

# **Clinical Study Protocol**

## **Johnson & Johnson Vision Care, Inc.**

Evaluation of Multifocal Contact Lens Designs with and without an HEV-Blocker on Visual Function

Protocol CR-6391

Version: 4.0

Date: 12 January 2022

Investigational Products: JJV Investigational Multifocal Contact Lens with and without HEV-Blocker

Control: ACUVUE® OASYS Multifocal Contact Lens

Keywords: JJV Investigational Multifocal, ACUVUE® OASYS Multifocal Contact Lens, HEV Blocker, Presbyopia, Randomized, senofilcon A (C3), senofilcon A, Daily Wear

### **Statement of Compliance to protocol, GCP and applicable regulatory guidelines:**

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

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**PROTOCOL TITLE, NUMBER, VERSION AND DATE**

Title: Evaluation of Multifocal Contact Lens Designs with and without an HEV-Blocker on Visual Function

Protocol Number: CR-6391

Version: 4.0

Date: 12 January 2022

**SPONSOR NAME AND ADDRESS**

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

**MEDICAL MONITOR**

Name: [REDACTED]

Title: [REDACTED]

Address: [REDACTED]

24 Hour Contact Telephone #: [REDACTED]

Email: [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.

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### AUTHORIZED SIGNATURES

The signatures below constitute 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,<sup>4</sup> ISO 14155:2020,<sup>1</sup> ICH guidelines,<sup>2</sup> and the Declaration of Helsinki.<sup>3</sup>

Author *See Electronic Signature Report*  DATE

Co-Author 

Clinical Operations Manager *See Electronic Signature Report*  DATE

Biostatistician *See Electronic Signature Report*  DATE

Data Management *See Electronic Signature Report*  DATE

Approver *See Electronic Signature Report*  DATE

**Clinical Study Protocol**  
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Reviewer

*See Electronic Signature Report*

DATE

Reviewer

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**CHANGE HISTORY**

Version	Originator	Description of Change(s) and Section Number(s) Affected	Justification for Change	Date
1.0	[REDACTED]	Original Protocol	NA	30-Jun-2021
2.0	[REDACTED]	Add OU visual acuity to Exit Evaluation and Unscheduled Visits	OU VA collected at baseline and should also be collected at Exit and Unscheduled Visits	08-Jul-2021
3.0	[REDACTED]	<p>Throughout Document-updated protocol version and date.</p> <p>Appendix G &amp; section 7.2-added fitting guide and clarified fitting procedure.</p> <p>Section 7.1-corrected follow-up days to <math>\pm 3</math> days.</p> <p>Section 4.3-updated estimated study duration.</p> <p>Section 7.2-clarified eye for color testing.</p> <p>Appendix H-updated to record findings OU.</p> <p>Updated to new protocol template.</p>	<p>Fitting guide in package insert has trouble shooting steps that are not included in this study so separate fitting guide included.</p> <p>Corrected typo and updated anticipated study timing.</p> <p>Clarification in Appendix H so that is matches the body of the protocol.</p>	13-Sep-2021

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Version	Originator	Description of Change(s) and Section Number(s) Affected	Justification for Change	Date
4.0	[REDACTED]	<p>Throughout Document-updated protocol version and date.</p> <p>Throughout Document-removed hyperopes, changed sample size to 35 to enroll and 25 to complete and removed reference to CLAIMs study. Corrected typos.</p> <p>Synopsis-corrected term used for control lens and study duration to be consistent with body of protocol.</p> <p>Section 3.3-added history of herpetic keratitis</p>	Business priorities dictated changes to study being a feasibility type study.	12 Jan 2022

**SYNOPSIS**

Protocol Title	Evaluation of Multifocal Contact Lens Designs with and without an HEV-Blocker on Visual Function
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Feasibility Design control phase: Phase 2
Trial Registration	This study will be registered on ClinicalTrials.gov based on the following: The study is not determined to be an early feasibility study.
Test Article(s)	Investigational Products: JJV Investigational Multifocal Contact Lens with HEV-Blocker Control: ACUVUE® OASYS Multifocal with Pupil Optimized Design Contact Lenses
Wear and Replacement Schedules	Wear Schedule: The study is non-dispensing and all lenses will be worn only during the visit.
Objectives	Characterize the effects of an HEV-Blocker on several measures of visual function in a presbyopic population and to compare the results to a multifocal lens without an HEV-blocker (ACUVUE® OASYS Multifocal).

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Study Endpoints	<p>Primary endpoints: disability glare, halo size (mm), and starburst size (mm).</p> <p>Secondary endpoints: two-point thresholds with and without 403 nm filter; heterochromatic contrast threshold and glare discomfort.</p> <p>Primary and secondary endpoints will be measured with natural, binocular viewing conditions.</p> <p>Other endpoints: Subjective ratings of glare discomfort, halo and starburst intensity and color perception.</p>
Study Design	<p>This is a single-masked, bilateral, controlled, randomized, 2x2 crossover, non-dispensing clinical trial. There will be two study visits. Eligible subjects will be randomized and fit into one study lens per visit based on the randomization schedule. There will be a <math>7\pm3</math> days washout between the study visits. Additional details of the procedures done at each study visit are located at the end of the synopsis in the flowchart (Figure 1).</p>
Sample Size	<p>A total of approximately 35 eligible subjects will be enrolled with 25 targeted to complete the study.</p>
Study Duration	<p>The study will last approximately 6-7 months.</p>
Anticipated Study Population	<p>Healthy male and female volunteers with presbyopia will be screened as per criteria outlined below. Subjects will be myopic with refractive astigmatism of <math>\leq 0.75</math> D and adapted soft contact lens wearers. In addition, an attempt will be made to recruit an even distribution in the following ADD groups: +0.75 to +1.25 D, +1.50 to +1.75 D and +2.00 to +2.50 D.</p>

