Clinical Study Protocol
Johnson & Johnson Vision Care, Inc.

Protocol Title: Evaluation of a daily disposable silicone hydrogel multifocal contact lens in myopes and hyperopes

Protocol CR-6477

Version: 2.0

Date: 05 January 2022

Investigational Products: JJVC Investigational Multifocal Contact Lenses manufactured in senofilcon A C3

Keywords:
Senofilcon A C3, Presbyopia, Daily Wear, Daily Disposable, Dispensing, Single arm

Statement of Compliance to protocol, GCP and applicable regulatory guidelines:
This trial will be conducted in compliance with the protocol, ISO 14155:2020,[1] the International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP),[2] the Declaration of Helsinki,[3] and all applicable regulatory requirements.

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION AND DATE

Protocol Title: Evaluation of a daily disposable silicone hydrogel multifocal contact lens in myopes and hyperopes
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SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

[redacted]

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

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

AUTHORIZED SIGNATURES

The signatures below constitutes the approval of this protocol and the attachments and provide the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations,[4] ISO 14155:2020,[1] ICH guidelines,[2] and the Declaration of Helsinki.[3]

Study Responsible Clinician	*See Electronic Signature Report* [redacted]	DATE
Clinical Operations Manager	*See Electronic Signature Report* [redacted]	DATE
Biostatistician	*See Electronic Signature Report* [redacted]	DATE
Data Management	*See Electronic Signature Report* [redacted]	DATE
Reviewer	*See Electronic Signature Report* [redacted]	DATE
Reviewer	*See Electronic Signature Report* [redacted]	DATE
Medical Safety Officer	*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	Justification for Change	Date
1.0	[redacted]	Original Protocol	N/A	10 Nov 2021
2.0	[redacted]	Throughout Protocol-updated version number and date. Section 7.2-biomicroscopy step corrected typo from grade 3 to grade 2.	Corrected typo of biomicroscopy grade.	05 January 2022

SYNOPSIS

Protocol Title	Evaluation of a daily disposable silicone hydrogel multifocal contact lens in myopes and hyperopes
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Design Validation Study Design control phase: Phase 3
Trial Registration	This study will be registered on ClinicalTrials.gov.
Test Article(s)	Investigational Product: JJVC Investigational Multifocal Contact Lenses manufactured in senofilcon A C3
Wear and Replacement Schedules	Wear Schedule: The test lenses will be used on a daily disposable basis. Replacement Schedule: The lenses will be replaced after a day of wear.
Objectives	The objective of this study is to demonstrate that the JJV Investigational senofilcon A C3 Multifocal Contact Lens in its final lens design made in the 4GT Manufacturing Platform meets the validation requirements related to objective and subjective vision, eye health and fit acceptance.
Study Endpoints	Primary Endpoints • CLUE vision scores • LogMAR visual acuity scores • Unacceptable lens fit (Yes/No) • Grade 3 or Higher Biomicroscopy Findings (Yes/No) Secondary Endpoints • Number of lenses needed to fit (optimize) the subject's vision • CLUE comfort scores • CLUE handling scores
Study Design	This is a single-masked, single-arm, dispensing clinical trial. Up to 120 subjects will be enrolled into the study with the aim of completing approximately 100 subjects. The subjects will be fit at (Visit 1) in the study lens and wear the lens for 3±1 day then undergo optimization (Visit 2) and wear the optimized pair for approximately 1 week (7±1 day). At the follow-up visit (Visit 3), logMAR acuity and final subjective responses will be collected and the subject will be exited from the study. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).

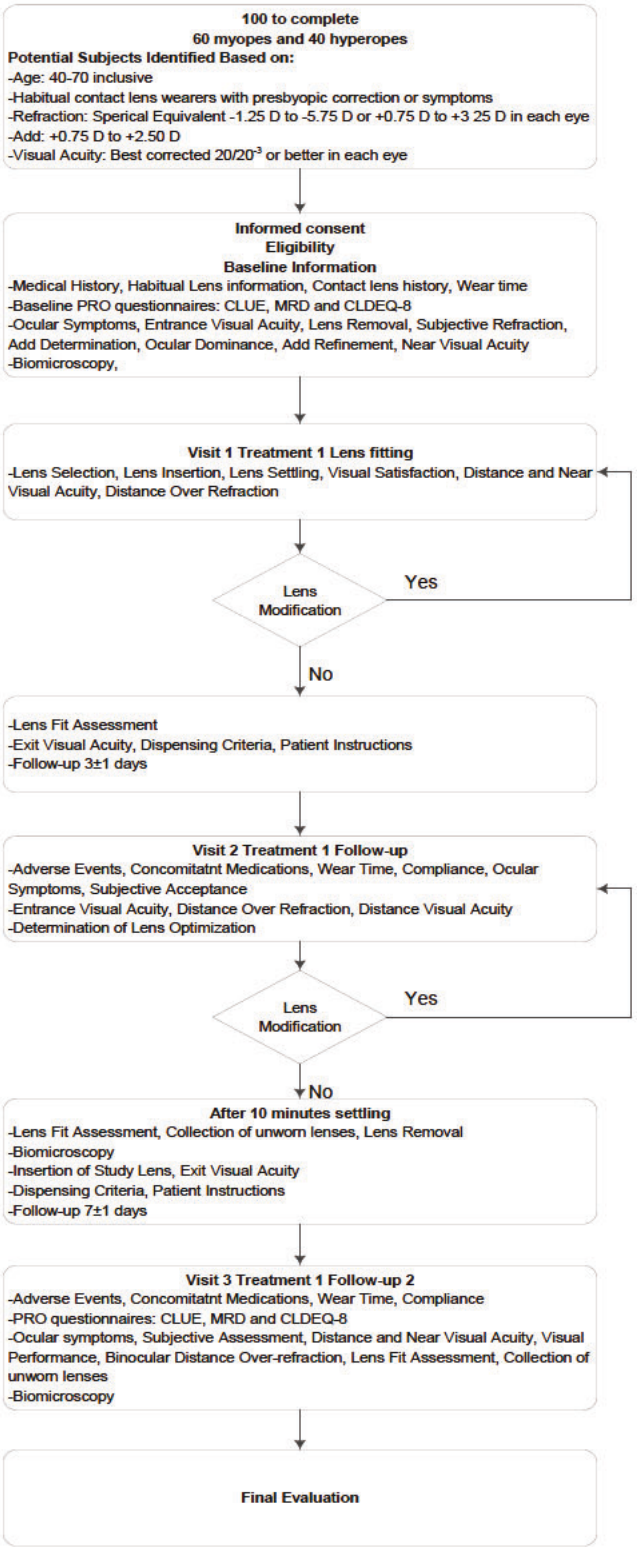
Sample Size	Approximately 120 eligible subjects will be enrolled (72 myopes and 48 hyperopes) with 100 subjects targeted to complete (60 myopes and 40 hyperopes).
Study Duration	The study will last approximately 2 to 3 months.
Anticipated Study Population	Healthy male and female volunteers with presbyopia will be screened as per criteria outlined below. All volunteers will have baseline measurements taken to ensure eligibility. The baseline procedures will occur after informed consent has been obtained. Subjects will have medical and contact lens history recorded, baseline questionnaires completed, and refractive and anterior segment status determined. For a detail flowchart of procedures below.

Eligibility Criteria - Inclusion	Potential subjects must satisfy all of the following criteria to be enrolled in the study Inclusion Criteria after Screening: The subject must: 1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Be at least 40 years of age and not greater than 70 years of age at the time of consent. 4. Own a wearable pair of spectacles if required for their distance vision. 5. Be an adapted soft contact lens wearer in both eyes (i.e. worn lenses a minimum of 2 days per week for at least 6 hours per wear day, for 1 month or more duration). 6. Either already be wearing a presbyopic contact lens correction (e.g., reading spectacles over contact lenses, multifocal or monovision contact lenses, etc.) or if not respond positively to at least one symptom on the "Presbyopic Symptoms Questionnaire". Inclusion Criteria at Baseline: 7. The subject's distance spherical equivalent refraction (vertex corrected if ≥-4.25 D) must be in the range of -1.25 D to -5.75 D or +0.75 D to +3.25 D in each eye. 8. The subject's refractive cylinder must be ≤0.75 D in each eye. 9. The subject's ADD power must be in the range of +0.75 D to +2.50 D. 10. The subject must have distance best corrected visual acuity of $20/20^{-3}$ or better in each eye.

Eligibility Criteria – Exclusion	Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria after Screening: The subject must not: 1. Be currently pregnant or lactating. 2. Have any active or ongoing ocular or systemic allergies that may interfere with contact lens wear. 3. Have any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis). 4. Have any previous, or planned, ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, dacryocystorhinostomy, peripheral iridotomy/iridectomy, cataract surgery, retinal surgery, etc.). 5. Have a history of amblyopia, strabismus or binocular vision abnormality. 6. Use of any of the following medications within 1 week prior to enrollment: oral retinoid, oral tetracyclines, anticholinergics, oral phenothiazines, oral/inhaled corticosteroids. See section 9.1 for further examples. 7. Use of any ocular medication, with the exception of rewetting drops. 8. Have a history of herpetic keratitis. 9. Have a history of irregular cornea. 10. Have a history of pathological dry eye. 11. Have Participated in any contact lens or lens care product clinical trial within 30 days prior to study enrollment. 12. Be and employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician). 13. Have any known hypersensitivity or allergic reaction to non-preserved rewetting drop solutions or sodium fluorescein. Exclusion Criteria at Baseline: The subject must not:

	14. Have clinically significant (Grade 2 or greater) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear. 15. Have any current ocular infection or inflammation. 16. Have any current ocular abnormality that may interfere with contact lens wear.
Disallowed Medications/Interventions	Use of any prescription or over-the-counter (OTC) medications that may affect contact lens wear. See section 9.1 in the protocol for details regarding disallowed systemic medications.
Measurements and Procedures	logMAR acuity, subjective responses, biomicroscopy and fit evaluations.
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any serious adverse event (SAE) where relationship to study agent cannot be ruled out, may 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	Non-Preserved Rewetting drops, lens cases, glass vials, saline, ETDRS light cabinet, 4 M logMAR charts, and Near logMAR charts.
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS, ACRONYMS 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
COVID-19	Coronavirus Disease 2019
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
MedDRA©	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NAVQ	Near Activity Visual Questionnaire
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

The purpose of this study is to evaluate the performance of a daily disposable silicone hydrogel multifocal contact lens containing a high energy visible light blocker. The performance of the lens will be compared to historical control values.

1.1. Name and Descriptions of Investigational Products Summary of Findings from Nonclinical Studies

Investigational Product: JJVC Investigational Multifocal-PG Contact Lenses manufactured in senofilcon A C3

Control: No active control lenses will be used. The Test lens performance will be compared to historical control values.

1.2. Intended Use of Investigational Products

All lenses are intended to correct spherical refractive error and presbyopia. For this study the lenses will be worn as a daily disposable lens, with the lenses being discarded after a day of wear.

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 Test lenses refer to the latest version of the CR-6477 Investigational Brochure.[5]

1.4. Summary of Known Risks and Benefits to Human Subjects

Anticipated risks and adverse reactions with this lens are similar to those with other soft daily wear contact lenses used to correct presbyopia. A listing of examples of adverse reactions is found in the section 13 of this protocol. The investigator should follow normal clinical guidelines regarding examination and care of subjects who participate in this trial. Refer to Investigational Brochure (IB) for the Investigational lens.

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

The Test lenses, or similar prototypes, have been previously tested in clinical studies [redacted] was discontinued early by the Sponsor due to the COVID-19 pandemic. There were no Adverse Events reported in [redacted] At the time of writing of this protocol study [redacted] was in the data collection phase. A summary of the lens performance in studies [redacted] is provided below.[6-13]

In [redacted] 30 subjects completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.057 and 0.091 at distance and near respectively. There was one adverse event reported during the study. The subject experienced mild upper respiratory virus and did not receive any treatment for this event. The event resolved and the subject completed the study. The investigator considered the event to be unrelated related to study article/procedure.[6]

In [redacted] 41 subjects completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.104 and 0.058 at distance and near respectively. There were no adverse events reported during the study.[7]

In [redacted] 67 subjects completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.078 and 0.062 at distance and near respectively. There were six adverse of events during the study. Two of the six were ocular adverse events were related to the control lens. Both were corneal infiltrative events; one was non-significant and the other was significant and both were classified as possibly related to the contact lenses.[9]

[redacted] was a single masked, randomized controlled, dispensing clinical trial and had a primary endpoint of logMAR visual acuity. There were 60 subjects that completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.132, -0.066 and 0.072 at distance, intermediate and near respectively. There were four adverse of events during the study. Three of the four were non-ocular adverse events. Two of those not related to the study lenses and one (headache) was related to the Control Contact lens. There was one ocular adverse event (non-significant infiltrative event) that was possibly related to the test lens.[10]

[redacted] was a single masked, randomized controlled, dispensing clinical trial on hyperopic presbyopes and had a primary endpoint of logMAR visual acuity. There were 64 subjects that completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.083, -0.013 and 0.090 at distance, intermediate and near respectively. There were four adverse of events during the study. Three of the four were non-ocular adverse events. None of the non-ocular adverse events were related to the test articles. There was one ocular adverse event (non-significant) that was mild corneal staining that was not related to the test lens.[101]

[redacted] was a single masked, randomized controlled, dispensing, 3x3 crossover clinical trial on hyperopic presbyopes and had a primary endpoint of subjective vision responses. There were 34 subjects that completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.10, -0.04 and 0.06 at distance, intermediate and near respectively. There were no adverse events reported during the study.[12]

[redacted] was a single masked, randomized controlled, dispensing clinical trial on myopic presbyopes and had a primary endpoint of logMAR visual acuity. There were 66 subjects

that completed the study per the protocol. The lenses displayed good clinical vision performance with binocular, high luminance, high contrast logMAR visual acuity of -0.128, -0.061 and 0.057 at distance, intermediate and near respectively. There was one adverse of event during the study. The one ocular adverse event was a non-significant grade 2 or less slit lamp finding requiring treatment. The event was classified as related and occurred while wearing the control lens.[13]

For information about the Investigational product refer to the CR-6477 Investigational Brochure.

