Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Evaluation of On-eye Optical Performances of the RMY-100 Lens

Protocol CR-6000

Version: 3.0, Amendment 2.0

Date: 05 June 2018

Investigational Products:
RMY-100: Daily disposable soft contact lens made in etafilcon A material with an optical design for myopia control

Key Words: Myopia control, Non-dispensing, Daily disposable, Etafilcon A, Orthokeratology, Wavefront aberration, Corneal topography, Accommodation, Off-axis refraction, Visual acuity

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

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION

Title: Evaluation of On-eye Optical Performances of the RMY-100 Lens

Protocol Number: CR- 6000
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Date: 05 June 2018

SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

[redacted]
Address: 7500 Centurion Pkwy, W-2A, Jacksonville, FL 32256
[redacted]

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, ICH guidelines,[1] ISO 14155[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	Fellow Designated SME Review 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	13-Oct-2017
2.0	[redacted]	1. Updated the Study Operation Manager in the section of AUTHORIZED SIGNATURES 2. Increased the sample size of the Control arm from a minimum of 8 subjects to completed to 15 to complete in sections of SYNOPSIS, 3.4 Enrollment Strategy and 4.3 Enrollment Target and Study Duration. 3. [redacted] 4. Updated the sample label in Section 6.4.	07-Feb-2018
3.0	[redacted]	1. Specified in Section 7.2 Detailed Study Procedure Visit 1 Step 1.1 that corneal topography will be collected on OD for the Test group subjects and better OK treated eye for the Control group subjects. 2. Specified in Section 15 Data Handling and Record Keeping/Archiving the external data sources. 3. Added Corneal Topography [redacted] 4. Added WAM [redacted]	05-Jun-2018

SYNOPSIS

Protocol Title	Evaluation of On-eye Optical Performances of the RMY-100 Lens
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Development phase, Phase 1
Trial Registration	The study will be registered on clinicaltrial.gov based on the following: This clinical study aims to understand the fundamental mechanisms of optical interventions for myopia control. The results of this study are expected to be published in peer-reviewed journals. In addition, this study will be conducted in Canada, clinicaltrial.gov registration is required by Health Canada.
Test Article(s)	Investigational Products: RMY-100: Daily disposable soft contact lens made in etafilcon A material with an optical design for myopia control.
Wear and Replacement Schedules	Wear Schedule: Daily wear Replacement Schedule: Daily disposable Subjects will wear the investigational test article during the study visits only. No study lenses will be dispensed for subjects to wear outside the office.
Objectives	The primary objective of the study is to evaluate the on-eye optical performances of the RMY-100 lens and compare with eyes treated with orthokeratology. The secondary objective of the study is to compare on-eye optical performances of the RMY-100 lens with eyes wearing sphero-cylindrical correction lenses in the spectacle trial frame.
Study Endpoints	Primary endpoint: • Wavefront aberrations measured at distance (0.25 D target vergence) and near (4 D target vergence) Secondary endpoint: • Off-axis refraction at both temporal and nasal fields of retina at ±10°, ±20°, ±30° with targets at 4 meters and ±30° only with targets at 25 cm. Other observations: • Corneal and test article on-eye topography • On-axis accommodative response with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D • Slit lamp findings • LogMAR visual acuity under HLHC, LLHC, and HLLC conditions • Lens fit assessment • Subjective vision assessment (CLUE Vision questionnaire)
Study Design	This is a two-arm parallel, non-masked, bilateral, non-dispensing study with one Test arm and one concurrent, non-randomized Control arm.

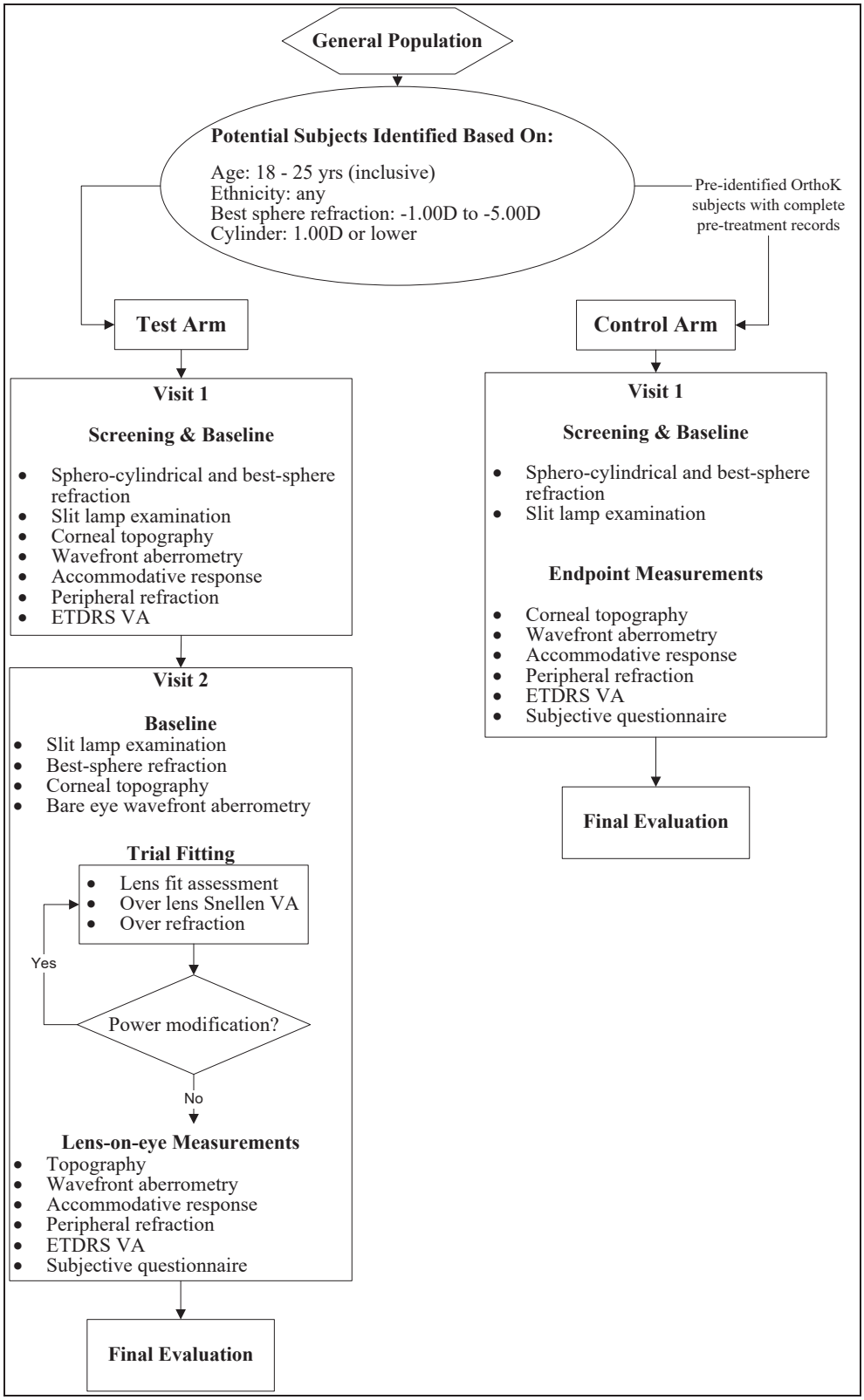
	For subjects enrolled in the Test arm, investigational test articles will be bilaterally fitted to the subject's eyes. Concurrently, a smaller sample of subjects who are established orthokeratology lens wearers will be enrolled to Control arm. Endpoint measures will be collected over one eye only (Test arm: OD only; Control arm: better OK fitted eyes). For subjects in the Test arm, there will be a total of 2 visits: Visit 1: Screening, baseline endpoint measures with bare eye/spectacles Visit 2: Lens fitting, endpoint measures over the study lenses and final evaluation. For the Control arm, subjects will be recruited through referrals from the university optometry clinic and independent Eye Care Professionals (ECPs) who will identify potential subjects by reviewing the case history of existing orthokeratology treated patients in their practices. Only subjects with complete pre-treatment record, e.g., spherocylindrical refraction and corneal topography will be invited to participate in the study. For subjects in the Control arm, there will be a total of 1 visit: Visit 1: Screening, baseline and endpoint measures over the selected eyes. 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 25 subjects will be enrolled in the Test arm of the study with a minimum of 20 subjects targeted to complete the study. Approximately 20 subjects will be enrolled in the Control arm of the study with a minimum of 15 subjects targeted to complete the study.
Study Duration	The total duration of the study is estimated to be about 14 weeks, including an approximately 10-week enrollment period.
Anticipated Study Population	Healthy male and female subjects between 7 and 25 years of age (inclusive) (prefer 7-15 if available within timeline) with best sphere refraction between -1.00 D to -5.00 D (inclusive) and 1.00 D or less astigmatism.
Eligibility Criteria	Potential subjects must satisfy all of the following criteria to be enrolled in the study: Inclusion Criteria after Screening: 1. Pediatric subjects (<18 years old) 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. Adult subjects (≥18 years old) and parent(s) or legal guardian(s) of pediatric subjects 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 25 years of age (inclusive). 5. Have normal eyes (i.e., no ocular medications or infections of any type). Below inclusion criterion is for subjects to be enrolled to the Control group only: 6. Are existing orthokeratology patients whose current treatment has been stabilized for at least 1 months and with complete pre-treatment record, e.g., spherocylindrical refraction and corneal topography. Pre-treatment wavefront aberration measures are preferred by not required. Inclusion Criteria after Baseline (apply to subjects to be enrolled to the Test group and to Control group subjects regarding their pre-OK treatment): 7. Vertex-corrected distance subjective best-sphere refraction must be between -1.00 D and -5.00 D (inclusive) in each eye. 8. Cylindrical refraction must be 1.00 D or less in each eye, by subjective sphero-cylindrical refraction. 9. Have sphero-cylindrical best-corrected visual acuity of 20/25 or better in each eye. 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 diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study. 3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear and/or participation in the study. 4. Any current use of ocular topical medication (occasional use of rewetting drops is allowed). 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 7 days prior to study enrollment. 7. Employee or their children/relatives of investigational clinic (e.g., Investigator, Coordinator, Technician). Below exclusion criteria are for subjects to be enrolled to the Test group only

	8. Current or recent (within 30 days from enrollment) rigid lens wearers. 9. History of orthokeratology treatment. Exclusion Criteria after Baseline: 10. 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. 11. Any Grade 3 or greater slit lamp findings (eg, edema, corneal neovascularization, corneal staining, tarsal abnormalities, and conjunctival injection) on the FDA scale. 12. Any ocular abnormality that is contraindicated contact lens wear. 13. Any corneal scar within central 5 mm. 14. Binocular vision abnormality, intermittent strabismus or strabismus. Below exclusion criteria are for subjects to be enrolled to the Test group only 15. Any corneal distortion resulting from ocular diseases or previous hard or rigid gas permeable contact lens wear.
Disallowed Medications / Interventions	Any current use of ocular topical medication such as eye drops (occasional use of re-wetting drops is allowed) and ointments. Any medication and therapies that would normally contraindicate contact lens wear.
Measurements and Procedures	For the Test group, all measurements will be taken over bare eye; sphero-cylindrical spectacle trial lenses and the test articles for OD only, and for the Control group, over bare eye for the better orthokeratology treated eye only, under binocular viewing conditions, unless otherwise specified: • Wavefront aberrations measured with target at distance (4 meters) and near (25 cm). • Off-axis refraction at both temporal and nasal fields of retina at ±10°, ±20°, ±30° with targets at 4 meters and ±30° only with targets at 25 cm. • On-axis accommodative response with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D • Slit lamp findings (OD, OS) • LogMAR visual acuity under HLHC, LLHC, and HLLC conditions • Lens fit assessment (OD, OS)

	• Subjective vision assessment (CLUE Vision questionnaire)
Microbiology or Other Laboratory Testing	None.
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	None.
Principal Investigator and Study Institution / Site	A detailed description of the principal Investigator, the clinical site, and the institution is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

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
CSF	Contrast Sensitivity Function
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 Council for Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
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

Among various optical interventions, orthokeratology (OK) has consistently shown to be effective in controlling myopia progression in clinical trials.[4-15] It is commonly believed that OK controls myopia progression through introducing positive power in the periphery of the cornea relative to the center power. Such optical intervention has shown to shift the retinal image shell to the myopic direction, therefore, potentially eliminating retinal hyperopic defocus as a growth signal to the eye.[16-23] With the hypothesis that the effectiveness of OK for myopia control is primarily optical driven, Johnson & Johnson Vision Care Myopia Control Platform developed the RMY-100 lens that is a soft contact lens with an optical design simulating the optical impact of an OK lens to the eye (the SimOK design). The safety and effectiveness of RMY-100 lens for controlling myopia progression was evaluated in [redacted] The results of the study indicated that axial elongation of the eye in the RMY-100 lens treated group was about 9% less than the spectacle lens control group. Although statistically significant, the magnitude of the effect was deemed clinically insignificant. In addition, there was no statistically significant difference in refraction change from baseline between the two study groups. Therefore, RMY-100 lens that simulates the optical impact of orthokeratology was largely ineffective in controlling myopia progression.[25]

Per the learning of [redacted] the study is designed with the objective of evaluating the on-eye optical performances of the RMY-100 lenses and comparing to the optical characteristics of eyes undergone orthokeratology treatment and with spectacle lens correction. The results of this study may provide information towards understanding of the mechanisms of orthokeratology for controlling myopia progression.