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Eligibility Criteria - Inclusion	<p>Potential subjects must satisfy all of the following criteria to be enrolled in the study:</p> <p>Inclusion Criteria following Screening:</p> <ol style="list-style-type: none"><li>1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.</li><li>2. The subject must appear able and willing to adhere to the instructions set forth in this clinical protocol.</li><li>3. The subject must be at least 40 and not more than 70 years of age at the time of screening.</li><li>4. Subjects must own a wearable pair of spectacles if required for their distance vision.</li><li>5. The subject must be an adapted soft contact lens wearer in both eyes (i.e., worn lenses a minimum of 2 days per week for at least 8 hours per wear day, for at least 1 month of duration).</li><li>6. The subject must 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".</li></ol> <p>Inclusion Criteria at Baseline Evaluation:</p> <ol style="list-style-type: none"><li>7. The subject must have normal color perception as evidenced by reading 17 out of the first 21 Ishihara plates correctly.</li><li>8. The subject's distance spherical equivalent of their refraction must be in the range of -1.00 D to -4.00 D.</li><li>9. The subject's refractive cylinder must be <math>\leq 0.75</math> D in each eye.</li><li>10. The subject's ADD power must be in the range of +0.75 D to +2.50 D in each eye.</li><li>11. The subject must have best corrected distance visual acuity of 20/20<sup>-3</sup> or better in each eye.</li></ol>
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Eligibility Criteria – Exclusion	<p>Potential subjects who meet any of the following criteria will be excluded from participating in the study:</p> <p>Exclusion Criteria following Screening:</p> <ol style="list-style-type: none"><li>1. Currently pregnant or lactating.</li><li>2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g., rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study.</li><li>3. Use of any of the following oral medications within 1 week prior to enrollment: oral retinoids, oral tetracyclines, oral phenothiazines, anticholinergics, oral/inhaled steroids, oral phosphodiesterase type 5 inhibitors, interferon alfa, antimycobacterial antibiotics, and nitroimidazole antibiotics. See section 9.1 for additional details regarding excluded systemic medications.</li><li>4. Any current use of ocular medication with the exception of rewetting drops.</li><li>5. Any known hypersensitivity or allergic reaction to single use preservative free rewetting drops or sodium fluorescein.</li><li>6. Any previous or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK dacryocystorhinostomy, cataract surgery, retinal surgery, peripheral iridotomy/iridectomy, etc.).</li><li>7. Participation in any contact lens or lens care product clinical trial within 7 days prior to study enrollment.</li><li>8. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).</li><li>9. Any active or ongoing ocular or systemic allergies that may interfere with contact lens wear.</li><li>10. A history of amblyopia, strabismus or binocular vision abnormality.</li><li>11. History of herpetic keratitis.</li><li>12. History of optic nerve or retinal disease or trauma.</li><li>13. Abnormal color vision.</li></ol>
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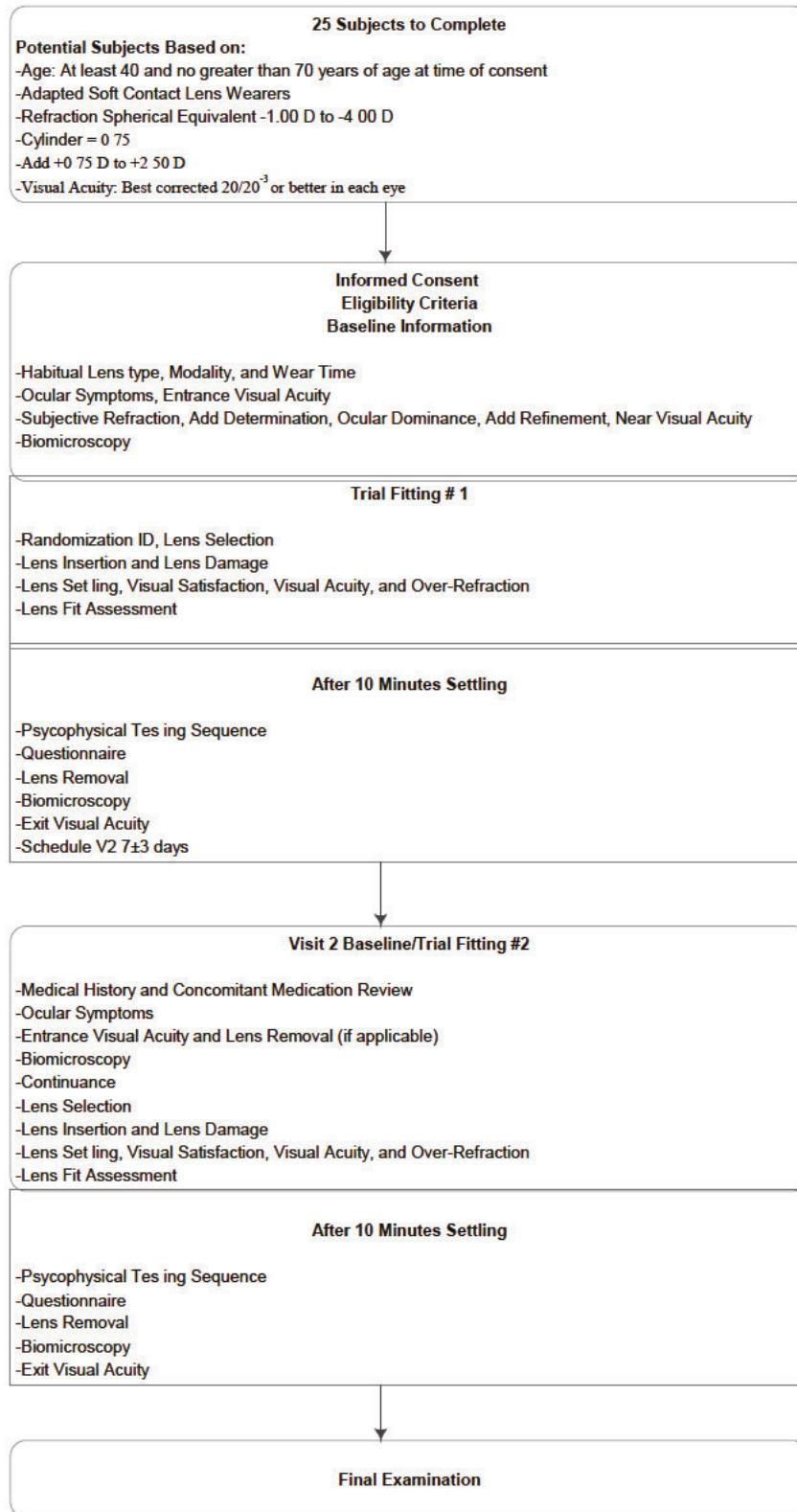
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	<p>Exclusion Criteria at Baseline Evaluation:</p> <p>14. Any other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, or corneal distortion</p> <p>15. Any grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA scale.</p> <p>16. Any current ocular infection or inflammation.</p>
Disallowed Medications/Interventions	<p>Use of any prescription or over-the-counter (OTC) medications that may affect contact lens wear.</p> <p>See Section 9.1 for details regarding disallowed systemic medications.</p>
Measurements and Procedures	<p>The addition of the HEV-Blocker may provide benefits beyond the benefits of the correction of only ametropia. The test procedures will evaluate objective test methods in an optical bench set-up to quantify some of these potential benefits. See Figure 1 in the synopsis and Section 7.2 in the protocol for the additional details on the procedures.</p>
Microbiology or Other Laboratory Testing	<p>None.</p>
Study Termination	<p>The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.</p>
Ancillary Supplies/ Study-Specific Materials	<p>Non-preserved rewetting drops and optical bench test methods.</p>
Principal Investigator(s) and Study Institution(s)/Site(s)	<p>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.</p>

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Figure 1: Study Flowchart



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### COMMONLY USED ABBREVIATIONS, ACRONYMS AND DEFINITIONS OF TERMS

Add	Near addition; the additional power required for near vision correction
ADE	Adverse Device Effect
ADHD	Attention Deficit Hyperactivity Disorder
AE	Adverse Event/Adverse Experience
AO1Dfa	ACUVUE OASYS® 1-DAY with HydraLuxe™ TECHNOLOGY for ASTIGMATISM
AOfA	ACUVUE OASYS® 2-WEEK for ASTIGMATISM
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COM	Clinical Operations Manager
COVID-19	Coronavirus Disease 2019
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
	
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ESD	Eyelid Stabilized Design
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICH	International Council for Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LASIK	Laser-Assisted in Situ Keratomileusis
LogMAR	Logarithm of Minimal Angle of Resolution
OD	Right Eye
OS	Left Eye
OU	Both Eyes
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRK	Photorefractive Keratectomy
PRO	Patient Reported Outcome

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QA	Quality Assurance
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VA	Visual Acuity

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### **1. INTRODUCTION AND BACKGROUND**

Filters have long been used in ophthalmic devices, with sunglasses probably the best-known example. Sunglasses help to minimize the deleterious effects of intense light. Intense light can lead to discomfort as well as degrade visual performance. Using light filters can help to improve the discomfort associated with intense light as well as improve the visual performance.

Johnson & Johnson currently has two multifocal contact lenses on the market. Multifocal contact lenses correct refractive errors through the use of simultaneous vision, where the distance, intermediate and near corrections are placed in front of the pupil at one time. This type of correction can reduce image contrast and create visual artifacts, thus reducing visual performance. Given the vision compromise created by simultaneous vision, the additional detrimental impact of intense light can further compound the problem.

The purpose of this study is to investigate the potential visual benefits of using a High Energy Visible (HEV) light blocker in multifocal contact lenses and evaluate its impact on performance. An investigational multifocal contact lens with an HEV blocker will be compared to a multifocal lens without an HEV blocker.

#### **1.1. Name and Descriptions of Investigational Products**

Investigational Products: JJV Investigational Multifocal Contact Lens with HEV blocker (Test Lens)

JJV Investigational Multifocal Contact Lens without HEV-Blocker (Control Lens)

#### **1.2. Intended Use of Investigational Products**

All lenses in this study are intended to correct spherical refractive error and presbyopia. The study is non-dispensing and all of the study lenses will be worn as a daily disposable lens, with the lenses being discarded after a wear at the clinical site. The lenses will be fit in a randomized fashion. After fitting, the subject will undergo a number of vision assessments. The sequence will then be repeated with the other study lens type.

#### **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 JJV investigational lenses used in this study refer to the latest version of the CR-6391 Investigator Brochure.

#### **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. 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 study lens package insert for

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additional details for the control lens and the Investigational Brochure (IB) for the Investigational lenses. The study multifocal contact lenses are designed for the correction of refractive spherical refractive error and presbyopia. The test lenses are manufactured in senofilcon A C3 material and the control lens in senofilcon A. The lenses will be worn in a daily wear, disposable modality. These lenses are not intended for extended wear.