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective:
The objective of this study is to demonstrate that the JJV Investigational senofilcon A C3 Multifocal Contact Lens in its final lens design made in the 4GT Manufacturing Platform meets the validation requirements related to objective and subjective vision, eye health and fit acceptance.

Secondary Objective:
The secondary objective of this study is to determine that the lenses meet the users' needs in overall subjective vision, lens handling, comfort and lens fit success.

2.2. Endpoints

Primary Efficacy Endpoints:

Visual Performance (logMAR)
Visual Performance will be assessed binocularly at the 1-week follow-up evaluation under high luminance high contrast conditions. At distance (4 meters), VA is assessed using ETDRS Charts; while near (40 cm) and intermediate (64 cm) assessments will be made using reduced Guillon-Poling charts. See [redacted] in Appendix H for details regarding the collection of visual acuity (logMAR) visual ability.

Subjective Vision
Subjective vision will be assessed using the Contact Lens User Experience (CLUE™) questionnaire at the 1-week follow-up evaluation. CLUE™ is a validated patient-reported outcomes questionnaire to assess patient-experience attributes of soft, disposable contact lenses (comfort, vision, handling, and packaging) in a contact-lens wearing population in the US, ages 18-65. Derived CLUE™ scores using Item Response Theory (IRT) follow a normal distribution with a population average score of 60 (SD 20), where higher scores indicate a more favorable/positive response with a range of 0-120. A 5-point increase in an average CLUE™ score translates into 10% shift in the distribution of scores for population of soft contact lens[23].

Primary Safety Endpoints:

Slit Lamp Findings (SLF)
Slit Lamp Findings (Grade 3 or higher) will be assessed for each subject eye at all study visits (schedule and unscheduled). SLFs will be evaluated and classified using the FDA Grading scale rating from 0 to 4, where Grade 0 represents the absence of findings and 1 to 4 representing successively worse findings (i.e. Grade 1=trace, Grade 2= mile, Grade 3=moderate and Grade 4= severe). The percentage of eyes with Grade 3 or higher slit lamp findings will be analyzed and will include corneal infiltrates. See [redacted] in Appendix H for more details on the collect of SLFs.

Unacceptable Lens Fit
Unacceptable lens fit will be assessed at all study visits (scheduled and unscheduled) for each subject eye. Unacceptable fit is a binary response where Y=1 if lens fit is unacceptable and Y=0 otherwise. Unacceptable fit was defined as unacceptable if any one of the following criteria:

- limbal exposure at primary gaze or with extreme eye movement;
- edge lift;
- excessive movement in primary up gaze;
- insufficient movement in all three of the following conditions: primary gaze, up gaze, and push up test.

Eyes with multiple unacceptable fitting events was counted only once. See [redacted] in Appendix H for additional details regarding lens fit assessments.

Secondary Endpoints

- CLUE™ Vision score
- CLUE™ Comfort score
- CLUE™ Handling core
- Lens Fit Success (Number of lenses needed to fit (optimize) the subject's vision)

2.3. Hypotheses

Co-Primary Safety Hypotheses

1. When wearing the Test lenses, the proportion (%) of eyes with at least one reported clinically significant slit-lamp finding (Grade 3 or 4) during the post-fit period will be statistically less than 5%.

2. When wearing the Test lenses, the proportion (%) of eyes with an unacceptable fit during the study will be statistically less than 5%.

Both co-primary safety hypotheses must be met in order to test any co-primary efficacy hypotheses.

Co-Primary Efficacy Hypotheses:

1. After approximately 1-week of wear in the optimized Test lenses, the mean overall quality of vision score of the Test lenses will be statistically better than 41 points for the myope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

2. After approximately 1-week of wear in the optimized Test lenses, the mean overall quality of vision score for the Test lenses will be statistically better than 36 points for the hyperope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

3. After approximately 1-week of wear in the optimized Test lenses, the mean distance, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.0 logMAR.

4. After approximately 1-week of wear in the optimized Test lenses, the mean intermediate, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.17 logMAR.

5. After approximately 1-week of wear in the optimized Test lenses, the mean near, binocular, high luminance, high contrast logMAR visual acuity score of the Test lens will be statistically lower than 0.17 logMAR.

   All safety and efficacy co-primary hypotheses must be satisfied in order to meet the study objectives and to test any secondary hypotheses.

Secondary Hypotheses

1. After approximately 1-week of wear in the optimized Test lenses, the mean overall quality of vision score of the Test lenses will be statistically better than 46 points for the myope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

2. After approximately 1-week of wear in the optimized Test lenses, the mean overall quality of vision score for the Test lenses will be statistically better than 41 points for

the hyperope population. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

3. After approximately 1-week of wear in the optimized Test lenses, the mean overall comfort score for the Test lenses will be statistically better than 52 points. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

4. After approximately 1-week of wear in the optimized Test lenses, the mean overall handling score for the Test lenses will be statistically better than 53 points. This will be recorded by the subject using the CLUE Follow-up Questionnaire.

5. The percentage of subjects who obtain the optimum lens pair in 4 lenses or less will be statistically better than 90%.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Healthy male and female subjects who are habitual soft contact lens wearers will be recruited. Subjects will be at least 40 years of age and not older than 70 years of age. Subjects enrolled in this study will be either myopic or hyperopic and have presbyopia**.**

3.2. Inclusion Criteria

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

Inclusion Criteria after Screening:
The subject must:

1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Be at least 40 years of age and not greater than 70 years of age at the time of consent.
4. Own a wearable pair of spectacles if required for their distance vision.
5. Be an adapted soft contact lens wearer in both eyes (i.e. worn lenses a minimum of 2 days per week for at least 6 hours per wear day, for 1 month or more duration).
6. Either already be wearing a presbyopic contact lens correction (e.g., reading spectacles over contact lenses, multifocal or monovision contact lenses, etc.) or if not respond positively to at least one symptom on the “Presbyopic Symptoms Questionnaire”.

Inclusion Criteria at Baseline:

7. The subject’s distance spherical equivalent refraction (vertex corrected if ≥-4.25 D) must be in the range of -1.25 D to -5.75 D or +0.75 D to +3.25 D in each eye.
8. The subject’s refractive cylinder must be ≤0.75 D in each eye.

9. The subject's ADD power must be in the range of +0.75 D to +2.50 D.
10. The subject must have distance best corrected visual acuity of $20/20^{-3}$ 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:
The subject must not:

1. Be currently pregnant or lactating.
2. Have any active or ongoing ocular or systemic allergies that may interfere with contact lens wear.
3. Have any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis).
4. Have any previous, or planned, ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, dacryocystorhinostomy, peripheral iridotomy/iridectomy, cataract surgery, retinal surgery, etc.).
5. Have a history of amblyopia, strabismus or binocular vision abnormality.
6. Use of any of the following medications within 1 week prior to enrollment: oral retinoid, oral tetracyclines, anticholinergics, oral phenothiazines, oral/inhaled corticosteroids. See section 9.1 for further examples.
7. Use of any ocular medication, with the exception of rewetting drops.
8. Have a history of herpetic keratitis.
9. Have a history of irregular cornea.
10. Have a history of pathological dry eye.
11. Have Participated in any contact lens or lens care product clinical trial within 30 days prior to study enrollment.
12. Be and employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).
13. Have any known hypersensitivity or allergic reaction to non-preserved rewetting drop solutions or sodium fluorescein.

Exclusion Criteria at Baseline:
The subject must not:

14. Have clinically significant (Grade 2 or greater) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear.
15. Have any current ocular infection or inflammation.

16. Have any current ocular abnormality that may interfere with 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.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is a single-masked, single-arm, dispensing clinical trial. Up to 120 subjects (72 myopes and 48 hyperopes) will be enrolled into the study with the aim of completing approximately 100 subjects (60 myopes and 40 hyperopes).

The study begins with an initial visit, Visit 1 (Day 0), if a subject is found to meet all eligibility criteria, they will be fit with the study lens, in both eyes; otherwise, the subject will be deemed ineligible and classified as a screen failure.

If a subject is dispensed lenses at the initial visit, then two additional visits will be conducted. Visit 2 will occur 3 ± 1 days after Visit 1. At Visit 2 subjects will undergo lens optimization if the subject reports unsatisfactory vision or is unable to obtain 20/30 binocular distance visual acuity with the study lenses. Subjects will return for Visit 3 (Final Evaluation) after 12±2 days. At the final visit, subjects will undergo subjective and objective assessments of vision.

Subjects will be advised to wear the study lenses every day while they are in the study for a minimum of 6 hours per day. The study lens will be replaced at the optimization visit. However, lost or damaged lenses maybe replaced when necessary. Unscheduled visit may be conducted.

4.2. Study Design Rationale

The study is intended to compare one study lens type and to characterize performance against predefined targets which are set in the Customer Requirements Document. Due to the predefined performance criteria a single-arm study design was chosen. The specifics of the lens design, beyond that the lenses are intended to correct for their distance and near vision, will be masked to the subject. The final optimized lenses are dispensed for approximately 1 week of daily disposable wear which is the intended modality of the lenses.

4.3. Enrollment Target and Study Duration

A total of approximately 120 eligible subjects will be enrolled (72 myopes and 48 hyperopes) with 100 subjects targeted to complete (60 myopes and 40 hyperopes). The study is anticipated to last 2-3 months.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn in a bilateral fashion using a single-arm design. Due to the nature of the design no randomization is required.

5.2. Masking

This is a single arm study and all subjects will be assigned to the same study lens. Subjects will be unaware of the identity of the investigational product. Investigators and clinical site personnel involved in the data collection will not be masked, however, the identity of the test device will be masked.

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

5.3. Procedures for Maintaining and Breaking the Masking

The identity of the test article shall not be broken unless information concerning the lens type is necessary for the urgent medical treatment of a subject. The Sponsor must be notified before the mask is broken.

Investigator or designee will pull the appropriate test articles from the study supply. All test articles that are opened, whether dispensed (placed/fit on eye or dispensed outside the clinical site) or not, must be recorded on the Test Article Accountability Log in the “Dispensed” section.

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	JJVC Investigational Multifocal Contact Lens Manufactured in senofilcon AC3
Manufacturer	Johnson & Johnson® Vision Care, Inc.
[redacted]	[redacted]
Lens Material	senofilcon A (C3)
Nominal Base Curve	8.35 mm
Nominal Diameter	14.3 mm
Nominal Distance Powers (D)	-1.00 D to -6.00 D and +0.50 D to +3.50 D in 0.25 D steps
Nominal ADD Powers (D)	LOW, MID, HI
Water Content	38%
Center Thickness	Varies with power
Oxygen Permeability (Dk)	103
Wear Schedule in Current Study	Daily Wear
Replacement Frequency	Daily
Packaging Form (vial, blister, etc.)	Blister
Packaging Form (vial, blister, etc.)	Blister

6.2. AncillarySupplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies

	Single-Use Preservative-Free Rewetting Solutions (any one of these three rewetting solutions options may be supplied)		
Solution Name/Description	Eye-Cept® Rewetting Drops	ScleralFil® Preservative Free Saline Solution	LacriPure Saline Solution
Manufacturer	Optics Laboratory	B&L	Menicon
Preservative	Non-Preserved	Non-preserved	Non-preserved

6.3. Administration of Test Articles

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

6.4. Packaging and Labeling

The test articles will be packaged in blisters, as the primary packaging. The test article will be over-labeled to mask the subject to the identity of the lens. The test articles will be in investigational cartons sealed with a tamper evident seal, commercial cartons, or in plastic bags as the secondary packaging form. The sample study label is shown below:

6.5. Storage Conditions

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

6.6. Collection and Storage of Samples

When possible, any lens or test article associated with an Adverse Event 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 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 articles must be kept in a locked storage cabinet, accessible only to those assigned by the Investigator for dispensing. The Investigator may delegate this activity to authorized study site personnel listed on the Site Delegation Log. All test articles must be accounted. This includes:

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

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

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 7±1 from V2
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hours
Statement of Informed Consent	x		
Demographics	x		
Medical History/Concomitant Medications	x		

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 7±1 from V2
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hours
Adverse Events and Concomitant Medications Review		x	x
Compliance		x	x
Habitual Contact Lens Information	x		
Contact Lens History	x		
Wear Time and Comfortable Wear Time with Habitual lenses	x		
Wear Time and Comfortable Wear Time with Study lenses		x	x
Screening Inclusion/Exclusion Criteria	x		
Subject Reported Ocular Symptoms	x	x	x
Baseline PRO (CLUE and MRD) Questionnaire	x		
CLDEQ-8 Questionnaire	x		x
Distance and Near Entrance Visual Acuity	x	x	x
Lens Removal	x	x	x
Subjective Refraction and Distance Visual Acuity	x		
Near ADD Determination	x		
Ocular Dominance	x		
ADD Refinement	x		
Near Visual Acuity	x		
Biomicroscopy	x	x	x