1.1. Name and Descriptions of Investigational Products

This study will test one investigational lens (RMY-100). The RMY-100 lens is a spherical soft contact lens with an aspheric optical design aimed to control myopia progression.

The RMY-100 lens is made of the same material and with the same manufacturing process as the marketed 1 Day Acuvue® Moist contact lenses. The diameter and base curve of the lens fall within the US FDA cleared range of VISTAKON® (etafilcon A) contact lenses parameters. 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 investigational test article is for daily disposable wear for correcting myopia and controlling the progression of myopia. During this study, each subject will wear the test article binocularly at the second visit of the study only, for no more than 3 hours. This is a non-dispensing study; no study lenses will be dispensed to the subjects to wear outside the study site.

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 RMY-100 lenses refer to the latest version of the Investigator's Brochure for the RMY-100 lens.[26]

1.4. Summary of Known Risks and Benefits to Human Subjects

The benefit of controlling myopia progression is considered to be substantial[27] as the prevalence and incidence of myopia has been increasing substantially over the past few decades.[28-30] 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.[31]

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 the RMY-100 lens, such as potential sub-optimal visual performances and long-term physiological and/or neurological impact. The assessment regarding the above identified risks concluded that the risks associated with the RMY-100 lens are expected to be the same as those normally attributed to the wear of soft hydrophilic contact lenses on a daily wear basis. In addition, 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. Due to the unique optical design of the RMY-100 lens, 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, if lenses are to be dispensed for wear at home, specific criteria regarding visual acuity and subjective vision acceptance will be imposed so that no study lenses will be dispensed and the subject will be discontinued from the study unless these vision criteria are met. Because the current study is a non-dispensing study with the maximum lens exposure time for each subject being limited to less than 3 hours, risks associated with vision as a result of the unique optical design of the RMY-100 lens are minimal and potential long-term physiological/neurological impact are not applicable to this study.

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. Per the clinical study risk assessment, this study is considered a non-significant risk study based 1) the study is a non-dispensing study; and 2) although the investigational lens is optically designed for the intent of myopia control, the lens will be used in this study for myopia correction only with limited wear time (i.e., subjects will wear study lenses for less than 3 hours).

For the most comprehensive risk and benefit information regarding RMY-100 lenses refer to the latest version of the Investigator's Brochure for the RMY-100 lens.[26]

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 the RMY-100 lens.[26]

To date, there have been a total of five clinical studies conducted during the development of the RMY-100 lenses.[25,32-35] Among these studies, four [redacted] were to evaluated the physiology responses and vision, comfort, handling and fit performances of the RMY-100 to ensure that the lens has satisfactory performances to be further evaluated in the long-term (up to 2 years), myopia control clinical trial in a pediatric population [redacted]. There were no serious, significant, or unanticipated ocular adverse events and no loss of best corrected visual acuity with wear of study test articles reported in these past clinical studies. For detailed information regarding prior clinical data refer to the latest version of the Investigator's Brochure for the RMY-100 lens.[26]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

The objective of the study is to evaluate the on-eye optical performances of the RMY-100 lenses and comparing to the optical characteristics of eyes undergone orthokeratology treatment and with spectacle lens correction.

This is an exploratory study for providing information towards understanding the difference in optical impact between RMY-100 lens and orthokeratology and the mechanisms of orthokeratology for controlling myopia progression.

Primary Objective:
The primary objective of the study is to evaluate the on-eye optical performances of the RMY-100 lens, and compare with eyes treated with orthokeratology.

Secondary Objective:
The secondary objective of the study is to compare the on-eye optical performances of the RMY-100 lens with eyes wearing sphero-cylindrical correction in the spectacle trial frame.

2.2. Endpoints

Primary Endpoint
The primary endpoint of this study is wavefront aberrations measured at 4-meter distance (0.25 D target vergence) and near (25 cm with 4 D target vergence).

Secondary Endpoint
The secondary endpoint of this study is Off-axis refraction at both temporal and nasal fields of retina at ±10°, ±20°, ±30° with targets at 4 meters and ±30° only with targets at 25 cm.

Other Exploratory Endpoints and observations include:

- Corneal and test article on-eye topography
- Accommodative response with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D
- Slit lamp findings
- LogMAR visual acuity under HLHC, LLHC, and HLLC conditions
- Lens fit assessment
- Subjective vision assessment (CLUE Vision)

2.3. Hypotheses

Primary Hypotheses:

1. After the 10-minute lens settling period, distance (4 meters) spherical aberration (Z_4^0) measured with RMY-100 on the eye will be similar or larger than that measured from the post-OK eyes.

2. After the 10-minute lens settling period, near (25 cm) spherical aberration (Z_4^0) measured with RMY-100 on the eye will be similar or larger than that measured from the post-OK eyes.

Secondary Hypotheses:

1. After the 10-minute lens settling period, distance (4 m) off-axis refraction at ±30° retinal eccentricity measured with RMY-100 on the eye will be similar or larger than that measured from the post-OK eyes.

2. After the 10-minute lens settling period, near (25 cm) off-axis refraction at ±30° retinal eccentricity measured with RMY-100 on the eye will be similar or larger than that measured from the post-OK eyes.

Other Hypotheses:

1. After the 10-minute lens settling period, the slope of accommodative response measured with RMY-100 on the eye will be similar as that measured from the post-OK eyes.

2. After the 10-minute lens settling period, distance (4 m) and near (25 cm) wavefront aberrations, off-axis refractions within ±30° retinal eccentricity, and the slope of accommodative response measured with RMY-100 on the eye will be different from that measured with spectacle trial lenses on eye.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Healthy male and female subjects between ages of 7 and 25 years (inclusive) with best sphere-refraction between -1.00 D to -5.00 D (inclusive) and 1.00 D or less astigmatism will be recruited. Subjects must have healthy eyes and satisfy all the eligibility criteria at enrollment. There are no restrictions as to gender or race/ethnicity. Subjects may be neophytes or current soft contact lens wearers.

3.2. Inclusion Criteria

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

Inclusion Criteria after Screening:

1. Pediatric subjects (<18 years old) 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. Adult subjects (≥18 years old) and parent(s) or legal guardian(s) of pediatric subjects 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 25 years of age (inclusive).
5. Have normal eyes (i.e., no ocular medications or infections of any type).

Below inclusion criterion is for subjects to be enrolled to the Control group only:

6. Are existing orthokeratology patients whose current treatment has been stabilized for at least 1 months and with complete pre-treatment record, e.g., spherocylindrical refraction and corneal topography. Pre-treatment wavefront aberration measures are preferred by not required.

Inclusion Criteria after Baseline (apply to subjects to be enrolled to the Test group and to Control group subjects regarding their pre-OK treatment):

7. Vertex-corrected distance subjective best-sphere refraction must be between -1.00 D and -5.00 D (inclusive) in each eye.
8. Cylindrical refraction must be 1.00 D or less in each eye, by subjective sphero-cylindrical refraction.
9. Have sphero-cylindrical best-corrected visual acuity of 20/25 or better in each eye.

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 diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study.
3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear and/or participation in the study.
4. Any current use of ocular topical medication (occasional use of re-wetting drops is allowed).
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 7 days prior to study enrollment.
7. Employee or their children/relatives of investigational clinic (e.g., Investigator, Coordinator, Technician).

Below exclusion criteria are for subjects to be enrolled to the Test group only

8. Current or recent (within 30 days from enrollment) rigid lens wearers.
9. History of orthokeratology treatment.

Exclusion Criteria after Baseline:

10. 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.
11. Any Grade 3 or greater slit lamp findings (eg, edema, corneal neovascularization, corneal staining, tarsal abnormalities, and conjunctival injection) on the FDA scale.
12. Any ocular abnormality that is contraindicated contact lens wear.
13. Any corneal scar within central 5mm
14. Binocular vision abnormality, intermittent strabismus or strabismus.

Below exclusion criteria are for subjects to be enrolled to the Test group only

15. Any corneal distortion resulting from ocular diseases or previous hard or rigid gas permeable contact lens wear.

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.

In addition, the Control group subjects will be recruited through referrals from the university optometry clinic and independent Eye Care Professionals (ECPs) who will identify potential

subjects by reviewing the case history of existing orthokeratology treated patients in their practices.

It is anticipated that the age distribution is likely to be different between the two study groups, e.g., orthokeratology patients may be of younger age than soft contact lens patients. Therefore, the study site is encouraged to recruit subjects in each study group with similar age, gender and baseline refraction distributions. Specifically, the site will aim to enroll approximately 15 subjects in the Test group who match the subjects enrolled in the Control group with regard to age, gender and baseline refraction as much as possible. The clinical site is encouraged to enroll subjects between 7 and 15 years of age, if available within the enrollment timeline.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is a two-arm parallel, non-masked, bilateral, non-dispensing study with one Test arm and one concurrent, non-randomized Control arm.

For subjects enrolled in the Test arm, investigational test articles will be bilaterally fitted to the subject's eyes. Concurrently, a smaller sample of subjects who are established orthokeratology lens wearers will be enrolled to Control arm. Endpoint measures will be collected over one eye only (Test arm: OD only; Control arm: better OK fitted eyes, eg, better centration and better myopia correction outcome, etc., based on the investigator's judgement. If both eyes are treated equally well, choose OD).

For subjects in the Test arm, there will be a total of 2 visits:
Visit 1: Screening, baseline endpoint measures with bare eye/spectacle trial lenses
Visit 2: Lens fitting, endpoint measures over the study lenses and final evaluation.

For the Control arm, the investigators will pre-identify subjects through reviewing the case history of existing orthokeratology treated patients. Only subjects with complete pre-treatment record, e.g., spherocylindrical refraction and corneal topography will be invited to participate in the study.

For subjects in the Control arm, there will be a total of 1 visit:
Visit 1: Screening, baseline and endpoint measures over the selected eyes.

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

4.2. Study Design Rationale

The study was designed to evaluate the on-eye optical performance of the RMY-100 lens. The RMY-100 lens was designed to have an optical profile that simulates the optical effect of an orthokeratology lens on the eye. As such optical characteristics and effects of RMY-100 lens on the eye, including wavefront aberrations, especially spherical aberration, lens-on-eye

topography, accommodative responses and off-axis refraction, will be measured and compared with those measured from eyes of patients of current orthokeratology treatment.
Due to the two populations to be investigated are different, ie., non-OK patients that will be fit with soft contact lenses and current over-night OK patients with no vison correction during the day, the study is designed to be a non-randomized, two-arm parallel, non-masked study.

4.3. Enrollment Target and Study Duration

Approximately 25 subjects will be enrolled in the Test arm of the study with a minimum of 20 subjects targeted to complete the study.

Approximately 20 subjects will be enrolled in the Control arm of the study with a minimum of 15 subjects targeted to complete the study.

The study will be conducted at one clinical site.

The total duration of the study enrollment will be approximately 10 weeks, unless otherwise approved by the Sponsor. The total duration of the study is expected to be 14 weeks (including the enrollment period).