For the most comprehensive risk and benefit information regarding JJV Investigational Multifocal Contact Lens with HEV blocker refer to the latest version of the Investigator's Brochure.

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

The Test lenses have been previously tested in clinical studies [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED], [REDACTED] and [REDACTED]. [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 studies [REDACTED], [REDACTED] did not have final study reports and [REDACTED] were still in the field. A summary of the lens performance in studies [REDACTED], [REDACTED], [REDACTED] and [REDACTED] is provided below.

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.

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.

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.

[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.

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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.

For information about the control product refer to study lens package insert for additional details (APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)) and the Investigational Brochure (IB) for the Investigational product.

## **2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES**

### **2.1. Objectives**

Characterize the effects of an HEV-blocker on several measures of visual function in a presbyopic population and to compare the results to a lens without an HEV-Blocker (ACUVUE® OASYS Multifocal).

#### **Primary Objective**

The primary objective is to evaluate the impact an HEV blocker used in a multifocal contact lens has on artifacts potentially caused by intense light with respect to glare disability threshold, starbursts and halos.

#### **Secondary Objective**

The secondary objective is to assess the impact an HEV blocker has on the deleterious effects of scatter, measured as two-point thresholds measured with and without a 403 nm filter, heterochromatic contrast threshold and glare discomfort.

#### **Exploratory Objectives**

The exploratory endpoints include subjective response to the visual artifacts and color perception.

### **2.2. Endpoints**

#### **Primary Endpoints**

##### **Glare Disability Threshold (change in log relative energy level) (GD)**

GD threshold will be evaluated by exposing subjects to various intensities of a white light annulus (~10-deg inner diameter; 12-degree outer diameter), which surrounds a mid-wave (580 nm), central grating target. GD will be quantified by the log relative energy level necessary to obscure the central target.

##### **Starburst diameter (mm)**

Starburst diameter will be quantified by the horizontal spread of the spokes emerging from the center of a small, point-like stimulus. A calibrated custom-made micrometer (two sides with reverse threading) will be used to spread two posts out from a central mid-point. The posts attach to a custom-designed ruler that indicates the lateral spread of the starburst.

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### Halos (mm)

Halos will be quantified by the diameter (mm) of outer edges of the halo of the white light point-like stimulus and is measured using the same micrometer as for starbursts.

### **Secondary Endpoints**

#### Two-point threshold (mm)

To create the two-point threshold stimulus, a single point-source like stimulus will be spread into two distinct points of light, using a custom-built, collapsible light baffle. The two-point threshold will be quantified as the minimum distance (mm) at which a participant can detect two distinct points of light, separated by a small black space.

#### Glare Discomfort (change in squint in mm) (GDC)

GDC will be evaluated by calculating the change in height of the palpebral fissure measured while the participant views the mid-wave central grating target, compared to the maximal squint during a 5-second photostress exposure induced by a solid, 10-degree broadband field, which completely obscures the target (~10-deg diameter). Both eyes will be recorded and averaged, to produce an average palpebral fissure height before and during the photostress exposure.

#### Heterochromic Contrast Threshold (HCT)

Using the same optical bench set-up described in GD above, to measure HCT, participants will view the mid-wave (580 nm) grating target presented on a short-wave (460 nm) “sky-light background.” The intensity of the background will be adjusted, until the participant is no longer able to resolve the grating target. The log-relative energy of the background needed to obscure the central target will be recorded as HCT.

### **Exploratory Endpoints**

#### Color perception testing

A custom-built device will be used to measure color perception. Participants will view a stimulus that consists of broadband light that is passed through integrating spheres, coated with an ultra-diffuse reflective material. The experimenters will then adjust a set of Wratten filters until the subject perceives a perfect, untinted white. CIE coordinates (x,y; u',v'; total illuminance; total irradiance) will be recorded.

Subjective discomfort while viewing halos, starbursts and the photostressor will be assessed. Subjective discomfort will be measured using a single Likert-type question following exposure to the photostressor and after viewing halo and starburst stimuli.

#### **2.3. Hypotheses**

Primary Hypotheses

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1. Glare disability thresholds measured using the optical bench will be significantly higher in the Test lens compared to the Control lens.
2. Halo sizes (mm) measured with the custom halometer device will be significantly smaller in the Test lens compared to the Control lens.
3. Starburst size (mm), as measured with the halometer, will be significantly smaller in the Test lens compared to the Control lens.

### **Secondary Hypotheses**

1. Two-point thresholds (mm) measured using the light shield and baffle device will be significantly lower in the Test lens compared to the Control lens with the 403 nm filter.
2. Two-point thresholds (mm) measured using the light shield and baffle device will be significantly lower in the Test lens compared to the Control lens without the 403 nm filter.
3. The Test lens will have a significantly lower change in squint response (mm) compared to the Control lens with respect to glare discomfort as measured on an optical bench.
4. Heterochromatic contrast thresholds measured using the optical bench will be significantly higher in the Test lens compared to the Control lens.

### **Exploratory Hypotheses**

1. Color appearance (x, y, u', v') measured using the custom colorimeter device will not differ between the Test lens and the Control lens.
2. The photostressor, halo and starburst stimuli will be perceived as significantly less intense / uncomfortable in the Test lens, compared to the Control lens.

## **3. TARGETED STUDY POPULATION**

### **3.1. General Characteristics**

Healthy male and female volunteers with presbyopia will be screened as per criteria outlined below. Subjects will be adapted soft contact lens wearers and be myopic with no or low levels of astigmatism ( $\leq 0.75$  D). In addition, an attempt will be made to recruit an even distribution of subjects in the following ADD groups: +0.75D to +1.25 D, +1.50D to +1.75 D and +2.00D to +2.50 D.

### **3.2. Inclusion Criteria**

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

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### **Inclusion Criteria following 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 between at least 40 and not more than 70 years of age at the time of screening.
4. Possess a wearable pair of spectacles that provide correction for 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 8 hours per wear day, for 1 month of more duration).
6. 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 Evaluation**

7. The subject must have normal color perception as evidenced by reading 17 out of the first 21 Ishihara plates correctly.
8. The subject’s distance spherical equivalent of their refraction must be in the range of -1.00 D to -4.00 D.
9. The subject’s refractive cylinder must be  $\leq$ 0.75 D in each eye.
10. The subject’s ADD power must be in the range of +0.75 D to +2.50 D in each eye.
11. The subject must have best corrected distance 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 following Screening**

The subject must not:

1. Be currently pregnant or lactating.
2. Any systemic disease (e.g., Sjögren’s Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g., rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study.
3. Use of any of the following oral medications within 1 week prior to enrollment: oral retinoids, oral tetracyclines, oral phenothiazines, anticholinergics, oral/inhaled steroids, oral phosphodiesterase type 5 inhibitors, interferon alfa, antimycobacterial antibiotics, and nitroimidazole antibiotics. See Section 9.1 for additional details regarding excluded systemic medications.
4. Any current use of ocular medication with the exception of rewetting drops.
5. Any known hypersensitivity or allergic reaction to single use preservative free rewetting drops or sodium fluorescein.

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6. Any previous or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK dacryocystorhinostomy, cataract surgery, retinal surgery, peripheral iridotomies/iridectomy, etc.).
7. Participation in any contact lens or lens care product clinical trial within 7 days prior to study enrollment.
8. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).
9. Any active or ongoing ocular or systemic allergies that may interfere with contact lens wear.
10. History of herpetic keratitis.
  
11. A history of amblyopia, strabismus or binocular vision abnormality.
12. History of optic nerve or retinal disease or trauma
13. Abnormal color vision.

### Exclusion Criteria at Baseline Evaluation

The subject must not have:

14. Any other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, or corneal distortion
15. Any grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA scale.
16. Any current ocular infection or inflammation.

### **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-site, 2-visit, single-masked (partial), bilateral, controlled, 2x2 crossover, randomized, non-dispensing clinical trial. There will be two study visits. Approximately 35 subjects will be enrolled with a target of 25 subjects to complete. If a subject meets all eligibility criteria, then the subject will be randomized at Visit 1 into one of two lens wear sequences using a 2x2 crossover design. The subjects will be fit into the study lenses at each visit per the randomization scheme. There will be a 7±3 days washout between study visits. Subjects will not wear the study lenses outside the study visit. Additional details of the procedures done at each study visit are contained in Section 7.2.