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 1 Follow-up 1 Optimization	Visit 3 Treatment 1 Follow-up 2
Time Point	Day 0	Day 3±1 from V1	Day 7±1 from V2
Estimated Visit Duration	2.5 hours	1.0 hour	1.5 hours
Baseline Inclusion/ Exclusion Criteria	x		
Continuance		x	x
Lens Selection	x	x (if modified)	x
Lens Insertion	x	x	x
10-Minute Settling	x	x (if modified)	
Visual Satisfaction / Subjective Acceptance	x	x	x
Study Lens Distance and Near Visual Acuity	x	x	x
Distance Over Refraction and Visual Acuity	x	x	x
Subjective Lens Fit Assessment	x	x	x
Binocular Over Refraction			x
Compliance		x	x
Follow-up PRO (CLUE / MRD) Questionnaire			x
Visual Performance			x
Modifications	x	x	
Distance and Near Exit Visual Acuity	x	x	x
Dispensing Criteria	x	x	x
Instructions	x	x	x
Schedule Follow-up	x	x	x
Final Evaluation			x

7.2. Detailed Study Procedures

VISIT 1

Subjects must report to the visit wearing their habitual contact lenses to accurately assess baseline PRO (CLUE and MRD) performance. If the subject is not wearing their lenses they must be rescheduled.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. ***NOTE**: The subject must be provided a signed copy of this document.*	
1.2	Demographics	Record the subject's age, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subject's medical history and concomitant medications.	
1.4	Habitual Lenses	Questions regarding the subject's habitual lens type and parameters.	
1.5	Habitual Lens Duration of Wear/Days per week	Questions regarding the subject's duration of contact lens wear and the minimum number of days they wear their lenses per week.	
1.6	Contact Lens History	Record the subject's correction type (i.e. monovision, multifocal, sphere with readers, etc.).	
1.7	Wear time and Comfortable Wear time with Habitual lenses	Record the subject's wear time and comfortable wear time with their habitual contact lenses.	
1.8	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. *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]
1.9	Baseline PRO (CLUE and MRD) and CLDEQ-8 Questionnaires	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of their habitual lenses using the PRO (CLUE and MRD) questions.	Appendix A [redacted]
1.10	Ocular Symptoms	The subject will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.11	Entrance Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the subject's habitual contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	[redacted]
1.12	Lens Removal	Have the subject remove their habitual lenses and store in an approved storage solution.	
1.13	Subjective Refraction and Distance Visual Acuity	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity to the nearest letter. **NOTE**: ***Best distance visual acuity with sphero-cylindrical refraction must be at least 20/20^{-3} in each eye for the subject to be eligible in the study.***	[redacted]
1.14	Near ADD Determination	The near reading addition will be determined using the binocular crossed cylinder technique (BCC) at 40 cm.	[redacted]
1.15	Ocular Dominance	Determine the distance ocular dominance with the best distance correction in place using a +1.00-blur test. If the results are equivocal use the sighting dominance test to determine the dominant eye used for the study.	Appendix E
1.16	ADD Refinement	Place the BCC result in the trial frame and refine the near prescription with trial lenses (or flippers) under binocular conditions.	[redacted]
1.17	Near Visual Acuity	Using the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm. Record the near visual acuity OD, OS and OU at 40 cm.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.18	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are Grade 2 or higher, the subject will be discontinued. If discontinued a final examination must be completed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	
1.19	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. If so, proceed to lens fitting. *If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.*	
Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.20	Lens Selection	Select the lens pair and power based on the spherical equivalent refraction and fitting guide for each eye. Record the Test lens parameters (power and lot number).	Appendix F (Fitting Guide)
1.21	Lens Insertion	Subjects will insert the lenses themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in labeled vial with sterile saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor. Complete the Product Quality Complaint form.	
1.22	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes.	
1.23	Determine Visual Satisfaction	Determine if the subject's vision is acceptable with the lenses. Allow the subject to look down a hallway or out of a	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		window for distance vision assessments, and for them to read a book, magazine or similar for near vision.	
1.24	Study Lens Distance and Near Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results. **Note:** Use the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm to measure the Near visual acuity	[redacted]
1.25	Distance Over-Refraction and Distance Visual Acuity	Perform a distance over-refraction OD and OS using loose lenses outside of the phoropter under ambient room illumination. The distance over-refraction may also be refined under binocular conditions. Record the results. The results of the distance over-refraction may also be checked for the impact on near vision under monocular and/or binocular conditions.	
1.26	Modifications	If the subject reports unsatisfactory vision or is unable to obtain 20/30 distance visual acuity OU with the lenses, then a modification must be attempted. If the subject reports satisfactory vision with the lenses a modification is not required, however at the Investigator's discretion and based upon their findings on the measured visual acuity and/or over- refraction the investigator may make a modification. Up to two attempts at modification are permitted, if necessary, in order to achieve an acceptable distance and near binocular performance for the subject, and to enable them to wear that particular lens type. Follow the fitting guide allowing for at least 10 minutes of settling time between each lens modification attempted. If modifications are required steps 1.22-1.27 will be repeated for each modification.	Appendix F (Fitting Guide)
1.27	Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). • The subject should not proceed to wear the lenses if any of the following is	[redacted]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in all three movement categories (primary gaze, upgaze, and push-up). NOTE: If lens fit is unacceptable subject will be discontinued from the study. Remove the lenses and complete the Final Evaluation forms.	
1.28	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU. ***NOTE: The distance visual acuity must be at least 20/30 OU for the lenses to be dispensed.***	[redacted]
1.29	Dispensing Criteria	The following criteria must be met for lenses to be dispensed and if all are not met the subject will be discontinued. • Distance Snellen acuity equal to or better than 20/30 OU • Subject must indicate that the vision is acceptable. • Subject must indicate that the comfort of the lenses is acceptable. • Lenses must have an acceptable general lens fit.	
1.30	Patient Instructions	Instruct the Subject the following: • The lenses will be worn on a daily wear basis. • Only enough lenses will be dispensed to the subject to wear for the required number of days until their follow-up	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		visit. No additional lenses will be dispensed. • A new lens will be opened and worn each day. • Instruct the subject to bring back all unworn study lenses. • Instruct the subject no cleaning or disinfecting solutions will be used for this lens type. • If determined necessary by the Investigator sterile non-preserved rewetting drops may be dispensed to be used as needed for dryness. • Subjects will be instructed to wear lenses for a minimum of 6 hours a day, every day during the study. • Subjects will be instructed to wear their glasses when not wearing the study lenses. • A patient instruction booklet will be provided. ***NOTE: In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.***	
1.31	Schedule Follow-up	The subject will be scheduled to return for their follow-up appointment in 3±1 days. ***NOTE: To count the follow-up visit as a day of wear the Subject must have worn the study lenses for 6 hours prior to the visit.***	

VISIT 2

The subjects must present to Visit 2 wearing the study lenses. To be counted as a day of wear the lenses need to have been worn for at least six (6) hours prior to the visit.

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
2.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
2.2	Wear time and Comfortable Wear time with Study lenses	Record the hours the subject has worn the study lenses and the comfortable wear time on the day of follow-up.	
2.3	Compliance	Record the subject's compliance with wearing the study lenses. ***NOTE: Subjects must have worn lenses for at least 6 hours per day.*** ***To be counted as a day of wear at this visit the Subject must have worn the study lenses for 6 hours prior to the visit.***	
2.4	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.5	Subjective Acceptance	Record whether the subject's distance and near vision with the lenses is acceptable.	
2.6	Distance and Near Entrance Visual Acuity	Measure the distance and near visual acuity OD, OS and OU. Record the results. Use the ETDRS 2000 Series Chart 1 or 2 near card placed at 40 cm to measure the Near visual acuity	[redacted]
2.7	Distance Over-Refraction and Distance Visual Acuity	Perform a distance over-refraction OD and OS using loose lenses outside of the phoropter under ambient room illumination. The distance over-refraction may also be refined under binocular conditions. Record the results and distance visual acuity OD and OS. The results of the distance over-refraction may also be checked for the impact on near vision under monocular and/or binocular conditions.	

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
2.8	Determination of Lens Optimization	If the subject reports unsatisfactory vision or is unable to obtain 20/30 distance visual acuity OU with the lenses, then a modification must be attempted. If the subject reports satisfactory vision with the lenses a modification is not required, however at the Investigator's discretion and based upon their findings on the measured visual acuity and/or over- refraction the investigator may make a modification. Up to two attempts at modification are permitted if necessary, in order to achieve an acceptable distance and near binocular performance for the subject, and to enable them to wear that particular lens type. Follow the fitting guide and steps 1.22-1.27 in Visit 1 Fitting allowing for at least 10 minutes of settling time between each lens modification.	Appendix F (Fitting Guide)
2.9	Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). • The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). ***<u>NOTE</u>: If lens fit is unacceptable subject will be discontinued from the study. Remove the lenses, and complete the Final Evaluation forms.***	[redacted]
2.10	Collection of unworn lenses (if applicable)	Collect unworn lenses returned by the subject when lens power has been optimized. If lens power was not changed allow the subject to use the unworn lenses dispensed at	

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
		Visit 1 and dispense enough lenses of the same power to last the subject until their next visit.	
2.11	Lens Removal	The study lenses will be removed and discarded.	
2.12	Biomicroscopy	Perform biomicroscopy OD and OS. Slit Lamp Classification Scales 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]
2.13	Insertion of Study Lenses	Dispense the subject a new pair of lenses that match the distance and ADD power of the lenses that were removed in Step 2.11 above.	
2.14	Distance and Near Exit Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place. For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU. ***NOTE: The distance visual acuity must be at least 20/30 OU for the lenses to be dispensed.***	[redacted]
2.15	Dispensing Criteria	The following criteria must be met for lenses to be dispensed and if all are not met the subject will be discontinued. • Distance Snellen acuity equal to or better than 20/30 OU • Subject must indicate that the vision is acceptable. • Subject must indicate that the comfort of the lenses is acceptable. • Lenses must have an acceptable general lens fit.	
2.16	Patient Instructions	Instruct the Subject the following: • The lenses will be worn on a daily wear basis.	

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
		• Only enough lenses will be dispensed to the subject to wear for the required number of days until their follow-up visit. No additional lenses will be dispensed. • A new lens will be opened and worn each day. • Instruct the subject to bring back all unworn study lenses. • Instruct the subject no cleaning or disinfecting solutions will be used for this lens type. • If determined necessary by the Investigator sterile non-preserved rewetting drops may be dispensed to be used as needed for dryness. • Subjects will be instructed to wear lenses for a minimum of 6 hours a day, every day during the study. • Subjects will be instructed to wear their glasses when not wearing the study lenses. • Remind the subject to bring their habitual correction to the follow-up visit. ***NOTE*: In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.**	
2.17	Schedule Follow-up	The subject will be scheduled to return for their follow-up appointment in 7±1 days.	

Visit 2: Treatment 1 Follow-up 1			
Step	Procedure	Details	[redacted]
		***NOTE**: To count the follow-up visit as a day of wear the Subject must have worn the study lenses for 6 hours prior to the visit.*	

VISIT 3

The subjects must present to Visit 3 wearing the study lenses. To be counted as a day of wear the lenses need to have been worn for at least six (6) hours prior to the visit.

Visit 3: Treatment 1 Follow-up 2			
Step	Procedure	Details	[redacted]
3.1	Adverse Events and Concomitant Medications Review	Review the subject's concomitant medications and record any changes from the previous study visit. Record any adverse events or medical history changes from the previous study visit.	
3.2	Wear time and Comfortable Wear time with Study lenses	Record the hours the subject has worn the study lenses and the comfortable wear time on the day of follow-up.	
3.3	Compliance	Record the subject's compliance with wearing the study lenses. ***NOTE**: Subjects must have worn lenses for at least 6 hours per day* ***To be counted as a day of wear at this visit the Subject must have worn the study lenses for 6 hours prior to the visit.***	
3.4	PRO (CLUE and MRD) and CLDEQ-8 Questionnaires	The subject will evaluate the vision characteristics, comfort characteristics, handling characteristics, and visual symptoms of the study lenses using the PRO (CLUE and MRD) & CLDEQ-8 questionnaires.	Appendix A [redacted]
3.5	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire	[redacted]
3.6	Subjective Acceptance	Record whether the subject's distance and near vision with the lenses is acceptable.	
3.7	Distance and Near Entrance Visual Acuity	Distance and near Snellen visual acuity will be measured for each eye with the study contact lenses in place.	[redacted]

Visit 3: Treatment 1 Follow-up 2			
Step	Procedure	Details	[redacted]
		For near measures use the ETDRS 2000 Series Chart 1 or 2. The acuity will be recorded to the nearest letter OD, OS and OU.	
3.8	Visual Performance Distance (4M) Intermediate (64 cm) Near (40 cm)	Binocular Visual performance will be recorded for the following: **Distance, Bright Illuminance** *High and Low Contrast ETDRS Charts* 4M- HC#3 and LC#3 **Near, Bright Illuminance** *Reduced Guillon-Poling Charts* Intermediate (64 cm) High Contrast and Low Contrast Near (40 cm) High Contrast and Low Contrast **Distance, Dim Illuminance (with *Distance* goggles)** *High Contrast ETDRS Charts 4*M- HC#6 **Near, Dim Illuminance (with *Near* goggles)** *Reduced Guillon-Poling charts* High Contrast Intermediate (64 cm) and Near (40 cm). **Note:** • **The room illuminance must be between 7.3 and 7.9 EV (394-597 lux).** • **Distance, HC-1 Chart luminance Acceptable Range 10.5-10.7 EV (181-208 cd/m^2).** • **Guillon-Poling, Near Chart Luminance Acceptable Range 10.8-11.1 EV (223-274 cd/m^2).** • **Do not use the Mesopic filter for Dim luminance (Dim luminance will be simulated by using the goggles)**	[redacted]
3.9	Binocular Distance Over-refraction and Distance Visual Acuity	Perform a binocular over-refraction and record the OD and OS results and distance visual acuity. Note: No lens changes are allowed based on the over-refraction.	Appendix G

Visit 3: Treatment 1 Follow-up 2			
Step	Procedure	Details	[redacted]
3.10	Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The subject should not proceed to wear the lenses if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). ***<u>NOTE</u>: If lens fit is unacceptable subject will be discontinued from the study. Remove the lenses, and complete the Final Evaluation forms.***	
3.11	Collection of unworn lenses (if applicable)	Collect unworn lenses returned by the subject.	
3.12	Lens Removal	Have the subject remove the study lenses and store in saline in a labeled glass vial. ***<u>NOTE</u>: Lenses do not need to be stored in a refrigerator.***	
3.13	Biomicroscopy	Perform biomicroscopy OD and OS. Slit Lamp Classification Scales 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]

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	Exit Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best-corrected distance visual acuity (OD, OS, OU) to the nearest letter. **Note**: This step is not necessary if the subject was exited due to screen failure.	[redacted]
F.3	Exit Slit Lamp Biomicroscopy (for subjects that are discontinued early)	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 or saline may be instilled. This step is not necessary if the subject was exited due to screen failure. **Note**: This step is not necessary if the subject was exited due to screen failure, or if biomicroscopy was performed as part of the final follow-up visit procedures (i.e., immediately prior to the final evaluation).	[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, as appropriate:

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

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

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

The following information will be collected during an unscheduled visit.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Reason for unscheduled visit	Indicate if the only reason for the visit is that the subject requires additional test articles. If the reason is other than resupply of previously dispensed lenses, specify the reason for the visit.	
U.2	Chief Complaints (if applicable)	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.3	Adverse Events and Concomitant Medications Review (if applicable)	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.4	Entrance VA (if applicable)	Record the entrance distance visual acuity (OD, OS) to the nearest letter.	[redacted]
U.5	Subjective Sphero-cylindrical Refraction (if applicable)	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).	[redacted]
U.6	Slit Lamp Biomicroscopy (if applicable)	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]
U.7	Dispensing (if applicable)	If the subject requires additional lenses to complete the wear period and is eligible to do so, provide additional lenses per the dispensing instructions given in the detailed study procedures.	
U.8	Exit Visual Acuity (if applicable)	Record the subject's exit distance visual acuity (OD, OS) to the nearest letter.	[redacted]

NOTE: If the only reason for the unscheduled visit is that the subject requires additional test articles, only the dispensing information needs to be recorded.