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

This is a non-randomized study. The study lens (RMY-100) will be fit bilaterally to the Test group subjects at the second visit of the study only.

5.2. Masking

This is a non-masked study.

5.3. Procedures for Maintaining and Breaking the Masking

Not applicable.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

	Test
Name	RMY-100
Manufacturer	JJVC
[redacted]	[redacted]
Lens Material	Etafilcon A
Nominal Base Curve @ 22ºC	7.9 mm
Nominal Diameter @ 22ºC	13.8 mm
Nominal Distance Powers (D)	-1.00 to -5.50 D in 0.25D step
Nominal Cylinder Powers (D) and Axes	N/A
Nominal ADD Powers (D)	N/A
Water Content	58 – 61%
Oxygen Permeability (Dk), Boundary corrected, Edge corrected	28.0
Modality in Current Study	Daily wear
Replacement Frequency	Daily disposable
Packaging Form (vial, blister, etc.)	Blister Pack

Per the study design, each subject in the Test group will likely use at least one (up to 4) lens per eye for lens fitting (including up to 3 lens power modifications). Therefore, it is estimated that up to 8 lenses per subject for up to 25 subjects, which is approximately 200 lenses, will be used for the study. The study lens will be worn for up to 3 hours for each subject in the Test group.

There will be no test article fit to the subjects in the Control group.

6.2. Ancillary Supplies/Products

This is a non-dispensing study with test articles worn during the study visit only. No lens care product will be used.

6.3. Administration of Test Articles

Test articles will be fitted to Test group subjects meeting all eligibility requirements during the study visit at the clinical site. No study lenses will be given to Test group subjects to wear out of the office or to the Control group subjects. 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 have an investigational primary label with the appropriate country-specific language. The test

articles will be in 6-pack cartons with the appropriate country-specific language on the secondary packaging.
The sample study labels are shown below:

Primary Package	Secondary Package Label
	

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

No samples will be collected as part of the study procedures.

When possible, any 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, 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.
2. The number and reason for unplanned replacements.

Following final reconciliation of test articles by the monitor, the Investigator or monitor will return all unused test articles to JJVC.

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

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

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 2: Time and Events

Visit Information	Visit 1 Screening, Baseline	Visit 2 Len Fitting
Time Point	Day 0	1 to 10 days after Visit 1
Estimated Visit Duration	3 hours	3 hours
Statement of Informed Consent	x	
Demographics	x	
Medical History/Concomitant Medications	x	x
Habitual Contact Lens Information	x	
Inclusion/Exclusion Criteria	x	
Subjective Sphero-Cylindrical Refraction with Best-corrected Distance Visual Acuity	x	x
Subjective Best-sphere Refraction	x	x
Subjective Best-sphere Over-refraction		x
Slit Lamp Classification	x	x
Lens Assignment		x
Lens Insertion & Settling		x
Lens Fit Assessment		x
Lens-on-Eye Visual Acuity		x
Lens Power Modification (if applicable)		x
ETDRS logMAR Distance VA (HLHC, HLLC and LLHC)	x	x
CLUE Vision Questionnaires (Baseline and Post Lens Fit)	x	x
Wavefront Aberrometry (Distance and Near)	x	x
Corneal and/or Lens-on-Eye Topography	x	x
Accommodative Response	x	x

Visit Information	Visit 1 Screening, Baseline	Visit 2 Len Fitting
Time Point	Day 0	1 to 10 days after Visit 1
Estimated Visit Duration	3 hours	3 hours
Off-axis Refraction	x	x
Study Completion (Final Evaluation)		x

7.2. Detailed Study Procedures

VISIT 1

Subjects should report to the initial visit wearing their habitual correction lenses, if available

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent & Children's Assent	Each adult subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. For pediatric subjects (<18 years old), each subject's parent or legal guardian must read, understand, and sign the Statement of Informed Consent, and each subject must read, 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 must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's date of birth, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.4	Habitual Vision Correction Information	Questions regarding the type of the subject's habitual vision correction (for the Test group subjects) and past mode of vision correction prior to orthokeratology treatment (for the Control group): • No correction • Spectacle lenses	

Visit 1: Screening			
Step	Procedure	Details	[redacted]
		• Soft contact lens • Rigid contact lens (other than orthokeratology) • Orthokeratology • Other, specify	

1.5	Habitual Soft Contact Lenses and Brand name of the current Orthokeratology Lenses	Questions regarding the subject's habitual soft contact lens type and parameters (Test group) and the Brand name of the current orthokeratology lenses (Control group).	
1.6	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]
1.7	Subjective Sphero-cylindrical Refraction	The investigator will complete subjective (spherocylindrical) refraction and record the resultant distance visual acuity (OD, OS and OU) to the nearest letter. **Note**: for the Control group subjects, the subject's latest sphero-cylindrical refraction prior to orthokeratology treatment will also be recorded in the CRF.	[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 best corrected 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.	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		However, if the subject's response changes from "red" to "green" with only a 0.25 D 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.	
1.9	Slit Lamp Findings	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are Grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to determine eligibility. If discontinued a final examination must be completed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
1.10	Eligibility after Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible. **Note**: If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.	
1.11	Corneal Topography	Collect 3 corneal topography maps over the subject's bare eye. For Test group subjects: OD only For Control group subjects: better OK treated eye **Note**: For subjects in the Control group, their latest corneal topography data prior to orthokeratology treatment will also be collected, if available.	[redacted]
1.12	Wavefront Aberrometry	Collect wavefront aberration measures 3 times under the following conditions: For Test group subjects (OD only): • Bare eye with Distance target (4m)	[redacted]

		• With sphero-cylindrical correction in the spectacle trial frame with Distance target (4 m) • With sphero-cylindrical correction in the spectacle trial frame with Near target (25 cm) <u>For Control group subjects (better OK treated eye)</u>: • Bare eye with Distance target (4 m) • Bare eye with Near target (25 cm) **<u>Note</u>**: For subjects in the Control group, their latest wavefront aberration data prior to orthokeratology treatment will also be collected, if available.	

1.13	Accommodative Response	Collect sphero-cylindrical auto-refraction with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D, respectively. Three repeated measurements per each target vergence: <u>For Test group subjects (OD only)</u>: • With sphero-cylindrical correction in the spectacle trial frame over the eye <u>For Control group subjects (better OK treated eye)</u>: • Bare eye	[redacted]
1.14	Off-axis Refraction	Collect off-axis refraction with an open-field autorefractor under the following conditions, 3 repeated measures per each condition: • With distance targets (4 m) at field angles of 0°, ±10°, ±20°, and ±30°; • With near targets (25 cm) at field angles of ±30° only. <u>For Test group subjects (OD only)</u>: • Bare Eye, with Distance target (4 m): 0°, ±10°, ±20°, and ±30° • With sphero-cylindrical correction in the spectacle trial frame over the eye, with Distance target (4 m): ±10°, ±20°, and ±30° • With sphero-cylindrical correction in the spectacle trial frame over the eye, with Near target (25 cm): ±30° <u>For Control group subjects (better OK treated eye)</u>:	[redacted]

		• Bare Eye with Distance target (4m): ±10°, ±20°, and ±30° • Bare Eye with Near target (25cm): ±30°	
1.15	Distance ETDRS LogMAR Visual Acuity	Perform monocular distance ETDRS LogMAR visual acuity test at a 4-meter distance under the following conditions with one measurement per condition. 1. Dim illumination (e.g., <2.5 lux), low luminance, with high contrast charts (LLHC); 2. Bright illumination (e.g., >400 lux), high luminance with low contrast charts (HLLC); 3. Bright illumination (eg, >400 lux), high luminance with high contrast charts (HLHC); <u>For Test group subjects (OD only)</u>: • VA will be measured with spherical refraction in the trial fame. <u>For Control subjects (better OK treated eye)</u>: • VA will be measured with Bare Eye. The Precision Vision 4-meter high and low contrast ETDRS charts (HC1, LC1 and HC2) will be used.	[redacted]
1.16	Baseline CLUE Vision Questionnaire	Ask the subject to complete the CLUE Vision questionnaire regarding current mode of correction.	[redacted]
1.17	Exit VA	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

VISIT 2 (Test Group Only)

Subjects in the Test group should report to the visit wearing their habitual correction lenses, if available, 1 to 10 days after Visit 1.

Visit 2			
Step	Procedure	Details	[redacted]
2.1	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.	

Visit 2			
Step	Procedure	Details	[redacted]
2.2	Entrance Visual Acuity	Record the distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]
2.3	Subjective Best-sphere Refraction	Perform subjective best-sphere refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity 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 0.25 D 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]
2.4	Slit Lamp Findings	FDA Slit Lamp Classification Scale will be used to grade the findings. If any of these slit lamp findings are Grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to determine continuance. If discontinued a final examination must be completed. Adverse events shall be documented and followed for significant slit lamp findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
2.5	Continuance	Determine is the subject is eligible to continue with the current study visit.	
2.6	Bare Eye Corneal Topography	Collect 3 corneal topography maps over the subject's bare eye (OD only).	[redacted]
2.7	Bare Eye Wavefront Aberrometry	Collect wavefront aberration measures 3 times over the subject's bare eye with Distance (4 m) and Near (25 cm) targets (OD only).	[redacted]

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
2.8	Lens Selection	Select the contact lens power based on subjective best sphere refraction.	
2.9	Lens Insertion	The subject or the investigator will 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.	
2.10	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
2.11	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]
2.12	Over the Lens Distance and Near VA	Record the subject's distance and near visual acuity to the nearest letter with the study lenses (OD, OS and OU).	[redacted]
2.13	Subjective Best-Sphere Over-refraction	Perform subjective best-sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU). **Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct.	[redacted]

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
		However, if the subject's response changes from "red" to "green" with only a 0.25 D 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.	
2.14	Lens Power Modification (if applicable)	The subject's best sphere over-refraction **cannot** be positive (>0.00 D) or, in the case of a myopic over-refraction, it **cannot** be -0.50 D or higher (≤-0.50 D). 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 -0.25 D 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 -0.25 D 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 -0.25 D 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 -0.50 D or more, increase the lens power by -0.25 D each step till the subject's best sphere over refraction is -0.25 D or plano based on the above lens power modification rule #2 - #4.	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
		For each study contact lens power modification, repeat steps 2.8 – 2.14. Up to three power modifications are allowed.	
2.15	LOE Corneal Topography	Collect 3 corneal topography maps with the study lens on-eye (OD only).	[redacted]
2.16	LOE Wavefront Aberrometry	Collect wavefront aberration measures 3 times with the study lens on-eye with Distance (4 m) and Near (25 cm) targets (OD only):	[redacted]
2.17	LOE Accommodative Response	Collect sphero-cylindrical auto-refraction 3 times with the study lens on-eye (OD only) with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D, respectively.	[redacted]
2.18	LOE Off-axis Refraction	Collect off-axis refraction with the study lens on-eye with an open-field autorefractor (OD only) under the following conditions, 3 repeated measures per each condition: • With distance targets (4 m) at field angles of ±10°, ±20°, and ±30°; • With near targets (25 cm) at field angles of ±30° only.	[redacted]
2.19	LOE Distance ETDRS LogMAR Visual Acuity	Perform monocular distance ETDRS LogMAR visual acuity test at a 4-meter distance with the subject wearing the study lenses under the following conditions, with one measurement per condition (OD only): • Dim illumination (e.g., <2.5 lux), low luminance, with high contrast charts (LLHC); • Bright illumination (e.g., >400 lux), high luminance with low contrast charts (HLLC); • Bright illumination (eg, >400 lux), high luminance with high contrast charts (HLHC); The Precision Vision 4-meter high and low contrast ETDRS charts (HC1, LC1 and HC2) will be used.	[redacted]
2.20	Visual Experience	Take the subjects to a waiting area where they can look out the window at distant objects to experience distance visual quality and provide the subjects reading materials to experience near visual quality under bright and dim lighting conditions.	

Visit 2: Lens Fitting			
Step	Procedure	Details	[redacted]
2.21	CLUE Vision Questionnaire	Ask the subject to complete the CLUE Vision questionnaire regarding the study lenses.	[redacted]
2.22	Lens Removal	Remove and discard the study 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 successfully. 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	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]

7.3. Unscheduled Visits

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

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

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

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

The following information will be collected during an unscheduled visit.

Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit	
U.2	Change of Medical History (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.	
U.3	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
U.4	Subjective Sphero-cylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU).	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. Adverse events shall be documented and followed for significant slit lamp findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
U.6	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

7.4. Laboratory Procedures

Not Applicable.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent;
- 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
- Subject lost to follow-up
- Subject no longer meets eligibility criteria (e.g., the subject becomes pregnant)
- Subject develops significant or serious adverse events, and unable to complete the scheduled visit
- 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)

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

An additional subject will be enrolled if a subject discontinues from the study prematurely 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: any medication that the investigator feels would be contraindicated in contact lens wear.

Concomitant therapies that are disallowed include: any therapies that the investigator feels 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."[2]

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 (eg, 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 - eg 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."[2]

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 – ie, 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, eg 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, eg, 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, eg, concomitant treatment of concomitant disease(s). The relationship in time is very suggestive, eg, 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 (eg, size, location, and depth, etc.)
- Date the clinical site was notified
- Date and time of onset
- Date and time of resolution
- Adverse event classification, severity, and relationship to test articles, as applicable
- Treatment regimen instituted, including concomitant medications prescribed, in accordance with applicable licensing requirements
- Any referral to another health care provider if needed

- Outcome, ocular damage (if any)
- Likely etiology
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event

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

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

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

13.4. Reporting Adverse Events

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to

their requirements (Section 13.4.2). The report will comment whether or not the adverse event was considered to be related to the test article, study treatment or study procedures.

13.4.1. Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events

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

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

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

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

Unanticipated (Serious) Adverse Device Effect (UADE)

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

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

Non-Serious Adverse Events

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

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

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

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

13.4.3. Event of Special Interest

None.

13.5. Reporting of Pregnancy

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

14. STATISTICAL METHODS

14.1. General Considerations

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.

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 all visits 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%. Due to the exploratory nature of the study, adjustment for multiple comparison will not be performed.

14.5. Primary Analysis

Primary efficacy analysis:
Distance and near wavefront aberration, specifically, spherical aberration (Z_4^0), will be analyzed using a linear mixed model. Each model will include the experimental design factors: treatment, distance and treatment by distance interaction and subject as random effect. Other baseline characteristics known of importance such as age and gender will be included as fixed covariates when appropriate. Kenward and Roger method will be used for the calculation of the denominator of degrees of freedom.[36]

Comparisons between the treatment groups will be carried out using 95% confidence intervals constructed of least-square means (LSM) differences (RMY-100 minus OK) from the linear mixed models at each distance. Statistical difference will be concluded in the lower limit is greater than 0 or the upper limit is less than 0.

14.6. Secondary Analysis

Secondary efficacy analysis:
Off-axis refraction at ±30° retinal eccentricities with targets at both distance (4 m) and near (25 cm) will be analyzed using a linear mixed model. Each model will include the experimental design factors: treatment, distance and treatment by distance interaction and subject as random effect. Other baseline characteristics known of importance such as age and gender will be included as fixed covariates when appropriate. Kenward and Roger method will be used for the calculation of the denominator of degrees of freedom.[36]

Comparisons between the treatment groups will be carried out using 95% confidence intervals constructed of least-square means (LSM) differences (RMY-100 minus OK) from the linear

mixed models at each distance. Statistical difference will be concluded in the lower limit is greater than 0 or the upper limit is less than 0.

14.7. Other Exploratory Analyses

Summary statistical analysis will be provided for the following other observations:

- Corneal and test article on-eye topography
- Accommodative response with target vergence of 0.25 D, 1 D, 2 D, 3 D and 4 D
- Slit lamp findings (OD, OS)
- LogMAR visual acuity under HLHC, LLHC, and HLLC conditions (OD, OU)
- Lens fit assessment (OD, OS)
- Subjective vision assessment (CLUE Vision)

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 5 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: Exported WAM sphero-cylindrical refraction measurements in the format of Excel files, Medmont corneal topography data in the format of raw data files (e.g., (.axl, .tgl, .dst, .hgt) and COAS wavefront aberration data in the format of raw data files (e.g., .DVB, .F8 and .WFB).

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.[2]

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

18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP),[1] 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),[1] and applicable regulatory requirements.

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

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

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

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

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

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

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

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

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

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

18.4. Informed Consent

Each subject must give written consent or assent and parental consent for minors according to local requirements after the nature of the study has been fully explained. The consent form for adults and assent and parental consent for minors must be signed before performance of any study-related activity. The consent form for adults and assent and parental consent for minors that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent for adults and assent and parental consent for minors is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[1] and ISO 14155[2] 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 subjects and their parents or guardians (if applicable) the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects and parents or guardians (if applicable) will be informed that their participation is voluntary and that they may withdraw consent to participate at any time.

The subject and parent or guardian (if applicable) will be given sufficient time to read the informed consent form and the opportunity to ask questions. After this explanation and before entry into the study, consent and assent (if applicable) should be appropriately recorded by means of the subject's dated signature on the consent form, or the minor subject's signature on the assent and the parent or guardian signature on the consent form. After having obtained the signed assent/consent form(s), a copy will be provided to the subject and parent or guardian (if applicable).

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 (eg, 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[37] 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,[1] 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[1] and ISO 14155[2] GCP guidance 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 based on the following:

This clinical study aims to understand the fundamental mechanisms of optical interventions for myopia control. The results of this study are expected to be published in peer-reviewed journals. In addition, this study will be conducted in Canada, clinicaltrial.gov registration is required by Health Canada.

22. REFERENCES

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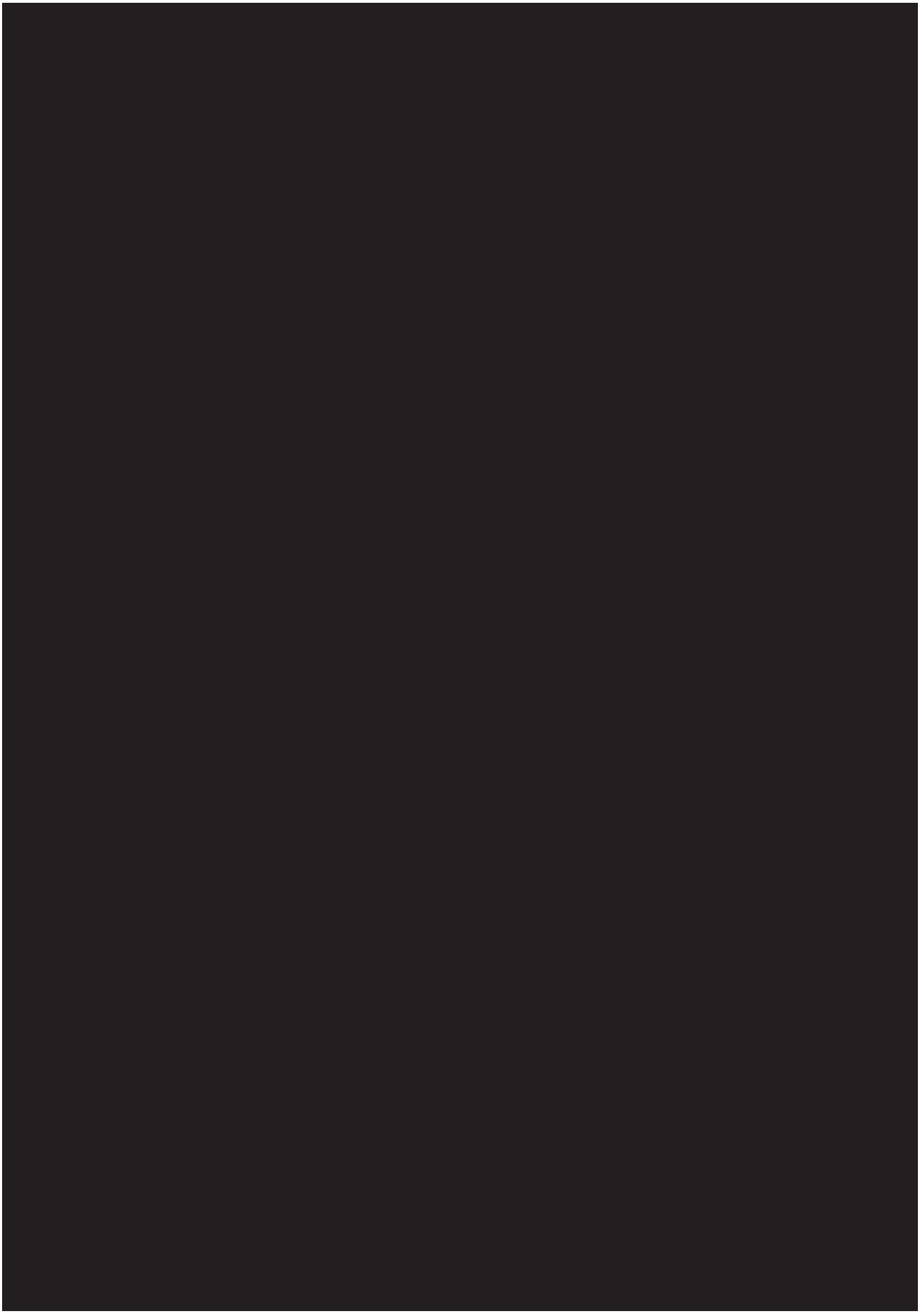
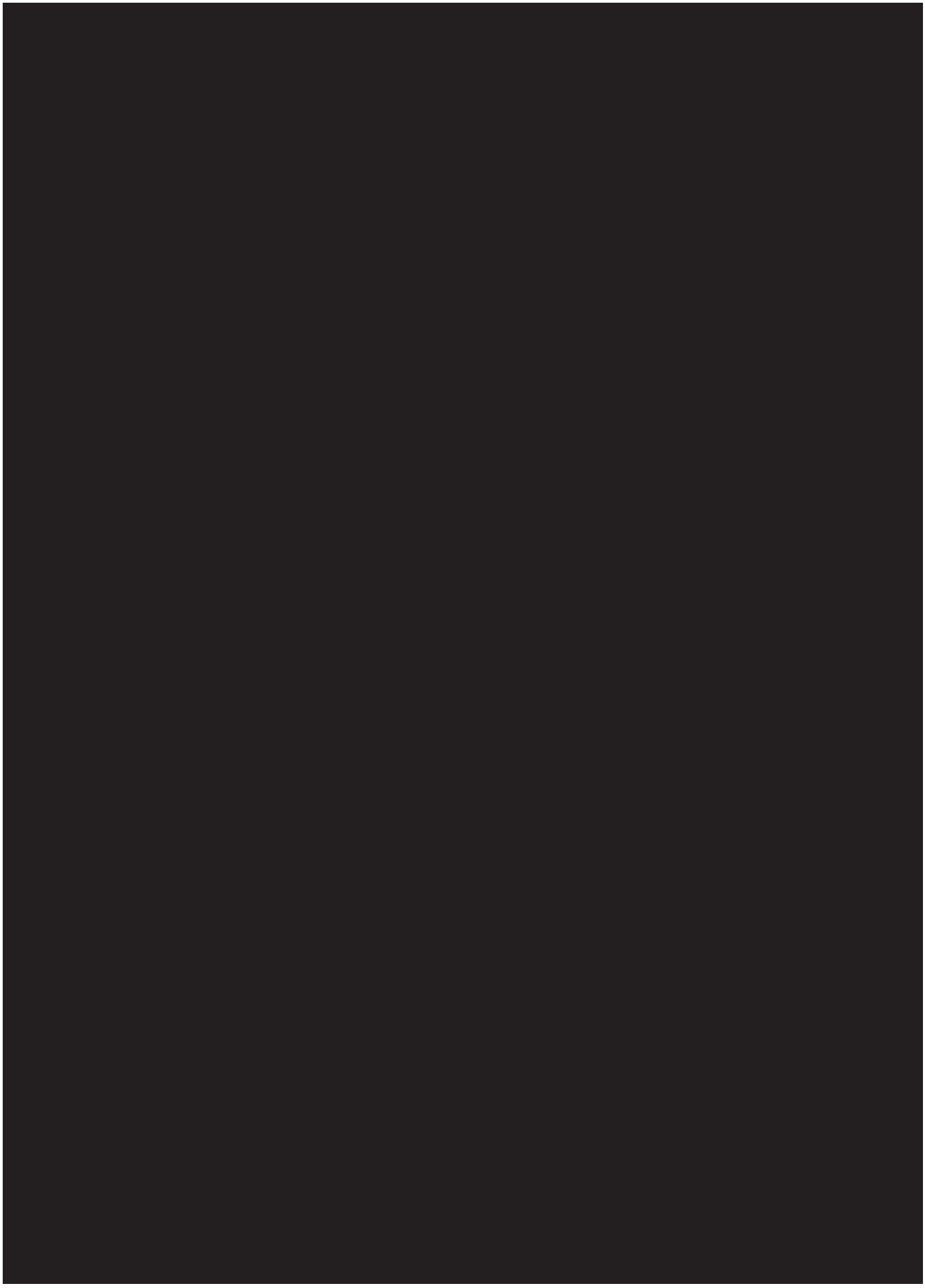
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)