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### **4.2. Study Design Rationale**

Crossover designs are a well-established study design in which subjects are exposed to multiple treatments during different time periods. A  $2\times 2$  bilateral crossover design was considered to be the optimal design since the study period is relatively short, the design can be cost effective, and more efficient comparisons between treatments can be made compared to a parallel, between-subjects design. In a crossover design, fewer subjects are required to achieve the same pre-specified statistical power. Each subject will act as their own control to reduce the influence of potential confounding factors such as age, gender and vision correction. A  $7\pm 3$  days washout period between study lens wear will be implemented to help reduce any potential bias.

### **4.3. Enrollment Target and Study Duration**

A total of approximately 35 eligible subjects will be enrolled with 25 targeted to complete the study. The study will last approximately 6-7 months.

## **5. TEST ARTICLE ALLOCATION AND MASKING**

### **5.1. Test Article Allocation**

A computer-generated randomization scheme will be used to randomly assign subjects to one of the 2 possible contact lens wear sequences in a bilateral fashion using a  $2\times 2$  crossover design with a block of size 2. The randomization scheme will be generated using the PROC PLAN procedure from Statistical Analysis System (SAS) Software Version 9.4 or higher (SAS Institute, Cary, NC)<sup>6</sup>. Please see below for details regarding the randomization by study period.

Table 1: Detailed Randomization Plan for all Study Visits

Sequence	Period 1 (Visit 1)	Period 2 (Visit 2)
1	Test	Control
2	Control	Test

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

The randomized assignment of subjects will be performed at the first visit prior to the first fitting. The following must have occurred prior to randomization:

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

When dispensing test articles, the following steps should be followed to maintain randomization codes:

1. Investigator or designee (documented on the Delegation Log) will consult the lens fitting schedule to obtain the test article assignment for that subject prior to dispensing.

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2. Investigator or designee will record the subject's number on the appropriate line of the lens fitting schedule
3. 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.

### **5.2. Masking**

This is a single masked (partial) study. It is impossible to totally mask the subjects as the lenses with the HEV blocker will have a different color, however subjects will not be informed of the differences in optical designs or any details regarding the intended performance of the HEV blocker. Masking will be used to reduce potential bias. 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 as to the identity of the investigational product.

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

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

### **5.3. Procedures for Maintaining and Breaking the Masking**

The test articles mask 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.

When dispensing test articles, the following steps should be followed to maintain randomization codes:

1. Investigator or designee (documented on the Delegation Log) will consult the lens fitting schedule/randomization scheme to obtain the test article assignment for that subject prior to dispensing.
2. Investigator or designee will record the subject's number on the appropriate line of the randomization scheme.
3. Investigator or designee will pull the appropriate test articles from the study supply. All test articles that 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.

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### 6. STUDY INTERVENTION

#### 6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 2: Test Articles

	Test Lens	Control
Name and Description	Investigational Multifocal Contact Lens-MF (HEV)	ACUVUE® OASYS Multifocal with Pupil Optimized Design Contact Lenses
Manufacturer	Johnson & Johnson® Vision Care, Inc.	Johnson & Johnson® Vision Care, Inc.
Compass or Protocol Management Protocol(s) and/or Lot Number or Other Identifier	[REDACTED]	Marketed Product
Lens Material	senofilcon A (C3) with HEV	senofilcon A
Nominal Base Curve	8.35	8.4 mm
Nominal Diameter	14.3 mm	14.3 mm
Nominal Distance Powers (D)	-1.00 D to -4.00 D in 0.25 D steps	-1.00 D to -4.00 D in 0.25 D steps
Nominal Cylinder Powers (D) and Axes	None	None
Nominal ADD Powers (D)	LOW, MID, HI	LOW, MID, HI
Water Content	38%	38%
Center Thickness	0.07 mm	0.07 mm
Oxygen Permeability (Dk)	103	103
Wear Schedule in Current Study	Daily Wear	Daily Wear
Replacement Frequency	Daily Disposable	Daily Disposable
Packaging Form (vial, blister, etc.)	Blister	Blister

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### **6.2. Ancillary Supplies/Products**

The following solutions will be used in this study:

Table 3: 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	LaciPure Saline Solution
Manufacturer	Optics Laboratory	B&L	Menicon
Preservative	Non-Preserved	Non-preserved	Non-preserved

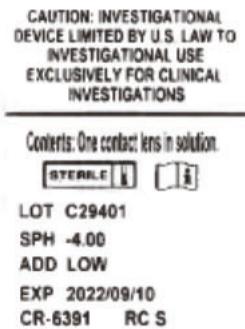
Lens cases and fluorescein strips (either 0.6 mg or 1.0 mg) will be supplied for use as needed.

### **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 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.

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### **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.

Reference [REDACTED]: Site Instructions for Test Article Receipt and Test Article Accountability for additional information.

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**7. STUDY EVALUATIONS**

**7.1. Time and Event Schedule**

Table 4: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 2
Time Point	Day 1	Day 7 ± 3
Estimated Visit Duration	2.5 hours	1.5 hours
Statement of Informed Consent	x	
Demographics	x	
Medical History and Concomitant Medications/Adverse Event Review	x	x
Habitual Lenses	x	
Habitual Lens Duration of Wear/Days per week	x	
Wear time and Comfortable Wear time with Habitual lenses	x	
Eligibility after Screening	x	
Ocular Symptoms	x	x
Entrance Distance Visual Acuity	x	x
Lens Removal (if applicable)	x	x
Subjective Sphero-cylindrical Refraction	x	
Near ADD Determination	x	
Ocular Dominance	x	
ADD Refinement	x	
Near Visual Acuity	x	
Ishihara Plates	x	
Biomicroscopy	x	x
Iris Color	x	
Eligibility after Baseline	x	
Randomization ID	x	x
Lens Selection	x	x

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Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Treatment 2
Time Point	Day 1	Day 7 ± 3
Estimated Visit Duration	2.5 hours	1.5 hours
Lens Insertion	X	X
Lens Settling	X	X
Visual Satisfaction	X	X
Visual Acuity	X	X
Distance Over-Refraction	X	X
Subjective Lens Fit Assessment	X	X
Psychophysical testing sequence	X	X
Lens Removal	X	X
Continuance		X
Exit Biomicroscopy	X	X
Exit Visual Acuity	X	X
Schedule Visit	X	
Final Evaluation		X

## 7.2. Detailed Study Procedures

### VISIT 1

The subjects must present to Visit 1 wearing habitual spectacles or contact lenses if required for their distance vision.

Visit 1: Screening		
Step	Procedure	Details
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.  <b>NOTE: The subject must be provided a signed copy of this document.</b>
1.2	Demographics	Record the subject's age, gender, race and ethnicity.
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.

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Visit 1: Screening		
Step	Procedure	Details
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	Wear time and Comfortable Wear time with Habitual lenses	Record the subjects wear time and comfortable wear time with their habitual contact lenses.
1.7	Eligibility after Screening	<p>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.</p> <p><i>If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.</i></p>

Visit 1: Baseline		
Step	Procedure	Details
1.8	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.
1.9	Entrance Distance Visual Acuity	<p>Distance Snellen visual acuity will be measured for each eye with the subject's habitual correction in place, if required for their distance vision.</p> <p>The acuity will be recorded to the nearest letter OD, OS and OU.</p>
1.10	Lens Removal (if applicable)	Have the subject remove their habitual lenses and store in an approved storage solution
1.11	Subjective Sphero-cylindrical Refraction	<p>Complete binocular subjective sphero-cylindrical refraction and record the resultant distance visual acuity (OD, OS, and OU) to the nearest letter.</p> <p><b>Note:</b> Best distance visual acuity with sphero-cylindrical refraction must be at least 20/20-3 in each eye for the subject to enroll in the study.</p>

