completed at least 30 days prior to any scheduled study visit. 7. Any chronic use of sulfa drugs. This includes but is not limited to 1) Sulfamethoxazole containing products, such as Bactrim, Septra 2) Carbonic anhydrase inhibitors such as dorzolamide and acetazolamide 3) Sulfasalazine 4) Topiramate 5) Thiazides diuretics such as hydrochlorothiazide & chlorthalidone Short-term use of above listed medications may be allowed, but must be completed at least 7 days prior to any scheduled study visit. 8. Any medications that has known ocular side effects. Concomitant therapies that are disallowed include: 1. Contact lens corneal reshaping/CRT/orthokeratology 2. Any vision training/vision therapy/orthoptics/patching 3. Use of reading spectacles or progressive addition lenses 4. Any therapies that the investigator felt would be contraindicated in contact lens wear.
Measurements and Procedures	• Axial length (by LENSTAR LS 900, or a similar device (e.g., IOLMaster) in Asian sites upon approval of the sponsor) • Cycloplegic auto refraction (by an open-field auto refractor) • Slit lamp examination per the ISO 11980 grading scale • Subjective ocular symptom questionnaires • Landolt C logMAR visual acuity under the high luminance high contrast conditions (OD, OS, OU) • Subjective lens fit assessment • Subjective assessment of vision, comfort and lens handling
Microbiology or Other Laboratory Testing	Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature.
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any Serious Adverse Event (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	Topical anesthetics (e.g., 0.5% proparacaine or equivalent approved in local markets) Cycloplegia agent (1% cyclopentolate) Precision Vision Landolt C 4-meter, high contrast, logMAR visual acuity charts (2210, 2210A and 2210B) Precision Vision Landolt C 40-cm, high contrast, logMAR visual acuity charts There will be no contact lens care solutions, e.g., disinfecting or storage used/provided in the study.
Principal Investigator and Study Sites	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

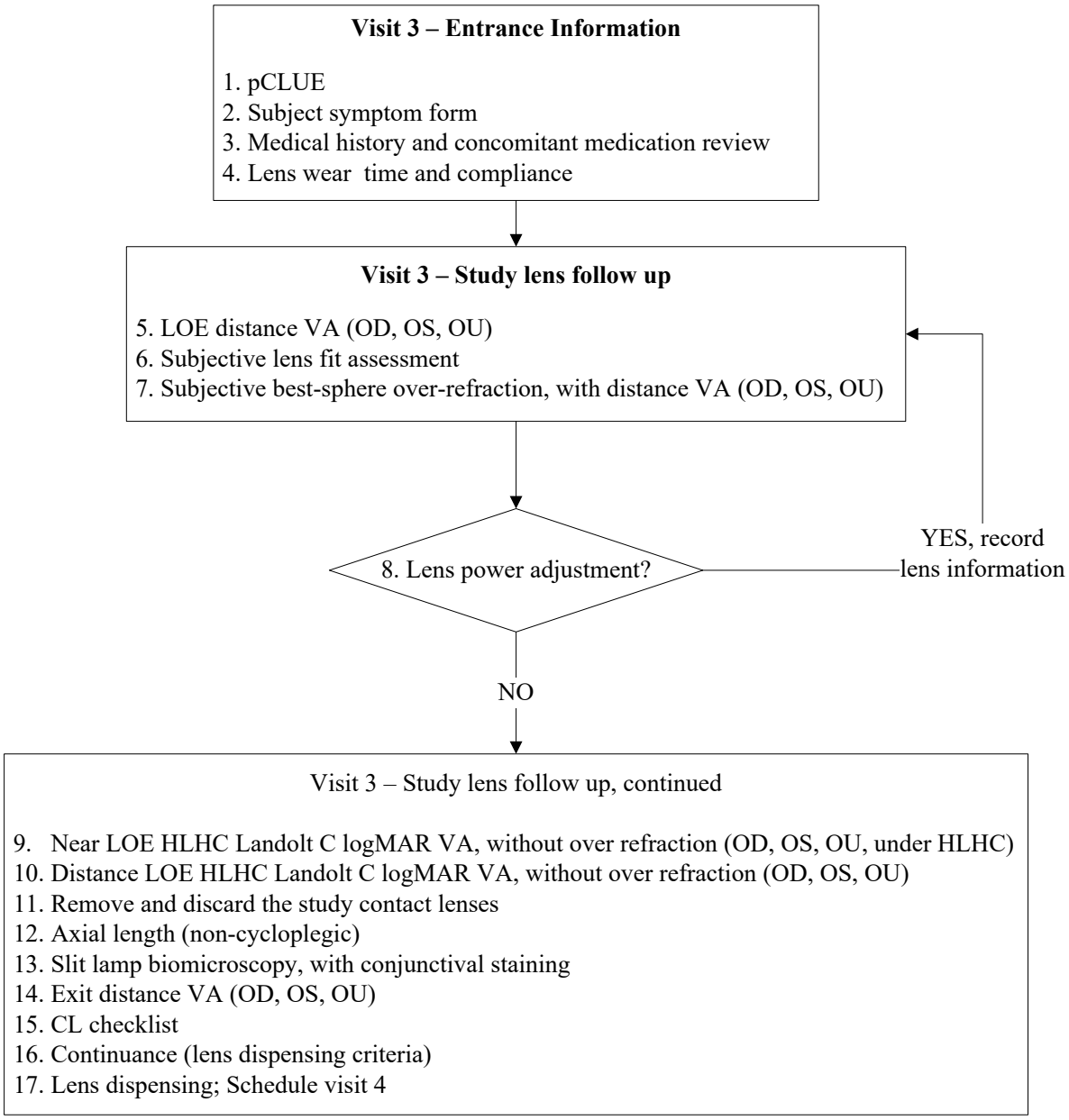


Flowchart, continued



Flowchart, continued

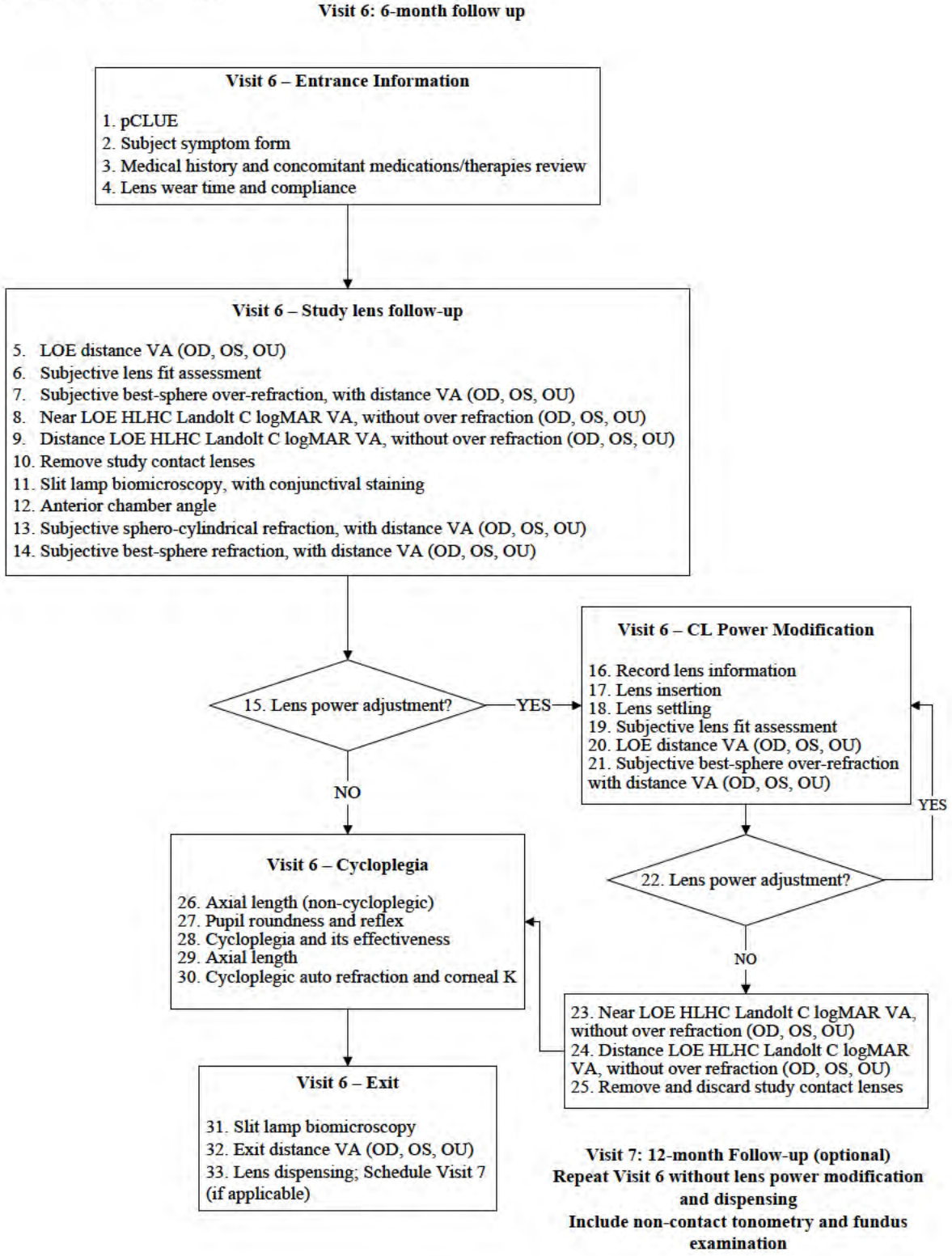
Visit 3: 1-week Follow-up



Visit 4: 1-month Follow-up
Repeat Visit 3

Visit 5: 3-month Follow-up
Repeat Visit 3

Flowchart, continued



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

ADD	Plus Power Required for Near Use
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
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager
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
IOP	Intraocular Pressure
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
MedDRA©	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NIH	National Institutes of Health
OD	Right Eye
OHRP	Office for Human Research Protections
OHSR	Office for Human Subjects Research
OS	Left Eye
OU	Both Eyes
PD	Protocol Deviation
PHI	Protected Health Information

PI	Principal Investigator
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRO	Patient Reported Outcome
QA	Quality Assurance
QC	Quality Control
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

Based on the literature reports and past experiences of developing soft contact lenses for controlling myopia progression at Johnson & Johnson Vision Care (JJVC),[5-10] it is hypothesized that introducing more "plus" power in the optical design of the lens that covers larger retinal area is likely to result in larger myopia control treatment effect. However, this approach may also lead to negative impact on vision. In order to balance between maximizing myopia control efficacy and minimizing visual impact, a series of new optical designs for myopia control are proposed. These prototypes were evaluated in pilot studies for their visual performances [redacted] in adult subjects. [11-13] Lens prototypes were also evaluated for their potential for controlling myopia progression via "in-vitro" modeling. The results of these studies indicated that two prototype designs (EMO-114 and EMO-118) provided satisfactory visual, comfort and fit performances[14,15] and are suitable to be further evaluated for their myopia control efficacy in a longitudinal clinical trial.

The purpose of the current study is to evaluate the safety and effectiveness of two new lens prototypes (EMO-114 and EMO-118) for controlling myopia progression. Also included in the study is a third investigational lens (EMO-116) that has an optical design simulating that of the MiSight lens (CooperVision, Inc.). The MiSight lens is CE-marked and indicated for myopia control in patients of 8-18 years of age.[6,16]

1.1. Name and Descriptions of Investigational Products

This study will test three investigational lenses (EMO-114, -116, and -118) for their myopia control effect against a marketed control lens. Two of the investigational lenses (Test1: EMO-114 and Test 2: EMO-118) are new lens prototypes designed for myopia control purpose. The third investigational lens (Test 3: EMO-116) has an optical design simulating the CE-marked MiSight lens and is included in the study serving as the positive control lens. An FDA-cleared, non-marketed lens (Control: EMO-117) is included in the study to serve as the negative control lens. All four study lenses are made in senofilcon A material and will be worn in the daily disposable modality. Further details about the test articles are found in Section 6 of this protocol.

1.2. Intended Use of Investigational Products

The intended use of the three investigational soft contact lenses (Test: EMO-114, -116, and -118) is for correcting myopia and controlling the progression of myopia. The fourth investigational lens (Control: EMO-117) is for correcting myopia only and is not intended for controlling myopia progression. During this study, each subject will wear one of the four types of contact lenses. All four types of contact lenses will be worn bilaterally in the daily wear, daily disposable modality for at least 8 hours per day, 5 days per week (subjects will be encouraged to wear study contact lenses 10 hours or more per day and 7 days per week) for a minimum of 6 months and up to 1 year.

1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. For the most comprehensive nonclinical information regarding the investigational lenses refer to the latest version of the Investigator's Brochure for EMO Design Family Lenses.[17]

1.4. Summary of Known Risks and Benefits to Human Subjects

The benefit of controlling myopia progression is considered to be substantial[18] as the prevalence and incidence of myopia has been increasing substantially over the past few decades.[19-21] In addition, significant health risks have been associated with myopia, including glaucoma, cataract, retinal detachment and myopic macular degeneration. Therefore, it can be considered most advantageous to control the progression of myopia and start treatment at an early age when myopia is at a low level. Based on theoretical predication, it is estimated that an effect of reducing myopia progression by 33% and 50% will result in a reduction in risk population (defined as the percentage of myopes being 5.00 D or higher) by 73% and over 90%, respectively.[22]

The risks associated with the wear of contact lenses for myopia control includes 1) contact lens risks in general population; 2) contact lens risks in pediatric population; and 3) risks specifically associated with EMO family of lenses, such as potential sub-optimal visual performances and long-term physiological and/or neurological impact.

Assessment regarding contact lens risks in general and in the pediatric population concluded that the risks associated with the EMO investigational lenses are expected to be the same as those normally attributed to the wear of soft hydrophilic contact lenses on a daily wear basis. The daily disposable modality of the investigational lenses further reduces risks associated with lens care and the use of care products (eg, cleaning, disinfecting, rinsing and storage, etc.). Anticipated adverse reactions with these lenses are the same as any other soft contact lens as listed in this study protocol Section 13.1. In addition, the most recent review on the safety of contact lens wear in children concluded that “the incidence of corneal infiltrative events in children is no higher than in adults, and in the youngest age range of 8 to 11 years, it may be markedly lower”.[23]

Due to the unique optical design of the EMO lenses, visual performance of these lenses may not be equivalent to that of lenses with a conventional spherical lens design. To manage the risk, special attention will be paid to visual acuity, visual complaints (eg, blurry vision or visual artifacts such as ghosting or haloes, etc.), and subjective visual acceptance while fitting the study lenses. In addition, the study lens power may be modified based on the refraction over the study lens and visual acuity. Finally, specific criteria regarding visual acuity and subjective vision acceptance will be imposed for lens dispensing. The study lenses will not be dispensed and the subject will be discontinued from the study if these vision criteria are not met. Finally, there has been no evidence in the literature suggesting any long-term physiological or neurological risks associated with children being exposed to chronic myopic defocus (e.g., due to under correction) or to multi-focal type optical interventions.

There have been no reports of loss of best corrected visual acuity in published pediatric clinical trials utilizing various methods for myopia control purposes or in any prior JJVC conducted myopia control trials.[24-30] None-the-less, best sphero-cylindrical corrected visual acuity (BSCVA) will be closely monitored at each follow-up visit throughout the course of the study. Should there be any confirmed case of development of amblyopia during the study, it will be investigated and followed per the procedures specified for unanticipated adverse device effects in the current protocol Section 13.5.

Per the risk-to-benefit analysis, it is proposed that the benefits of slowing myopia progression outweigh the risks associated with daily disposable soft contact lens wear.

The US Food & Drug Administration has traditionally considered that daily wear contact lens studies are non-significant risk studies (FDA Premarket Notification [510(k)] Guidance Document for Daily Wear Contact Lens [May 1994],[31] and FDA Information Sheets: Significant Risk and Non-significant Risk Medical Device Studies [October, 1995][32]). However, due to the proposed new intended use of soft contact lenses for controlling myopia progression in the pediatric population, the US FDA considers such soft contact lenses to be significant risk devices and clinical investigations of these lenses in pediatric populations in the US must be conducted in accordance with Investigational Device Exemption (IDE) regulations as stated in CFR Title 21, Part 812.[4]

For the most comprehensive risk and benefit information regarding the EMO lenses refer to the latest version of the Investigator's Brochure for EMO Design Family Lenses.[17]

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

The review of the scientific literature examined the current state of published information contact lens safety and myopia control with soft contact lenses. Potential applicable literature was identified through a literature search on PubMed.org dated back to 1980's, as well as through examination of review articles published on the subject. A list of relevant literature references is provided in latest version of the Investigator's Brochure for EMO Design Family Lenses.[17]

To date, there have been only three clinical studies involving the EMO family of lenses [redacted] (non-dispensing), [redacted] (short-term dispensing for up to 3 days) and [redacted] (non-dispensing) were pilot studies with a primary objective of evaluating the visual performances of EMO lens design prototypes in adult subjects. A total of seven lens prototypes were examined, including the EMO-114, -116, and -118 lenses that will be investigated in the current study. There were no ocular adverse events reported in these studies. For detailed information regarding prior clinical data refer to the latest version of the Investigator's Brochure for EMO Design Family Lenses.[17]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

The objective of the study is to evaluate the safety and effectiveness of three soft contact lens prototypes for controlling myopia progression by comparing to a control soft contact lens.

Primary Objective:
The primary objective of the study is to evaluate the performance of three soft contact lens prototypes for slowing myopia progression in children age 7 to 12 years old (inclusive) after 6-month of lens wear by comparing to a control soft contact lens.

Secondary Objective:
The secondary objective of the study is to evaluate the safety of three new soft contact lens prototypes. The evaluation of the safety of the test articles will be based on monitoring adverse events, slit lamp findings and subject reported ocular symptoms throughout the study.