7.4. Laboratory Procedures

Not Applicable

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent.
- they are eligible.
- completed all study visits

8.2. Withdrawal/Discontinuation from the Study

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

- 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 necessitating discontinuation of study lens wear
- Subjects who have experienced a Corneal Infiltrative Event (CIE).
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment).
- Subject not compliant with study lens wear schedule
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit.

For discontinued subjects, the Investigator will:

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

Additional subjects will be enrolled if a subject discontinues from the study prematurely.

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications and therapies are medications or therapies that contraindicate contact lens wear. See the Exclusion criteria for specific details.

9.1. Systemic Medications

The following table lists the medications disallowed in this study.

Table 4: Disallowed systemic medications

Class of Drug	Common Indication(s)	Common Examples
Anticholinergics	Irritable bowel syndrome, Parkinson's disease, peptic ulcer, cystitis, nasal congestion, cold symptoms, overactive bladder, COPD	Bentyl, Spiriva, Atrovent, Hyosyne, Levsin, Symax Fastab, Symax SL, Homax SL, Cogentin, Transderm Scop, etc., …
Oral Phenothiazines	Antipsychotic disorders (schizophrenia, mania)	Compazine, Mellarill, Thorazine, Phenagran, etc.…
Oral Retinoids	Cystic acne	Isotretinoin
Corticosteroids	Arthritis, colitis, asthma, bronchitis, allergic or inflammatory conditions	Cortisone, Prednisone, Hydrocortisone, Medrol, Kenalog etc., …
Oral Tetracycline	Urinary Tract Infection, acne, chlamydia, gonorrhea	Sumcyin, Acitsite, Achromycin V, etc.

10. DEVIATIONS FROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. 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, to the IEC/IRB.

If the deviation potentially impacts the safety of patient or changes the technical integrity of the study, then it must be reported to IEC/IRB. This is a "Major Deviation". Deviations that contradict the information contained in the Informed Consent/Assent forms will be considered Major Deviations.

Minor deviations have no substantive effect on patient safety or technical integrity of the study. They are often logistical in nature.

Protocol waivers are prohibited.

Table 5 lists examples of deviations that will constitute major and minor protocol deviations for this study.

Table 5: Examples of major and minor protocol deviations

Deviation category	Major deviation	Minor deviation
Out-of-window visit	Visit attended more than 2 days out of visit t window defined in study procedures	Visit attended 2 or fewer days out of visit window defined in study procedures
Unanswered PRO questions	For questionnaires where data is related to a primary or secondary endpoint, more than 2 PRO questions are unanswered (i.e., left blank).	For questionnaires where data is related to a primary or secondary endpoint, 2 or fewer PRO questions are unanswered (i.e., left blank). For questionnaires where data where data is not related to a primary or secondary endpoint, any PRO questions are unanswered (i.e., left blank).

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 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 apply 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: This definition includes events related to the investigational medical device or the comparator, and to the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.

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.

Note: 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 adverse event that led to any of the following:

- Death
- Serious deterioration in the health of the subject that resulted in any of the following:
- Life-threatening illness or injury
- Permanent or persistent impairment of a body structure or a body function
- Hospitalization or prolongation of patient hospitalization
- Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.

- Chronic disease
- Foetal distress, foetal death or a congenital physical or mental impairment of birth defect.

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 – are defined as events that are symptomatic and warrant discontinuation (temporary or permanent) of the contact lens wear

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

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

Non-Significant Adverse Events – are defined as those events that are usually asymptomatic and usually do not warrant discontinuation of contact lens wear but may cause a reduction in wear time. However, the Investigator may choose to prescribe treatment 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: 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: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

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

13.2. Assessing Adverse Events

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

- Seriousness/Classifications (see definition in section 13.1).
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related, unlikely related, possibly related, or 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, or severe - 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, or other.

13.2.1. Causality Assessment

Causality Assessment – A determination of the relationship between an adverse event and the test article. The test article relationship for each adverse event should be determined by the investigator using these explanations:

- Not Related- An adverse event that is not related to the use of the test article, study treatment or study procedures.

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

13.2.2. Severity Assessment

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

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

13.3. Documentation and Follow-Up of Adverse Events

The recording and documenting of adverse events (ocular and non-ocular) begin 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 and complete the Adverse Event eCRF.

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

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

- Adverse event (diagnosis not symptom).

- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.).
- Date the clinical site was notified.
- Date and time of onset.
- Date and time of resolution.
- Adverse event classification, severity, and relationship to test articles, as applicable.
- Treatment regimen instituted (where appropriate), 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, if the AE is related to the visual system.

Upon discovery of an AE that is deemed 'possibly related' or 'related' to the test article or study procedures (whether related to the visual system or not), an AE review form [redacted] must be completed. Additional dated and initialed entries should be made at follow-up evaluations. Separate forms must be completed for each eye if the AE is bilateral.

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 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 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 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 to the written guidelines, including reporting timelines.

13.5. Event of Special Interest

None

13.6. Reporting of Pregnancy

Subjects reporting pregnancy (by self-report) during 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. Pregnant participants are not discontinued from contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below. More details will be included in the stand-alone Statistical Analysis Plan (SAP). The SAP will be developed and finalized prior to database lock.

All data summaries and statistical analyses will be performed using the Statistical Analysis System (SAS) software Version 9.4 or higher (SAS Institute, Cary, NC).[14] 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.

Summaries will be presented by separately for each time point (Baseline, fitting, 3-Day follow-up, 1-week follow-up) and will be performed separately by completion status (Safety Population, Per-Protocol Population or Intent-to-treat, when appropriate).

14.2. Sample Size Justification

This study was designed and powered to test for superiority of the Test lens after 1-week of optimized lens wear with respect to the following: binocular HLHC visual performance at distance, intermediate and near, subjective Vision scores for both the hyperopic and myopic groups grade 3 or higher slit lamp findings and unacceptable lens fitting. Additionally, this study was also powered to test for superiority with respect to CLUE Comfort and Handling and Lens Fit success.

The sample size for co-primary efficacy endpoints was estimated to achieve a minimum statistical power of 99% for visual performance and CLUE Vision using a 2-sided type I error rate of 1%. Co-primary safety endpoints (slit lamp findings and unacceptable lens fitting) were estimated to achieve a minimum statistical power of 90% with 95% central posterior credible interval. The sample size for secondary endpoints (with the exception of lens fit success) were estimated to achieve a minimum statistical power of 80% using a two-sided type I error rate of 1% each. a minimum statistical power of 80% for lens fit success with the 99% central posterior credible interval.

With respect to safety endpoints, historical data from 7 studies were utilized, however, for primary efficacy and secondary endpoints historical data from only two studies were utilized in the sample size calculation since there were the only studies that have completed after design-lock (Phase2b). A summary of historical studies utilized in the sample size calculation are summarized in Table 6 below. For the sample size estimate for this study, only data from period 1 was utilized. Table 7 below summaries the historical data by endpoint.

Table 6: Historical Studies Utilized for Sample Size Calculations

Study Number	Design	Population	Number Enrolled	Number in Safety Population	Number in PP population	Endpoints utilized for sample size
[redacted]	2x2	Myopes	34	33	30	Primary Safety
	2x2	Hyperopes	48	44	41	Primary Safety
	2x3	Hyperopes	81	78	67	Primary Safety
	2x3	Myopes	71	68	60	Primary Safety
	2x3	Hyperopes	78	75	64	Primary Safety, Efficacy, Secondary
[redacted]	2x3	Myopes	81	78	66	Primary Safety, Efficacy Secondary,
[redacted]	2 Phase 3x3	Hyperopes	40	37	34	Primary Safety

PP: Per-Protocol

Table 7: Historical Data by Endpoint

Endpoint Type	Endpoint	Data Type	Value
*Primary Efficacy	VP - Distance	Mean (SD)	-0.109 (0.0848)
	VP - Intermediate		-0.024 (0.1129)
	VP - Near		0.085 (0.1264)
	CLUE Vision (Hyperopes)		57.1 (17.27)
	CLUE Vision (Myopes)		60.6 (16.84)
**Primary Safety	Grade 3 + SLF (Adverse Event)	Rate	0.24% (1 eye)
	Unacceptable Lens Fitting		0% (0 eye)
*Secondary	CLUE Vision Hyperopes	Mean (SD)	57.1 (17.27)
	CLUE Vision Myopes		60.9 (16.65)
	CLUE Comfort (Hyperopes + Myopes)		72.3 (17.43)
	CLUE Handling (Hyperopes + Myopes)		71.7 (17.09
	Lens Fit Success	Rate	100%

VP: Visual Performance, SD=Standard Deviation
*Summaries for primary efficacy and secondary endpoints were provided for the per-protocol population at the 1-week follow-up evaluation for period 1 only.
** Summaries for the primary safety endpoints were provided for the safety population; all available data was included

Primary Safety Endpoint Sample Size Calculations:

Grade 3 or Higher Slit Lamp Findings (SLF) and Unacceptable Lens Fitting

Sample size estimates for SLFs grade 3 or higher and unacceptable lens fitting were calculated using the same technique and assumptions. Since both safety endpoints are testing against a 5% threshold and have an event rate less than 0.5% both endpoints require the same sample to achieve the same pre-specified confidence level of 95%. Furthermore, it should be noted that why both endpoints are collected on all subjects they are clinically independent.

For Grade 3 or Higher SLF was converted to a binary response as $Y = 1$ if a subject eye has a clinically significant SLF and $Y = 0$ otherwise for analysis purpose (Unacceptable lens fitting is derived as a binary response as Y=1 is a subject had an unacceptable lens fit and 0 otherwise). From the historical data there was no/extremely low rate (< 1%) for clinically significant SLFs (Grade 3 or higher) or unacceptable lens fitting for the study lens. Assuming a correlation of 0.70 between left and right eyes within the same subject, a total of 2000 replicating trials were simulated with a reference rate of 2% (worse-case scenario). Given the rare event binary outcome of slit lamp findings, (or unacceptable lens fit) each replicated sample was analyzed using a Bayesian beta-binomial model with correlated binary data (Diniza et al; 2010). For each simulated trial, the upper bound of the 95% central posterior credible interval constructed for the percentage of Grade 3 or higher SLFs for the Test lens was compared to a margin of 5%. With the proposed sample size, there was at least 90% of the estimated 95% credible intervals with the upper bound being below 5%.

Primary Efficacy Endpoint Sample Size Calculations:

Binocular HLHC Visual Performance and CLUE Vision Scores

Sample size calculations for each co-primary efficacy endpoint were carried separately out using a 2-sided one sample mean t-test, with a two-sided type I rate of 1%. The calculation was performed using the POWER procedure in SAS Version 9.4.

Secondary Endpoint Sample Size Calculations:

CLUE Vision, Comfort and Handling

Sample size calculations for each secondary endpoint (with the exception of lens fit Success) were carried separately out using a 2-sided one sample mean t-test, with a two-sided type I rate of 1%. The calculation was performed using the POWER procedure in SAS Version 9.4.

Lens Fit Success

Lens fit success was converted to a binary response as $Y = 1$ if lens optimization was achieved in 4 lenses or less and $Y = 0$ otherwise for analysis purposes. From the historical data there was 100% rate for lens fit success there for a worst-case scenario of 98% was used as the reference rate. Assuming a correlation of 0.70 between left and right eyes within the same subject, a total of 2000 replicating trials were simulated. Given the rare event binary outcome, Y=0 each replicated sample was analyzed using a Bayesian beta-binomial model with correlated binary data (Diniza et al; 2010). For each simulated trial, the lower bound of the 99% central posterior credible interval constructed for the percentage successful lens fit for the Test lens was compared to a margin of 90%. With the proposed sample size, there was at least 80% of the estimated 99% credible intervals with the lower bound being above 90%.