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 to study participants and their parents separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not Applicable

APPENDIX D: [redacted]

- [redacted] Lens Fitting Characteristics
- [redacted] Determination of Distance Spherocylindrical Refractions
- [redacted] Biomicroscopy Scale
- [redacted] Distance and Near Visual Acuity Evaluation
- [redacted] Distance LogMAR Visual Acuity Measurement Procedure
- [redacted] Measurement of COAS Wavefront Aberrations
- [redacted] Patient Reported Outcomes
- [redacted] Visual Acuity Chart Luminance and Room Illumination Testing
- [redacted] Topography Measurement Using Medmont E300 Corneal Topographer
- [redacted] Using an Open-field Autorefractor (WAM-5500) for Measuring Accommodative Response and Off-axis Refraction

[redacted] LENS FITTING CHARACTERISTICS

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Lens Fitting Characteristics

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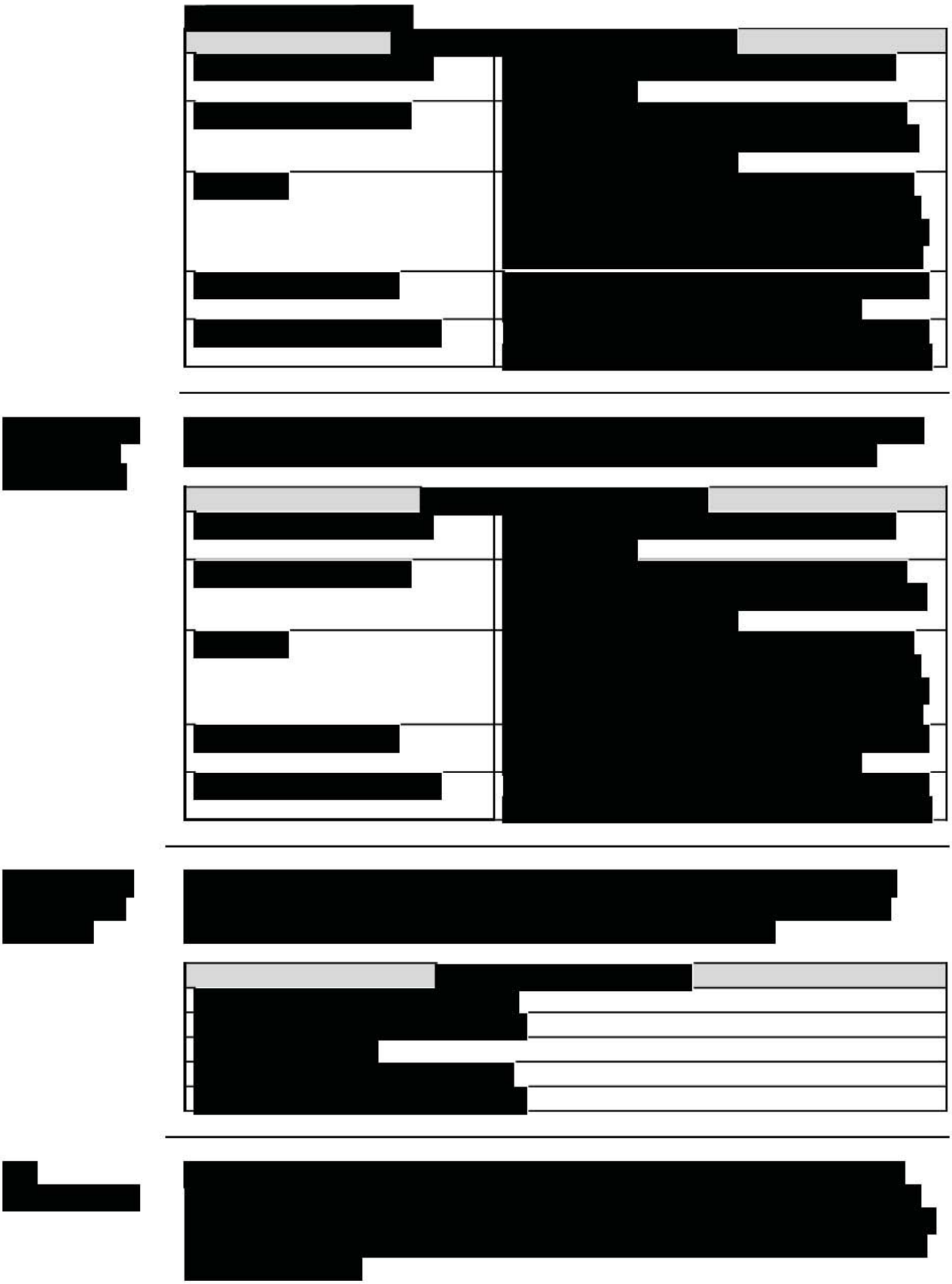

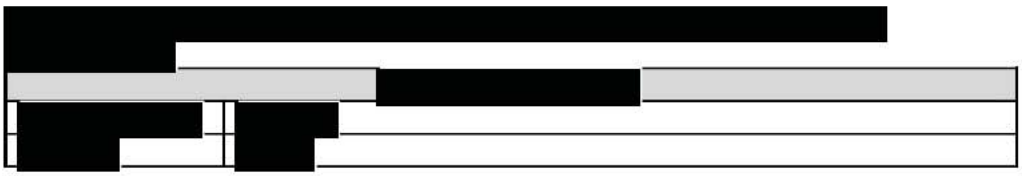

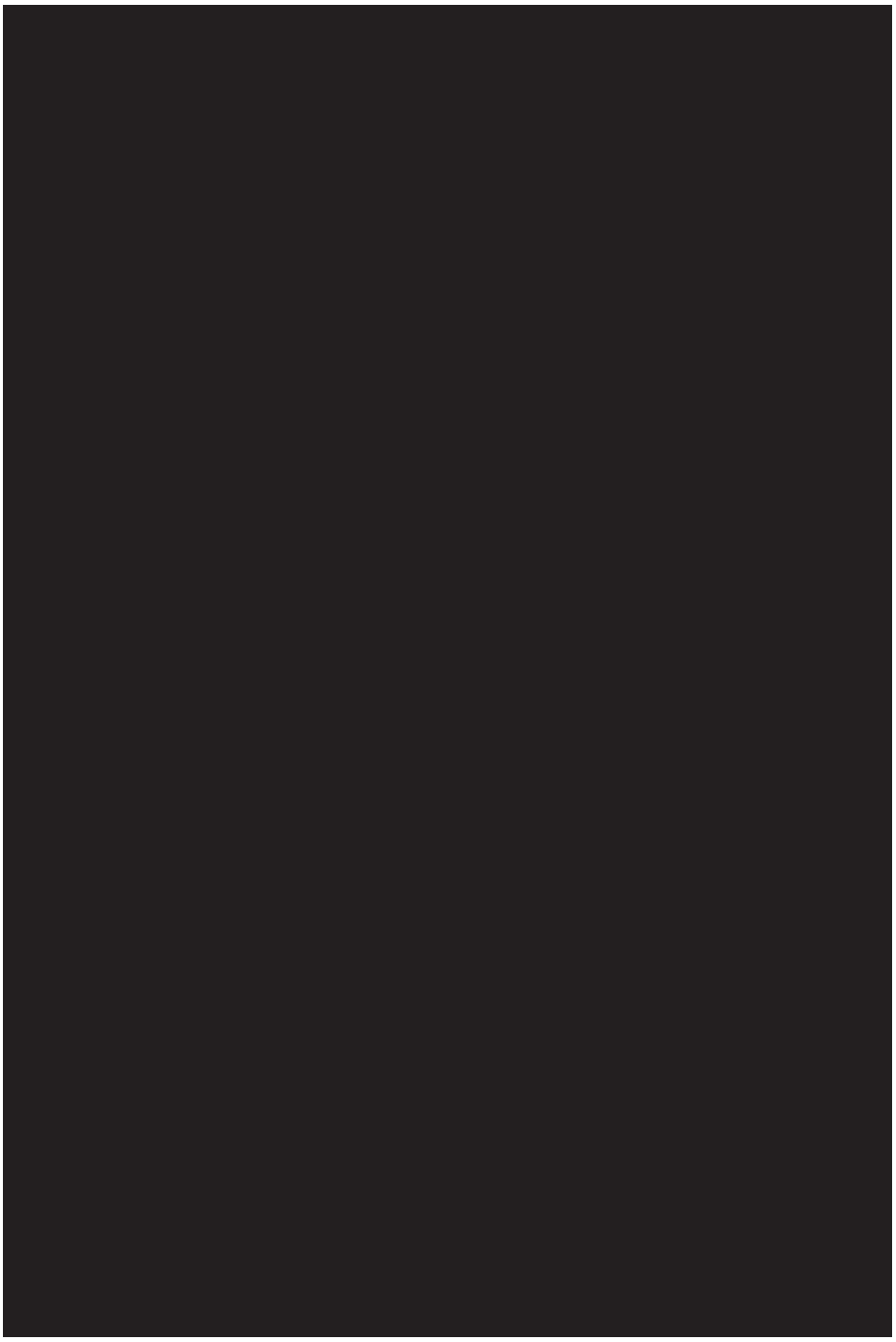

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted] **Determination of Distance Spherocylindrical Refractions**

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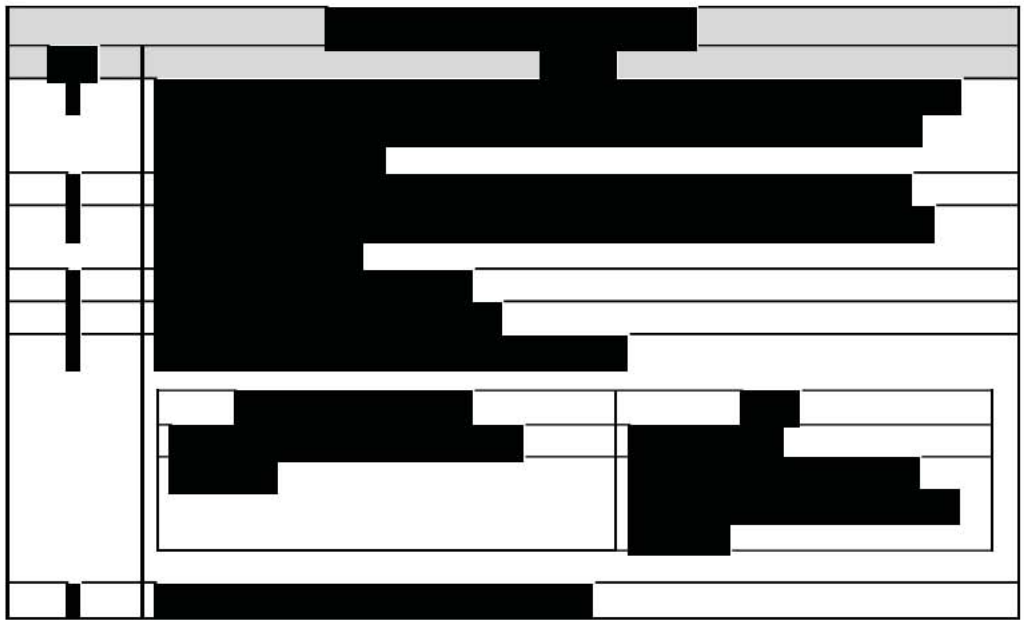