Other Objectives:
Other exploratory objectives include:

1. Assessing visual acuity with the study lenses;
2. Assessing lens fit characteristics;
3. Assessing lens wear time compliance;
4. Assessing subject's responses regarding lens vision, comfort and handling performances.

In addition, the performance of the three Test lenses (EMO-114, -116, and -118) for myopia control may be evaluated and compared with the Control lens (EMO-117) for one year of lens wear, if applicable. Summary statistical analyses will be performed on safety and efficacy parameters of available 1-year data.

2.2. Endpoints

Primary Endpoints
There are two co-primary endpoints in this study:

1. Change of axial length (AL) from baseline at 6 months;
   Axial length (in the unit of mm) will be measured using LENSTAR LS 900 manufactured by Haag-Streit, or a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor.
2. Change of spherical equivalent of cycloplegic auto refraction (SECAR) from baseline at 6 months
   SECAR (in the unit of D) will be computed from the sphero-cylindrical refraction measured by a commercially available autorefraction such as WAM-5500 manufactured by Grand Seiko.

Secondary Endpoints

- Serious and significant ocular Adverse Events (AEs)

Other Endpoints:

1. Non-significant AEs and non-ocular AEs
2. Slit lamp findings per the ISO 11980 grading scale
3. Subject-reported ocular symptoms
4. Corneal radius of curvature measured by an autorefractor
5. Over-the-lens near visual acuity
6. Subjective best-sphere over-refraction
7. Number of power modification per each prescription update
8. Number of prescription update during the study
9. Lens fit characteristics
10. Distance logMAR visual acuity under High Luminance High Contrast (HLHC) conditions
11. Subjective vision, comfort, and handling scores based on the Pediatric Contact Lens User Experience (pCLUE) questionnaire.
    pCLUE is a subjective questionnaire that is currently being developed specific for pediatric populations based on the existing CLUE™ questionnaire for the adult population. 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.[33]
12. Lens wear time compliance
13. Number of visits for contact lens insertion/removal training

In addition, the following observations will be recorded or monitored throughout the study:

1. Subject's demographics
2. Subject's disposition, number and reasons for discontinuation
3. Number and reasons for unscheduled visits
4. Lens accountability, including reasons for lens dispensing or replacement
5. Protocol deviations
6. Product quality complaints

2.3. Hypotheses

Primary Hypotheses:

After approximately 6 months of lens wear, at least one of the three Test lenses (EMO-114, -116, and -118) will be efficacious in slowing the progression of myopia compared to the Control lens (EMO-117) such that:

1. the change of axial length (AL) of the eye from baseline will be statistically significantly less for the Test lens compared with the Control lens.
2. the change of Spherical Equivalent of Cycloplegic Auto Refraction (SECAR) of the eye from baseline will be statistically significantly less in magnitude with the Test lens compared with the Control lens.

Both conditions regarding the performance of the Test lens must be met in order to meet the primary objective.

Secondary Hypothesis:
Secondary endpoint and all other safety endpoints will be summarized descriptively. No secondary endpoint hypothesis testing will be performed.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Healthy male and female children between 7 and 12 years of age (inclusive) with best sphere refraction between -0.75D and -4.50D (inclusive), 1.00D or less astigmatism. Potential subjects can be spectacle lens wearers, current soft lens wearers, or symptomatic myopes (e.g., with complaints of blurry vision) but currently with no correction. Each study site will aim to enroll at least 50% of subjects in the age group of 7 – 9 years as well as subjects with 0.50D or more myopia progression in the past 12 months (documented or by self-report) to their best effort. There are no restrictions as to gender or race/ethnicity.

3.2. Inclusion Criteria

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

Inclusion Criteria after Screening:
1. The subject must read (or be read to), understand, and sign the Statement of Information and Assent and receive a fully executed copy of the form.
2. The subject's parent(s) or legal guardian(s) must read, understand and sign the Statement of Informed Consent and receive a fully executed copy of the form.
3. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
4. Between 7 and 12 years of age (inclusive).
5. Have normal eyes (i.e., no ocular medications or infections of any type).

Inclusion Criteria after Baseline 1:
6. Distance subjective best-sphere refraction must be between -0.75D and -4.50D (inclusive) in each eye.
7. Cylindrical refraction must be 1.00D or less in each eye, by subjective sphero-cylindrical refraction.
8. Have sphero-cylindrical best-corrected visual acuity of 20/25 (ie, 0.8 in decimal convention or 0.10 logMAR) or better in each eye.

Inclusion Criteria after Baseline 2:
9. Cycloplegic objective sphero-cylindrical refraction (by auto refraction) must be between -0.75D and -4.50D in sphere and is 1.00D or less in cylinder in each eye (based on the average of 5 repeated sphero-cylindrical refraction measures).
10. The difference in spherical equivalent power between the two eyes must be less than 1.50D (based on the average of 5 repeated sphero-cylindrical refraction measures).

3.3. Exclusion Criteria

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

Exclusion Criteria after Screening:

1. Currently pregnant or lactating.
2. Any systemic allergies, infectious disease (e.g., hepatitis, tuberculosis), autoimmune disease (e.g., rheumatoid arthritis), or other systemic diseases (e.g., diabetes), by the parent or legal guardian's 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 current use of ocular topical medication.
5. Any previous or planned ocular or intraocular surgery, including refractive surgery.
6. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment.
7. Participation in any prior myopia control clinical study in the test group.
8. Current or recent (within 30 days from enrollment) rigid lens wearers.
9. History of orthokeratology treatment or use of other ophthalmic devices (e.g., bifocal, multifocal contact or spectacle lenses) or drugs (e.g., atropine or pirenzepine) for the purpose of controlling myopia progression.
10. Any known hypersensitivity or allergic reaction to EyeCept® (or sponsor approved equivalent) Rewetting Drop Solution.
11. Relatives of employee of investigational clinic (e.g., Investigator, Coordinator, Technician).

Exclusion Criteria after Baseline:

12. 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, aphakia, uveitis, ocular hypertension, glaucoma, severe keratoconjunctivitis sicca, history of recurrent corneal erosions, keratoconus, keratoconus suspect, pellucid marginal degeneration, entropion, ectropion, extrusions, chalazia, and recurrent styes.
13. Grade 3 or greater palpebral conjunctival observations or any other Grade 2 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, conjunctival injection) on the ISO 11980 classification scale.
14. 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 may contraindicate contact lens wear.
15. Any central corneal scar
16. Any corneal distortion resulting from ocular diseases or previous hard or rigid gas permeable contact lens wear.
17. Binocular vision abnormality, intermittent strabismus or strabismus.
18. Anterior chamber angle is Grade 2 or narrower in either eye.
19. IOP is 21 mmHg or higher in either eye.

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 multi-site, prospective, randomized, controlled, double-masked, four-arm-parallel-group, dispensing study.

Each subject will be bilaterally fitted with one of the four types of test articles and wear lenses of the assigned lens type during the entire course of the study. Test articles will be worn a minimum 8 hours per day and 5 days per week (subjects will be encouraged to wear study contact lenses 10 hours or more per day and 7 days per week) in a daily disposable modality for a minimum of 6 months and up to 1 year*.

There will be a total of 7 scheduled visits.
Visit 1: Screening and baseline evaluation
Visit 2: Baseline, randomization, lens fit and dispensing
Visit 3: 1-week follow-up
Visit 4: 1-month follow-up
Visit 5: 3-month follow-up
Visit 6: 6-month follow-up
Visit 7: 1-year follow-up (optional)*

* The study will complete after all subjects have completed the 6-month follow-up (Visit 6). Considering the extensive enrollment period (e.g., approximately 8 months), while waiting for the last enrolled subjects to complete the 6-months follow-up, the study allows subjects enrolled at the beginning of the enrollment period to continue wearing study lenses for up to 1 year and complete the 1-year follow-up (Visit 7) before completing the final evaluation and exiting the study.

Study participants will have no access to test articles at study closure.

4.2. Study Design Rationale

The study is designed as a study for proof of concept that soft contact lenses with novel optical designs have the potential for controlling myopia progression. A total of three investigational soft contact lenses will be evaluated for their safety and effectiveness of controlling myopia progression in children of 7 to 12 years of age by comparing to an FDA-cleared, non-marketed control contact lens.

Among the three Test lenses, two are of novel optical designs for myopia control (EMO-114 and EMO-118). The third Test lens (EMO-116) with an optical design simulating the MiSight lens (CE-marked for the myopia control indication, not marketed in the US, Canada or China) is included in the study to serve as a reference (positive control) for evaluating the myopia control efficacy of the two novel lens design prototypes (EMO-114 and EMO-118).

The Control lens (EMO-117) used in this study is an FDA-cleared, non-marketed soft contact lens with conventional, single-vision spherical optical design. This lens is selected as the

placebo control for evaluating the optical impact of the three Test lenses on myopia progression.

All four types of test articles are identical in all aspects (lens material, diameter, base curve, modality, and manufacturing process) except for different optical designs.

Since evaluating myopia progression of a subject and the lens effect of controlling myopia progression is longitudinal in nature, a bilateral dispensing, parallel-group study design is required. The designs of the four test articles allow the study to be conducted as a randomized, placebo-controlled, double-masked trial, which is considered to be the gold-standard for a clinical trial. Such clinical trial design and the selection of a soft contact lens as the control are recommended by the expert panel during the FDA workshop to inform the premarket evaluation of contact lenses designed to control myopia progression (Silver Spring, MD, September 30, 2016).

For the purpose of minimizing potential seasonal effect on a subject's rate of myopia progression, the complete evaluation of the effectiveness of a Test lens typically requires at least 1 year of lens wear. The study, however, is designed to have a minimum of 6 months of lens wear follow-up and evaluates the myopia control effect of Test lenses at 6 months instead of 1 year. The reason for selecting the 6-month study duration is that based on clinical trials reported in the literature and conducted by JJVC on evaluating lenses for myopia control,[5-10] it appears that the treatment effect, if any, is largest within the first 6 months treatment, and the effect appears to diminish over time. Therefore, as a first study for proof of concept of EMO lens design prototypes, a 6-month treatment period is expected to be sufficient to identify lenses that have potential myopia control effect.

4.3. Enrollment Target and Study Duration

Approximately 240 subjects will be enrolled in the study with a minimum of 160 subjects (40/arm) targeted to complete the 6-month follow-up. The point of enrollment is defined as the execution of the informed consent and assent at Visit 1.

Approximately 6-8 multi-national clinical sites, including sites in the US, Canada and China will participate in the study. Each site is expected to enroll approximately 30 to 40 subjects with 20 to 32 subjects (approximately 5 to 8 subjects per arm, per site) targeted to complete the study.

The duration of study enrollment will be approximately 8 months, unless otherwise approved by the Sponsor.

Eligible subjects will be randomly assigned to one of the four study arms and complete up to six scheduled visits. Details of the visit schedule are provided in Sections 4.1 and 7.1 of the current study protocol.

The total duration of the study is estimated to be 18 months, including approximately 8 months of enrollment period.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn in a bilateral and random fashion using parallel design with 4 lens types. Using a computer-generated randomization scheme provided by the study biostatistician, each subject will randomly be assigned to one of four study arms with a 1:1:1:1 ratio. Randomization will be first stratified by site. At each site, the study sample will be further stratified based on age (7 – 9 years and 10 – 12 years) and best-sphere refraction at baseline (lower than -2.00D myopia vs. -2.00D or more myopia). Each study site will aim to enroll at least 50% of subjects in the age group of 7 – 9 years.

Randomly-permuted block randomization will be used to avoid bias in the assignment of subjects to treatment, and to enhance the validity of statistical comparisons across treatment groups. Each block will contain four different lenses.

The clinical site will follow the randomization scheme provided and will complete enrollment according to the randomization list and will not pre-select or assign subjects.

Randomization must be performed at Visit 2. The following must have occurred prior to randomization:

- Informed consent and assent have been obtained from participant's parent/legal guardian and the participant
- 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 study will be double-masked. Both subjects and investigators (including clinical site personnel involved in the data collection) will be masked to the identity of the investigational product during the study. 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 test articles. 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 the Masking

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. Subjects who are discontinued will be replaced before completion of enrollment, with sponsor approval.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

	Test 1	Test 2	Test 3	Control
Name	EMO-114	EMO-116	EMO-118	EMO-117
Manufacturer	JJVC	JJVC	JJVC	JJVC
[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Lens Material	Senofilcon A	Senofilcon A	Senofilcon A	Senofilcon A
Nominal Base Curve @ 22 ℃	7.9 mm	7.9 mm	7.9 mm	7.9 mm
Nominal Diameter @ 22 ℃	13.8 mm	13.8 mm	13.8 mm	13.8 mm
Nominal Distance Powers (D)	-0.75 to -5.50 D in 0.25D step	-0.75 to -5.50 D in 0.25D step	-0.75 to -5.50 D in 0.25D step	-0.75 to -5.50 D in 0.25D step
Nominal Cylinder Powers (D) and Axes	N/A	N/A	N/A	N/A
Nominal ADD Powers (D)	N/A	N/A	N/A	N/A
Water Content	38%	38%	38%	38%
Oxygen Permeability (Dk), Boundary corrected	103	103	103	103

	Test 1	Test 2	Test 3	Control
Wear Schedule in Current Study	Daily wear	Daily wear	Daily wear	Daily wear
Replacement Frequency	Daily disposable	Daily disposable	Daily disposable	Daily disposable
Packaging Form (vial, blister, etc.)	Blister Pack	Blister Pack	Blister Pack	Blister Pack

Per the study design and lens wear modality, it is estimated that for each lens type, up to 60 subjects will complete the 6-month follow-up, each of whom will use approximately 400 lenses during the 6-month period. In addition, it is projected that up to 30 subjects in each lens group may complete 1 year follow-up, each of whom will use approximately 400 additional lenses during the second 6-month period. Therefore, for each lens type, the total number of study lenses to be used is approximately 36,000. The total number of study lenses to be used is approximately 144,000 for all four types of study lenses.

6.2. Ancillary Supplies/Products

This is a study with test articles worn in a daily disposable modality. No lens care product will be used. Ophthalmic solutions used in this study are listed in Table 2 below. Sponsor-approved re-wetting drops that are approved in local markets will be used as the Investigator's discretion.

Table 2: Ancillary Supplies/Products used in this study

Solution Name/Description	Proparacaine hydrochloride 0.5% Ophthalmic Solution	Cyclopentolate hydrochloride 1% Ophthalmic Solution
Manufacturer	Alcon® (Alcaine®) Akorn, Inc. Bausch & Lomb or other registered manufactures in the local markets	Alcon® (Cyclogyl®) Akorn, Inc. Bausch & Lomb or other registered manufactures in the local markets
Preservative(s)	Benzalkonium chloride 0.01%	Benzalkonium chloride 0.01%

The following visual acuity charts will be provided to the clinical sites:

Precision Vision Landolt C 4-meter, high contrast, logMAR visual acuity charts (2210, 2210A and 2210B)

Precision Vision Landolt C 40-cm, high contrast, logMAR visual acuity charts

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 labeled as investigational lenses with the identity of the lens masked to the subject/Investigators. The test articles will be in cartons, in arrays of six blisters, as the secondary packaging form. The sample study label is shown below:

6.5. Storage Conditions

Test articles will be maintained at ambient temperatures at the clinical site. Test articles must be kept under secure conditions.

6.6. Collection and Storage of Samples

Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. Refer Section 13.5.1 for determination of corneal culture and [redacted] for specimen collection procedures for corneal culture.

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 JJVC.

6.7. Accountability of Test Articles

JJVC 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 or room, 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 either destruct all unused test articles on site or return all unused test articles to JJVC per the instructions of the Sponsor.

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

[redacted]

In addition, the study will provide each subject with a pair of backup spectacle lenses. Dispensing of each pair of backup spectacle lenses and reasons for dispensing and replacement will be documented. Subjects will keep the study provided backup spectacle lenses at the end of the study.