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Visit 1: Baseline			
Step	Procedure	Details	
1.12	Near ADD Determination	The near reading addition will be determined using the binocular crossed cylinder technique at 40 cm followed by optimization in a trial frame in step 1.14 below.	
1.13	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
1.14	ADD Refinement	Place the BCC result in the trial frame and refine the near prescription with trial lenses (or flippers) under binocular conditions.	
1.15	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.	
1.16	Ishihara Plates	Perform Ishihara OD and OS with the best near correction. The subject must correctly identify 17 of the first 21 plates to continue.	
1.17	Biomicroscopy	<p>FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.</p> <p>If any of these slit lamp findings are grade 3 or higher. If discontinued a final examination must be completed.</p> <p>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.</p>	
1.18	Iris Color	Record the subjects Iris Color on the scale provided.	Appendix F
1.19	Eligibility after Baseline	<p>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.</p> <p><i>If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.</i></p>	

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Visit 1: Treatment 1 Lens Fitting		
Step	Procedure	Details
1.20	Randomization ID	Record the Randomization ID per the random scheme.
1.21	Lens Selection	<p>Select the lens pair based on the Randomization Scheme. Record the test lens parameters (power and lot number). The lens power selected will be the spherical equivalent for of the distance prescription for each eye. Select the ADD power based on upon the measured ADD power and the lens table in Appendix G.</p>
1.22	Lens Insertion	<p>The Investigator, or designee, will insert the lenses on the subjects eyes. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary.</p> <p>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 Quality Product Complaint form.</p> <p><b><u>NOTE:</u></b> <i>A Patient Instruction Guide will be given to the subject in any study where a lens is placed on eye. The subject will wear the study lenses only at the clinical site.</i></p>
1.23	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes before proceeding.
1.24	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 window for distance vision assessments, and for them to read a book, magazine or similar for near vision.
1.25	Visual Acuity	Distance and Near Snellen visual acuity will be measured OD, OS and OU..

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Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	
1.26	Distance Over- Refraction and Distance Visual Acuity	<p>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.</p>	
1.27	Subjective Lens Fit Assessment	<p>Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The subject will not proceed to wear the lenses if any of the following is observed:</p> <ul style="list-style-type: none"> <li>• presence of limbal exposure (appearance of clear cornea) in any gaze</li> <li>• presence of edge lift</li> <li>• presence of unacceptable movement (excessive or insufficient) in all three movement categories (primary gaze, upgaze, and push-up).</li> </ul> <p><i>If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.</i></p>	
1.28	Psychophysical testing sequence	<p>The following psychophysical testing sequence will be performed under binocular conditions.</p> <ul style="list-style-type: none"> <li>• Disability glare thresholds</li> <li>• Heterochromatic contrast thresholds</li> <li>• Discomfort glare</li> <li>• Subjective glare discomfort</li> <li>• Two-point threshold with and without filter</li> <li>• Halo Geometry</li> <li>• Subjective halo intensity</li> <li>• Starburst geometry</li> <li>• Subjective starburst intensity</li> <li>• Color Vision Testing (monocular-OD only)</li> </ul>	Appendix H

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Visit 1: Treatment 1 Lens Fitting		
Step	Procedure	Details
1.29	Lens Removal	Have the subject remove the study lenses and store in saline in a labeled glass vial. <i>NOTE: Lenses do not need to be stored in a refrigerator.</i>
1.30	Exit Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.  Adverse events shall be documented and followed for significant slit lamp findings.  If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.
1.31	Exit Visual Acuity	Record subjects' distance visual acuity, OD, OS, and OU to the nearest letter with their habitual lenses.
1.32	Schedule Visit	The subject will be scheduled for their next visit within $7\pm3$ days.

**VISIT 2**

The subjects must present to Visit 2 wearing habitual spectacles or contact lenses if required for their distance vision.

Visit 2: Baseline		
Step	Procedure	Details
2.1.	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.
2.2.	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.
2.3.	Distance Visual Acuity	Distance Snellen visual acuity will be measured for each eye with the subject's habitual correction in place, if required for their distance vision.  The acuity will be recorded to the nearest letter OD, OS and OU.

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Visit 2: Baseline			
Step	Procedure	Details	
2.4.	Lens Removal (if applicable)	Have the subject remove their habitual lenses and store in an approved storage solution	
2.5.	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.  If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	
2.6.	Continuance	Determine whether the subject is eligible to continue in the study based on the examination findings.	
2.7	Lens Selection	Select the lens pair based on the Randomization Scheme. Record the test lens parameters (power and lot number). The lens power selected will be the spherical equivalent for of the distance prescription for each eye. . Select the ADD power based on upon the measured ADD power and the lens table in Appendix G.	Appendix G
2.8	Lens Insertion	<p>The Investigator, or designee, will insert the lenses on the Subjects eyes themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary.</p> <p>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 Quality Product Complaint form.</p> <p><b><i>NOTE: A Patient Instruction Guide will be given to the subject in any study where a lens is placed on eye. The subject will wear the study lenses only at the clinical site.</i></b></p>	
2.9	Lens Settling	Allow the study lenses to settle for a minimum of 10 minutes before proceeding.	

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Visit 2: Baseline		
Step	Procedure	Details
2.10	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 window for distance vision assessments, and for them to read a book, magazine or similar for near vision.
2.11	Visual Acuity	Distance and Near Snellen visual acuity will be measured OD, OS and OU.
2.12	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.
2.13	Subjective Lens Fit Assessment	<p>Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The subject will not proceed to wear the lenses if any of the following is observed:</p> <ul style="list-style-type: none"> <li>• presence of limbal exposure (appearance of clear cornea) in any gaze</li> <li>• presence of edge lift</li> <li>• presence of unacceptable movement (excessive or insufficient) in all three movement categories (primary gaze, upgaze, and push-up).</li> </ul> <p><i>If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.</i></p>

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Visit 2: Baseline			
Step	Procedure	Details	
2.14	Psychophysical testing sequence	<p>The following psychophysical testing sequence will be performed under binocular conditions.</p> <ul style="list-style-type: none"> <li>• Disability glare thresholds</li> <li>• Heterochromatic contrast thresholds</li> <li>• Discomfort glare</li> <li>• Subjective glare discomfort</li> <li>• Two-point threshold with and without 403 nm interference filter</li> <li>• Halo geometry</li> <li>• Subjective halo intensity</li> <li>• Starburst geometry</li> <li>• Subjective starburst intensity</li> <li>• Color Vision Testing (monocular-OD only)</li> </ul>	Appendix H
2.15	Lens Removal	<p>Have the subject remove the study lenses and store in saline in a labeled glass vial.</p> <p><i>NOTE: Lenses do not need to be stored in a refrigerator.</i></p>	
2.16	Exit Biomicroscopy	<p>FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.</p> <p>Adverse events shall be documented and followed for significant slit lamp findings.</p> <p>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.</p>	

**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
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study, indicate the reason.

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Final Evaluation		
Step	Procedure	Details
F.2	Exit Refraction	<p>Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best-corrected distance visual acuity (OD, OS, and OU) to the nearest letter.</p> <p><b>Note:</b> This step is not necessary if the subject was exited due to screen failure.</p>
F.3	Exit Slit Lamp Biomicroscopy (for subjects that are discontinued early)	<p>FDA Slit Lamp Classification Scale will be used to grade the findings.</p> <p>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.</p> <p><b>Note:</b> 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).</p>

### 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.

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The following information will be collected during an unscheduled visit.

Unscheduled Visit		
Step	Procedure	Details
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 and OU) to the nearest letter.
U.5	Subjective Sphero-cylindrical Refraction (if applicable)	Perform bare-eye subjective sphero-cylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected <u>distance</u> visual acuity to the nearest letter (OD, OS, and OU).
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.
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 and OU) to the nearest letter.

#### 7.4. Laboratory Procedures

None

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### **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 visits through the final visit 2.

#### **8.2. Withdrawal/Discontinuation from the Study**

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

- Subject 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 missed any study visits
- Subject not compliant with study lens wear schedule
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit.

For discontinued subjects, the Investigator will:

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

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### **9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION**

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include medications that contraindicate contact lens wear.

Concomitant therapies that are disallowed include therapies that contraindicate contact lens wear.

#### **9.1. Systemic Medications**

Certain systemic medications are known to have a higher likelihood to interfere with contact lens wear, chiefly by disrupting the tear film.

A summary of disallowed systemic medications is shown in Table 5. Subjects with a history of taking these medications will be allowed to enroll only if:

- The medications have been taken on a continual, routine basis for at least 6 months, and
- The subject has demonstrated successful contact lens wear during this time.