Table 8 displays the sample size estimates and associated power by endpoints. As indicated below, co-primary safety endpoints were powered ~92% individually yielding a combined power of ~84%. With respect to co-primary efficacy each hypothesis was powered to ~99% power provided a combine power of ~95%. Therefore, the overall combined study power for co-primary safety and co-primary efficacy hypotheses is ~79% and is considered reasonable to support any conclusions from these analyses. Furthermore, secondary endpoints were powered to achieve at least 80% statistical power. This was considered to have a minimal impact on overall study power because of the multibranch gate keeping approach being implemented.

Table 8: Sample Size Estimates by Endpoint

Endpoint Type	Endpoint	Test Type	Sample Size	Power (%)
Primary Efficacy	VP - Distance	Superiority (0.00)	17	99.4
	VP - Intermediate	Superiority (0.17)	11	99.3
	VP - Near	Superiority (0.17)	48	99.0
	CLUE Vision-Hyperopes	Superiority (36)	14	99.4
	CLUE Vision Myopes	Superiority (41)	18	99.0

Endpoint Type	Endpoint	Test Type	Sample Size	Power (%)
Primary Safety	Grade 3 + SLF	Statistically less then (5%)	100	92.6
	Unacceptable Lens fitting	Statistically less then (5%)	100	92.6
Secondary	CLUE Vision-Hyperopes	Superiority (41)	16	82.4
	CLUE Vision Myopes	Superiority (46)	15	82.3
	CLUE Comfort (Hyperopes + Myopes)	Superiority (52)	11	83.8
	CLUE Handling (Hyperopes + Myopes)	Superiority (53)	17	83.7
	Lens Fit Success	Superiority (90%)	92	82.1

Based on the table above a total of at least 100 subjects a required to complete the study. To account for screen failures and subject dropout Up to 120 subjects (72 myopes and 48 hyperopes) will be enrolled to ensure at least 100 (60 myopes and 40 hyperopes) complete the study.

14.3. Analysis Populations

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

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 *co-primary safety*, *co-primary efficacy* and *secondary* hypotheses will be tested using a multibranch gate keeping strategy. Study hypotheses will be evaluated sequentially as follows: First, co-primary safety hypotheses will be tested using 95% central posterior credible intervals for the probability of Grade or higher and unacceptable lens fitting. Both hypotheses must be met in order to test co-primary efficacy hypotheses. Since both hypotheses must pass to continue testing primary hypotheses, an overall family-wise type I error rate of 5% will be allocated to co-primary efficacy hypotheses using a Bonferroni[24] approach. Each co-primary efficacy hypothesis will be tested using two-sided type I error rate of 1% (5 hypotheses total

=5%). All co-primary safety and co-primary efficacy hypotheses must be met to test any secondary hypotheses.

Secondary hypotheses (except for lens fit success) will be tested with using an overall two-sided family-wise type I error rate of 5% (1% individually). Lens fit success will be tested using a 99% credible interval.

14.5. Primary Analysis

Primary Safety Analyses:
All primary safety analysis will be conducted on the safety population.

Grade 3 or Higher SLF
Grade 3 of Higher SLFs will be analyzed using a Bayesian beta-binomial model with correlated binary data[17].

The Model:
Let Y_1 and Y_2 denote the binary outcomes of lens fit acceptance (Yes/No) in left and right eyes, respectively, across dispensing and follow-up visits when wearing the Test lens. Considering the correlation, ρ, between Y_1 and Y_2, the distribution of the sum $Y = Y_1 + Y_2$ is obtained by the mixture of two variables. One of them follow a binomial distribution $Bin(2,p)$ with mixing probability $(1-\rho)$ and the other one follows a modified Bernoulli distribution, $MBern(p)$, taking value 0 and 2 rather than conventional 0 and 1, with mixing probability ρ:

$$P(Y = y|\, p,\rho) = (1-\rho)Bin(2,p)I_{A1} + \rho MBern(p)I_{A2}\,,$$

where $I_{A1} = \{0,1,2\}$, $I_{A2} = \{0,2\}$ and p is the probability of success (i.e., acceptable lens fitting).

To overcome the complexity of the mixture likelihood a latent variable Z_i, i = 1, 2 is introduced in the model to indicate in which component of the model the observation y_i, i=1, 2, belongs to, that is,

$$Z_i = \begin{cases} 1, \text{if the observation belong to the MBern(p)}, \\ 0, \text{if the observation belong to the Bin(2, p)} \end{cases}$$

The joint distribution of the augmented data $(Y_i, Z_i), i = 1,2$, is given by

$$\mathrm{P}(\mathrm{Y}=\mathrm{y_i}, \mathrm{Z}=\mathrm{z_i}|\, \mathrm{p}, \rho) = \rho^{\mathrm{z_i}}\mathrm{p}^{\mathrm{y_i z_i}/2}(1-\mathrm{p})^{(2-\mathrm{y_i})\mathrm{z_i}/2}(1-\rho)^{1-\mathrm{z_i}}\binom{2}{\mathrm{y_i}}\mathrm{p}^{\mathrm{y_i}(1-\mathrm{z_i})}(1-\mathrm{p})^{(2-\mathrm{y_i})(1-\mathrm{z_i})}$$

The probability p links to the regression variables through a logit transformation as follow:

$$\text{logit}\,(\mathrm{p}) = \beta_0 + \beta_1 \mathrm{lens}$$

It is assumed that β_0, β_1 and ρ to be independent with a non-informative prior N(0, 1000) for β_0 and β_1, and beta(0.5, 0.5) for ρ. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC Procedure[14] will be used to estimate the posterior distributions of the

parameters (β_0, β_1, ρ). Inferences will be made based on a posterior credible interval for the relevant parameters.

Bayesian Estimation and Statistical Evaluation of Hypothesis:
Superiority of the Test lens relative to the pre-defined threshold with respect to Grade 3 or higher will be evaluated using Bayesian statistics.

Primary Safety Hypothesis 1:
The null and alternative hypotheses for evaluating superiority of the Test lens relative to 5% are as follows:

$$H_0: p_{\mathrm{T}} \geq 0.05$$
$$H_A: p_{\mathrm{T}} < 0.05,$$

where p_{T} is the probability of a Grade 3 or higher SLF across all study visits for Test lens. Based on Bayesian posterior probability distribution of the proportion p_T, superiority is interpreted as 95% probability of Test being statistically lower than the threshold of 5% (i.e., $p_{\mathrm{T}} < 0.05$). If the upper bound of the 95% central posterior credible interval is below 0.05, it can be concluded that there is 95% probability that the Test lens is superior to 5% (statistically less than) based on the observed sample.

In the case of zero clinically significant SLF, a Bayesian hierarchical model accounting for zero event problem will be considered[18].

Unacceptable Lens Fitting
Lens fit acceptance will be analyzed using a Bayesian beta-binomial model with correlated binary data[17].

Bayesian Estimation and Statistical Evaluation of Hypothesis:
Superiority of the Test lens relative to the pre-defined threshold with respect to unacceptable lens fitting will be evaluated using Bayesian statistics.

Primary Safety Hypothesis 2:
The null and alternative hypotheses for evaluating superiority of the Test lens relative to 5% are as follows:

$$H_0: p_{\mathrm{T}} \geq 0.05$$
$$H_A: p_{\mathrm{T}} < 0.05,$$

where p_{T} is the probability of event (i.e., probability of unacceptable lens fitting while wearing the test lens). Based on Bayesian posterior probability distribution of the proportion p_T, superiority is interpreted as 95% probability of the Test lens being statistically lower than the pre-defined threshold of 5% (i.e., $p_{\mathrm{T}} < 0.05$) with respect to unacceptable lens fitting rate. If the upper bound of the 95% central posterior credible interval is below 0.05, it can be

concluded that there is 95% probability that the Test lens is superior to the 5% threshold (statistically less) based on the observed sample.

In the case of all eyes have an acceptable lens fit (i.e., zero unacceptable lens fit), a Bayesian hierarchical model accounting for zero event problem will be considered. Details of this model will be provided in the stand-along SAP[18].

Primary Efficacy Analyses:
All primary efficacy analyses will be conducted on the intent-to-treat population.

Threshold utilized in hypothesis testing related to CLUE vision scores were based on a meta-analysis of CLUE vision scores for the Market leader for multifocal lenses, Air Optix[21].

CLUE Vision Scores
Mean population estimates and two-sided 95% confidence intervals will be computed separately for each stratum (hyperopes and myopes) using a bootstrap methodology. At least a total of 20000 bootstrap iterations will be used following the suggestions of Samuelson and Petrick[19]. A minimum threshold of 4000 bootstrap iterations was recommended for an alpha=0.05, however, since each test will be performed using alpha=0.01, it is more appropriate to increase number of bootstrap iterations. The assessment of the impact of the autocorrelation for between subjects repeated measurements, is defined by the difference between the observed statistic compared to the bootstrapped population mean (bias= observed minus bootstrapped population mean). This approach was recommended for all estimations of statistical inference since this approach accommodates correlated data. The bootstrap analysis that will be performed followed a procedure as discussed by Davison, AC and Hinkley, DV[20].

Primary Efficacy Hypothesis 1:
The null and alternative hypothesis to test for superiority of Myopes relative to the threshold 41 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 41$$
$$H_A: \mu_{Test} > 41$$

Where μ_{Test}, represents the population mean for Myopes at the 1-week follow-up with respect to CLUE vision scores. Superiority will be declared if the lower limit of the 95% CI is above 41.

Primary Efficacy Hypothesis 2:
The null and alternative hypothesis to test for superiority of Hyperopes relative to the threshold 36 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 36$$
$$H_A: \mu_{Test} > 36$$

Where μ_{Test}, represents the population mean for Hyperopes at the 1-week follow-up with respect to CLUE vision scores. Superiority will be declared if the lower limit of the 95% CI is above 36.

Visual Performance (logMAR)

Binocular HLHC visual performance will utilize the same bootstrapping methodology as described above for CLUE vision. However, with respect to VP, mean population estimates and two-sided 95% confidence intervals will be computed separately for each distance (distance 4m, intermediate 64cm and near 40cm) but will combine the hyperopic and myopic populations. At least a total of 20000 bootstrap iterations will be used following the suggestions of Samuelson and Petrick[19]. A minimum threshold of 4000 bootstrap iterations was recommended for an alpha=0.05, however, since each test will be performed using alpha=0.01, it is more appropriate to increase number of bootstrap iterations. The assessment of the impact of the autocorrelation for between subjects repeated measurements, is defined by the difference between the observed statistic compared to the bootstrapped population mean (bias= observed minus bootstrapped population mean). This approach was recommended for all estimations of statistical inference since this approach accommodates correlated data. The bootstrap analysis that will be performed followed a procedure as discussed by Davison, AC and Hinkley, DV[20].

Primary Efficacy Hypothesis 3:

The null and alternative hypothesis for binocular distance HLHC visual performance to test for superiority of Aurora relative to the threshold 0.0 logMAR are as follows:

$$H_o: \mu_{Test} \geq 0 \text{ logMAR}$$
$$H_A: \mu_{Test} < 0 \text{ logMAR}$$

Where μ_{Test}, represents the population mean for Aurora at the 1-week follow-up with respect to distance HLHC visual performance. Superiority will be declared if the upper limit of the 95% CI is below 0.0.

Primary Efficacy Hypotheses 4 and 5:

The null and alternative hypothesis for binocular intermediate and near HLHC visual performance to test for superiority of Aurora relative to the threshold 0.17 logMAR are as follows:

$$H_o: \mu_{Test} \geq 0.17 \text{ logMAR}$$
$$H_A: \mu_{Test} < 0.17 \text{ logMAR}$$

Where μ_{Test}, represents the population mean for Aurora at the 1-week follow-up with respect to HLHC visual performance. Superiority will be declared if the upper limit of the 95% CI for either intermediate or near is below 0.17.

14.6. Secondary Analysis

All secondary analyses will be conducted on the Intent-to-Treat population.
Threshold utilized in hypothesis testing related to CLUE vision, comfort and handling scores were based on a meta-analysis of CLUE vision, comfort and handling scores for the Market leader for multifocal lenses, Air Optix[21].

CLUE Vision
Secondary hypotheses 1 and 2 will be tested using the same estimates and 95% CIs from the analysis as described for CLUE Vision in section 14.5. The hypotheses tests will be performed separately for Hyperopes and Myopes using 2-sided 95% confidence intervals constructed for the population mean at the 1-week follow-up evaluation.

Secondary Hypothesis 1:
The null and alternative hypothesis to test for superiority of Myopes relative to the threshold 46 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 46$$
$$H_A: \mu_{Test} > 46$$

Where μ_{Test}, represents the population mean for Aurora Hyperopes at the 1-week follow-up with respect to CLUE vision scores. Superiority will be declared if the lower limit of the 95% CI is above 46.

Secondary Hypothesis 2:
The null and alternative hypothesis to test for superiority of Hyperopes relative to the threshold 41 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 41$$
$$H_A: \mu_{Test} > 41$$

Where μ_{Test}, represents the population mean for Aurora Hyperopes at the 1-week follow-up with respect to CLUE vision scores. Superiority will be declared if the lower limit of the 95% CI is above 41.

CLUE Comfort and Handling
Mean population estimates and 95% CIs for CLUE comfort and handling will be calculated separately using bootstrapping techniques. For both comfort and handling scores, a minimum of 20000 bootstrap iterations will be used following the suggestions of Samuelson and Petrick[19]. A minimum threshold of 4000 bootstrap iterations was recommended for an alpha=0.05, however, since each test will be performed using alpha=0.01, it is more appropriate to increase number of bootstrap iterations. The assessment of the impact of the autocorrelation for between subjects repeated measurements, is defined by the difference between the observed statistic compared to the bootstrapped population mean (bias= observed

minus bootstrapped population mean). This approach was recommended for all estimations of statistical inference since this approach accommodates correlated data. The bootstrap analysis that will be performed followed a procedure as discussed by Davison, AC and Hinkley, DV[20]. Secondary hypotheses 3 and 4 will be tested using the data from hyperopes and myopes combined since there is not a significant difference in performance between these two populations. The hypotheses tests will be performed separately for Comfort and Handling using 2-sided 95% confidence intervals constructed for the population means at the 1-week follow-up evaluation.