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Information	Visit 1 Screening, Baseline	Visit 2 Lens Fitting, Dispensing	Visit 3 (1-week), Visit 4 (1-month) Visit 5 (3-months) Lens Follow-up	Visit 6 Lens Follow-up 6-months	Visit 7 Lens Follow-up 1-year (Optional)
Time Point	-	Day 0 Within 3 weeks from V1	V3: 7±3 days; V4: 28±7 days; V5: 91±7 days after V2	182±14 days after V2	364±21 days after V2
Estimated Visit Duration	3.5 hours	3.0 hours	2.0 hour	3.0 hours	3.0 hours
Statement of Informed Consent and Assent	x				
Demographics	x				
Subject & Family History of Myopia	x				
Habitual Vision Correction Information	x				
Medical History/Concomitant Medications	x	x	x	x	x
Cover Test	x				
Screen for Corneal Distortion	x				
Inclusion/Exclusion Criteria	x				
Lens Wear Compliance			x	x	x
Subject Reported Ocular Symptoms		x	x	x	x
Entrance Snellen Distance Visual Acuity		x	x	x	x
Subjective Sphero-Cylindrical Refraction	x			x	x
Subjective Best-sphere Refraction	x	x		x	x
Slit Lamp Classification	x	x	x	x	x
Anterior chamber angle	x			x	x
Distance Landolt C logMAR VA (HLHC)	x	x	x	x	x
Near Landolt C logMAR VA (HLHC)		x	x	x	x
Pupil diameter	x				

Visit Information	Visit 1 Screening, Baseline	Visit 2 Lens Fitting, Dispensing	Visit 3 (1-week), Visit 4 (1-month) Visit 5 (3-months) Lens Follow-up	Visit 6 Lens Follow-up 6-months	Visit 7 Lens Follow-up 1-year (Optional)
Time Point	-	Day 0 Within 3 weeks from V1	V3: 7±3 days; V4: 28±7 days; V5: 91±7 days after V2	182±14 days after V2	364±21 days after V2
Estimated Visit Duration	3.5 hours	3.0 hours	2.0 hour	3.0 hours	3.0 hours
Pupil reflex	x			x	x
Non-contact tonometry	x				x
Cycloplegia & Effectiveness of Cycloplegia	x			x	x
Axial Length	x		x	x	x
Cycloplegic Auto Refraction and Corneal K	x			x	x
Fundus Examination	x				x
Lens Assignment		x			
Lens Insertion & Settling		x	(x)	(x)	
Lens Fit Assessment		x	x	x	x
Lens-on-Eye Distance Visual Acuity		x	x	x	
Subjective Best-sphere Over-refraction		x	x	x	x
Lens Power Modification (if applicable)		x	x	x	
CLUE Baseline Questionnaire	x				
CLUE Follow-up Questionnaire			x	x	x
Subject Activity Information	x				
Dispense Subject Diary		x	x	(x)	
Exit Distance Visual Acuity	x	x	x	(x)	
I/R Training, Contact Lens Checklist		x	x	(x)	
Dispense Parent/Patient Instruction Guide		x			
Dispense Test Article		x	x	(x)	

Visit Information	Visit 1 Screening, Baseline	Visit 2 Lens Fitting, Dispensing	Visit 3 (1-week), Visit 4 (1-month) Visit 5 (3-months) Lens Follow-up	Visit 6 Lens Follow-up 6-months	Visit 7 Lens Follow-up 1-year (Optional)
Time Point	-	Day 0 Within 3 weeks from V1	V3: 7±3 days; V4: 28±7 days; V5: 91±7 days after V2	182±14 days after V2	364±21 days after V2
Estimated Visit Duration	3.5 hours	3.0 hours	2.0 hour	3.0 hours	3.0 hours
Study Lens Removal			x	x	x
Study Completion, Final Evaluation		x		(x)	x

"(x)" indicates procedures if applicable

7.2. Detailed Study Procedures

VISIT 1 – Screening and Baseline

Potential subjects who currently wear myopia correcting lenses (spectacles or soft contact lenses) should report to the visit wearing their spectacle lenses.

It is preferred, but not required that on an individual basis, each subject reports to baseline, 6- and 12-month (if applicable) visits at approximately the same time frame of the day, eg, morning, noon, early or late afternoon.

Instructions for breaking Visit 1 into two sections (as needed):

Due to the length of Visit 1, it is foreseeable that some subjects may not be able to complete all procedures within one visit. In such cases, subjects will complete Visit 1 procedures up to 1.16 (pupil diameter) without being cyclopleged. If Visit 1 is to be completed on two separate days, the subject's exit visual acuity must be collected at the end of the first part of the Visit 1, before the subject exits the visit.

The subject may return on a different day (up to 21 days from the initial visit) to complete the rest of procedures in Visit 1 including all procedures under the sections of "Questionnaires" and "Cycloplegia and Endpoint Data Collection" below.

When the subject returns to complete the rest of the procedures of visit 1, the following information will be collected prior to performing any other testing procedures:

- Visit date,
- Review of medical history and concomitant medications/therapies
- Entrance visual acuity
- Slit lamp biomicroscopy

Results of procedures under the second part of Visit 1 will be recorded in Visit 1 EDC.

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent & Children's Assent	Each subject's parent or legal guardian must read, understand, and sign the Statement of Informed Consent, and each subject must read (or be read to), understand and sign the Statement of Information and Assent before the subject is enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the Consent and Assent forms. **Note**: The subject and parent (legal guardian) must be provided a signed copy of both documents.	
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 Vision Correction Information	Questions regarding the type of the subject's habitual vision correction: • No correction • Spectacle lenses • Soft contact lens • Rigid contact lens (other than orthokeratology) • Orthokeratology • Other, specify	
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. **Note:** If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.6	Entrance VA	Record the entrance distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]
1.7	Subjective Sphero-cylindrical Refraction	Perform subjective sphero-cylindrical 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 resultant distance visual acuity (OD, OS and 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]
1.8	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 resultant distance visual acuity (OD, OS, OU) to the nearest letter. **Note**: Use the same endpoint criterion for the duo-chrome test as specified for sphero-cylindrical refraction.	[redacted]
1.9	Cover test	Perform distance and near cover-uncover test to rule out the presence of strabismus.	[redacted]
1.10	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. **Note**: Except for subjects with Grade 2 palpebral conjunctival observations that are eligible to be enrolled, if any other slit lamp finding (per ISO 11980) is graded as 2 or worse, the subject may not continue at this time, but may return up to one additional time to determine eligibility. If the subject is discontinued from the study, 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]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.11	Anterior chamber angle evaluation	Evaluate anterior chamber angle with the slit lamp using van Herrick method, Grade 0 - 4. If Grade 2 and narrower, do not perform cycloplegia, and the subject will be discontinued.	
1.12	Screen for corneal distortion	Examine the keratometer mires or corneal topography Placido ring pattern to rule out corneal distortion.	
1.13	Non-contact Tonometry	Measure intraocular pressure via non-contact tonometry. Take three valid IOP measurements. The average of three IOP measurements must be <21 mmHg in each eye.	
1.14	Eligibility after Baseline 1	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. **Note**: If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.	
1.15	Distance Landolt C LogMAR Visual Acuity	Perform ***monocular and binocular*** distance Landolt C LogMAR visual acuity test at 4-meter distance under: • Bright illumination (>400 lux), High Luminance with High Contrast charts (HLHC). The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. Both eyes will be measured with subject's best sphere correction in the trial frame. One measurement per eye, per condition.	[redacted]
1.16	Pupil Diameter	Measure pupil diameter under the following two lighting conditions: 1. dim illumination (<2.5 lux), 4 meters away from a low luminance, high contrast charts (LLHC); 2. bright illumination (>400 lux), 4 meters away from a high luminance, high contrast chart (HLHC). One measurement per eye, per condition.	[redacted]

Visit 1: Questionnaires			
Step	Procedure	Details	[redacted]
1.17	Baseline pCLUE (for current contact lens wearers only)	Ask the subject to complete the pCLUE questionnaire regarding own lenses.	
1.18	Family History of Myopia	Record the subject's Family History of Myopia.	
1.19	Subject's History of Myopia Progression and Activity Information	Record the subject's History of Myopia Progression and Activity Information.	

Visit 1: Cycloplegia and Endpoint Data Collection			
Step	Procedure	Details	[redacted]
1.20	Axial Length (prior to Cycloplegia)	Measure axial length minimum of 5 times per eye with the LENSTAR LS 900 or a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor. **Note**: each measurement should be within 0.02mm from each other (the range of the 5 measurements should be 0.02mm or less), to the investigator's best attempt.	
1.21	Pupil Roundness and Reflex	Check subject's pupil equal round, reactive to light and accommodation and pupil afferent reflex.	
1.22	Cycloplegia and Its Effectiveness	Administer 1 drop of 0.5% proparacaine followed by 2 drops of 1% cyclopentolate 5 minutes apart. Record the time of administration Check effectiveness of cycloplegia 30 minutes after the second drop of cyclopentolate. Subject must have less than 2D residual accommodation before proceeding to axial length measurement.	
1.23	Axial Length	Measure axial length minimum of 5 times per eye with the LENSTAR LS 900, or a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor. **Note**: each measurement should be within 0.02mm from each other (the range of the 5	

Visit 1: Cyclopleg ia and Endpoint Data Collection			
Step	Procedure	Details	[redacted]
		measurements should be 0.02mm or less), to the investigator's best attempt.	
1.24	Cycloplegic Auto Refraction	Measure sphero-cylindrical refraction a minimum of 5 times per eye with the WAM-5500 auto refractor. Record sphere, cylinder and axis, and corneal K. **Note**: each measurement should be within 0.37D from each other for both sphere and cylinder (the range of the 5 measurements should be 0.37D or less), to the investigator's best attempt.	[redacted]
1.25	Fundus Examination	Perform fundus examination and record any abnormality	
1.26	Baseline Eligibility 2	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. **Note**: If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.	
1.27	Order Spectacle Glasses	A pair of non-aspheric, polycarbonate spectacle lenses will be ordered based on today's sphero-cylindrical refraction from each individual clinical site's choice of reputable venders. Each clinical site is responsible for ordering and dispensing the spectacle glasses for each eligible subject. **Note**: a cylindrical refraction of 0.25D will be prescribed to the subjects if it results in noticeable vision improvement, i.e., 3 or more letters of improvement in visual acuity.	
1.28	Schedule Visit 2	Schedule the subject to return for Visit 2 within one week after spectacle lenses are available.	
1.29	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

VISIT 2 – Study Lens Fitting and Dispensing

Subjects who currently wear myopia correcting lenses should report to the visit wearing their spectacle lenses.

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

Visit 2: Baseline			
Step	Procedure	Details	[redacted]
2.1	Backup Spectacle Lenses Dispensing	Record the following information: • Date dispensed, • Spectacle lenses prescription (sphere, cylinder, axis OD/OS), and • Reason for dispensing (e.g., initial dispensing, prescription modification, lost, damage, other (specify)). • Distance visual acuity with the backup spectacle lenses (OD, OS, OU) to the nearest letter. • Spherical over-refraction with the backup spectacle lenses. **Note**: for the backup spectacle lenses to be dispensed, distance visual acuity must be $20/25^{-2}$ (0.14 logMAR) or better and spherical over-refraction must not exceed ±0.25D in each eye. If the backup spectacle lenses cannot be dispensed, the subject will not continue with Visit 2. Update the subject's prescription, if applicable, and order a new pair of backup spectacle lenses. Reschedule Visit 2 when the new backup spectacle lenses are available.	
2.2	Change of Medical History (Adverse Events) and Concomitant Medications Review	Record any adverse events or medical history changes from the previous study visit. Review the subject's concomitant medications and record any changes from the previous study visit.	
2.3	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire with regard to their habitual correction.	[redacted]
2.4	Entrance Visual Acuity	Record the entrance distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]

Visit 2: Baseline			
Step	Procedure	Details	[redacted]
2.5	Slit Lamp Biomicroscopy	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding (per ISO 11980) is graded as 2 (except for subjects with Grade 2 baseline palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. The subject may not continue at this time. After the slit lamp findings are resolved, the subject may return up to one additional time to determine eligibility. If the subject is discontinued from the study, 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.	
2.6	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 resultant distance and near 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.	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
2.7	Lens Selection	Assign the study lens based on the randomization scheme. Select the contact lens power based on subjective best sphere refraction.	
2.8	Lens Insertion	The investigator shall insert 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.	
2.9	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
2.10	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 <u>all three</u> of the following conditions: primary gaze, up gaze, and Josephson push up. **<u>Note</u>**: if lens fit is unacceptable subject will be discontinued from the study.	[redacted]
2.11	Over the Lens Distance VA	Record the subject's <u>distance</u> visual acuity to the nearest letter with the study lenses (OD, OS and OU).	[redacted]
2.12	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 resultant <u>distance</u> visual acuity to the nearest letter (OD, OS, OU). **<u>Note</u>**: 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.	[redacted]

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
		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.	
2.13	Lens Power Modification (if applicable)	The subject's best sphere over-refraction **cannot** be positive (>0.00D) or, in the case of a myopic over-refraction, it **cannot** be -0.50D or higher (≤-0.50D). Adjust the study contact lens power when necessary based on the following rules: 1. If subject's best sphere over-refraction is positive, re-refract the subject and adjust the lens power accordingly. 2. If the subject's best sphere over-refraction is plano, continue with the study without lens power modification, regardless of subject's distance VA. 3. If subject's best sphere over-refraction is -0.25D and distance VA without over refraction is 20/25 (0.10 logMAR) or better, continue with the study without lens power modification. 4. If the subject's spherical over-refraction is -0.25D and distance visual acuity without over-refraction is worse than 20/25 (0.10 logMAR), and distance visual acuity is 3 or more letters better with over refraction than without over refraction, increase the lens power by -0.25D and refit the subject to achieve either 20/25 (0.10 logMAR) or better distance VA without over refraction or plano over refraction. 5. If subject's best sphere over-refraction is -0.50D or more, increase the lens power by -0.25D each step till the subject's best sphere over refraction is -0.25D or plano based on the above lens power modification rule #2 - #4. For each study contact lens power modification, repeat steps 2.7 – 2.13. Up to three power modifications are allowed.	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
2.14	Over the Lens Near VA	Record the subject's near visual acuity to the nearest letter with the study lenses (OD, OS and OU) with a Landolt C near visual acuity chart at 40cm.	
2.15	Distance Landolt C HLHC LogMAR Visual Acuity	Perform distance Landolt C LogMAR visual acuity test (OD, OS, OU) at a 4-meter distance with the subject wearing the study lenses under the following conditions: • Bight illumination (e.g., >400 lux), High Luminance with High Contrast charts (HLHC); The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. One measurement per eye, per condition.	
2.16	I/R Training & Contact Lens Checklist	Teach contact lens insertion, removal and lens safe wear practices. Review the training material(s) including training video, if applicable. The subject's parent or legal guardian must be present during I/R training. I/R training will be deemed successful only if the subject and/or the parent can successfully insert the study contact lenses, and the subject him/herself can remove the lenses without any assistance. Investigator will observe and record if lens insertion and removal is successful by the parent or by the subject. If I/R training is successful, ask the subject to complete the Contact Lens Checklist (repeat till the subject can answer all the questions correctly) and continue with lens dispensing; otherwise, schedule the subject and parent to return for additional I/R training visit without dispensing the study lenses. **Note:** I/R training should be successfully completed within 3 weeks from V1. If more than 3 weeks have passed and the study lenses still cannot be dispensed to the subjects (due to, for example, prolonged I/R training), a repeat of baseline measures for the two primary outcomes	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
		(cycloplegic auto refraction and axial length) shall be performed. Specifically, protocol procedures of anterior chamber angle, pupil examination, cycloplegia, auto refraction and axial length measurements will be repeated before study lenses are dispensed to the subjects.	
2.17	Exit VA	Record subjects' distance visual acuity, OD, OS and OU to the nearest letter.	[redacted]
2.18	Continuance (Lens Dispensing Criteria)	For the subject to continue in the study, they must meet all five of the following criteria: 1. The subject's distance Landolt C LogMAR visual acuity with the test article measured under bright illumination and high luminance conditions with the high contrast charts must be 0.10 logMAR or better binocularly, and 0.14 logMAR or better in each eye for the test articles to be dispensed to the subjects. 2. Vision with the study lenses must be acceptable to the subjects. 3. The lens fit is acceptable OD and OS 4. Investigator approval. If the Investigator does not approve the dispensing of the study lens, then the study is terminated for that subject. 5. The subject has successfully completed the I/R training and answered all questions in the Contact Lens Checklist correctly.	
2.19	Lens Dispense	The lenses will be dispensed for a wearing period of 7±3 days (e.g., approximately 15 lenses per eye). The lenses will be worn as daily wear/daily disposable only. At the investigator's discretion, provide the subject with rewetting drops approved in local markets (No solutions, e.g., disinfecting or storage, will be given to the subject). The study lens will be worn on a basis of a daily disposable modality. Study contact lens dispensing instructions checklist: 1. Habitual contact lens wearers should wear the study lenses at least 8 hours a day, 5 days a week	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
		(recommend 10 hours or more a day, 7 days a week) till the next visit. 2. Neophytes may wear the study lenses 4 hours today, 6 hours the next day and at least 8 hours a day every day afterwards till the next visit. 3. Never sleep in the lenses and to remove the study lenses 1 hour before bedtime every night. 4. Always throw away any lens that is taken out of the eye and use only the new lens with each lens insertion. 5. Always have the study provided glasses at hand while wearing the study contact lenses. 6. Only wear the study provided glasses while not wearing the study contact lenses. 7. Bring the study provided spectacle glasses to the next visit. 8. Provide the subject with a copy of the parent instruction guide, the instruction pamphlet, the lens insertion/removal information cards, and the instruction video, if applicable. 9. Schedule the subject for Visit 3 (1-week follow up, 7 ± 3 days from Visit 2 or the day the subject completes initial lens dispensing). 10. Instruct the subject to wear study lenses to the next visit. 11. Instruct the subject to fill out the lens wear and activity diary <u>every day</u> till the next visit. If paper diary is provided, instruct the subject to bring the filled diary to the next visit. **<u>Note</u>**: In the event a lens is lost or damaged, the subject will use a new lens from the most recently dispensed lenses. 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 may be returned to the Sponsor, if any.	

VISIT 3 – 1-week Follow-up

The Subject must report to the visit wearing the test article.

It is preferred, but not required that on an individual basis, each subject reports to the visit at approximately the same time frame as the baseline visit.