Or:

- The subject was taking the medication on a temporary basis and ceased taking that medication at least 2 weeks prior to signing the informed consent (this is considered sufficient time for the medication to have left the body prior to enrollment).

Subjects with a history of taking medications listed in Table 5 on a long-term, routine basis for less than 6 months will not be allowed to participate in the study.

Table 5: Disallowed systemic medications

Class of Drug	Common Indication(s)	Common Examples
Estrogens (not including contraceptive medication)	Menopause, osteoporosis, vaginitis	Vagifem, Estrace, Climara, Vivelle-Dot, Premarin, Minivelle, etc.
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.
Beta-blockers	Hypertension, angina, heart attack, migraine, atrial fibrillation, adrenal cancer, essential tumor, glaucoma	Toprol XL, Lopressor, Tenormin, Propranolol, Timoptic, Trandate, Inderal LA, etc.
Psychotropics	Antipsychotic (schizophrenia, mania), antidepression,	Zoloft, Celexa, Prozac, Lexapro, Effexor, Cymbalta, Ativan, Xanax, Desyrel, Wellbutrin, etc.

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Class of Drug	Common Indication(s)	Common Examples
	antiobsessive, antianxiety, mood stabilizer, stimulants (ADHD)	
Vitamin A analogs	Cystic acne	Isotretinoin

Examples of disallowed systemic antihistamines are given in Table 6. Subjects with a history of taking systemic antihistamines will be allowed to enroll only if:

- They have taken antihistamines continuously for at least 2 weeks, and
- They have demonstrated successful wear while taking the medication

Table 6: Disallowed systemic antihistamines

Class of Drug	Common Indication(s)	Common Examples
Antihistamines	Allergic rhinitis, sedation, hives, allergic conjunctivitis, skin allergy, itching, motion sickness	Hydroxyzine, Promethagan, Phenadoz, Vistaril, Claritin, Zyrtec, Astepro, Astelin, Optivar, Allegra, Benadryl, 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, 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.

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Table 7 lists examples of deviations that will constitute major and minor protocol deviations for this study.

Table 7: Examples of major and minor protocol deviations

<b>Deviation category</b>	<b>Major deviation</b>	<b>Minor deviation</b>
Out-of-window visit	Visit attended more than 7 days out of visit window defined in study procedures	Visit attended 6 or fewer days out of visit window defined in study procedures

## **11. STUDY TERMINATION**

If more than 2 subjects in the investigational soft contact lens group develop serious expected (e.g., definite or probable MK) or unexpected device related adverse events, the study will be suspended. Upon review and consultation with IRB, DMC, and JJVC Safety Management Team, the study may be terminated. This potential stopping rule is established based on our trial involving approximately 200 subjects wearing the investigational soft contact lens for up to 3 years with an assumed MK rate that is below 0.2% per patient-year. The rate of 0.2% per patient year is the established rate for extended wear lenses in adults, which was requested by the FDA as a criterion for evaluating a contact lens for pediatric use in an FDA response to a pre-IDE submission. To be conservative, 200 independent patient years were used in the calculation. The probability of observing 2 cases or more incidents of MK is 0.061, and 3 cases or more incidents of MK is 0.007 (given an MK rate of 0.2% per patient year).

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.

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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.

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- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return (Refer to Form Control No. [REDACTED] for test article return instructions).

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

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

### 13. ADVERSE EVENTS

#### 13.1. Definitions and Classifications

**Adverse Event (AE)** – An AE is “any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device.”

**Note:** 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.<sup>1</sup>

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.

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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

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- 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.<sup>1</sup>**

**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.

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- 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.).

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- 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 (████████) 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,

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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

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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 Analyses 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.

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).<sup>6</sup> 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 study lens type, Test (Investigational Multifocal Contact Lens-MF (HEV) and Control (Investigational Multifocal Contact Lens-MF) and will be performed separately by completion status (Safety Population, Per-Protocol Population and Intent-to-Treat Population, when appropriate).

All primary and secondary analyses will be performed on the Intent-to-Treat Population (see Section 14.3 for additional details).

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### 14.2. Sample Size Justification

This study was not designed or powered to demonstrate any primary or secondary hypotheses. This is a feasibility study; therefore, the sample size was chosen by the study responsible clinician. Data collected from this study will be utilized to power future studies. A power analysis under different scenarios of intraclass correlations and effects sizes was performed using data from [REDACTED] since this study evaluated older subjects aged 40-65 and the Test lens from [REDACTED] has similar lens properties (HEV blocker formulation) and the same test psychophysiological endpoints were measured, and therefore this data was considered to best represent the lenses in this study. Table 8 below displays the descriptive summary for each endpoint and lens for the historical data.

Table 8: [REDACTED] Descriptive Summaries by Endpoint and Lens Type: 40-65 years

Endpoint	Mean (SD)		
	AO1D	Test	Difference
Glare Disability Threshold	1.125 (0.0636)	1.163 (0.0895)	0.0378 (0.03974)
Halo size (mm)	60.94 (19.829)	42.76 (17.747)	-18.180 (17.5803)
Starburst size (mm)	104.06 (19.785)	80.50 (15.666)	-23.557 (13.6529)

SD: Standard Deviation

AO1D: Acuvue Oasys 1-Day

Statistical power for each hypothesis based on 25 subjects to completed was calculated separately for each endpoint using a one-sided paired t-test with a type I error rate of 5%. The power estimates were conducted using the POWER procedure in SAS. The power for each endpoint for 25 subjects is provided in Table 9 below.

Table 9: Power Estimates by Endpoint for 25 Subjects to Complete

Endpoint	Effect Size	Power (%)		
		0.3	0.5	0.7
Glare Disability Threshold	0	5.0	5.0	5.0
	0.03	45.0	55.4	72.9
	0.05	81.2	90.7	98.3
Halo size (mm)	-14	91.5	97.2	99.8
	-16	96.4	99.2	>.999
	-18	98.7	99.8	>.999
Starburst size (mm)	-17	98.2	99.7	>.999
	-20	>.999	>.999	>.999
	-23	>.999	>.999	>.999

To account for subject dropouts and screen failures, up to 35 subjects will be enrolled into this study to ensure 25 complete.

### 14.3. Analysis Populations

**Safety Population:**

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

### **Per-Protocol Population:**

All subjects who successfully complete all visits and do not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock. Justification for the exclusion of subjects with protocol deviations from the per-protocol population set will be documented in a memo to file.

### **Intent-to-Treat (ITT) Population:**

All 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**

Primary and secondary hypotheses will be tested with a two-sided type I error rate of 5%. All primary and secondary hypotheses must be met in order to test any exploratory hypotheses.

#### **14.5. Primary Analysis**

##### **Starbursts (mm) and Halos (mm)**

Starbursts and Halos will be analyzed separately using a linear mixed model. Sequence of lens wear, period and lens type will be included as fixed effects. ADD Power, gender, race and dominant eye (Left or Right) may be included in the model as covariates when appropriate. Residual errors between measurements within the same subject across study periods will be modeled using an unstructured covariance structure (UN). The Kenward and Roger Method will be used for the denominator degrees of freedom. Comparisons between the study lenses will be carried out using two-sided 95% CIs for the least-square mean (LSM) difference (Test minus Control). Superiority will be declared if the upper limit of the 95% confidence interval is below 0.

The model will be constructed as follows:

We denote  $y_{ijkl}$  as the Starburst (or Halo) measurement for the  $l^{\text{th}}$  subject in the assigned to the  $k^{\text{th}}$  lens sequence during the  $j^{\text{th}}$  period for the  $i^{\text{th}}$  study lens (Test or Control).