Secondary Hypothesis 3:
The null and alternative hypothesis to test for superiority for Comfort of the Test lens relative to the threshold 52 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 52$$
$$H_A: \mu_{Test} > 52$$

Where μ_{Test}, represents the population mean for the Test lens at the 1-week follow-up with respect to CLUE comfort scores. Superiority will be declared if the lower limit of the 95% CI is above 52.

Secondary Hypothesis 4:
The null and alternative hypothesis to test for superiority for Handling of Test lens relative to the threshold 53 CLUE points are as follows:

$$H_o: \mu_{Test} \leq 53$$
$$H_A: \mu_{Test} > 53$$

Where μ_{Test}, represents the population mean for the Test lens at the 1-week follow-up with respect to CLUE Handling scores. Superiority will be declared if the lower limit of the 95% CI is above 53.

Number of Lenses Required to Achieve Optimization
Number of lenses required to achieve lens optimization will be analyzed using a Bayesian beta-binomial model with correlated binary data[17].

Bayesian Estimation and Statistical Evaluation of Hypothesis:
Superiority of the Test lens relative to the pre-defined threshold with respect to unacceptable lens fitting will be evaluated using Bayesian statistics. The null and alternative hypotheses for evaluating superiority of the Test lens relative to 5% are as follows:

$$H_0: p_{\mathrm{T}} \leq 0.90$$
$$H_A: p_{\mathrm{T}} > 0.90,$$

where p_{T} is the probability of event (i.e., proportion of subjects to achieve optimization in 4 lenses or less while wearing the test lens). Based on Bayesian posterior probability distribution of the proportion p_T, superiority is interpreted as 95% probability of the Test lens being statistically greater than the pre-defined threshold of 90% (i.e., $p_{\mathrm{T}} > 0.90$) with respect to

unacceptable lens fitting rate. If the upper bound of the 95% central posterior credible interval is above 0.90, it can be concluded that there is 95% probability that the Test lens is superior to the 90% threshold (statistically better) based on the observed sample.

In the case of all eyes have an acceptable lens fit (i.e., zero event of non-optimization), a Bayesian hierarchical model accounting for zero event problem will be considered. Details of this model will be provided in the stand-along SAP[18].

14.7. Other Exploratory Analysis

A meta-analysis will be performed on individual items from the study questionnaire utilizing data from all historical studies with database hard-lock, completed after design-lock [Phase 2b]. This will include [redacted]. The approximate number of subjects expected from the historical data is approximately 213. The allocation of subjects by study is displayed in Table 9.

Table 9: Clinical Studies Planned to be Utilized in Exploratory Meta-Analysis

Study Number	Population Included	Approximate Allocation of Subjects
[redacted]	Hyperopes	75
[redacted]	Myopes	78
[redacted]	Hyperopes	60

[redacted] is currently in execution

Any analyses performed on exploratory endpoints will be on the intent-to-treat population. Statistical analysis will follow the Meta-Analysis approach as discussed in Whitehead[22]. This analysis will be discussed completely in the stand-alone SAP.

The stand-alone SAP will include full details describing the following:

1. Specific items from questionnaire to be included
2. Historical data to be utilized
3. Structure for grouping questions assessing similar areas of performance (e.g., comfort or vision)
4. Methodology for assessing associations between endpoints within a grouping
5. Model details to be utilized for each grouping
6. Strategy for adjustments for multiple testing
7. Strategies regarding utilizing subject data, if a subject participate in more than 1 historical study
8. Methodology for accounting for different study designs

This planned exploratory meta-analysis is intended to support stand-alone claims for the JJVC Investigational Multifocal Contact Lenses manufactured in senofilcon A C3.

14.8. Interim Analysis

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

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 10%. The SAS/STAT procedures PROC MI and PROC MIANALYZE will be utilized with a parametric regression method used to make at least 50 imputations.

14.10. Procedure for Reporting Deviations from Statistical Plan

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

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

The data for this study will be captured on electronic case report forms (eCRFs) using the BioClinica EDC system. 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 data sources for this study include: Not Applicable

The clinical data will be recorded on dedicated eCRFs specifically designed to match the study procedures for each visit. Only specifically delegated staff can enter data on a CRF. 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 ISO14155:2020.**Error! Reference source not found.**

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.

15.3. Trial Registration on ClinicalTrials.gov

This study will be registered on ClinicalTrials.gov based on the following: This study is not an early feasibility study.

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.

16.4. Data Monitoring Committee (DMC)

Not Applicable.

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

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

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(R2) guidelines on Good Clinical Practice (GCP),[Error! Reference source not found.] 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[Error! Reference source not found.] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with section 8 of the ICH E6(R2) guidelines on Good Clinical Practice (GCP),[Error! Reference source not found.] 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.
- Sponsor-approved informed consent form (and any other written materials to be provided to the subjects)
- Investigator's Brochure (or equivalent information).
- 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, 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 revisions
- 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 revisions
- 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 revisions that increase subject risk, the revisions 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 or their representative, must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,**Error! Reference source not found.Error! Reference source not found.** current ICH GCP**Error! Reference source not found.** and ISO 14155:2020**Error! Reference source not found.** guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential subject the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Subjects will be informed

that their participation is voluntary and that they may withdraw consent to participate at any time.

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) and other applicable personal data protection and security laws and regulations.[15,16] 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, the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH GCP and all study documents as specified by the applicable regulatory requirement(s).**Error! Reference source not found.** The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

If it becomes necessary for the Sponsor or the appropriate regulatory authority to review any documentation relating to this study, the Investigator must permit access to such reports.
If the Investigator has a question regarding retention of study records, he/she should contact JJVC.

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

There is no plan to publish the outcome of this investigation.

22. REFERENCES

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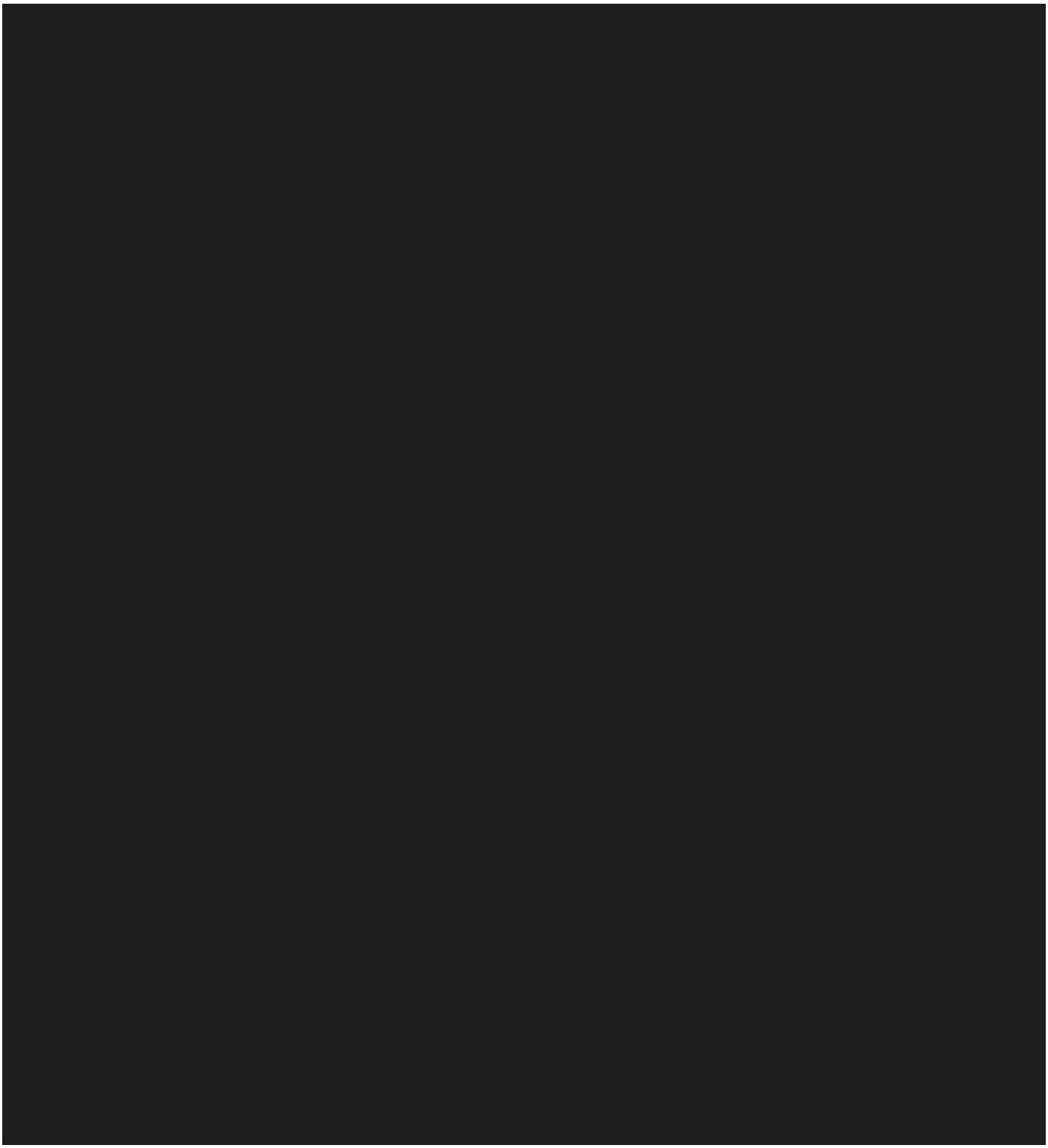
24. Bonferroni C. Calculation of the insurance groups of heads. Studies in Honour of Professor Salvatore Ortu Carboni. 1935;Rome: Italy:13-60

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

[redacted]

[redacted]



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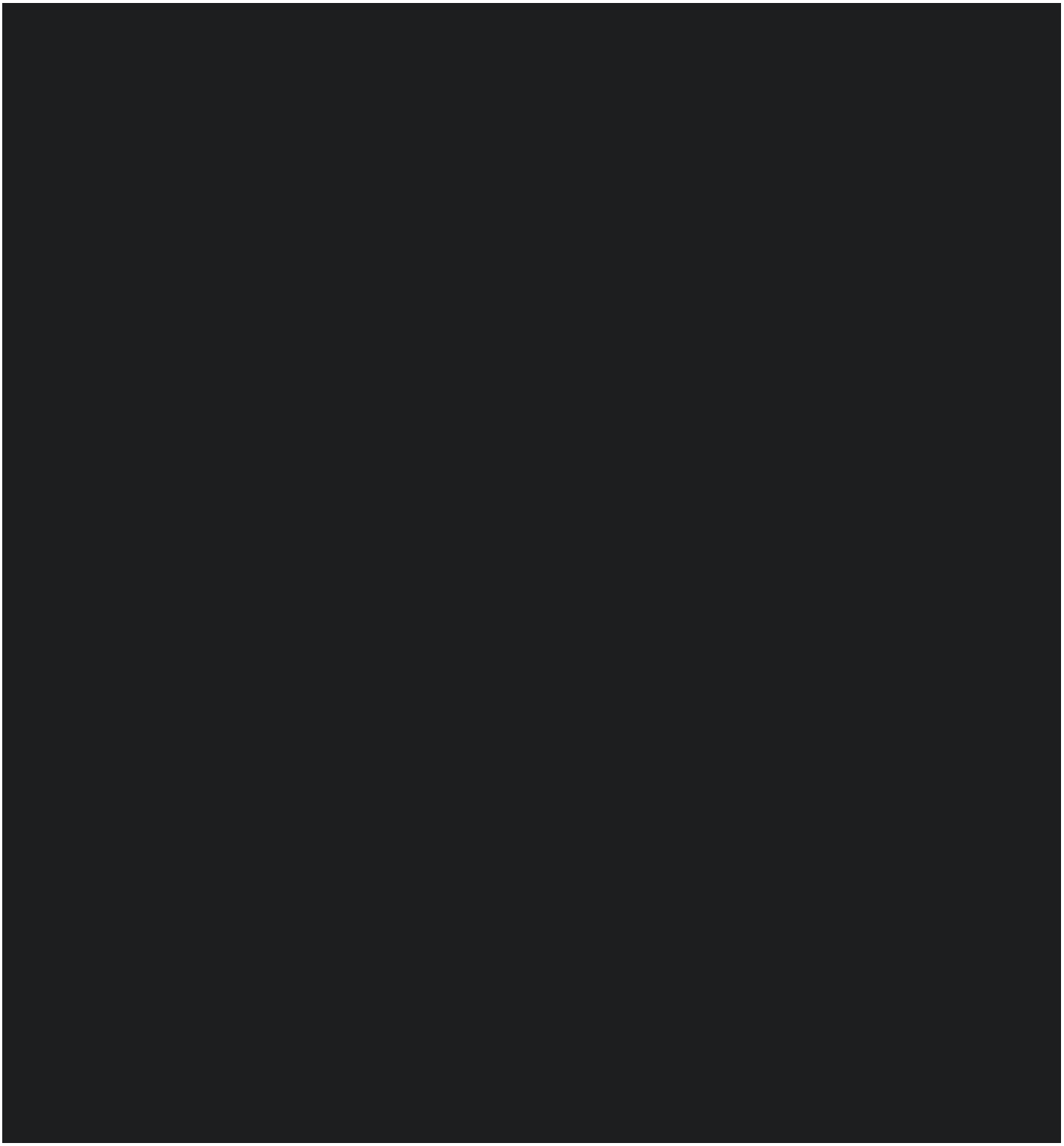
[redacted]