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

Visit 3: 1-week Follow-up			
Step	Procedure	Details	[redacted]
3.1	pCLUE Follow-Up Questionnaire	The subject will fill out the pCLUE Follow-Up Questionnaire.	[redacted]
3.2	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire regarding the test article.	[redacted]
3.3	Change of Medical History (Adverse Events) and Concomitant Medications / Therapies Review	Record any adverse events or medical history changes from the previous study visit. Review the subject's concomitant medications/therapies and record any changes from the previous study visit.	
3.4	Wearing Time and Compliance	Record the average wearing time (including number of hours per day during weekdays and weekends, and number of days per week) and average daily comfortable wearing time. Confirm compliance with the prescribed wear schedule. • Review the lens wear and activity diary. • Record and discuss the lens wear compliance based on the subject's self-report and diary information. For example, the subjects will be asked the time of the day the subject typically puts on the study lenses in the morning and takes off in the evening, and number of days the subject didn't wear the study lenses, etc.	
3.5	Lens-on-eye Distance VA	Record the distance Snellen visual acuity with the study lenses (OD, OS, and OU) to the nearest letter.	[redacted]
3.6	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:	[redacted]

Visit 3: 1-week Follow-up			
Step	Procedure	Details	[redacted]
		• limbal exposure at primary gaze or with extreme eye movement; • edge lift; • excessive movement in primary and up gaze; or • insufficient movement in <u>all three</u> of the following conditions: primary gaze, up gaze, and Josephson push up. **<u>Note</u>**: if lens fit is unacceptable subject will be discontinued from the study.	
3.7	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 <u>distance</u> visual acuity to the nearest letter (OD, OS, OU).	[redacted]
3.8	Lens Power Modification (if applicable)	The same lens power modification rules for study contact lenses as specified in Visit 2 apply. For each study contact lens power modification, record lens information and repeat steps 3.5 – 3.8.	
3.9	Over the Lens Near VA	Record the subject's <u>near</u> visual acuity to the nearest letter with the study lenses (OD, OS and OU) with a Landolt C near visual acuity chart at 40cm.	[redacted]
3.10	Distance Landolt C HLHC LogMAR Visual Acuity	Perform distance Landolt C LogMAR visual acuity test (OD, OS, OU) at a 4-meter distance with the subject wearing the study lenses under the following conditions: • Bight illumination (e.g., >400 lux), High Luminance with High Contrast charts (HLHC); The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. One measurement per eye, per condition.	[redacted]
3.11	Remove Study Contact Lenses	Investigator will observe the subject removing the study contact lenses, and record if the subject can remove the study contact lenses without assistance. Discard the removed study contact lenses.	
3.12	Axial Length	Measure axial length minimum of 5 times per eye with the LENSTAR LS 900, or a similar device	[redacted]

Visit 3: 1-week Follow-up			
Step	Procedure	Details	[redacted]
		(e.g., IOLMaster) in selected Asian sites upon approval of the sponsor. **Note**: each measurement should be within 0.02mm from each other (the range of the 5 measurements should be 0.02mm or less), to the investigator's best attempt.	
3.13	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding is graded as 2 (except for subjects with Grade 2 baseline palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. A subject with significant slit lamp findings (e.g., Grade 3 corneal staining and Grade 2 corneal vascularization, etc.) may not be dispensed with the study contact lens at this time, and an adverse event form must be filled. The subject must be followed till slit lamp findings are resolved and the investigator deems it's appropriate for the subject to continue with the study before study lens dispensing. If the subject is discontinued from the study, 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]
3.14	Exit VA	Record subjects' distance visual acuity with either the test article or the study provided glasses (OD, OS and OU) to the nearest letter.	[redacted]
3.15	Contact Lens Checklist	Ask the subject to complete the Contact Lens Checklist (repeat till the subject can answer all the questions correctly)	
3.16	Continuance (Lens Dispensing Criteria)	For the subject to continue in the study, they must meet all five criteria as specified in Visit 2.	
3.17	Lens Dispense	The lenses will be dispensed for a wearing period of 3 weeks (e.g., approximately 40 lenses per eye). The lenses will be worn as daily wear/daily disposable only. At the investigator's discretion, provide the subject with rewetting drops approved in local markets	

Visit 3: 1-week Follow-up			
Step	Procedure	Details	[redacted]
		(No solutions, e.g., disinfecting or storage, will be given to the subject). The study lens will be worn on a basis of a daily disposable modality. Study contact lens dispensing instructions checklist: 1. Subject shall wear the study lenses at least 8 hours a day, 5 days a week (recommend 10 hours or more a day, 7 days a week) till the next visit. 2. Never sleep in the lenses and to remove the study lenses 1 hour before bedtime every night. 3. Always throw away any lens that is taken out of the eye and use only the new lens with each lens insertion. 4. Always have the study provided glasses at hand while wearing the study contact lenses. 5. Only wear the study provided glasses while not wearing the study contact lenses. 6. Bring the study provided spectacle glasses to the next visit. 7. Schedule the subject for Visit 4 (1-month follow up, 28 ± 7 days from Visit 2, or from the day the subject completes initial lens dispensing). 8. Instruct the subject to wear study lenses to the next visit. 9. Instruct the subject to fill out the lens wear and activity diary <u>every week</u> till the next visit. If paper diary is provided, instruct the subject to bring the filled diary to the next visit. **<u>Note</u>**: In the event a lens is lost or damaged, the subject will use a new lens from the most recently dispensed lenses. 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 may be returned to the Sponsor, if any.	

VISIT 4 – 1-month Follow-up

The Subject must report to the visit wearing the test article.

It is preferred, but not required that on an individual basis, each subject reports to the visit at approximately the same time frame as the baseline visit.

Repeat all procedures listed under Visit 3, 1-week follow-up visit.

Dispense the study contact lenses for a wearing period of 2 months (up to 90 lenses per eye).

Instruct the subject to fill out the lens wear and activity diary every month till the next visit. If paper diary is provided, instruct the subject to bring the diary to the next visit.

Schedule the subject for Visit 5 (3-month follow-up, 91 ± 7 days from Visit 2).

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

VISIT 5 – 3-month Follow-up

The Subject must report to the visit wearing the test article.

It is preferred, but not required that on an individual basis, each subject reports to the visit at approximately the same time frame as the baseline visit.

Repeat all procedures listed under Visit 3, 1-week follow-up visit.

Dispense the study contact lenses for a wearing period of 3 months (up to 120 lenses per eye).

Instruct the subject to fill out the lens wear and activity diary every month till the next visit. If paper diary is provided, instruct the subject to bring the diary to the next visit.
Schedule the subject for Visit 6 (6-month follow up, 182 ± 14 days from Visit 2).

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

VISIT 6 – 6-month Follow-up

The Subject must report to the visit wearing the test article.

It is preferred, but not required that on an individual basis, each subject reports to the visit at approximately the same time frame as the baseline visit.

Instructions for breaking Visit 6 into two sections (as needed):

Due to the length of the visit, it is foreseeable that some subjects may not be able to complete all procedures within one visit. In such cases, subjects will complete the visit on two separate days. The two parts of the visit should be performed within 7 days, and the second half of the visit shall be completed within the originally specified visit window.

During the first part of the visit, the subject will complete all procedures before step 6.26, the section of "Cycloplegia and Endpoint Data Collection". The subject's exit visual acuity must be collected at the end of the first part of the visit before the subject exits the visit.

When the subject returns to complete the rest of the procedures of the visit, the following information will be collected prior to performing any other testing procedures:

- Visit date,
- Review of medical history and concomitant medications/therapies
- Entrance visual acuity
- Slit lamp biomicroscopy

Results of procedures performed during the second part of the visit will be recorded in EDC of the corresponding visit. Subjects shall continue wearing the assigned test articles during the break of the two parts of the visit.

Instructions for managing subjects presenting to Visit 6 while the study is in the process of being terminated:

Until the clinical site receives the written notification from the sponsor that the study is terminated without the subject completing the 1-year follow-up, all active subjects shall complete the 6-month follow-up visit (Visit 6) with their lens prescription updated (if applicable), additional study lenses dispensed and Visit 7 (1-year follow-up visit) scheduled.

In the event that the study is terminated, the subject will complete Visit 6 without lens modification and dispensing. The subject will complete final evaluation before exiting the study.

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

Visit 6: 6-Month Follow-up			
Step	Procedure	Details	[redacted]
6.1	pCLUE Follow-Up Questionnaire	The subject will fill out the pCLUE Follow-Up Questionnaire.	[redacted]
6.2	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire regarding the test article.	[redacted]
6.3	Change of Medical History (Adverse Events) and Concomitant Medications / Therapies Review	Record any adverse events or medical history changes from the previous study visit. Review the subject's concomitant medications/therapies and record any changes from the previous study visit.	
6.4	Wearing Time and Compliance	Record the average wearing time (including number of hours per day during weekdays and weekends, and number of days per week) and average daily comfortable wearing time. Confirm compliance with the prescribed wear schedule. • Review the lens wear and activity diary. • Record and discuss the lens wear compliance based on the subject's self-report and diary information. For example, the subjects will be asked the time of the day the subject typically puts on the study lenses in the morning and takes off in the evening, and number of days the subject didn't wear the study lenses, etc.	
6.5	Lens-on-eye Distance VA	Record the distance Snellen visual acuity with the study 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]
6.6	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 <u>all three</u> of the following conditions: primary gaze, up gaze, and Josephson push up.	[redacted]

Visit 6: 6-Month Follow-up			
Step	Procedure	Details	[redacted]
		Note: if lens fit is unacceptable subject will be discontinued from the study.	
6.7	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).	[redacted]
6.8	Over the Lens Near VA	Record the subject's near visual acuity to the nearest letter with the study lenses (OD, OS and OU) with a Landolt C near visual acuity chart at 40cm.	[redacted]
6.9	Distance Landolt C HLHC LogMAR Visual Acuity	Perform distance Landolt C LogMAR visual acuity test (OD, OS, OU) at a 4-meter distance with the subject wearing the study lenses under the following conditions: • Bight illumination (e.g., >400 lux), High Luminance with High Contrast charts (HLHC); The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. One measurement per eye, per condition.	[redacted]
6.10	Remove Study Contact Lenses	Investigator will observe the subject removing the study contact lenses, and record if the subject can remove the study contact lenses without assistance. Discard the removed study contact lenses.	
6.11	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding is graded as 2 (except for subjects with Grade 2 baseline palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. A subject with significant slit lamp findings (e.g., Grade 3 corneal staining and Grade 2 corneal vascularization, etc.) may not be dispensed with the study contact lens at this time, and an adverse event form must be filled. The subject must be followed till slit lamp findings are resolved and the investigator deems it's appropriate for the subject to continue with the	[redacted]

Visit 6: 6-Month Follow-up			
Step	Procedure	Details	[redacted]
		study before study lens dispensing. If the subject is discontinued from the study, 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.	
6.12	Anterior chamber angle evaluation	Evaluate anterior chamber angle with the slit lamp using van Herrick method, Grade 0 - 4. If Grade 2 and narrower, do not perform cycloplegia, and the subject will be discontinued.	[redacted]
6.13	Subjective Sphero-cylindrical Refraction	Perform subjective sphero-cylindrical 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 resultant distance visual acuity (OD, OS and 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]
6.14	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 resultant distance visual acuity (OD, OS, OU) to the nearest letter. **Note**: Use the same endpoint criterion for the duo-chrome test as specified for sphero-cylindrical refraction.	[redacted]

Visit 6: Lens Prescription Update (If Applicable) **Note**: This Section will only be performed if the subject will continue with the study for 1-year follow-up			
Step	Procedure	Details	[redacted]
6.15	Lens Prescription update (if applicable)	Adjust the subject's contact lens power only if the spherical equivalent power of the subject's sphero-cylindrical prescription has changed from the current prescription by more than or equal to ±0.375D. Re-fit the subject with the same type of study lens based on adjusted lens power. **Note**: the backup spectacle lenses will be updated, if needed per the same prescription update criterion.	
6.16	Lens Selection	Select the lens power based on today's (V6) subjective best sphere refraction.	
6.17	Lens Insertion	Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable.	
6.18	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
6.19	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 Josephson push up. **Note**: if lens fit is unacceptable subject will be discontinued from the study.	[redacted]

Visit 6: Lens Prescription Update (If Applicable) **Note**: This Section will only be performed if the subject will continue with the study for 1-year follow-up			
Step	Procedure	Details	[redacted]
6.20	Over the Lens Distance VA	Record the subject's distance visual acuity to the nearest letter with the study lenses (OD, OS and OU).	
6.21	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 resultant 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.	
6.22	Lens Power Modification (if applicable)	The same lens power modification rules for study contact lenses as specified in Visit 2 apply. For each study contact lens power modification, record lens information and repeat steps 6.17 – 6.22.	
6.23	Over the Lens Near VA	Record the subject's near visual acuity to the nearest letter with the study lenses (OD, OS and OU) with a Landolt C near visual acuity chart at 40cm.	[redacted]
6.24	Distance Landolt C HLHC LogMAR Visual Acuity	Perform distance Landolt C LogMAR visual acuity test (OD, OS, OU) at a 4-meter distance with the subject wearing the study lenses under the following conditions: • Bight illumination (e.g., >400 lux), High Luminance with High Contrast charts (HLHC); The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. One measurement per eye, per condition.	[redacted]
6.25	Remove Study Contact Lenses	Remove and discard the study contact lenses.	

Visit 6: Cyclopegia and Endpoint Data Collection			
Step	Procedure	Details	[redacted]
6.26	Axial Length	Measure axial length minimum of 5 times per eye with the LENSTAR LS 900, or a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor. **Note**: each measurement should be within 0.02mm from each other (the range of the 5 measurements should be 0.02mm or less), to the investigator's best attempt.	[redacted]
6.27	Pupil Roundness and Reflex	Check subject's pupil equal round, reactive to light and accommodation and pupil afferent reflex.	
6.28	Cycloplegia and Its Effectiveness	Administer 1 drop of 0.5% proparacaine followed by 2 drops of 1% cyclopentolate 5 minutes apart. Record the time of administration Check effectiveness of cycloplegia 30 minutes after the second drop of cyclopentolate. Subject must have less than 2D residual accommodation before proceeding to axial length measurement.	[redacted]
6.29	Axial Length	Measure axial length minimum of 5 times per eye with the LENSTAR LS 900, or a similar device (e.g., IOLMaster) in selected Asian sites upon approval of the sponsor. **Note**: each measurement should be within 0.02mm from each other (the range of the 5 measurements should be 0.02mm or less), to the investigator's best attempt.	[redacted]
6.30	Cycloplegic Auto Refraction	Measure sphero-cylindrical refraction a minimum of 5 times per eye with the WAM-5500 auto refractor. Record sphere, cylinder and axis, and corneal K. **Note**: each measurement should be within 0.37D from each other for both sphere and cylinder (the range of the 5 measurements should be 0.37D or less), to the investigator's best attempt.	[redacted]
6.31	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding is graded as 2 (except for subjects with Grade 2 baseline	[redacted]

Visit 6: Cycloplegia and Endpoint Data Collection			
Step	Procedure	Details	[redacted]
		palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. A subject with significant slit lamp findings (e.g., Grade 3 corneal staining and Grade 2 corneal vascularization, etc.) may not be dispensed with the study contact lens at this time, and an adverse event form must be filled. The subject must be followed till slit lamp findings are resolved and the investigator deems it's appropriate for the subject to continue with the study before study lens dispensing. If the subject is discontinued from the study, 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.	
6.32	Exit VA	Record subjects' distance visual acuity with either the test article or the study provided glasses (OD, OS and OU) to the nearest letter.	[redacted]

Visit 6: Lens Dispensing (If Applicable) **Note**: This Section will only be performed if the subject will continue with the study for 1-year follow-up			
Step	Procedure	Details	[redacted]
6.33	Contact Lens Checklist	Ask the subject to complete the Contact Lens Checklist (repeat till the subject can answer all the questions correctly)	
6.34	Continuance (Lens Dispensing Criteria)	For the subject to continue in the study, they must meet all five criteria as specified in Visit 2.	
6.35	Lens Dispense	The lenses will be dispensed for a wearing period of 6 months (e.g., up to 210 lenses per eye). The lenses will be worn as daily wear/daily disposable only. At the investigator's discretion, provide the subject with rewetting drops approved in local markets (No solutions, e.g., disinfecting or storage, will be given to the subject). The study lens will be worn on a basis of a daily disposable modality.	

Visit 6: Lens Dispensing (If Applicable) **Note**: This Section will only be performed if the subject will continue with the study for 1-year follow-up			
Step	Procedure	Details	[redacted]
		The same lens dispensing criteria and instructions as specified in Visit 3 apply, except that: 1. Schedule the subject for Visit 7 (1-year follow up, 364 ± 14 days from Visit 2, or from the day the subject completes initial lens dispensing). 2. Instruct the subject to fill out the lens wear and activity diary every month till the next visit. If paper diary is provided, instruct the subject to bring the filled diary to the next 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 may be returned to the Sponsor, if any.	

VISIT 7 – 12-month Follow-up (Optional)

This visit shall be performed for all active subjects who have completed the 6-month visit (Visit 6) with study lenses dispensed for 1-year follow-up, and date of the subject's scheduled 1-year follow-up visit is prior to the sponsor-specified date of last subject last visit (LSLV) in the written notice for study termination.

The Subject must report to the visit wearing the test article.

It is preferred, but not required that on an individual basis, each subject reports to the visit at approximately the same time frame as the baseline visit.

Repeat all procedures listed under Visit 6, 6-month follow-up visit without lens power modification and lens dispensing. In addition, non-contact tonometry and fundus examination will be performed.

Collect all unused contact lenses from the subject.

This visit may be performed on two different days (see details specified under Visit 6).

Note: verify and document device accuracy [redacted] and appropriate room and acuity chart lighting levels [redacted] before the visit.