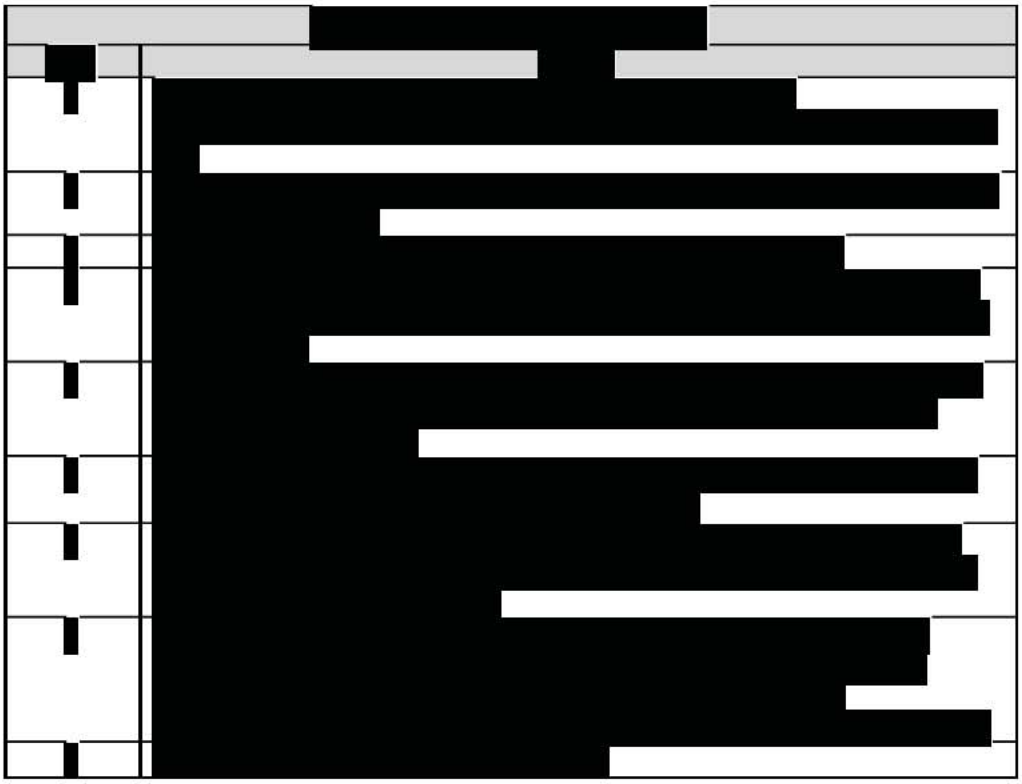

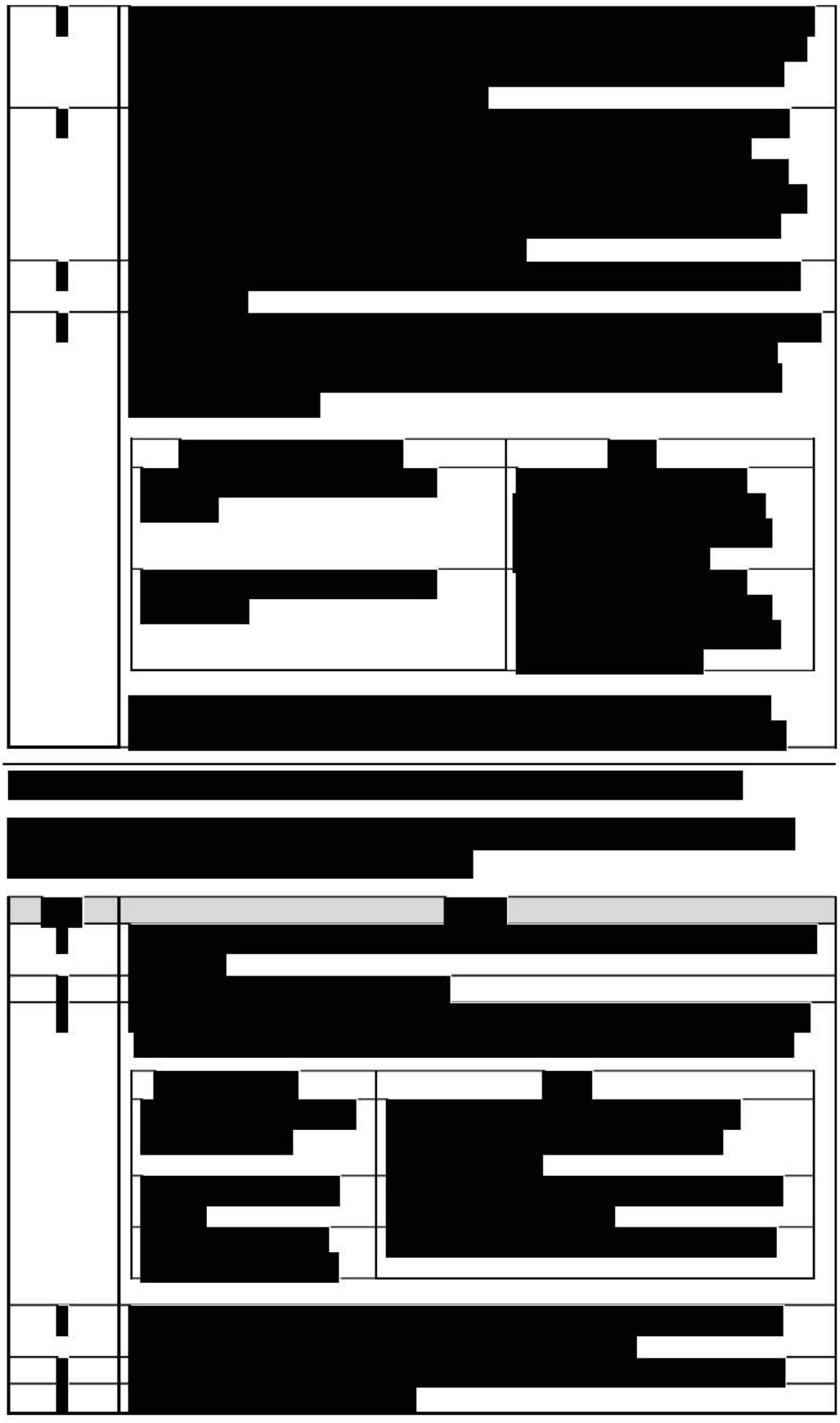

[redacted] BIOMICROSCOPY SCALE

[redacted] **Biomicroscopy Scale**

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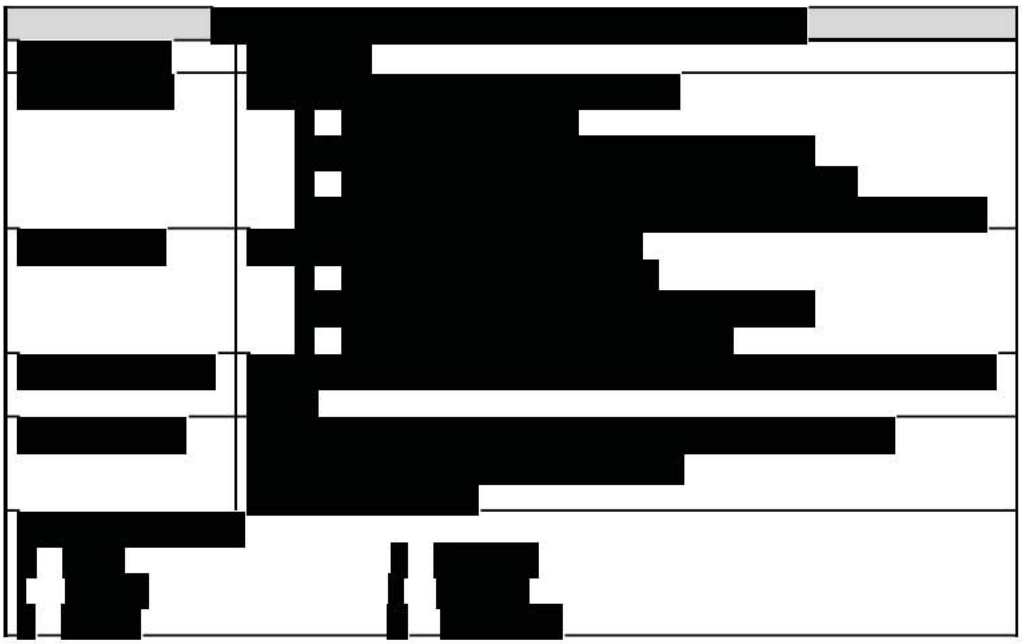

[redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION

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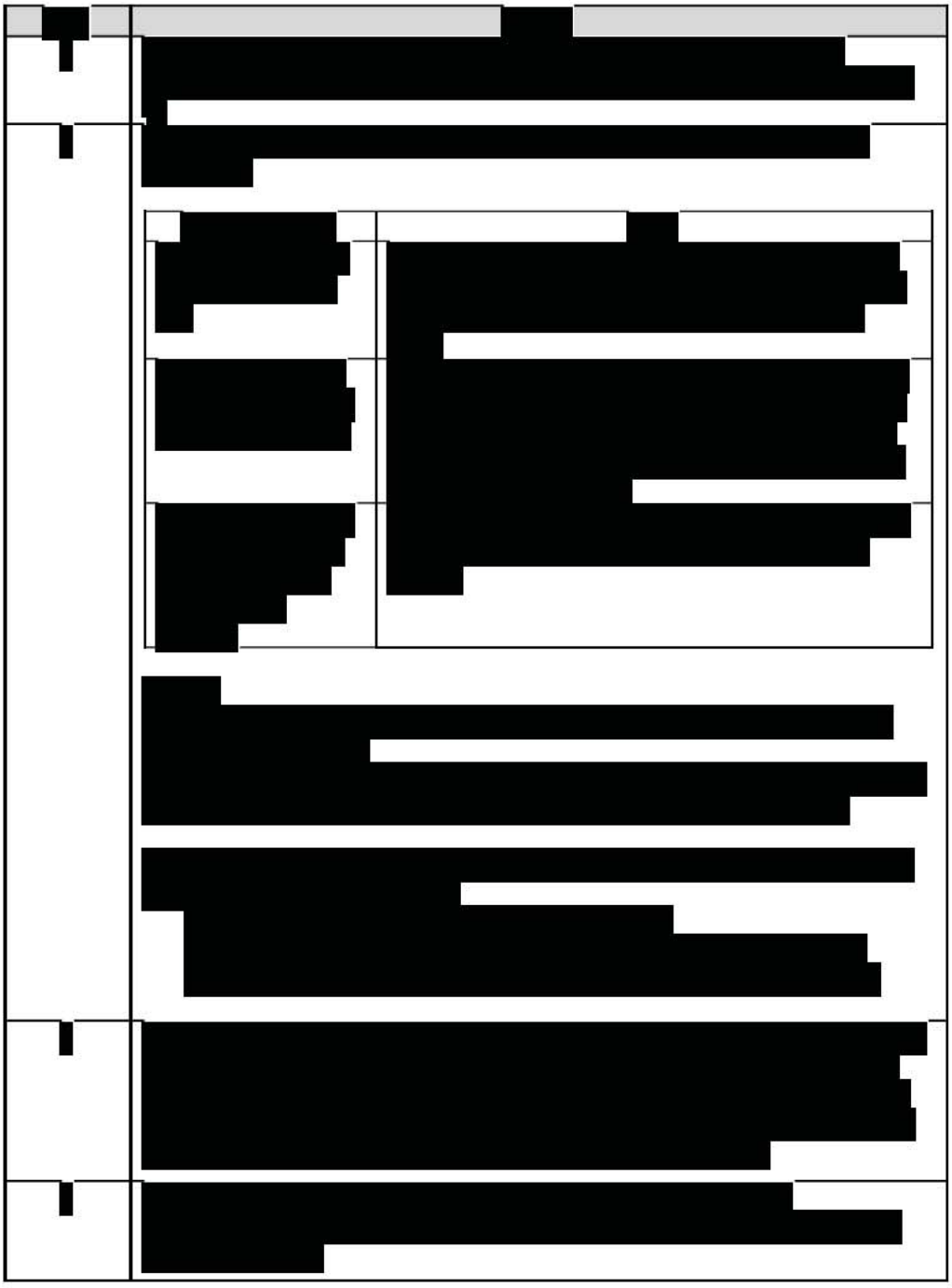