[redacted]

[redacted]



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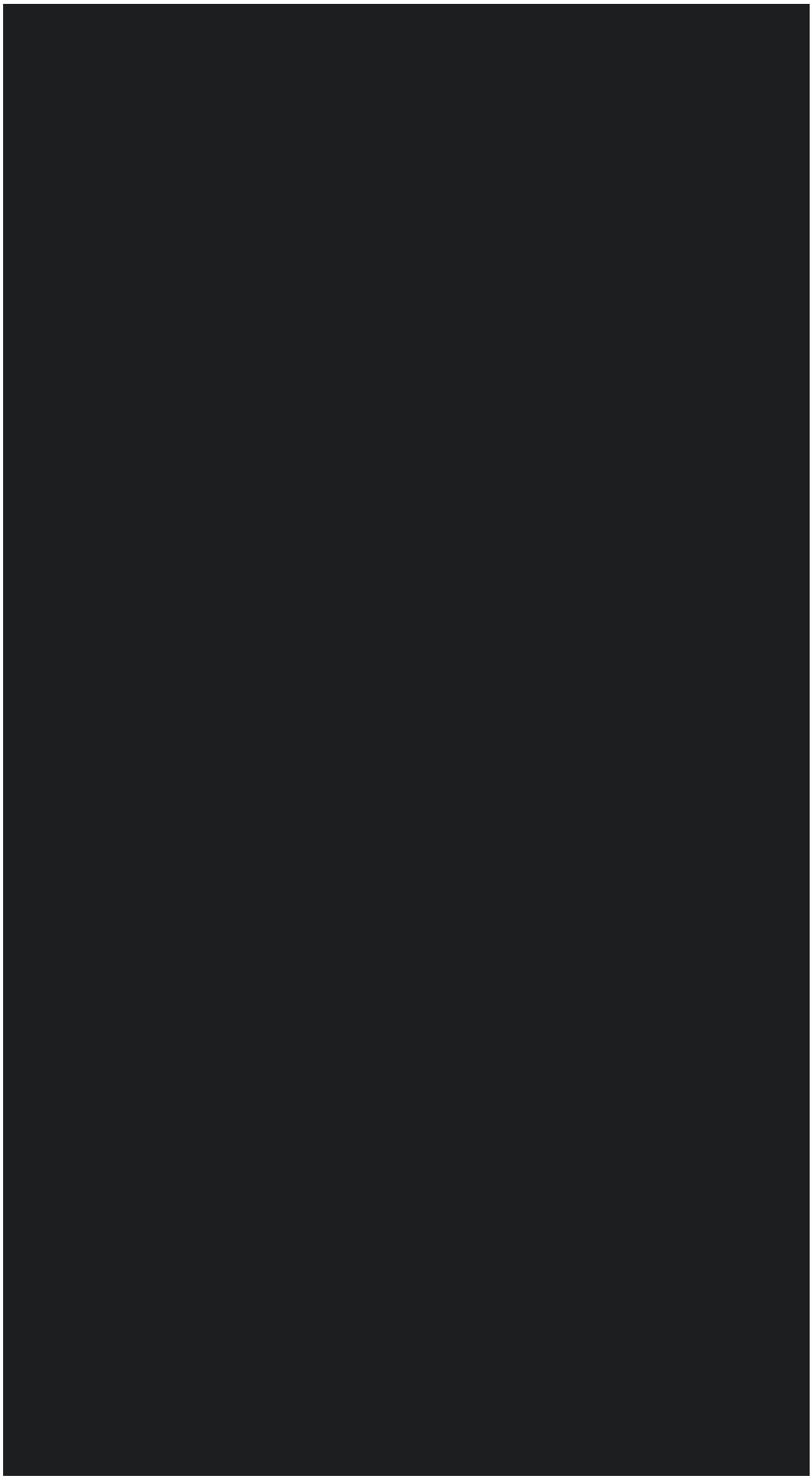
[redacted]

[redacted]

[redacted]



APPENDIX B: PATIENT INSTRUCTION GUIDE

[redacted].

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not applicable.

APPENDIX D: PRESBYOPIC SYMPTOMS QUESTIONNAIRE

[redacted]

APPENDIX E: OCULAR DOMINANCE

[redacted]

APPENDIX F: LENS FITTING GUIDE

Step 1.

[redacted]

[redacted]

APPENDIX G: BINOCULAR OVER REFRACTION

APPENDIX H: [redacted]

- [redacted] DETERMINATION OF NEAR ADDITION
- [redacted] NEAR LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE
- [redacted] LENS FITTING CHARACTERISTICS
- [redacted] SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS
- [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIVE ERROR
- [redacted] BIOMICROSCOPY SCALE
- [redacted] DISTANCE AND NEAR SNELLEN VISUAL ACUITY EVALUATION
- [redacted] DISTANCE LOGMAR VISUAL ACUITY MEASURMENT PROCEDURE
- [redacted] PATIENT REPORTED OUTCOMES
- [redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION

[redacted] DETERMINATION OF NEAR ADDITION

Title: Determination of Near Addition

Document Type: [redacted]

Document Number: [redacted] **Revision Number: 5**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Title:	**Determination of Near Addition**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 5**

[redacted]

[redacted] NEAR LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE

Title: Near LogMAR Visual Acuity Measurement Procedure

Document Type: [redacted]

Document Number: [redacted] **Revision Number:** 9

[redacted]

Title:	**Near LogMAR Visual Acuity Measurement Procedure**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 9**

[redacted]

[redacted] LENS FITTING CHARACTERISTICS

Title: Lens Fitting Characteristics

Document Type: [redacted]

Document Number: [redacted] **Revision Number:** 6

[redacted]

[redacted]

Title:	**Lens Fitting Characteristics**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 6**

[redacted]

[redacted]

[redacted]

[redacted] SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS

Title: Subject Reported Ocular Symptoms/Problems

Document Type: [redacted]

Document Number: [redacted] **Revision Number:** 4

[redacted]

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIVE ERROR

Title: Determination of Distance Spherocylindrical Refractive Error

Document Type: [redacted]

Document Number: [redacted] **Revision Number: 5**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] BIOMICROSCOPY SCALE

Title:	**Biomicroscopy Scale**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 10**

[redacted]

[redacted]

[redacted]

[redacted]

Title:	**Biomicroscopy Scale**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 10**

[redacted]

[redacted] DISTANCE AND NEAR SNELLEN VISUAL ACUITY EVALUATION

Title: Distance and Near Snellen Visual Acuity Evaluation

Document Type: [redacted]

Document Number: [redacted] **Revision Number: 5**

[redacted]

[redacted]

Title:	**Distance and Near Snellen Visual Acuity Evaluation**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 5**

[redacted]

Title:	**Distance and Near Snellen Visual Acuity Evaluation**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 5**

[redacted]

[redacted] DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE

Title:	**Distance LogMAR Visual Acuity Measurement Procedure**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 5**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Title:	**Distance LogMAR Visual Acuity Measurement Procedure**
Document Type:	[redacted]
Document Number:	[redacted] **Revision Number: 5**

[redacted]

[redacted] PATIENT REPORTED OUTCOMES

Title: Patient Reported Outcomes
Document Type: [redacted]
Document Number: [redacted] **Revision Number:** 3

[redacted]

[redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

Title: Visual Acuity Chart Luminance and Room Illumination Testing

Document Type: [redacted]

Document Number: [redacted] **Revision Number: 4**

[redacted]

Title: Visual Acuity Chart Luminance and Room Illumination Testing

Document Type: [redacted]

Document Number: [redacted] **Revision Number: 4**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

APPENDIX I: GUIDELINES FOR COVID-19 RISK MITIGATION

1.0 PURPOSE

The purpose of this document is to provide guidelines for the re-opening or initiation of clinical study sites participating in Johnson & Johnson Vision Care, Inc. (JJVCI) clinical studies during the COVID-19 pandemic.

2.0 SCOPE

This document provides guidelines for Johnson & Johnson Vision Care (JJVCI) to address the potential risks from COVID-19 to study subjects, investigators, study site staff, and monitors at study sites. The guidance provided in this document is in effect from the date of approval through the date of retirement of this Work Instruction. At a minimum, this Work Instruction will be reviewed and updated on a quarterly basis, as appropriate.

NOTE: Re-opening of sites outside of the US will be evaluated on a country by country basis subject to local health authority guidance.

3.0 DEFINITIONS

American Academy of Optometry (AAO): The American Academy of Optometry is an organization of optometrists based in Orlando, Florida. Its goal is to maintain and enhance excellence in optometric practice, by both promoting research and the dissemination of knowledge. The AAO holds an annual meeting, publishes a monthly scientific journal, gives credentials to optometrists through the fellowship process and publishes position statements.

American Optometric Association (AOA): The American Optometric Association, founded in 1898, is the leading authority on quality care and an advocate for our nation's health, representing more than 44,000 Doctors of Optometry (O.D.), optometric professionals, and optometry students. Doctor of Optometry take a leading role in patient care with respect to eye and vision care, as well as general health and well-being. As primary health care providers, Doctor of Optometry have extensive, ongoing training to examine, diagnose, treat and manage ocular disorders, diseases and injuries and systemic diseases that manifest in the eye. The American Optometric Association is a federation of state, student, and armed forces optometric associations. Through these affiliations, the AOA serves members consisting of optometrists, students of optometry, paraoptometric assistants and technicians. The AOA and its affiliates work to provide the public with quality vision and eye care.

Centers for Disease Control and Prevention (CDC): The Centers for Disease Control and Prevention is a national public health institute in the United States. It is a United States federal agency, under the Department of Health and Human Services, and is headquartered in Atlanta, Georgia.

COVID-19: Current outbreak of respiratory disease caused by a novel coronavirus. The virus has been named "SARS-CoV-2" and the disease it causes has been named "Coronavirus Disease 2019" (COVID-19).

Clinical Study: Voluntary research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drugs, vaccines, other therapies, or new ways of using existing treatments. May also be called clinical trials, studies, research, trials, or protocols.

Clinical Study Site: Location where a clinical study is conducted, such as a doctor's office, university, or laboratory. Clinical studies are conducted by Investigators who are individual(s) responsible for the conduct of the clinical study at a study site. If a study is conducted by a team of individuals, the Investigator is the responsible leader of the team and may be called the Principal Investigator.

Clinical Operations Manager (COM): The Johnson & Johnson Vision Care (JJVCI) individual responsible for the overall management of a clinical trial.

Monitor: An individual designated to oversee the progress of a clinical study and ensure that it is conducted, recorded, and reported in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and applicable regulatory requirements.

Medical Safety Officer (MSO): Physician who has primary accountability in their product portfolio for product health and safety, and who serves as an independent medical voice for patient safety.

Safety Management Team (SMT): A cross-functional, collaborative team responsible for review, assessment and evaluation of medical safety data arising from any source throughout the product life cycle.

4.0 GUIDANCE FOR STUDY DOCUMENTS

In alignment with recent health authority guidance, JJVCI is providing recommendations for study-related management in the event of disruption to the conduct of the clinical study. This guidance does not supersede any local or government requirements or the clinical judgement of the investigator to protect the health, safety and well-being of participants and site staff. If, at any time, a participant's safety is considered to be at risk, study intervention will be discontinued, and study follow-up will be conducted as outlined in the protocol.

During the COVID-19 pandemic, the additional risks listed below need to be considered for study participants and study personnel:

4.1 Additional Risks Related to the COVID-19 Pandemic:

- The possible transmission of the Coronavirus infection and consequent complications, beyond the risk of adverse events due to the investigational device and/or procedures.
- The risk may be higher in an optometric clinical study because of the close contact the subject will have with health care professionals during the procedures and assessments (since the investigator must make the measurements close to the subject's face) and, in addition the need for multiple follow-up visits/exams which may expose the subject to other patients and/or healthcare professionals who might be transmitting the virus, even if they do not have symptoms.
- Potential disruptions to the study may be necessary due to current or future pandemic-related emergency restrictions, which may lead to delays in scheduled follow-up visits.
- Subjects experiencing an adverse event related to contact lens wear may receive delayed treatment due to COVID-19 restrictions. In this event, all assessments that can be conducted virtually will be completed by the investigator to determine the best course of treatment for the subject, including an unscheduled visit, up to discontinuation from the study, as appropriate.

If a study subject is found to have contracted COVID-19 during participation in a study, he/she will be discontinued from the study and followed until COVID-19 Adverse Event (AE) resolution.

To help minimize the above potential risks, JJVCI recommend reviewing/complying with local, state, and governmental guidance for COVID-19 risks.

JJVCI will provide the following study specific documents with language pertaining to COVID-19 risks:

4.1.1 Informed Consent:

Will include information concerning the study-associated risks related to the COVID-19 pandemic in bold font and/or boxed on the first page of the Informed Consent document:

STUDY ASSOCIATED RISKS RELATED TO COVID-19 (CORONAVIRUS) PANDEMIC

It is important to note that this study will be conducted, at least in part, during the COVID-19 pandemic. As such, additional risks associated with the infection with COVID-19 exist for you. This is particularly important for this study due, in part, to the closeness of the doctor during the study examinations.

The potential effects of the disease are not fully known, at this time, and may include long-term serious health consequences. In severe cases, this may result in hospitalization and/or death. Based on current knowledge from the Centers for Disease Control and Prevention (CDC), those at high-risk for severe illness from COVID-19 include older adults and people with underlying medical conditions.

During this study, all appropriate measures will be taken to minimize risks including the use of personal protective equipment such as masks and gloves, as well as proper sanitization. This is in conformance to guidance from the CDC, local health departments, and the state and county in which the study doctor's office is located. However, these measures may not completely eliminate the risks associated with contracting COVID-19.