I/R TRAINING VISIT

The following information will be collected during an I/R training visit, note, I/R training visit can be repeated as needed:

Contact Lens I/R Training			
Step	Procedure	Details	[redacted]
T.1	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter with the subjects wearing the study provided spectacle lenses. [redacted]	[redacted]
T.2	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding is graded as 2 (except for subjects with Grade 2 baseline palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. A subject with significant slit lamp findings (e.g., Grade 3 corneal staining and Grade 2 corneal vascularization, etc.) may not be dispensed with the study contact lens at this time, and an adverse event form must be filled. The subject must be followed till slit lamp findings are resolved and the investigator deems it's appropriate for the subject to continue with the study before study lens dispensing. If the subject is discontinued from the study, 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]
T.3	I/R Training	Instruct and teach contact lens insertion, removal and lens safe wear practices. Review the training material(s) including training video, if applicable. The subject's parent or legal guardian must be present during I/R training. I/R training will be deemed successful only if the subject and/or the parent can successfully insert the study contact lenses, and the subject	

Contact Lens I/R Training			
Step	Procedure	Details	[redacted]
		him/herself can remove the lenses without any assistance. Investigator observes and record if lens Insertion and removal is successful by the parent or by the subject. If I/R training is successful, continue with lens dispensing; otherwise, schedule the subject and parent to return for additional I/R training visit without dispensing the study lenses. **Note:** I/R training should be successfully completed within 3 weeks from V1. If more than 3 weeks have passed and the study lenses still cannot be dispensed to the subjects (due to, for example, prolonged I/R training), a repeat of baseline measures of study endpoints shall be performed. Specifically, the following protocol procedures will be repeated before study lenses are dispensed to the subjects. • anterior chamber angle, • pupil examinations, • non-cycloplegic axial length, • cycloplegia • cycloplegic auto refraction • cycloplegic axial length	
T.4	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter with the subjects wearing the study contact lenses (if study contact lenses are to be dispensed).	[redacted]
T.5	Lens Dispensing	Dispense the study lenses if I/R training is successful. The same lens dispensing criteria and instructions as specified in Visit 2 apply and must be followed.	

BACKUP SPECTACLE LENS DISPENSING

The following information will be collected during a Spectacle Lens Dispensing:

Spectacle Lens Dispensing			
Step	Procedure	Details	[redacted]
S.1	Date of Dispensing	Record the date of the spectacle lens dispensing visit.	
S.2	Spectacle Lens Prescription	Record the subject's spectacle lens prescription OD/OS.	
S.3	Reason Dispensed	Record the reason for dispensing the spectacles (initial dispensing, prescription modification, lost, damage, other (specify)).	
S.4	Visual Acuity	Record the subject's distance visual acuity (OD, OS and OU) to the nearest letter with the subjects wearing the study provided spectacle lenses. [redacted]	[redacted]
S.5	Spherical Over-Refraction	Record the spherical over-refraction with the backup spectacle lenses.	
S.6	Backup Spectacle Lens Dispensing Criteria	For the backup spectacle lenses to be dispensed, the following two criteria must be met: 1. Distance visual acuity must be $20/25^{-2}$ (0.14 logMAR) or better; 2. Spherical over-refraction must not exceed ±0.25D in each eye. **Note**: If either of the above two dispensing criteria is not met, update the subject's prescription if applicable and order a new pair of backup spectacle lenses. Schedule another Backup Spectacle Lens Dispensing visit when the new backup spectacle lenses are available.	
S.7	Backup Spectacle Lens Dispensing	Dispense the backup spectacle lenses.	

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. If subject discontinued from the study indicate the reason.	
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]
F.3	Exit Slit Lamp Biomicroscopy	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]

MANAGING SUBJECTS THROUGH STUDY TERMINATION

At any given time that the study is being terminated, a written notification with a specific date by when all subjects must exit the study will be provided to each study site and IRB/IEC. The date will the chosen based on the expectation that all active subjects will have completed, at a minimum, the 6-month study visit (Visit 6).

All subjects with a scheduled study visit (as defined in Section 7.2 of the protocol) before the termination date will complete the scheduled visit as planned. A final evaluation will be performed at this last scheduled visit before the subject exits the study.

Any subject that will not have a scheduled study visit before the termination date will be asked to return for an unscheduled visit (refer Section 7.3) followed by a final evaluation before exiting the study. During the unscheduled visit, the following information will be collected:

- Visit Date
- Reasons for the unscheduled visit – Study termination (U.1)
- Review of medical history and concomitant medications/therapies (U.2)
- Compliance and wear time (U.3)
- Entrance visual acuity (U.4)
- Sphero-cylindrical refraction (U.6)
- Slit lamp biomicroscopy (U.10)

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.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit	
U.2	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.3	Compliance and Wear Time	Record the lens wear time information including number of days study lenses are not worn since the last visit.	
U.4	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
U.5	Subjective Best Sphere Over Refraction (for subjects whose chief complaint is blurry vision and require lens power modification)	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).	[redacted]

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.6	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.7	Subjective Best-sphere Refraction (for subjects whose chief complaint is blurry vision and require lens power modification)	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 resultant distance and near 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]
U.8	Lens Power Modification (if applicable)	Considering subject's chief complaints, over-refraction (if available), bare-eye sphero-cylindrical and best-sphere refraction, adjust lens power, if necessary. For each study contact lens power modification, record lens information and performs steps 3.5 – 3.8.	
U.9	Distance Landolt C HLHC LogMAR Visual Acuity (for subjects whose chief complaint is blurry vision and requires lens power modification)	Perform distance Landolt C LogMAR visual acuity test (OD, OS, OU) at a 4-meter distance with the subject wearing the study lenses under the following conditions: • Bight illumination (e.g., >400 lux), High Luminance with High Contrast charts (HLHC) The Precision Vision 4-meter high contrast Landolt C charts (No. 2210, 2210A, and 2210B) will be used. One measurement per eye, per condition.	[redacted]

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.10	Slit Lamp Findings	Slit Lamp Classification Scale per ISO 11980 will be used to grade the findings. In addition, conjunctival staining will be evaluated if present. **Note**: If any slit lamp finding is graded as 2 (except for subjects with Grade 2 baseline palpebral conjunctival observations) or worse, it may warrant classification of an adverse event, and shall be followed accordingly. A subject with significant slit lamp findings (e.g., Grade 3 corneal staining and Grade 2 corneal vascularization, etc.) may not be dispensed with the study contact lens at this time, and an adverse event form must be filled. The subject must be followed till slit lamp findings are resolved and the investigator deems it's appropriate for the subject to continue with the study before study lens dispensing. If the subject is discontinued from the study, 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.	
U.11	Lens Dispensing (if applicable)	Dispense the study lenses. The same dispensing criteria and instructions as specified in Visit 2 apply.	

7.4. Laboratory Procedures

Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. Detailed procedures for specimen collection for corneal culture and recommended culture media are provided in [redacted]

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent;
- are eligible;
- completed all visits through the final visit

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, including significant non-compliant to lens wear time schedule, e.g., the subject is found to have lens wear time that is less than 6 hours per day or less than 5 days per week for two consecutive follow-up visits (e.g., at both Visits 4 and 5, Visits 5 and 6, or Visits 6 and 7)
- 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 for more than 3 consecutive weeks during the first 6-month dispensing period
- 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 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 may be enrolled if a subject discontinues from the study during the study enrollment period.

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 for this study include the following:

1. Any chronic (3 months or more) or seasonal (30 days or more) use of topical ophthalmic medication except for artificial tears or contact lens rewetting drops. This includes but is not be limited to, topical ophthalmic anti-histamine, topical ophthalmic mast cell stabilizers, topical ophthalmic antibiotics, topical ophthalmic vasoconstricting agents, and topical decongestants, including nasal decongestants (naphazoline, tetrahydrozoline, and phenylephrine), etc.

Short-term use of above listed topical ophthalmic medication may be allowed, but must be completed at least 7 days prior to the study or scheduled follow-up visits during the study.

2. Any outside the study use of topical agents with anti-muscarinic properties for more than 3 consecutive days (i.e., other than for diagnostic use), or repeated single use of these agents for more than 3 doses within the last 6 months. This includes but is not limited to atropine, scopolamine, pirenzepine, tropicamide, cyclopentolate and homatropine. Occasional use of these agents (i.e., three doses or less during the last 6 months) must be completed 21 days prior to the study or any scheduled follow-up visit during the study.
3. Any chronic use of oral agents with anti-muscarinic properties. This includes, but is not limited to

    1) Any GI anti-spasmodic medicine containing atropine, hyoscyamine, and dicyclomine
    2) Over-the-counter cold & allergy preparations and sleeping agents that contain first generation anti-histamines (diphenhydramine, chlorpheniramine)
    3) Tricyclic anti-depressant (amitriptyline, imipramine, nortriptyline)
    4) Anti-psychotics agents (chlorpromazine, thioridazine)
    5) Anti-nausea/ anti-cough medication containing promethazine, prochlorperazine, meclizine and scopolamine
    6) Anti-anxiety agent (hydroxyzine)
    7) Ipratropium bromide

    Short-term use of above listed oral agents with anti-muscarinic properties may be allowed but must be completed at least 7 days prior to the study or scheduled follow-up visits during the study.

4. Any chronic use of human growth hormone products containing somatropin, e.g., Genotropin, Nutropin, Saizen, etc. Short-term use of these medications may be allowed but must be completed at least 30 days prior to the study or scheduled follow-up visits during the study.
5. Any chronic use of oral beta-blocker. Short-term use of oral beta-blockers may be allowed but must be completed at least 7 days prior to the study or scheduled follow-up visits during the study.
6. Any chronic use of anti-psychotic and neurological. This includes but is not limited to,

    1) ADHD medications containing methylphenidates, amphetamines & its derivatives (Ritalin, Concerta, Adderall, and Strattera, etc.)
    2) Anti-psychotic agents phenothiazines (chlorpromazine, thioridazine)

    Short-term use of above listed medications may be allowed, but must be completed at least 30 days prior to the study or scheduled follow-up visits during the study.

7. Any chronic use of sulfa drugs. This includes but is not limited to

    1) Sulfamethoxazole containing products, such as Bactrim, Septra
    2) Carbonic anhydrase inhibitors such as dorzolamide and acetazolamide
    3) Sulfasalazine
    4) Topiramate
    5) Thiazides diuretics such as hydrochlorothiazide & chlorthalidone

    Short-term use of above listed medications may be allowed, but must be completed at least 7 days prior to the study or scheduled follow-up visits during the study.

8. Any medications that has known ocular side effects.

Concomitant therapies that are disallowed include:

1. Contact lens corneal reshaping/CRT/orthokeratology
2. Any vision training/vision therapy/orthoptics/patching
3. Use of reading spectacles or progressive addition lenses
4. Any therapies that the investigator felt would be contraindicated in 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.

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 [redacted]

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, or 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. The test article relationship for each adverse event should 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 [redacted]. 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.

13.5. Event of Special Interest

13.5.1. Specific Requirements for Recording and Diagnosing Possible Microbial Keratitis

The signs of a presumed infectious ulcer (defined as progressive erosion of the corneal tissue) may include irregular focal infiltrates (>1 mm); active lesions with raised edges; significant diffuse infiltration; anterior corneal to mid-stromal involvement; erosion with overlying staining; conjunctival and lid edema; anterior chamber reaction (iritis); severe bulbar and limbal redness. Symptoms associated with a presumed infectious ulcer (microbial keratitis, MK) may include pain of rapid onset; severe redness; purulent or mucopurulent discharge; tearing; photophobia. For the purpose of reporting, per the ISO 11980, a presumed corneal ulcer which has any of the following characteristics should be reported as a serious adverse event[34]:

1. Central (6 mm) or paracentral (8 mm) location;
2. Penetration of Bowman's membrane;
3. Infiltrate> 2mm diameter
4. Associated with iritis ≥ Grade 2;
5. Associated with any increase in intraocular pressure;
6. Culture positive for microorganisms;
7. Increasing size of severity at subsequent visits.

In the event of any case of possible microbial keratitis (e.g., presence of an infiltrative lesion), the investigators shall provide complete descriptions of the event. A comprehensive description of diagnostic procedures is provided [redacted].

The investigator shall record the following in the CRF:

- Presence and severity of pain;
- Presence and type of discharge;
- Presence of lid edema;
- Presence of chemosis;
- Pattern and grading of redness (bulbar/limbal);

- Characterization of infiltrates (size, shape, location, depth) on the Infiltrate Assessment Form;
- Characterization of the epithelial defect (size/depth);
- Involvement of surrounding cornea;
- Endothelial involvement;
- Grading of anterior chamber cell and flare

The investigator shall record the diagnosis and specific treatment on the Adverse Event Form.

Where necessary, a culture of the corneal lesion will be collected to determine if the infection is microbial in nature. For example, if an overlying epithelial defect is present and any one of the conditions listed below is present when the infiltrate is first evaluated, the infiltrate must be cultured.

- Diameter greater than 1mm
- Location within the central (6 mm) optical zone
- Purulent discharge
- Pain
- Photophobia
- Iris/Anterior chamber inflammation

Any corneal lesions meeting the criteria set forth above must be cultured as outlined in the Premarket Notification (510(k)) Guidance Document for Daily Wear Contact Lenses (Revised May 1994).[31] Cultures will be collected with the Sponsor approved culture kits and sent to a study designated laboratory for analysis. The results will be communicated to the Investigator and the Sponsor. See [redacted] for specific procedures that should be followed for culturing of possible cases of infectious keratitis.

For other infiltrative events that do not meet the criteria as specified above, the investigators may culture the lesion when deemed appropriate. If cultures are collected, a source document note should be completed specifying the date of culture collection and laboratory utilized. An eCRF documenting this should be completed.

All cases of symptomatic corneal infiltrates shall be reported to DMC. The DMC will serve as an independent committee to adjudicate whether the event should be classified as infectious or non-infectious by majority vote. The following definitions will be used to classify whether the case is definite MK, probable MK, probably not MK, definitely not MK, or MK unrelated to contact lens wear. [35]

- **Definite MK**: one or more central (6 mm) or paracentral (8 mm) corneal stromal infiltrates greater than 2mm in size with pain rated more than mild, and one of the following:
    - anterior chamber reaction (iritis) Grade 2 or higher
    - mucopurulent discharge
    - positive corneal culture

- **Probable MK**: same definition as that of definite MK but failing to meet all of the specified criteria, e.g., the size of the lesion was less than 2mm, the pain was minimal, or there was less than Grade 2 anterior chamber reaction, no mucopurulent discharge, or negative corneal culture.
- **Probably not MK**: not meeting any of the above specified MK definitions.
- **Definitely not MK**: not meeting any of the above specified MK definitions and with significant evidence that suggests non-infectious etiology (e.g. reduction in severity without pharmacologic treatment).
- **MK unrelated to contact lens wear**: cases such as *Herpes simplex* keratitis or *Staphylococcal* marginal keratitis, where, in the judgment of the panel, the etiology is unrelated to the wear of contact lenses.

13.5.2. Loss of Best Sphero-cylindrical Corrected Visual Acuity without Physical Cause

During the course of the study, if it is found that best sphero-cylindrical corrected visual acuity (BSCVA) of a subject is less than 20/25 (0.1 logMAR) in either eye and is more than 1.5 lines worse than that was measured at baseline without any physical cause (confirmed through up to 3 repeated independent measures to rule out potential measurement errors or variations), the subject will cease wearing the study lenses and an adverse event will be filed. The subject will be followed until the best corrected visual acuity is no more than 1.5 lines worse than baseline or is stabilized before being discontinued from the study. A decrease of more than 1.5 lines of BSCVA is considered a significant change. This criterion is established based on the 95% limits of agreement of repeated measures of visual acuity in children. [36]

It is not anticipated that development of amblyopia (defined as a reduction of BSCVA to 20/30 or worse or a two-line difference between the two eyes, in the absence of pathology [37-39]) will occur while wearing the investigational soft contact lens. Upon identifying the first confirmed case of amblyopia during the course of the study, the event will be investigated and followed according to procedures specified for an Unanticipated Adverse Device Effect (Sections 11 and 13.1).

13.6. 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. A general description of the statistical methods to be implemented in this clinical trial is outlined below.

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 (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. Unscheduled visits will be summarized separately and will be excluded from the 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.

All statistical analysis will be conducted on the per-protocol population defined in section 14.3.

14.2. Sample Size Justification

This is a pilot study for assessing the investigational test articles. As such, the sample size was not determined based on any power analysis with regard to the primary endpoint. The collected data will be used to design future trials. Below sample size calculation is for reference only.

Using the POWER procedure in SAS 9.4, below is the summary of different statistical powers based on the different assumptions of the true difference in each of the primary endpoint at the given sample size (40 per arm). The estimated standard deviation is from the change at 6 months for the test group of the historical study [redacted] The power analysis was conducted controlling 2-sided type I error of 0.05.

Assuming the true difference in change of axial length (AL) from baseline at 6 months is between 0.05mm to 0.12mm, the table below demonstrates the table below demonstrates the power analysis for the given sample size (40 per arm).

Difference (Test-Control)	Estimated Standard Deviation	# of subjects per arm	Power
0.05	0.10	40	0.60
0.08	0.10	40	0.94
0.10	0.10	40	0.99
0.12	0.10	40	0.99

Assuming the true difference in change of spherical equivalent of cycloplegic auto refraction (SECAR) from baseline at 6 months (in magnitude) is between 0.10D to 0.25D, the table below demonstrates the power analysis for the given sample size (40 per arm).

Difference (Test-Control)	Estimated Standard Deviation	# of subjects per arm	Power
0.10	0.32	40	0.03
0.15	0.32	40	0.54
0.20	0.32	40	0.79
0.25	0.32	40	0.93

14.3. Analysis Populations

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

Per-Protocol Population:
All subjects who have successfully completed the initial screening and baseline visit (Visit 1), the study lens fitting and dispensing visit (Visit 2), and the 6-month follow up visit (Visit 6), and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock (Per-Protocol Population). Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

Intent-to-Treat (ITT) Population:
All randomized subjects regardless of actual treatment and subsequent withdrawal from study or deviation from protocol. At least one observation should be recorded.

14.4. Level of Statistical Significance

All planned analysis for this study will be conducted with an overall type I error rate of 5%.