The Model was as follows:

$$y_{ijkl} = \mu_0 + \beta_1 \text{Lens}_{i[j,k]} + \beta_2 \text{Period}_j + \beta_3 \text{Sequence}_k + \varepsilon_{ijkl}$$

- $\mu_0$ : overall intercept;
- $\text{Lens}_{i[j,k]}$ : Lens indicator;  $\text{Lens}_{i[j,k]}=1$  for Test and 0 otherwise;
- $\text{Period}_j$  : effect of the  $j^{\text{th}}$  period; period=1 if analysis period=1 and 0 otherwise
- $\varepsilon_{ijkl}$ : random error associated with the  $j^{\text{th}}$  period for the  $l^{\text{th}}$  subject for the  $i^{\text{th}}$  treatment assigned to the  $k^{\text{th}}$  lens sequence

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- $\begin{bmatrix} \varepsilon_{1kl} \\ \varepsilon_{2kl} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{11}^2 & \sigma_{12} \\ \sigma_{21} & \sigma_{22}^2 \end{bmatrix} \right)$

### Hypothesis Testing

The null and alternative hypotheses are as follows and will be conducted separately for both starbursts and halos :

$$H_0: \mu_{Test} - \mu_{Control} \geq 0$$
$$H_A: \mu_{Test} - \mu_{Control} < 0$$

where  $\mu_{Test} - \mu_{Control}$  is the population mean difference between the Test and the Control lenses. If the upper limit of the 95% confidence limit is below 0 then the results favor the *Test lens*. If the lower limit of the 95% confidence limit is above 0 then the results favor the *Control lens*.

### GD Threshold (change in log relative energy level)

GD Threshold will be analyzed using a linear mixed model. Sequence of lens wear, period and lens type will be included as fixed effects. ADD Power, gender, race and dominant eye (Left or Right) may be included in the model as covariates when appropriate. Residual errors between measurements within the same subject across study periods will be modeled using an unstructured covariance structure (UN). The Kenward and Roger Method will be used for the denominator degrees of freedom. Comparisons between the study lenses will be carried out using two-sided 95% CIs for the least-square mean (LSM) difference (Test minus Control). Superiority will be declared if the upper limit of the 95% confidence interval is below 0.

The model will be constructed as follows:

We denote  $y_{ijkl}$  as the GD threshold for the  $l^{\text{th}}$  subject in the assigned to the  $k^{\text{th}}$  lens sequence during the  $j^{\text{th}}$  period for the  $i^{\text{th}}$  study lens (Test or Control).

The Model was as follows:

$$y_{ijkl} = \mu_0 + \beta_1 \text{Lens}_{i[j,k]} + \beta_2 \text{Period}_j + \beta_3 \text{Sequence}_k + \varepsilon_{ijkl}$$

- $\mu_0$ : overall intercept;
- $\text{Lens}_{i[j,k]}$ : Lens indicator;  $\text{Lens}_{i[j,k]}=1$  for Test and 0 otherwise;
- $\text{Period}_j$  : effect of the  $j^{\text{th}}$  period; period=1 if analysis period=1 and 0 otherwise
- $\varepsilon_{ijkl}$ : random error associated with the  $j^{\text{th}}$  period for the  $l^{\text{th}}$  subject for the  $i^{\text{th}}$  treatment assigned to the  $k^{\text{th}}$  lens sequence
- $\begin{bmatrix} \varepsilon_{1kl} \\ \varepsilon_{2kl} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{11}^2 & \sigma_{12} \\ \sigma_{21} & \sigma_{22}^2 \end{bmatrix} \right)$

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### Hypothesis Testing

The null and alternative hypotheses for glare disability are as follows:

$$H_0: \mu_{Test} - \mu_{Control} \leq 0$$
$$H_A: \mu_{Test} - \mu_{Control} > 0$$

where  $\mu_{Test} - \mu_{Control}$  is the population mean difference between the Test and the Control lenses. If the upper limit of the 95% confidence limit is below 0 then the results favor the *Control lens*. If the lower limit of the 95% confidence limit is above 0 then the results favor the *Test lens*.

#### **Note:**

Prior to fitting any linear models for any endpoints, the distribution of each endpoint will be assessed to ensure the assumption of normality is fulfilled, this will be evaluated using the Shapiro-Wilks test for each study lens separately under the UNIVARIATE PROCEDURE in SAS Version 9.4. If an endpoint is concluded to follow a non-normal distribution, then a generalized linear model will be fit instead of the proposed linear models. If this occurs, the distribution that best fits the data will be chosen for the model and associated endpoint.

### **14.6. Secondary Analysis**

#### **Light Scattering with and without 403nm filter and Glare Discomfort (mm)**

Light scattering with and without a 403nm filter and glare discomfort will be analyzed separately using a linear mixed model. Sequence of lens wear, period and lens type will be included as fixed effects. ADD Power, gender, race and dominant eye (Left or Right) may be included in the model as covariates when appropriate. Residual errors between measurements within the same subject across study periods will be modeled using an unstructured covariance structure (UN). The Kenward and Roger Method will be used for the denominator degrees of freedom. Comparisons between the study lenses will be carried out using two-sided 95% CIs for the least-square mean (LSM) difference (Test minus Control). Superiority will be declared if the upper limit of the 95% confidence interval is below 0.

The model will be constructed as follows:

We denote  $y_{ijkl}$  as the Light scattering (with or without 403nm filter) measurement for the  $l^{\text{th}}$  subject in the assigned to the  $k^{\text{th}}$  lens sequence during the  $j^{\text{th}}$  period for the  $i^{\text{th}}$  study lens (Test or Control).

The Model was as follows:

$$y_{ijkl} = \mu_0 + \beta_1 Lens_{i[j,k]} + \beta_2 Period_j + \beta_3 Sequence_k + \varepsilon_{ijkl}$$

- $\mu_0$ : overall intercept;
- $Lens_{i[j,k]}$ : Lens indicator;  $Lens_{i[j,k]}=1$  for Test and 0 otherwise;
- $Period_j$  : effect of the  $j^{\text{th}}$  period; period=1 if analysis period=1 and 0 otherwise

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- $\varepsilon_{jkl}$ : random error associated with the  $j^{\text{th}}$  period for the  $l^{\text{th}}$  subject for the  $i^{\text{th}}$  treatment assigned to the  $k^{\text{th}}$  lens sequence
- $[\varepsilon_{1kl} \ \varepsilon_{2kl}] \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{11}^2 & \sigma_{12} \\ \sigma_{21} & \sigma_{22}^2 \end{bmatrix} \right)$

### Hypothesis Testing

The null and alternative hypotheses are as follows and will be conducted separately for both starbursts and halos :

$$H_0: \mu_{\text{Test}} - \mu_{\text{Control}} \geq 0$$
$$H_A: \mu_{\text{Test}} - \mu_{\text{Control}} < 0$$

where  $\mu_{\text{Test}} - \mu_{\text{Control}}$  is the population mean difference between the Test and the Control lenses. If the upper limit of the 95% confidence limit is below 0 then the results favor the *Test lens*. If the lower limit of the 95% confidence limit is above 0 then the results favor the *Control lens*.

### Heterochromatic Contrast Threshold (HCT)

HCT will be analyzed using a linear mixed model. Sequence of lens wear, period and lens type will be included as fixed effects. ADD Power, gender, race and dominant eye (Left or Right) may be included in the model as covariates when appropriate. Residual errors between measurements within the same subject across study periods will be modeled using an unstructured covariance structure (UN). The Kenward and Roger Method will be used for the denominator degrees of freedom. Comparisons between the study lenses will be carried out using two-sided 95% CIs for the least-square mean (LSM) difference (Test minus Control). Superiority will be declared if the upper limit of the 95% confidence interval is below 0.

The model will be constructed as follows:

We denote  $y_{ijkl}$  as the HCT measurement for the  $l^{\text{th}}$  subject in the assigned to the  $k^{\text{th}}$  lens sequence during the  $j^{\text{th}}$  period for the  $i^{\text{th}}$  study lens (Test or Control).

The Model was as follows:

$$y_{ijkl} = \mu_0 + \beta_1 \text{Lens}_{i[j,k]} + \beta_2 \text{Period}_j + \beta_3 \text{Sequence}_k + \varepsilon_{ijkl}$$

- $\mu_0$ : overall intercept;
- $\text{Lens}_{i[j,k]}$ : Lens indicator;  $\text{Lens}_{i[j,k]}=1$  for Test and 0 otherwise;
- $\text{Period}_j$  : effect of the  $j^{\text{th}}$  period; period=1 if analysis period=1 and 0 otherwise
- $\varepsilon_{ijkl}$ : random error associated with the  $j^{\text{th}}$  period for the  $l^{\text{th}}$  subject for the  $i^{\text{th}}$  treatment assigned to the  $k^{\text{th}}$  lens sequence
- $[\varepsilon_{1kl} \ \varepsilon_{2kl}] \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{11}^2 & \sigma_{12} \\ \sigma_{21} & \sigma_{22}^2 \end{bmatrix} \right)$

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### Hypothesis Testing

The null and alternative hypotheses for HCT are as follows:

$$H_0: \mu_{Test} - \mu_{Control} \leq 0$$
$$H_A: \mu_{Test} - \mu_{Control} > 0$$

where  $\mu_{Test} - \mu_{Control}$  is the population mean difference between the Test and the Control lenses. If the upper limit of the 95% confidence limit is below 0 then the results favor the *Control lens*. If the lower limit of the 95% confidence limit is above 0 then the results favor the *Test lens*.