If you are found to have contracted COVID-19 or feel ill with flu-like symptoms during participation in the study, you will not be permitted to continue in-office study follow-up visits, but you will receive instructions and your condition will be monitored by the doctor and/or study staff.

4.1.2 COVID-19 Risk Control Checklist (Attachment-B):

Will include COVID-19 risk control methods that are required by a site to conduct JJVCI clinical studies. The risk controls are consistent with CDC, AOA, AAO Guidance. The Principal Investigator will review/sign the study specific checklist prior to the Site Initiation Meeting.

4.1.3 Protocol Compliance Investigator(s) Signature Page:

Will include a statement indicating that the Principal Investigator (PI) agrees to conduct the study in compliance with all local, state, and governmental guidance's for COVID-19 risk mitigation.

I have read the suggested guidance provided by JJVCI pertaining to the COVID-19 risk mitigation, (COVID-19 Work Instruction in the Appendix of this protocol). I agree to conduct this study in compliance with local, state, governmental guidance for COVID-19 risks.

4.1.4 Study Site Initiation Training Slides:

Will include suggestions to help mitigate potential transmission of COVID-19. Suggestions may include maintaining social distancing in the clinical site by staggered scheduling of study patients, wearing proper PPEs, frequent disinfection, and installing shields on the slit lamp and other applicable equipment.

5.0 GUIDANCE FOR REMOTE SUBJECT VISITS

Potential disruptions to the study may be necessary due to current or future pandemic-related emergency restrictions. Possible disruption of the study as a result of COVID-19 control measures may lead to delays in scheduled follow-up visits.

Subjects may be delayed in being seen for study follow up visit(s), for example due to COVID-19 control measures or due to the subject's concerns or fears about COVID-19 risk. When appropriate, the remote assessment will be conducted to the extent possible. Discussions with the subject during remote assessments may include:

Procedure	Details
Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire regarding the test article when applicable and feasible.
Change of Medical History (Adverse Events) and Concomitant Medications / Therapies Review	Record any adverse events or medical history changes from the previous study visit with the subject/parents. Review the subject's concomitant medications/therapies and record any changes from the previous study visit.
Wearing Time and Compliance	Record the average wearing time (including number of hours per day during weekdays and weekends, and number of days per week). Confirm compliance with the prescribed wear schedule. • Record and discuss the lens wear compliance based on the subject's self-report. For example, the subjects will be asked the time of the day the subject typically puts on the study lenses in the morning and takes off in the evening, the number of days per week lenses were worn, and the number of consecutive days the subject didn't wear the study lenses, etc.

The discussion with the subject will be documented in EDC under Tele-Visit and a minor protocol deviation will be noted. If during the telephone consultation, a subject states he/she wishes to discontinue participating in the study, instruct the subject to stop wearing the study lenses and schedule the subject to return to the clinic for a Final Evaluation at the at earliest possible time. Subjects should return all unused lenses to the clinic at the last visit.

Changes in study visit schedules, missed visits, or participant discontinuations may lead to missing data, including data related to protocol-specified procedures. Case report forms should capture specific information regarding the basis of missing data, including the relationship to the COVID-19 pandemic.

6.0 STUDY CONDUCT DURING PANDEMIC

It is recognized that the Coronavirus Disease 2019 (COVID-19) pandemic may have an impact on the conduct of this clinical study due to, for example, self-isolation/quarantine by participants and study-site personnel; travel restrictions/limited access to public places, including Optometry Clinics; and changes in clinic procedures required to address the COVID-19 challenge.

Every effort should be made to adhere to protocol-specified assessments for study participants, including follow-up. However, if scheduled visits cannot be conducted in person at the study site it is suggested that assessments be performed to the extent possible remotely/virtually or delayed until such time that on-site visits can be resumed in order to continue participant monitoring in accordance with the protocol where possible. At each contact, participants will be interviewed to collect safety data. Key efficacy endpoint assessments should be performed if required and as feasible.

Modifications to protocol-required assessments may be permitted via COVID-19 Appendix after consultation with the participant, investigator, and the sponsor. Missed assessments/visits will be captured in the clinical trial management system for protocol deviations. Interruptions of test article wear or discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the case report form (CRF).

The sponsor will continue to monitor the conduct and progress of the clinical study, and any changes will be communicated to the sites and to the health authorities according to local guidance.

If a participant has tested positive for COVID-19, the investigator should contact the sponsor's responsible medical monitor to discuss initial plans for study intervention and follow-up. The medical monitor will notify the Safety Management Team of any subject(s) that have reported "COVID-19", "Asymptomatic COVID-19", or "Suspected COVID-19" adverse events within 24 hours of the notification.

Modifications made to the study conduct as a result of the COVID-19 pandemic will be summarized in the clinical study report.

COVID-19 screening procedures that may be mandated by local healthcare systems do not need to be reported as an amendment to the protocol even if done during clinical study visits.

6.1 Monitoring Visits

When on-site monitoring by the sponsor is not feasible, the sponsor's site monitor will contact the study site to schedule remote visits. In such cases, on-site monitoring visits will resume when feasible, with increased frequency to address the source data verification backlog.

Even with staffing limitations during this COVID-19 pandemic, all routine operations related to clinical trials should be well-documented and archived as part of standard process. When conditions permit, all parties involved in this clinical trial should communicate relevant information in a timely manner so that all relevant parties remain sufficiently informed.

6.1.1 Study Site Initiation:

During the period that this Work Instruction is in effect, Site Initiation Meetings and training of study site staff will be conducted remotely. The JJVCI study team will conduct training via Skype, Zoom, Microsoft Teams or similar software as well as utilize online training materials, as applicable. Study site training will be documented utilizing Site Initiation Report [redacted] per Study Site Initiation [redacted]

On-site visits may be considered when, for example, hands-on training or evaluation of site facilities is required. While on site, the Clinical Research Associate (CRA) will follow all local, state, and governmental policies for COVID-19 Risk Mitigation, including social distancing, wearing of PPE, etc. as applicable for the location of the study site.

6.1.2 Interim Monitoring Visits (if applicable):

During the period that this Work Instruction is in effect, Interim Monitoring On-site visits will be kept to a minimum and include only those tasks that the CRA cannot perform remotely (e.g., source document verification, test article reconciliation, etc.).

To ensure data integrity during the conduct of all JJVC studies, clinical study teams will follow the study specific Clinical Monitoring Plan [redacted]

While on site, the CRA will follow all local, state, and governmental policies for COVID-19 Risk Mitigation, including social distancing, wearing of PPE, etc. as applicable for the location of the study site.

6.1.3 Study Site Closure:

During the period that this Work Instruction is in effect, the duration of the Study Site Closure Visit will be limited to tasks that the CRA cannot perform remotely (e.g., source document verification, test article final reconciliation and return, etc.).

Attachment A: Study Site Correspondence

XXXX XX, 2020

Re: COVID-19 Mitigation Plan, <<CR-xxxx/protocol title>>

Dear <<Principal Investigator>> and Study Team,

Coronavirus (COVID-19) has impacted several communities and business activities over the past several months. While we work toward the successful conduct of clinical studies, our commitment continues to be the safety of patients, healthcare professionals, and to our communities.

Therefore, we would like to share the following revisions/additions related to the above referenced Johnson & Johnson Vision Care company sponsored clinical trial(s) you are currently working on or considering participation within.

Protocol:

- Guidelines for COVID-19 Risk Mitigation provided in the Appendix section.

Protocol Signature Page:

- Will include a statement indicating the Principal Investigator agrees to conduct the study in compliance with all local, state, and governmental guidelines for COVID-19 risk mitigation.

Informed Consent:

- Will include information concerning the study-associated risks related to the COVID-19 pandemic in bold font and/or boxed on the first page of the Informed consent document.

COVID-19 Risk Control Checklist for Clinical Studies:

- Will include COVID-19 risk control measures that are required to ensure the safety and health of subjects, site staff and monitors during the pandemic.

We want to encourage the need for open lines of communication about potential challenges you may foresee as the result of the current COVID-19 situation. Therefore, we encourage you to regularly connect with your respective Johnson & Johnson clinical study team (Clinical Research Associate (CRA), Lead CRA or Study Managers).

Thank you for your continued engagement, collaboration, and dedication to your study subjects during this challenging time.

Please file this letter in your site file study correspondence.

Attachment B: COVID-19 Risk Control Checklist

Study Number
Site Number
Principal Investigator (PI) Name

The following COVID-19 risk control methods are required to conduct Johnson & Johnson Vison Care clinical studies. Please review the following requirements and Initial each requirement.

PI Initials	General Site Safety Planning Measures
	Signage within site describing Risk Control methods
	Social Distancing practices throughout site (waiting rooms, lobby, exam rooms, etc.)
	Non-contact thermometer available to assess temperatures of staff and patients
	Training on patient flow and physical distancing in waiting room
	Establish longer time frame between patient appointments to reduce persons in the site
	Staff should receive job-specific training on PPE and demonstrate competency with selection and proper use of PPE and wear at all times during interactions with subjects (e.g., putting on and removing without self-contamination)

PI Initials	Site Staff Daily Safety Measures
	As part of routine practice, site staff should regularly monitor themselves for fever and symptoms of COVID-19, including temperature checks
	Any staff member (including non-study clinic staff and Investigators) showing signs of being sick or testing positive for COVID-19 must not be permitted to work on activity that may expose study related staff and subject and the Sponsor shall be informed **NOTE: Inform JJVC in 24 hours of any COVID-19 cases and all potential exposure during the clinical study.**
	Ensure that all staff wear a mask Gloves should be required when working directly with patients and changed between each patient
	Have staff thoroughly wash hands for at least 20 seconds or use an alcohol-based hand sanitizer when they arrive, before and after each patient, before eating and after using the bathroom.
	Cleaning and disinfection procedures for exam rooms and instruments or equipment between patients with gloves.
	Cleaning and disinfection procedures for commonly touched surfaces (doors, chairs, computers, phones, etc.) with gloves.

PI Initials	Before a Patient or Study Visit:
	Patients should be asked prior to entering the site about fever and respiratory illness and whether they or a family member have had contact with another person with confirmed COVID-19 in the past 14 days. Patients exhibiting signs of being sick should be rescheduled when their symptoms resolve.
	Instruct patients that companions should remain outside of the facility and not accompany the patient into the facility unless they are a parent/guardian of the patient or if they are a true caregiver and need to assist the patient
	Request the patient to call or text the office upon arrival so entrance to and movement through facility can be coordinated by site staff

PI Initials	Patients Entering the site:
	Temperature checks utilizing a non-contact thermometer for all patients and companions entering the site.
	All patients and companions must wear cloth or disposable mask at all times in the site
	Maintain social distancing. Waiting rooms or lobbies should be as empty as possible. Advise seated patients to remain at least 6 feet from one another.
	Communal objects in (e.g. toys, reading materials, etc.) should be removed or cleaned regularly.

I certify that I have read and agree to implement all the listed COVID-19 Risk Control Measures required for the conduct of Johnson & Johnson Vision Care studies.

Principal Investigator Signature and Date

RESOURCE LINKS

US Resource Links

- OSHA Training
  https://www.osha.gov/SLTC/covid-19/controlprevention.html

  Personal Protective Equipment (PPE) Training
  CDC: https://www.cdc.gov/coronavirus/2019-ncov/hcp/using-ppe.html

- I&R Training
  ACUVUE® LensAssist: https://www.acuvue.com/lensassist

- Clinic Preparedness Guides
  CDC: https://www.cdc.gov/coronavirus/2019-ncov/hcp/clinic-preparedness html
  AOA: https://aoa.uberflip.com/i/1240437-aoa-guidance-for-re-opening-practices-covid·19/1?m4=
  American Optometric Association: https://www.aoa.org/optometry-practice-reactivation-preparedness-guide

- In-Office Disinfection of Multi-Patient Use Diagnostic Contact Lenses
  https://www.gpli.info/wp-content/uploads/2020/03/2020-01-15-in-office-disinfecting-of-diagnostic-lenses.pdf

OUS Resource Links

- Updates on local regulations in Hong Kong
  https://www.coronavirus.gov hk/eng/index.html

- Resumption of optical services in England: Letter from Matt Neligan and Poonam Sharma
  https://www.england nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/04/C0601-reopening-of-optical-services-letter-17-june-2020.pdf

- NHS Optical Letter
  https://www.england nhs.uk/coronavirus/wp-content/uploads/sites/52/2020/04/C0127-optical-letter-1-april-2020.pdf

- The College of Optometrists primary eye care COVID-19 guidance: Red phase
  https://www.college-optometrists.org/the-college/media-hub/news-listing/coronavirus-covid-19-guidance-for-optometrists.html

- The College of Optometrists COVID-19: College updates
  https://www.college-optometrists.org/the-college/media-hub/news-listing/coronavirus-2019-advice-for-optometrists.html#CollegeGuidelines

- Infection Control Guidelines. (n.d.). Retrieved from Canadian Association Of Optometrists: https://opto.ca/sites/default/files/resources/documents/infection_control_guidelines_2016.pdf

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6477 Protocol Title: Evaluation of a daily disposable silicone hydrogel multifocal contact lens in myopes and hyperopes

Version and Date: 2.0 05 January 2022

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

I agree to conduct this study according to ISO 14155:2020,[1] GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] United States (US) Code of Federal Regulations (CFR),[4] and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. The Principal Investigator is responsible for ensuring that all clinical site personnel, including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

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

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

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

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

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

I have read the suggested guidance provided by JJVCI pertaining to the COVID-19 risk mitigation, (COVID-19 Work Instruction in the Appendix I of this protocol). I agree to conduct this study in compliance with local, state, governmental guidance for COVID-19 risks.

Principal Investigator: _____ _____
Signature Date

_____
Name and Professional Position (Printed)

Institution/Site: _____ _____
Institution/Site Name

_____
Institution/Site Address