14.5. Primary Analysis

The two primary endpoints, changes of axial length (AL) and cycloplegic auto refraction (SECAR) from baseline at 6 months follow-up, will be analyzed separately using a linear mixed model for longitudinal data. Each model will include treatment group, time period (in weeks) and treatment group by time interaction as fixed effect factors; and site, subject nested in site, and eye nested in subject as random effect factors when appropriate. Other baseline characteristics known of importance such as age, gender, refractive error at baseline, axial length at baseline, pupil size, parental history of myopia and other factors will be included as fixed covariates when appropriate. The covariance between residual errors from the same subject/eye across lens wearing time periods will be selected based on the finite-sample corrected Akaike's Information Criterion.[41] Covariance structures considered may include: Homogeneous Compound Symmetry (CS), first-order autoregressive (AR(1)) and Unstructured covariance structure (UN). For AR (1) structure, site, subject nested in site and eye nested in subject will be included in each model as random effects. For the remaining structures, only site and subject will be included as random effects. The covariance structure that returns the lowest Akaike Information Criteria Corrected (AICC) will be selected as the structure that best fit the data. Heterogeneous residuals covariance structures (R-side) across treatment 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 for the denominator degree of freedom.[42]

The null and alternative hypotheses for superiority for each test lens relative to the control are as follows for AL and SECAR:

$$H_0: \Delta_{AL} \geq 0; H_A: \Delta_{AL} < 0;$$

$$H_0: \Delta_{SECAR} \geq 0; H_A: \Delta_{SECAR} < 0,$$

where Δ_{AL} and Δ_{SECAR} are the mean differences (Test minus Control) in change from baseline of AL and SECAR at 6 months follow-up respectively.

For each primary endpoint, the comparison between the treatment groups at 6-Month time period will be conducted using a t-test on least-square means from the final model. The corresponding CI of least-square mean (LSM) difference (i.e. LSM change from baseline of test group minus LSM change from baseline for control group) will be calculated with 95% confidence to test the primary hypothesis.

Superiority of the test lens relative to the control lens in reducing change from baseline in axial length at 6-Month will be claimed if the corresponding upper confidence limits of the LSM differences is smaller than 0.

Superiority of the test lens relative to the control lens in reducing the magnitude of change from baseline in cycloplegic auto refraction at 6-Month will be claimed if the corresponding lower confidence limits of the LSM differences is greater than 0.

14.6. Secondary Analysis

Secondary endpoint – serious and significant ocular adverse events will be summarized descriptively using all available data from the entire study, including data from unscheduled visits.

14.7. Other Analyses

If the primary objective of the study is met, additional analysis may be performed to compare among three Test lenses, including comparisons between Test 1 and Test 2 vs. Test 3 lenses.

In addition, the performance of the three Test lenses (EMO-114, -116, and -118) for myopia control may be evaluated and compared with the Control lens (EMO-117) after 1-year of lens wear, if data are available.

Summary statistical analysis will be provided for the following other observations for the entire study, including 1-year data, if available:

1. Non-significant AEs and non-ocular AEs
2. Slit lamp findings per the ISO 11980 grading scale
3. Subject-reported ocular symptoms
4. Corneal radius of curvature measured by an autorefractor

5. Over-the-lens near visual acuity
6. Subjective best-sphere over-refraction
7. Number of power modification per each prescription update
8. Number of prescription update during the study
9. Lens fit characteristics
10. Distance logMAR visual acuity under High Luminance High Contrast (HLHC) conditions
11. Subjective vision, comfort, and handling scores based on the Pediatric Contact Lens User Experience (pCLUE) questionnaire.
12. Lens wear time compliance, including weighted average of daily lens wear time (in hours), average number of lens wear days per week, and a composite lens wear time compliance score (%) relative to protocol specified minimum and recommended lens wear time requirements, per each dispensing period and for the entire study
13. Number of visits for contact lens insertion/removal training
14. Subject's demographics
15. Subject's disposition, number and reasons for discontinuation
16. Number and reasons for unscheduled visits
17. Lens accountability, including reasons for lens dispensing or replacement
18. Protocol deviations
19. Product quality complaints

Further exploratory analysis will be considered at discretion of the Study Responsible Clinician.

14.8. Interim Analysis

Not applicable.

14.9. Procedure for Handling Missing Data and Drop-Outs

Missing or spurious values will not be imputed. 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, sensitivity analysis will be conducted using multiple imputation methods if the proportion of subject dropout is greater than the 15%. The SAS/STAT procedures PROC MI and PROC MIANALYZE will be utilized with a parametric regression method used to make at least 50 imputations.

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 an EDC system (Bioclinica). An authorized data originator will enter study data into the eCRFs using the EDC system. Data collected on equipment that is not captured in EDC 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.[1]

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 and their parents/legal guardians will be fully informed of the risks and requirements of the study and, during the study, subjects and their parents/legal guardians will be given any new information that may affect their decision to continue participation. Subjects and their parents/legal guardians will be told that their consent/assent 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 whose parents are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily, and subjects who provides their assent 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),[2] 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[3] 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),[2] 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 assent and their parents (legal guardians) must give written consent according to local requirements after the nature of the study has been fully explained. The consent and assent forms must be signed before performance of any study-related activity. The consent and assent forms that are used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent and assent are in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and ISO14155[1] GCP 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 and the parent (legal guardian) the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects and their parents (legal guardians) will be informed that their participation is voluntary and that they may withdraw consent to participate at any time.

The subject and parent (legal guardian) will be given sufficient time to read the information and assent form and the informed consent form, respectively, and the opportunity to ask questions. After this explanation and before entry into the study, assent and consent should be appropriately recorded by means of the subject's and parent/legal guardian's dated signatures. After having obtained the consent and assent, a copy of the informed consent and assent forms must be given to the subject.

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,[43] the Personal Information Protection and Electronic Documents Act (PIPEDA) in Canada,[44] and other applicable personal data protection and security laws and regulations. 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/ISO 14155 GCP guidance[1,2] 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 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 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 based on the following:

This is an interventional clinical trial for evaluating safety and effectiveness of novel soft contact lenses for controlling myopia progression in pediatric populations.

22. REFERENCES

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15. Cheng X. *Clinical Report* [redacted] *Evaluation of Visual Performances of Soft Contact Lens Prototypes for Myopia Control.* TBD.
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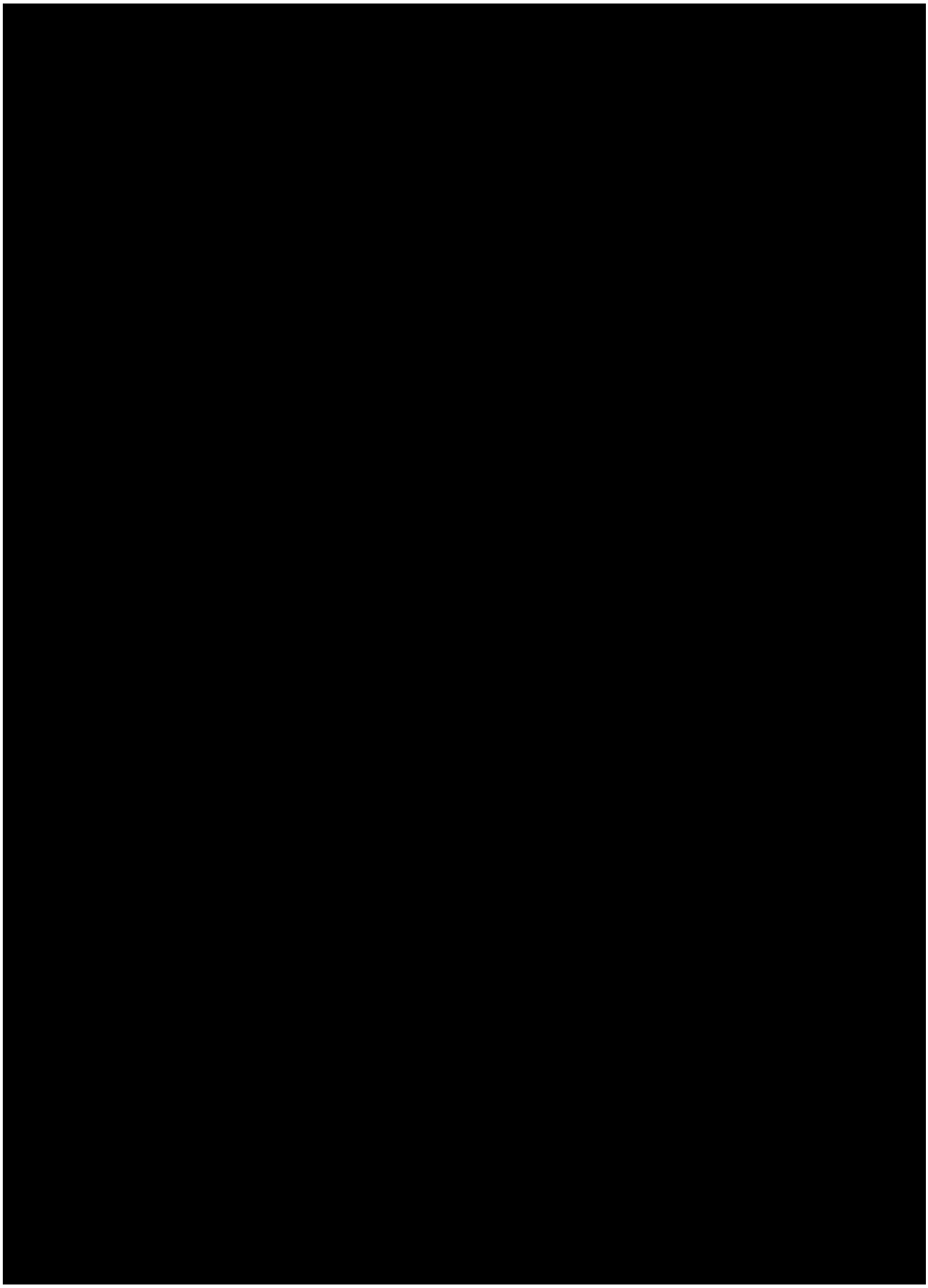
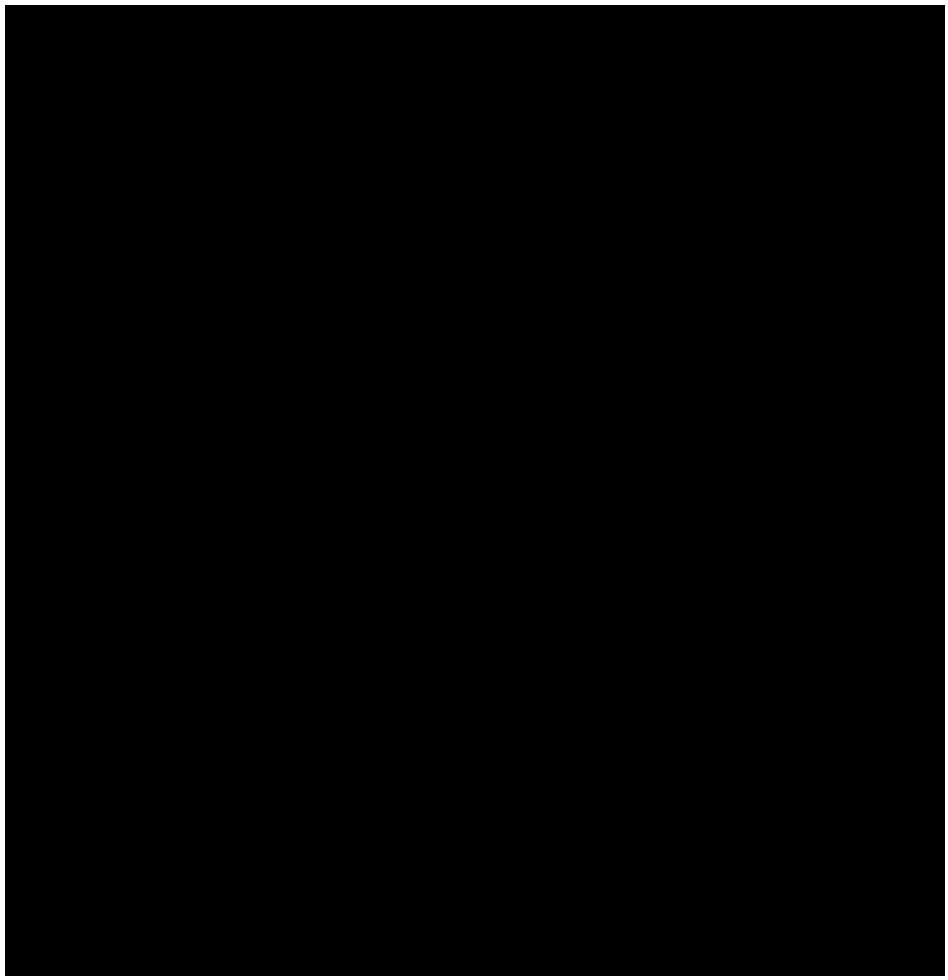
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)





APPENDIX B: PARENT/PATIENT INSTRUCTION GUIDE

A parent/patient instruction guide, contact lens insertion and removal instructions, insertion and removal instructional video, and a study pamphlet will be provided separately to study participant's and their parent's.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not Applicable

APPENDIX D: [redacted]

[redacted] Lens Fitting Characteristics
Subject Reported Ocular Symptoms Problems
Determination of Distance Spherocylindrical Refractions
Conjunctival Staining
Distance and Near Visual Acuity Evaluation
Distance LogMAR Visual Acuity Measurement Procedure
Patient Reported Outcomes
Administration of Cylcloplegia
Anterior Chamber Angle Grading Scale
Cover-Uncover Test
ISO Biomicroscopy Scale
Measuring Axial Length & Ocular Biometrics with the LENSTAR 900
Measuring Pupil Diameter with NeurOptics VIP-200 Pupillometer
Specimen Collection Procedures for Corneal Culture
Visual Acuity Chart Luminance and Room Illumination Testing
WAM-5500 On-axis Auto Refraction Measurement
Corneal Infiltrate Assessment
[redacted] Diagnosis of Microbial Keratitis
Work Aid: Measuring Axial Length & Other Ocular Biometrics with IOLMaster

[redacted] **LENS FITTING CHARACTERISTICS**

[redacted]

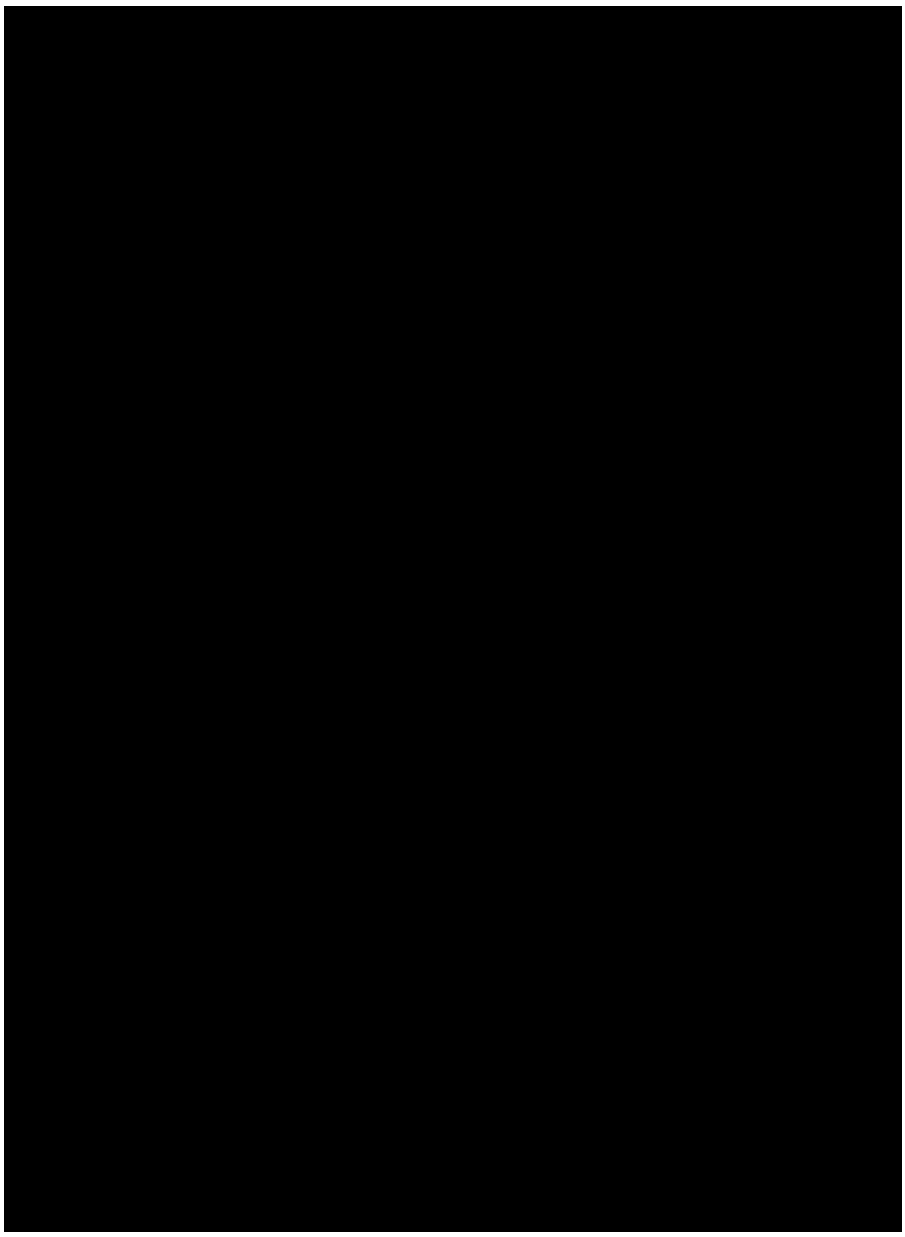
[redacted]

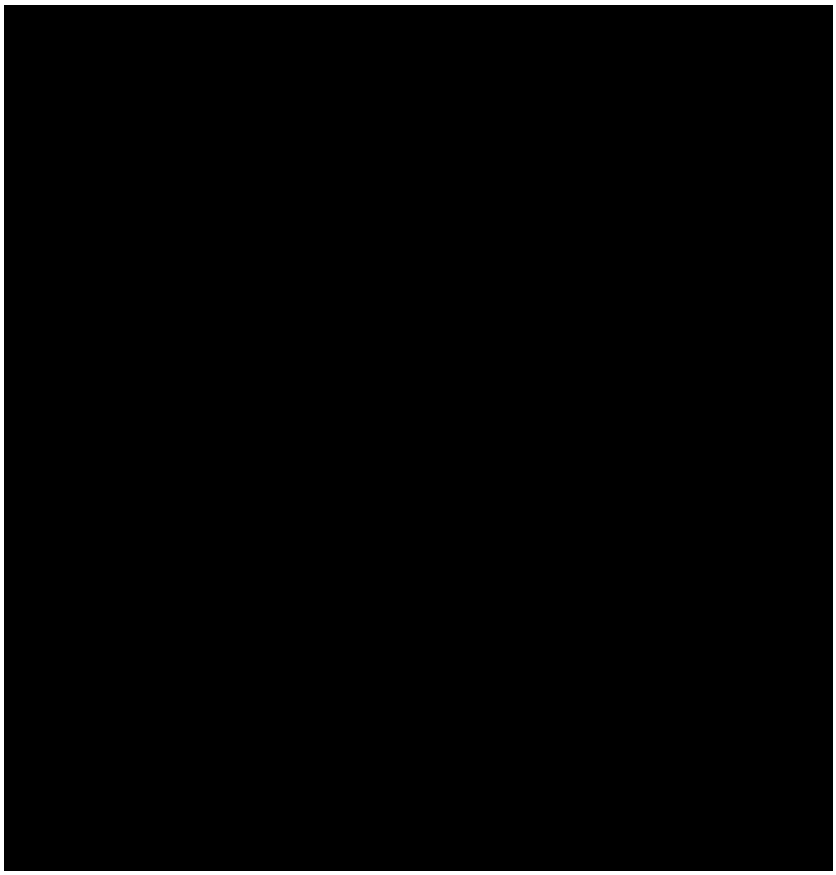
[redacted]

[redacted]

[redacted]

[redacted]





[redacted] SUBJECT REPORTED OCULAR SYMPTOMS PROBLEMS

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted]

[redacted]

[redacted] **CONJUNCTIVAL STAINING**

[redacted] [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

- [redacted]
- [redacted]

[redacted]

[redacted]

[redacted] **DISTANCE AND NEAR VISUAL ACUITY EVALUATION**

[redacted] [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **PATIENT REPORTED OUTCOMES**

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted]

- [redacted]
- [redacted].