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Measurement of COAS Wavefront Aberrations

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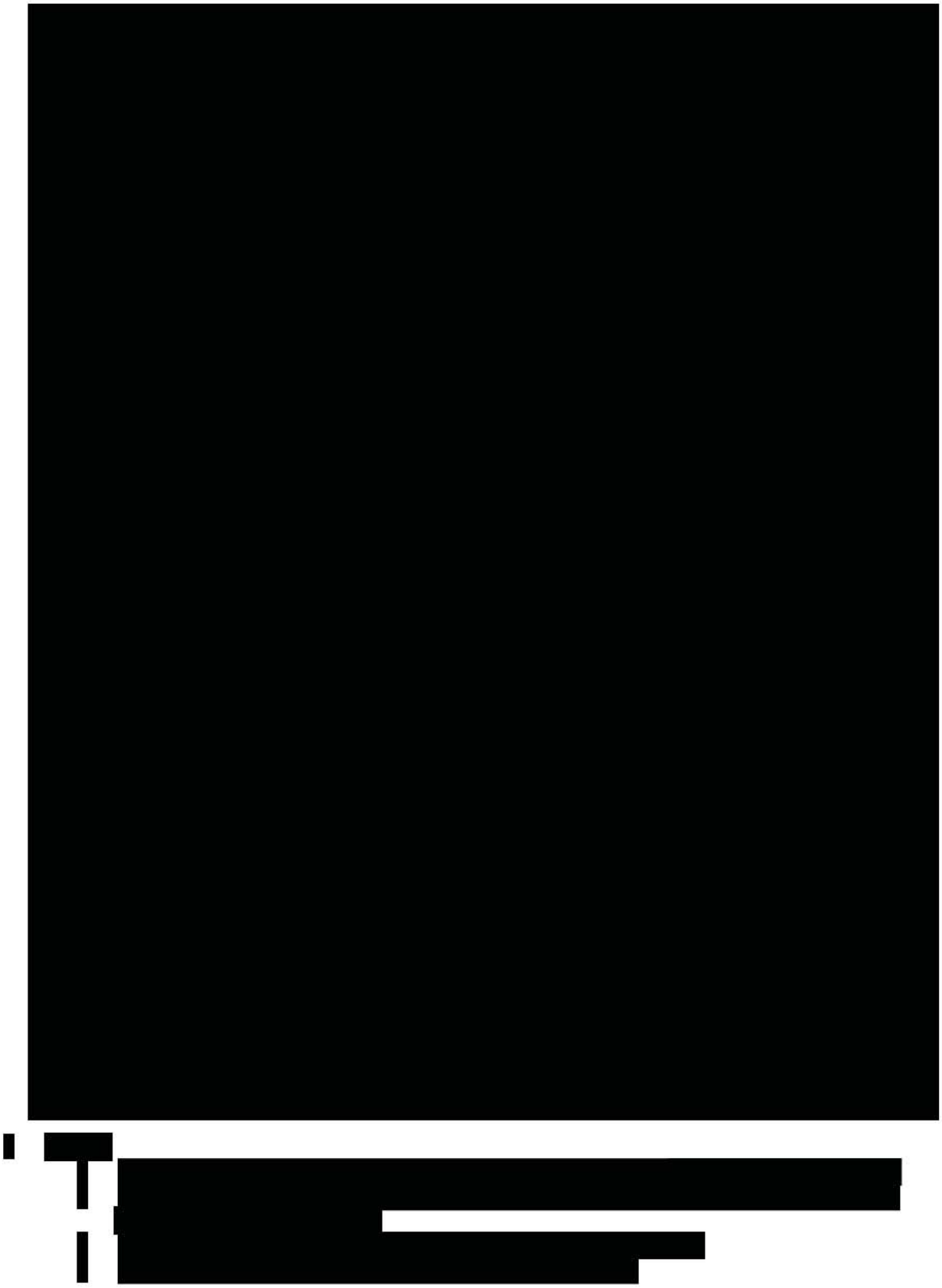