[redacted] [redacted]

[redacted] **ADMINISTRATION OF CYLCLOPLEGIA**

[redacted] [redacted]

[redacted] [redacted]

[redacted] [redacted]

[redacted]

[redacted]

[redacted] **ANTERIOR CHAMBER ANGLE GRADING SCALE**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

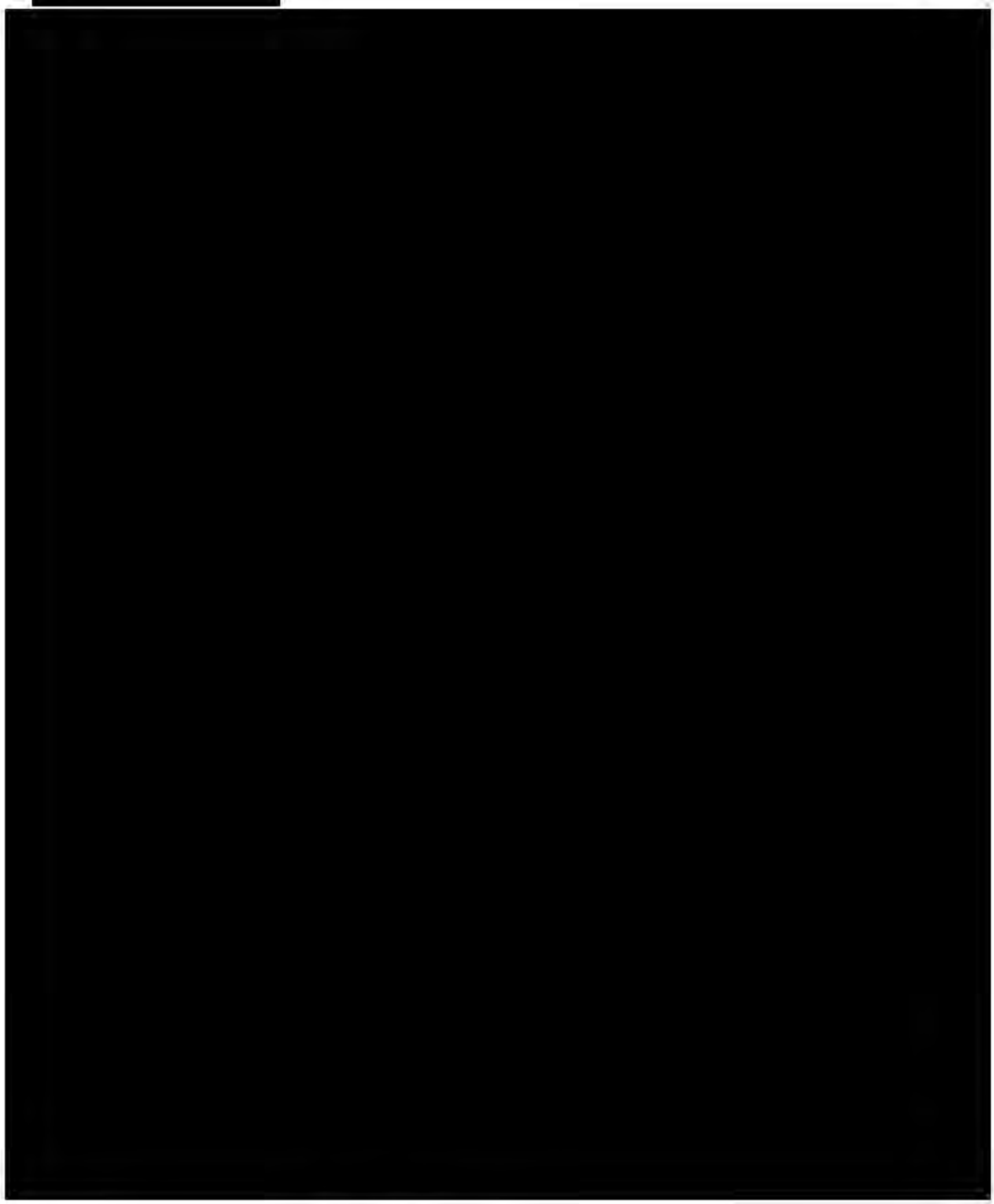
[redacted]

[redacted]

[redacted]

[redacted] **COVER-UNCOVER TEST**

[redacted]



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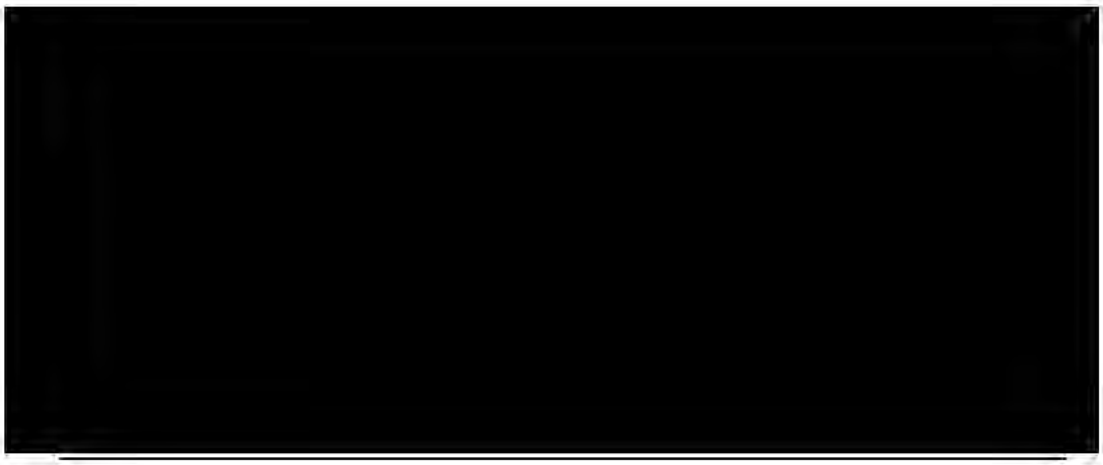

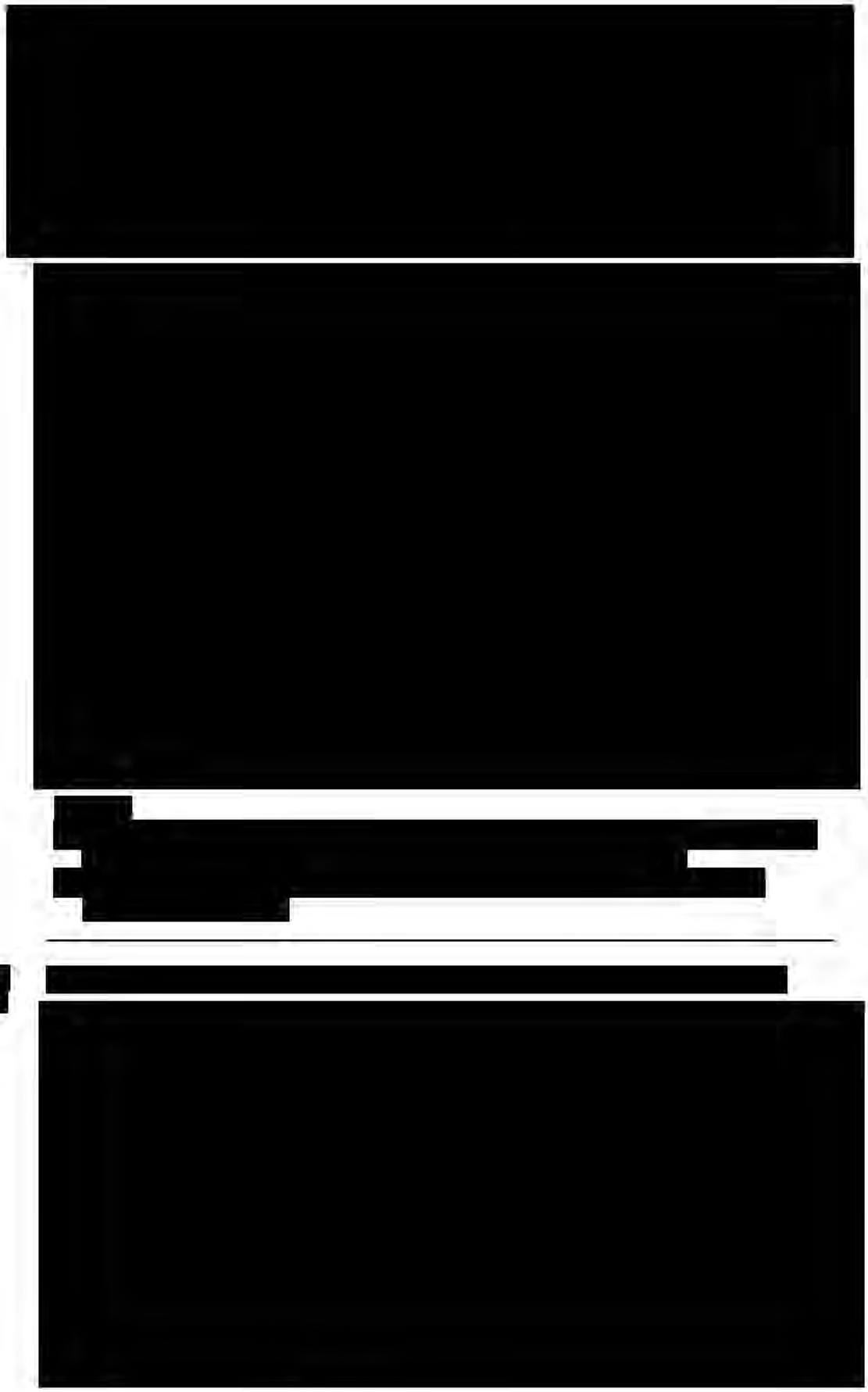

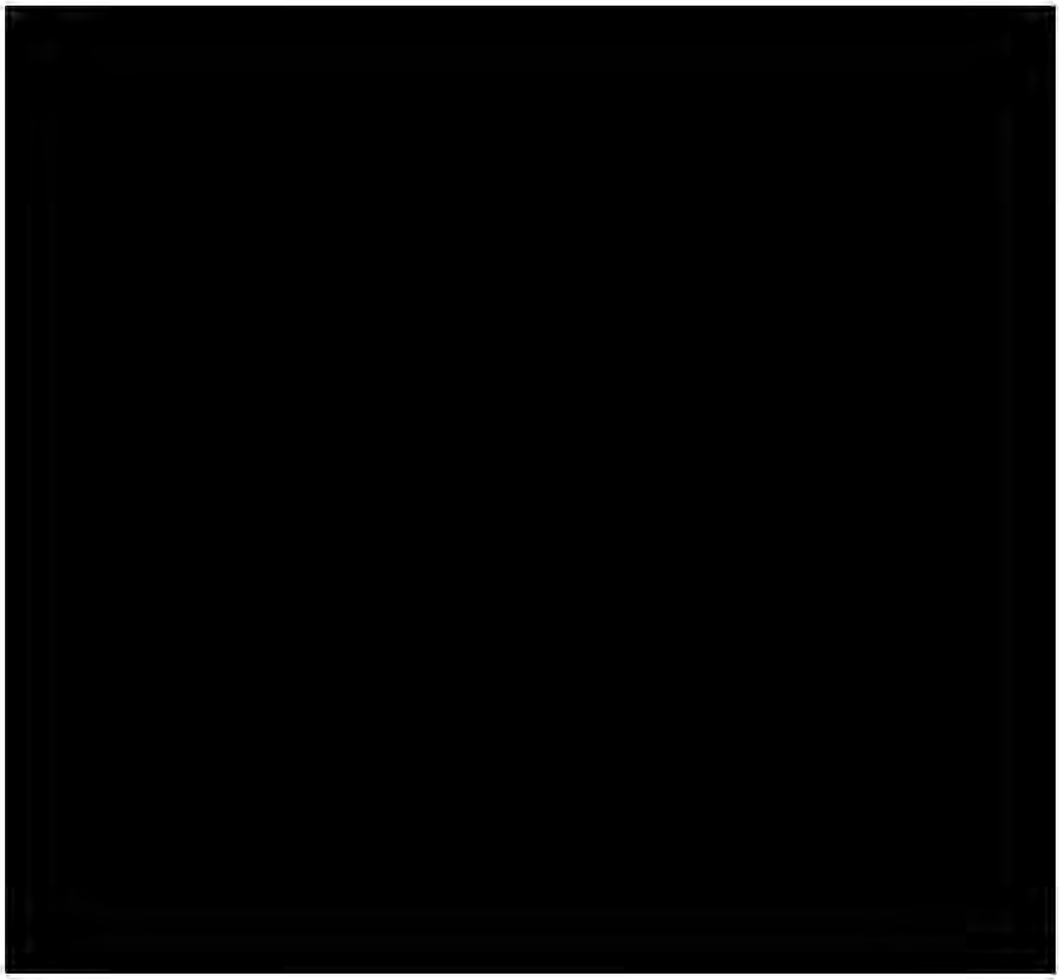

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[redacted] **MEASURING AXIAL LENGTH & OCULAR BIOMETRICS WITH THE LENSTAR 900**

[redacted]

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Title:	**Measuring Axial Length & Ocular Biometrics with the LENSTAR 900**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 2**

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[redacted] **MEASURING PUPIL DIAMETER WITH NEUROPTICS VIP-200 PUPILLOMETER**

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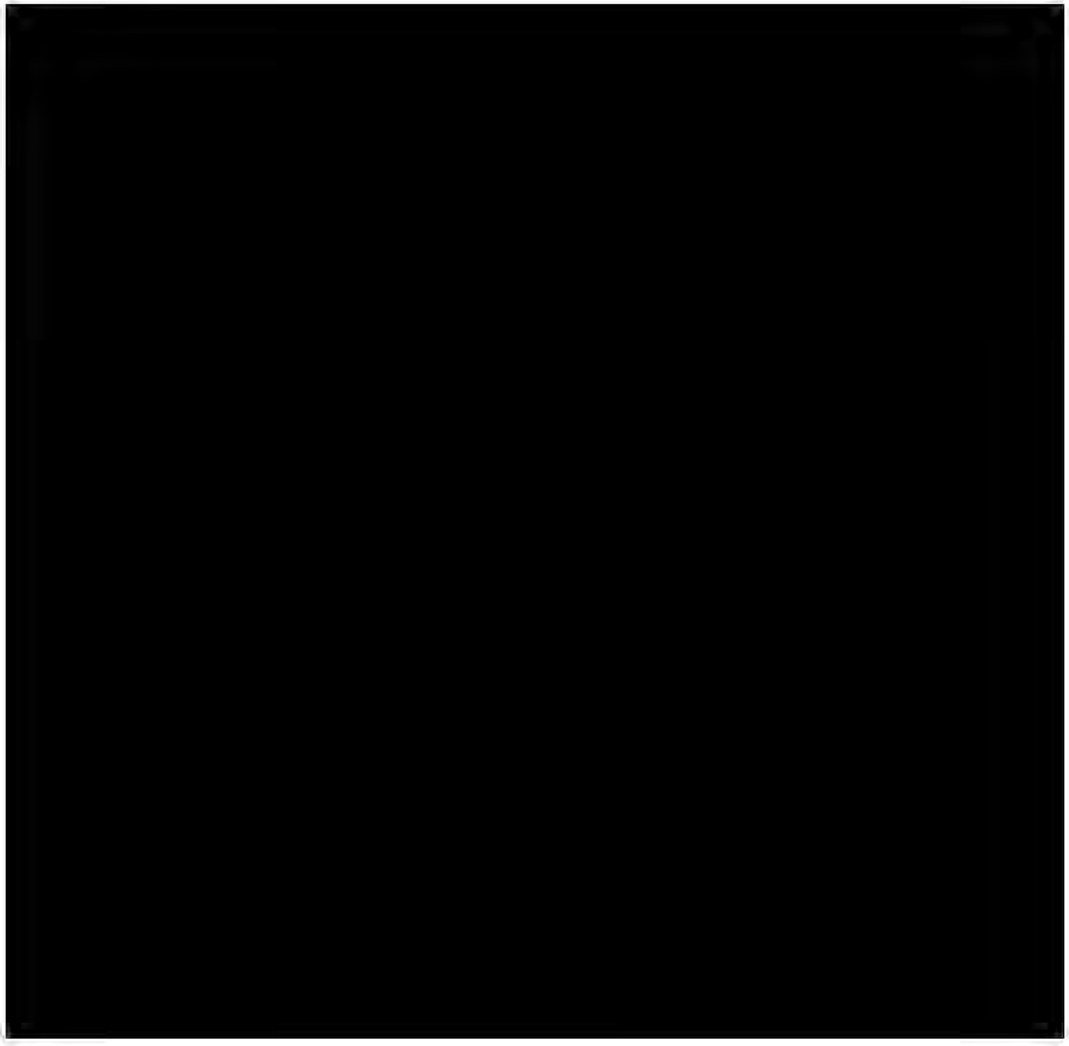