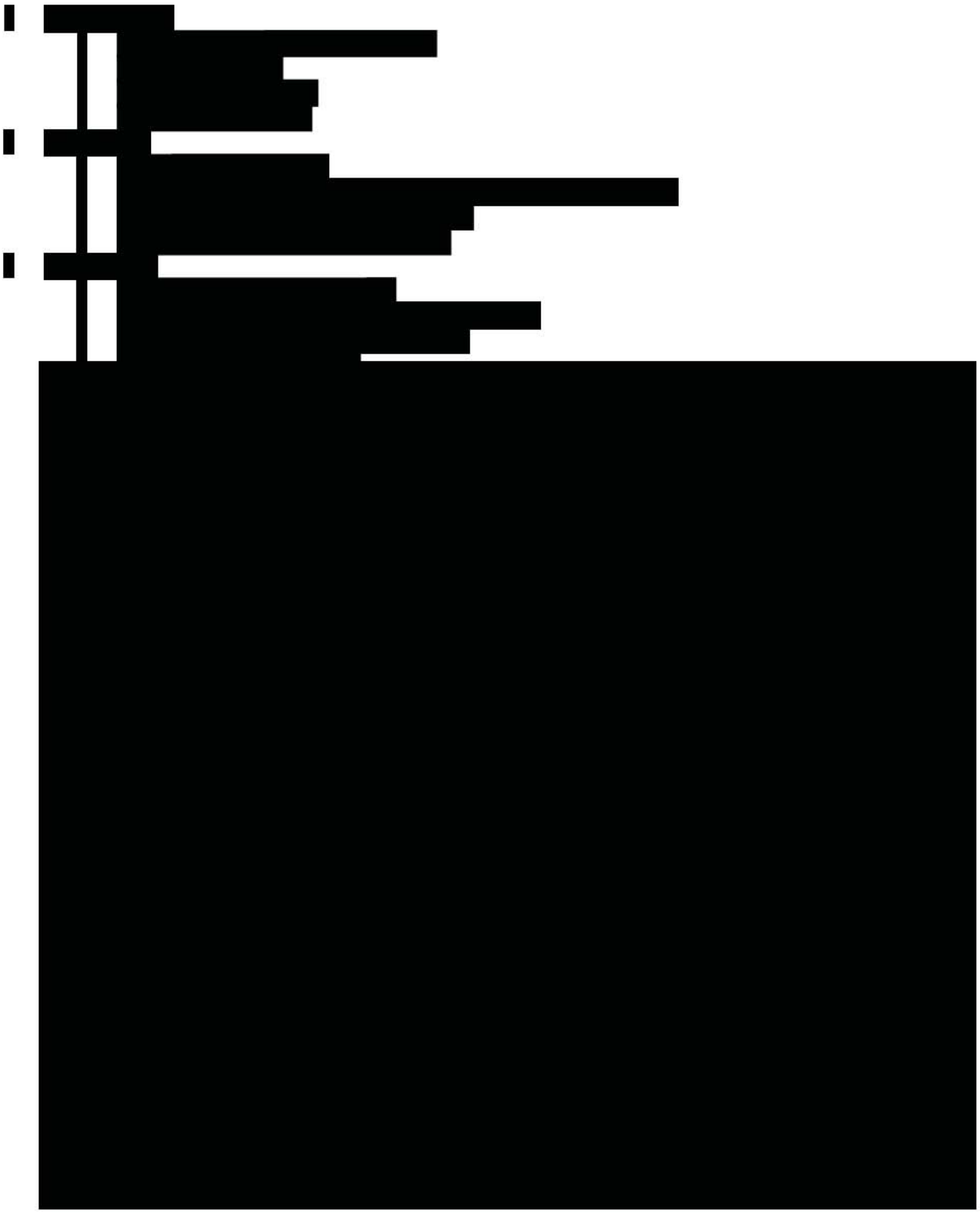

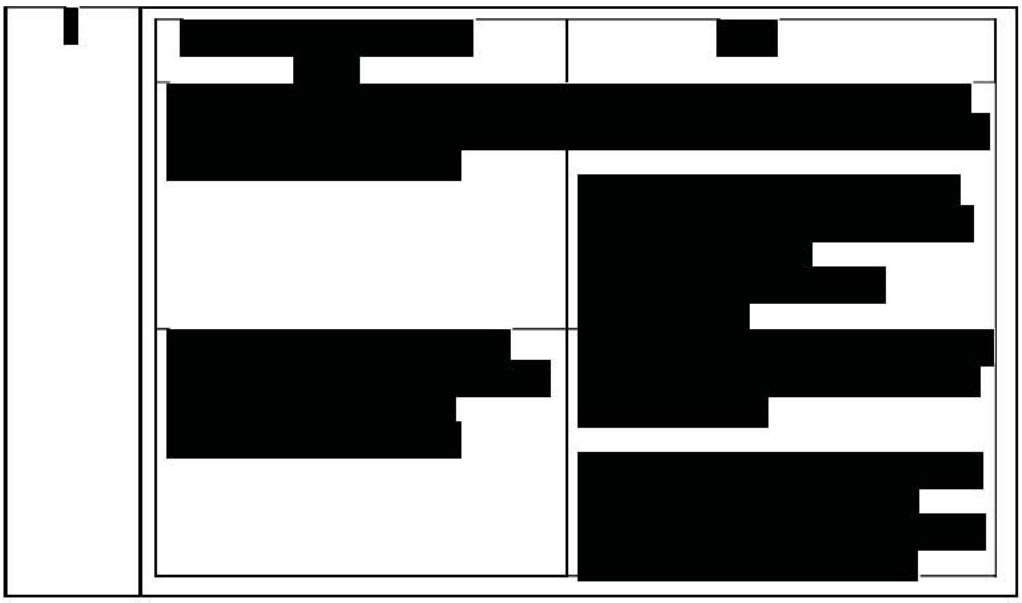

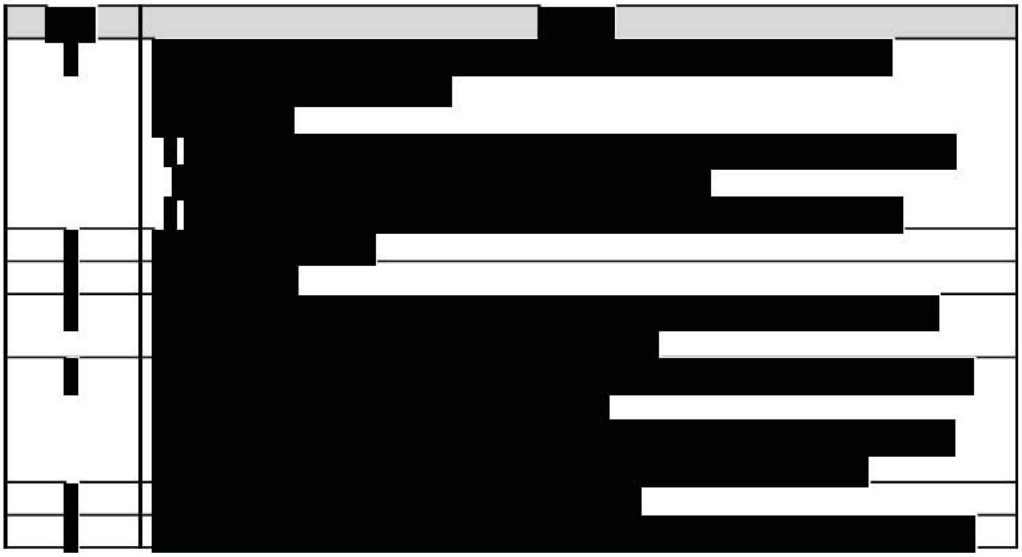

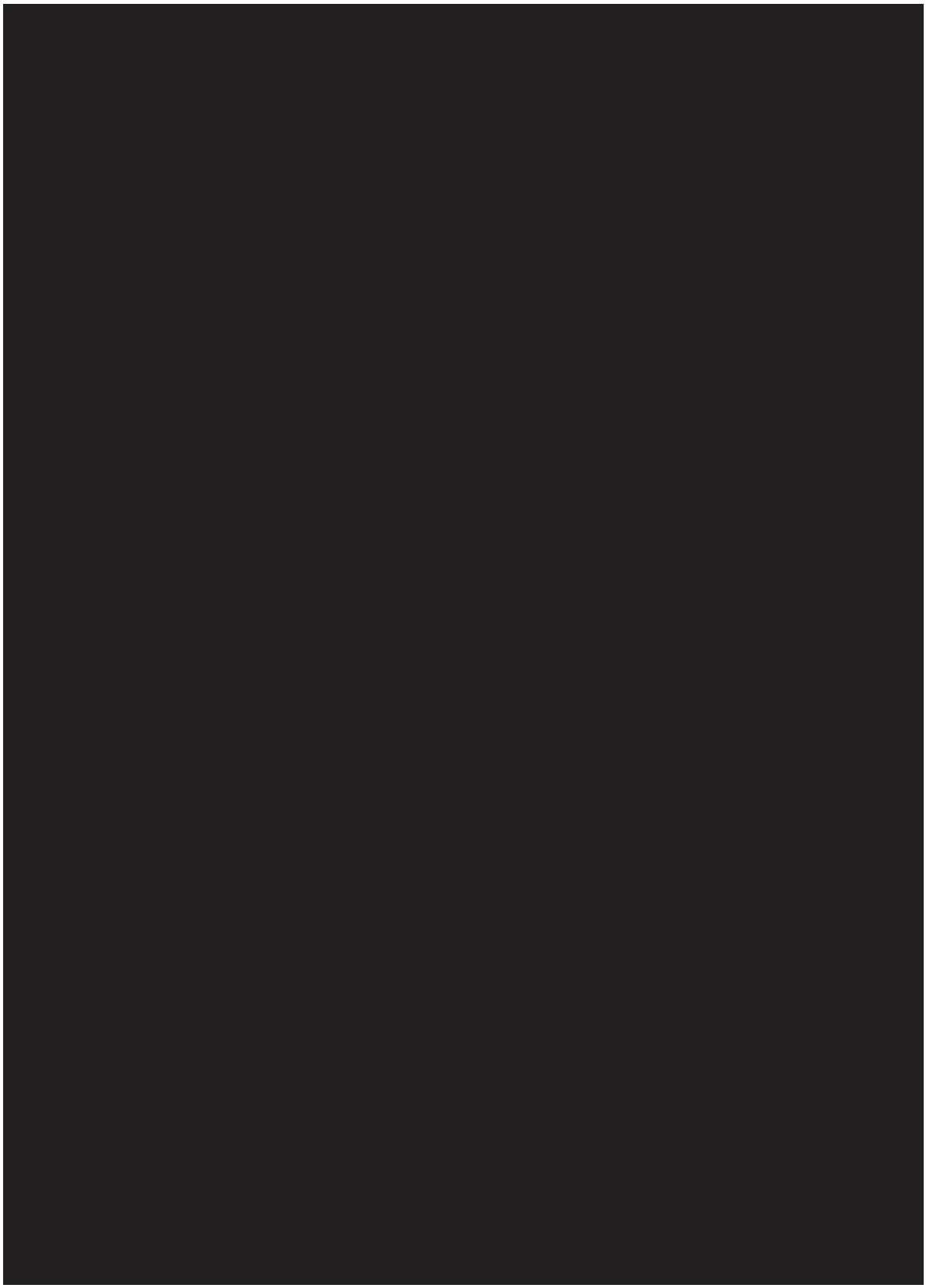

[redacted] **Patient Reported Outcomes**

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[redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

Title: Visual Acuity Chart Luminance and Room Illumination Testing

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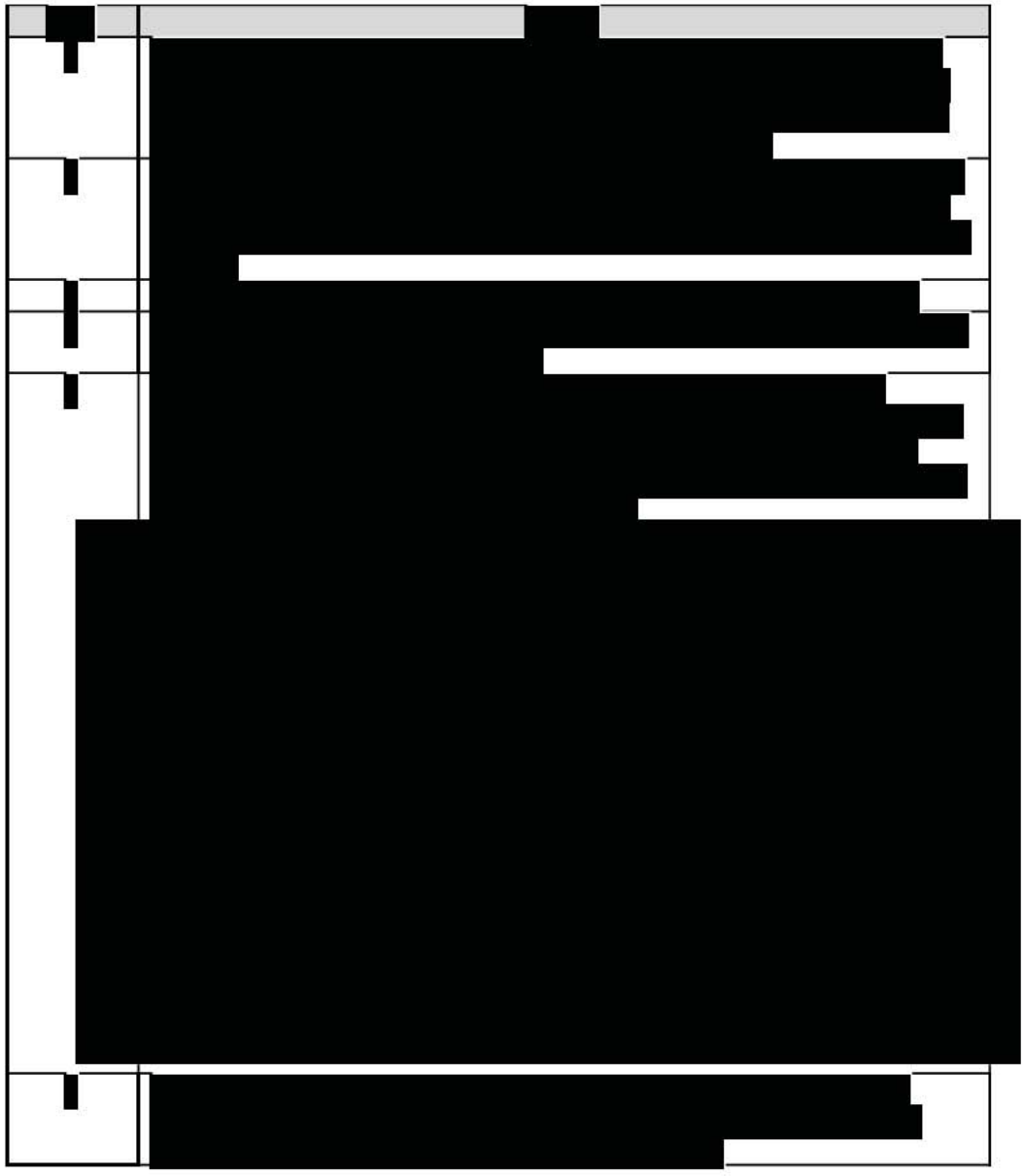

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[redacted] [redacted] TOPOGRAPHY MEASUREMENT USING MEDMONT E300 CORNEAL TOPOGRAPHER

Work aid will be provided separately.

[redacted] USING AN OPEN-FIELD AUTOREFRACTOR (WAM-5500) FOR MEASURING ACCOMMODATIVE RESPONSE AND OFF-AXIS REFRACTION

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Using an Open-field Autorefractor (WAM-5500) for Measuring Accommodative Response and Off-axis Refraction

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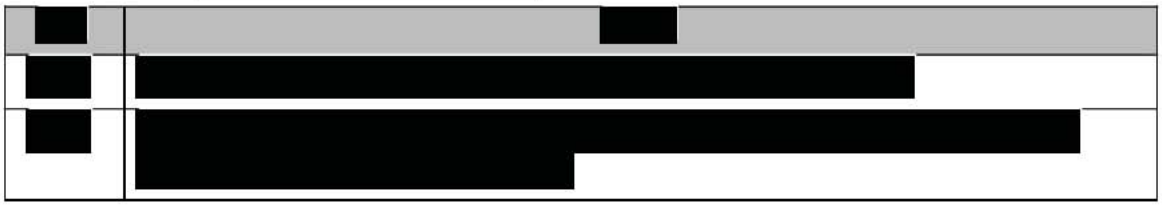

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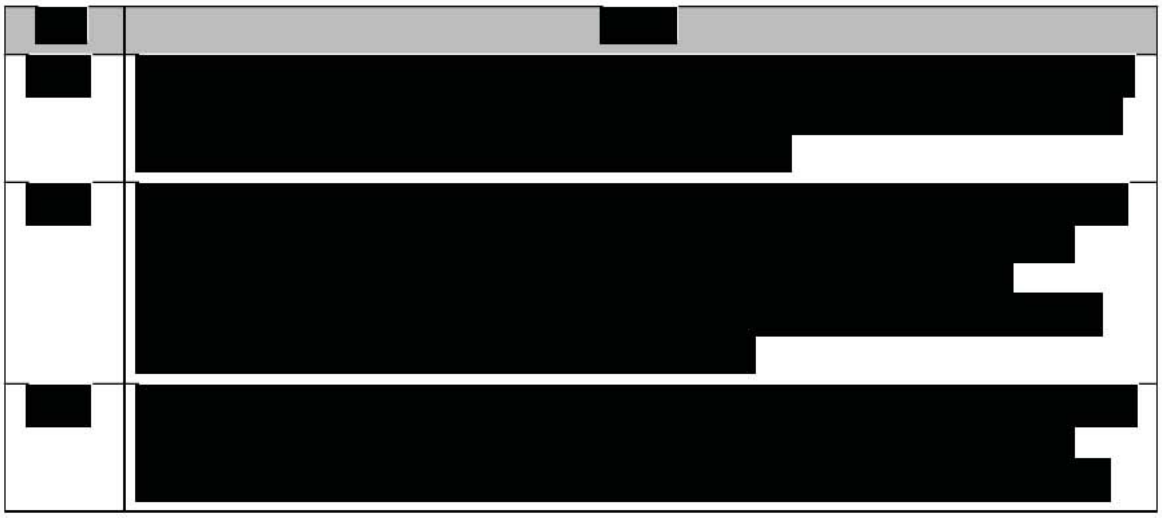

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6000 Evaluation of On-eye Optical Performances of the RMY-100 Lens

Version and Date: Version 3.0, Amendment 2.0, 05-Jun-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,[1] the Declaration of Helsinki,[3] ISO 14155,[2] United States (US) Code of Federal Regulations (CFR),[38] 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[1] 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[1] regulations and GCP guidelines regarding clinical trials during and after study completion.

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

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

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

Principal Investigator:

_____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site:

_____

Institution/Site Name

_____

Institution/Site Address

Electronic Signature Report

Job Name: VIS-CR-006000/A-R&D Clinical Study
Revision: VIS-CSPR-005828/3-Clinical Protocol
Title: VIS Clinical Study Protocol Approval
Status: Approved
System: Vision Care R&D Knowledge Management
Generated By: Thomas, Ashley
Generated On: 2018-06-15 11:21:50

Signoff Details

Function/Role	Approval Details			
Biostatistician Approval	Participant	WWID	Decision	Decision Date
	Xu, Jasper	1015493	Approved	2018-06-14T15:55:49

Function/Role	Approval Details			
Clinician Approval	Participant	WWID	Decision	Decision Date
	Cheng, Xu	330285	Approved	2018-06-14T17:01:29

Function/Role	Approval Details			
Clinical Research Manager Approval	Participant	WWID	Decision	Decision Date
	Balsamo,Margaret	1011701	Approved	2018-06-14T15:37:05

Function/Role	Approval Details			
	Participant	WWID	Decision	Decision Date
Other Approval	Paulk, Randall	375676	Approved	2018-06-15T10:49:17
	Moody, Kurt	358947	Approved	2018-06-14T15:45:33
	Brennan, Noel	1018516	Approved	2018-06-14T15:50:52