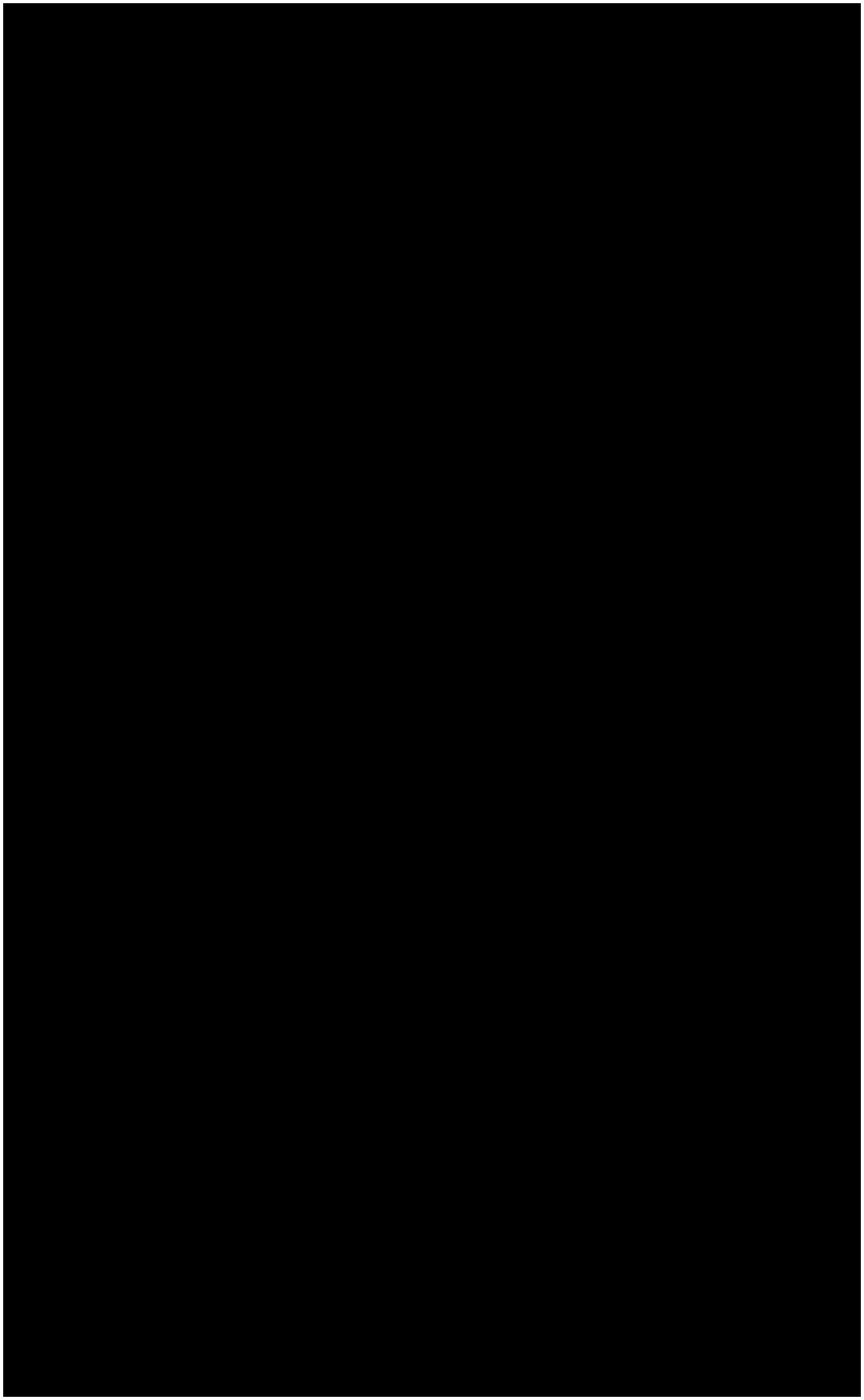

[redacted] **SPECIMEN COLLECTION PROCEDURES FOR CORNEAL CULTURE**

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[redacted]VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

Title:	**Visual Acuity Chart Luminance and Room Illumination Testing**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 3**

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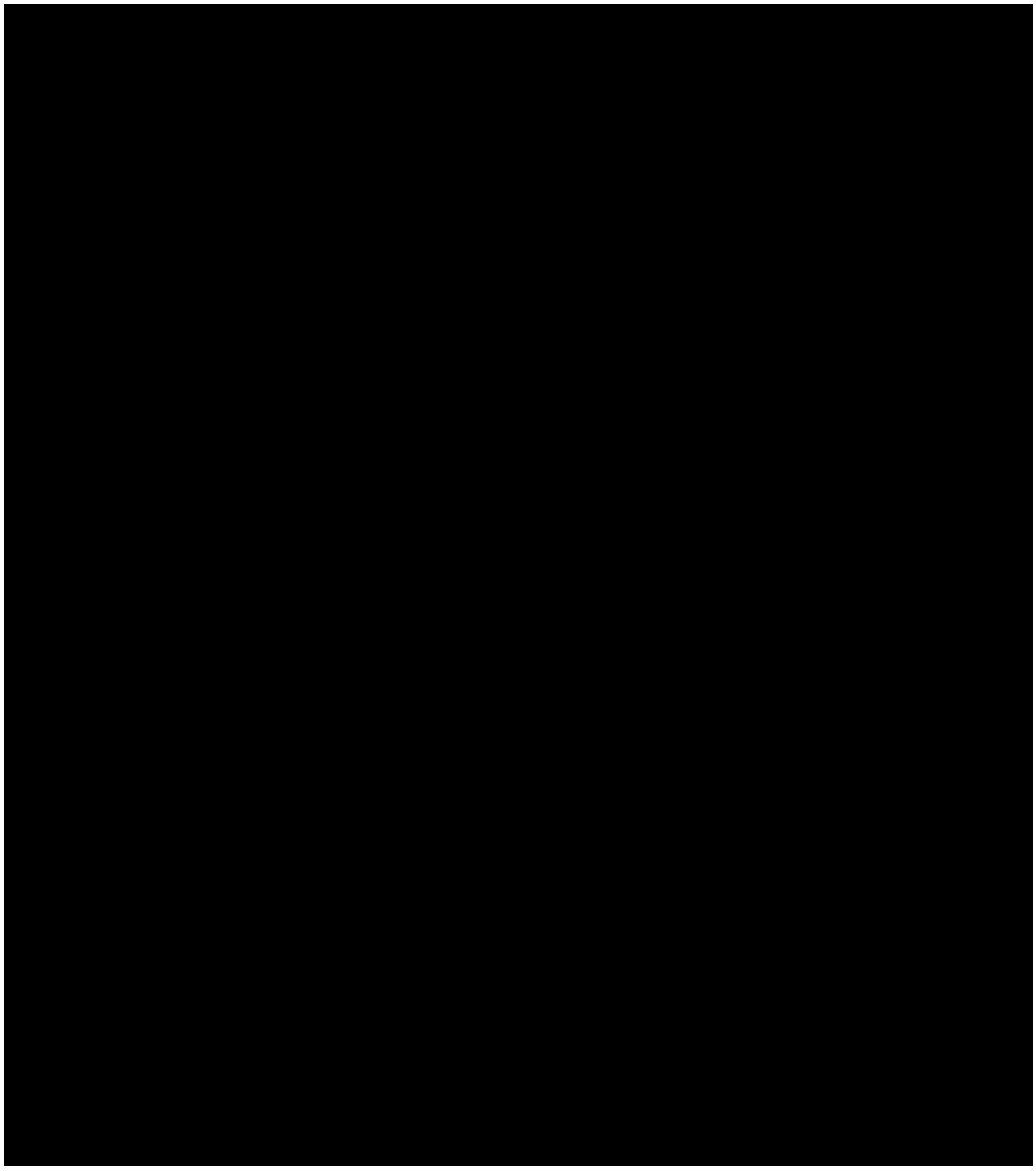

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[redacted] **CORNEAL INFILTRATE ASSESSMENT**

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Further documentation, such as diagrams or photographs, may be recorded in the site source documents [redacted]

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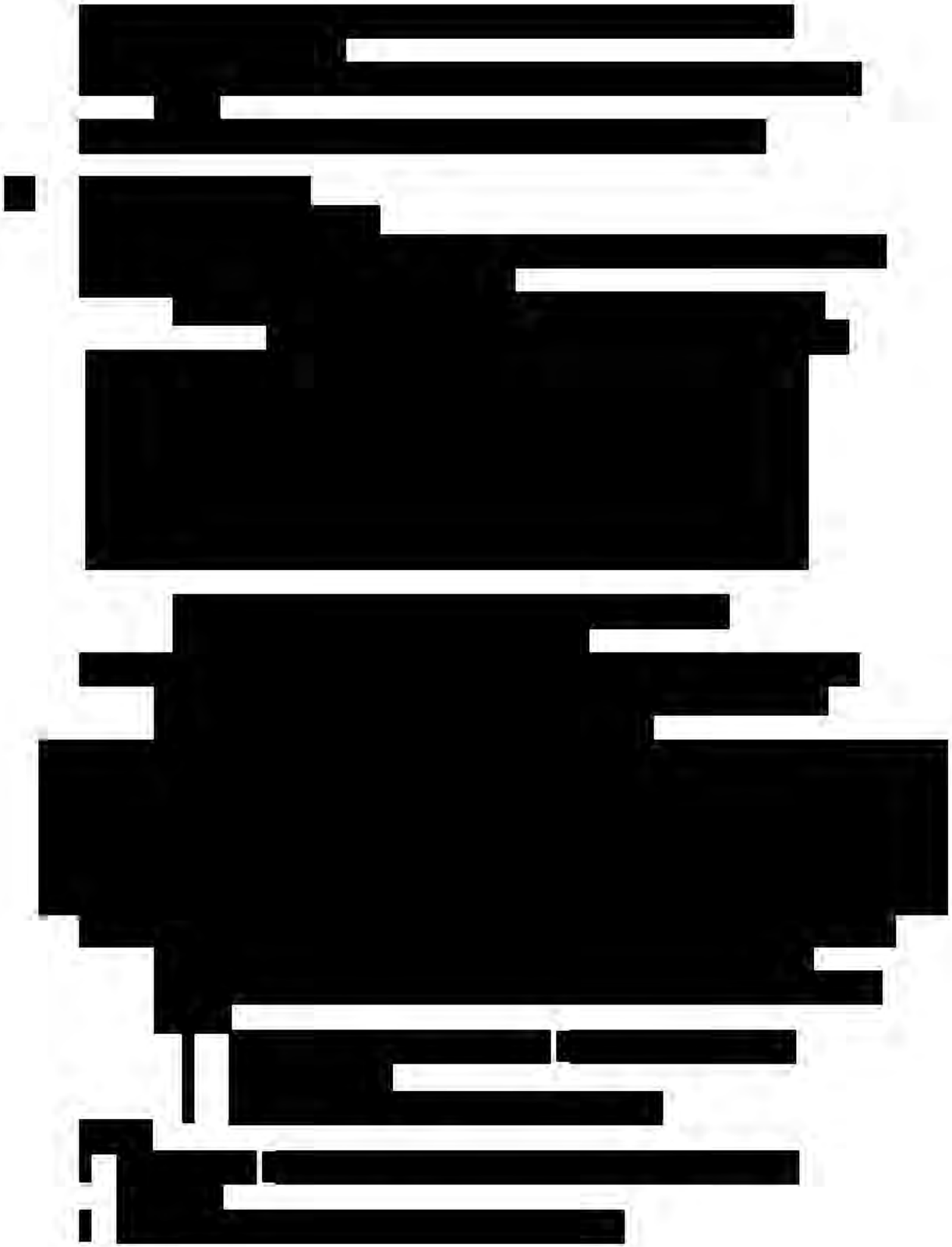
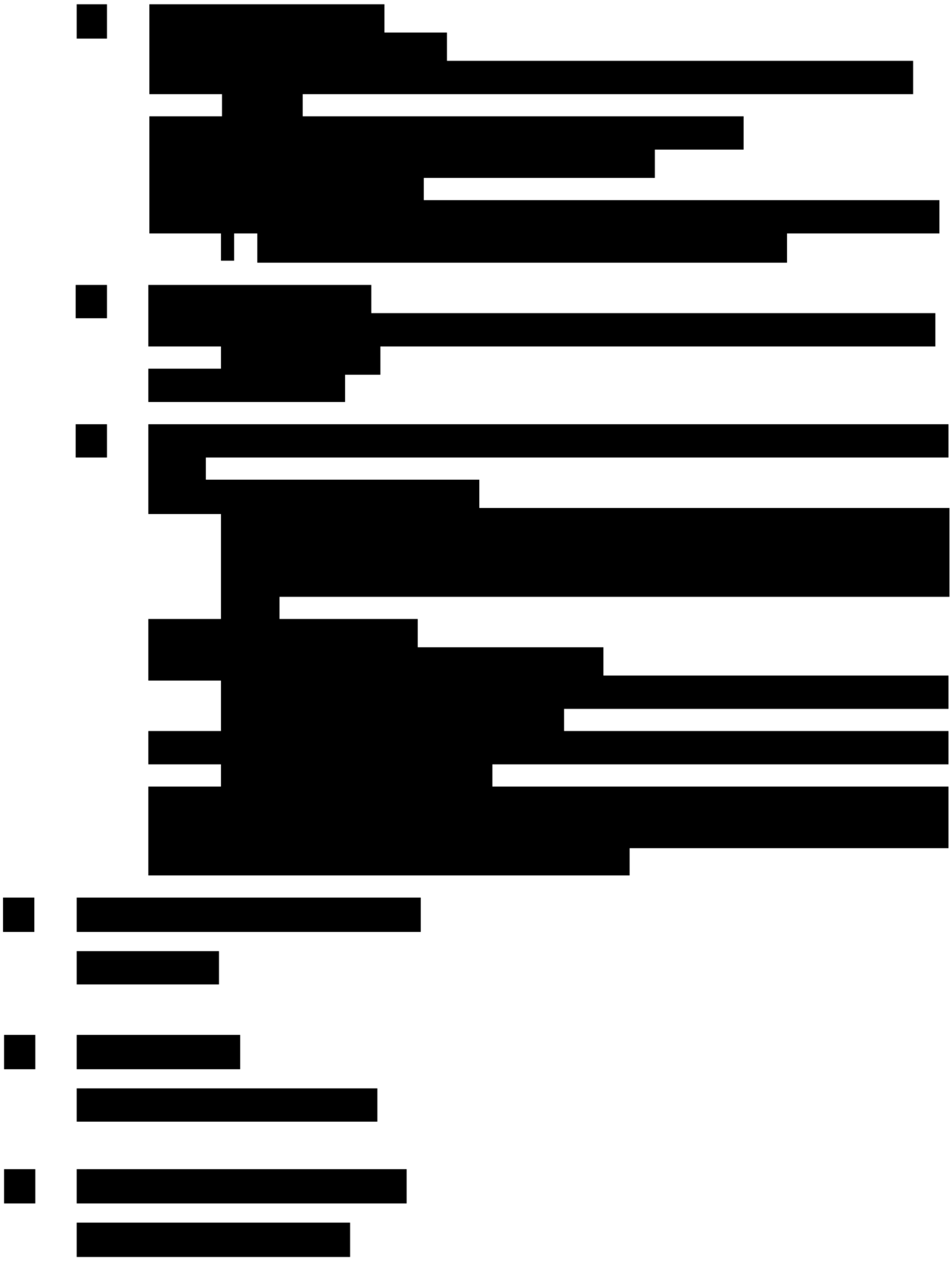
[redacted] **DIAGNOSIS OF MICROBIAL KERATITIS**

MEASURING AXIAL LENGTH & OTHER OCULAR BIOMETRICS WITH IOL MASTER WORK AID





PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title:
CR- 5959 Evaluating Soft Contact Lens Prototypes for Myopia Control

Version and Date: Version: 3.0, Amendment 2, Date: 11-Sep-2018

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

I agree to conduct this study according to GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] ISO 14155,[1] 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[11] 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