### 14.7. Other Exploratory Analysis

#### Color Appearance (white point)

The four chromaticity coordinates ( $xx$ ,  $yy$ ,  $uu'$ , and  $vv'$ ) from the color appearance test will be analyzed using a linear mixed model. Sequence of lens wear, period and lens type will be included as fixed effects. ADD Power, gender, race and dominant eye (Left or Right) may be included in the model as covariates when appropriate. Residual errors between measurements within the same subject across study periods will be modeled using an unstructured covariance structure (UN). The Kenward and Roger Method will be used for the denominator degrees of freedom. Comparisons between the study lenses will be carried out using two-sided 95% CIs for the least-square mean (LSM) difference (Test minus Control). Superiority will be declared if the upper limit of the 95% confidence interval is below 0.

The model will be constructed as follows:

We denote  $y_{ijkl}$  as the Light scattering (with or without 403nm filter) measurement for the  $l^{th}$  subject in the assigned to the  $k^{th}$  lens sequence during the  $j^{th}$  period for the  $i^{th}$  study lens (Test or Control).

The Model was as follows:

$$y_{ijkl} = \mu_0 + \beta_1 Lens_{i[j,k]} + \beta_2 Period_j + \beta_3 Sequence_k + \varepsilon_{ijkl}$$

- $\mu_0$ : overall intercept;
- $Lens_{i[j,k]}$ : Lens indicator;  $Lens_{i[j,k]}=1$  for Test and 0 otherwise;
- $Period_j$  : effect of the  $j^{th}$  period; period=1 if analysis period=1 and 0 otherwise
- $\varepsilon_{ijkl}$ : random error associated with the  $j^{th}$  period for the  $l^{th}$  subject for the  $i^{th}$  treatment assigned to the  $k^{th}$  lens sequence
- $$\begin{bmatrix} \varepsilon_{1kl} \\ \varepsilon_{2kl} \end{bmatrix} \sim N \left( \begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma_{11}^2 & \sigma_{12} \\ \sigma_{21} & \sigma_{22}^2 \end{bmatrix} \right)$$

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### Hypothesis Testing

The null and alternative hypotheses for the significance testing between the Test lens and the Control lens with respects to each chromaticity coordinate for color appearance are presented below:

$$H_0: \mu_{Test} - \mu_{Control} = 0$$

$$H_A: \mu_{Test} - \mu_{Control} \neq 0$$

where  $\mu_{Test} - \mu_{Control}$  is the population mean difference between the Test and the Control lenses. Statistical differences will be concluded if 0 is not contained within the 95% confidence interval.

### **14.8. Interim Analysis**

Not applicable.

### **14.9. Procedure for Handling Missing Data and Drop-Outs**

Missing or spurious values will not be imputed. The count of missing values will be included in the summary tables and listings.

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, sensitivity analysis will be conducted using multiple imputation methods if the proportion of subject dropout is greater than the 15%. The SAS/STAT procedures PROC MI and PROC MIANALYZE will be utilized with a parametric regression method used to make at least 50 imputations.

### **14.10. Procedure for Reporting Deviations from Statistical Plan**

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

## **15. DATA HANDLING AND RECORD KEEPING/ARCHIVING**

### **15.1. Electronic Case Report Form/Data Collection**

The data for this study will be captured on electronic case report forms (eCRFs) using 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

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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.<sup>1</sup>

### **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: The study is determined not to be an early feasibility study.

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### **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

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### **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),<sup>2</sup> 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 64<sup>th</sup> WMA General Assembly 2013<sup>3</sup> 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),<sup>2</sup> 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.

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- 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.

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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,<sup>3</sup> current ICH GCP<sup>2</sup> and ISO 14155:2020<sup>1</sup> guidelines, applicable regulatory requirements, and Sponsor Policy.

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

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

### **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)<sup>4</sup> and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

# **Clinical Study Protocol**

## **Johnson & Johnson Vision Care, Inc.**

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,<sup>2</sup> 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<sup>2</sup> and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

# **Clinical Study Protocol**

## **Johnson & Johnson Vision Care, Inc.**

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 this outcome of this investigation.

## **22. REFERENCES**

1. ISO 14155:2011: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at: <https://www.iso.org/standard/45557.html>
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at: <http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html>
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at: <https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/>
4. United States (US) Code of Federal Regulations (CFR). Available at: <https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR>
5. Health Information Portability and Accountability Act (HIPAA). Available at: <https://www.hhs.gov/hipaa/for-professionals/privacy/index.html>
6. SAS Institute Inc. 2016 SAS/STAT® 14.3 User's Guide. Cary, NC: SAS Institute Inc.
7. Keselman HJ, Algina J, Kowalchuk RK, Wolfinger RD. A comparison of two approaches for selecting covariance structures in the analysis of repeated measurements. *Communications in Statistics - Simulation and Computation*. 1998;27(3):591-604.
8. Kenward MG, Roger JH. Small Sample Inference for Fixed Effects from Restricted Maximum Likelihood. *Biometrics*. 1997;53(3):983.

**Clinical Study Protocol**  
**Johnson & Johnson Vision Care, Inc.**

9. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices. Available at:  
<http://data.europa.eu/eli/reg/2017/745/2017-05-05>

**Clinical Study Protocol  
Johnson & Johnson Vision Care, Inc.**

**APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)**

Not Applicable.

**Clinical Study Protocol  
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**APPENDIX B: PATIENT INSTRUCTION GUIDE**

A Patient Instruction Guide (PIG) will be provided separately.

**Clinical Study Protocol  
Johnson & Johnson Vision Care, Inc.**

**APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)**

**IMPORTANT: Please read carefully and keep this information for future use.**

**This Package Insert and Fitting Guide is intended for the Eye Care Professional, but should be made available to patients upon request. The Eye Care Professional should provide the patient with the patient instructions that pertain to the patient's prescribed lenses.**



**ACUVUE® OASYS MULTIFOCAL Contact Lenses with PUPIL OPTIMIZED DESIGN**

**PACKAGE INSERT & FITTING INSTRUCTION GUIDE**

**ACUVUE® OASYS MULTIFOCAL (senofilcon A) Contact Lens  
Soft (hydrophilic) Contact Lenses Visibility Tinted with UV  
Blocker for Daily & Extended Wear**



CAUTION: US Federal law restricts this device to sale by or on the order of a licensed practitioner

## SYMBOLS KEY

The following symbols may appear on the label or packaging:

**Multifocal Lenses For:** Presbyopia, Phakic or Aphakic

SYMBOL	DEFINITION
	Caution, Consult Instructions for Use
	Date of Manufacture
	Manufacturer
	Use By Date (expiration date)
<b>LOT</b>	Batch Code
<b>STERILE</b> 	Sterilized Using Steam Heat
	Indicates a Single Sterile Barrier System
<b>DIA</b>	Diameter
<b>BC</b>	Base Curve
<b>D</b>	Diopter (lens power)
<b>MD</b>	Medical Device Symbol
<b>MAX ADD</b>	Near ADD
<b>LOW</b>	“Low” near ADD
<b>MID</b>	“Medium” near ADD
<b>HGH</b>	“High” near ADD
	CE-mark and Identification Number of Notified Body
UV BLOCKING	UV Blocking
	Fee Paid for Waste Management
	CAUTION: US Federal law restricts this device to sale by or on the order of a licensed practitioner

**SYMBOL**   **DEFINITION**

	Lens Orientation Correct
	Lens Orientation Incorrect (Lens Inside Out)
<b>EC REP</b>	Authorized Representative in the European Community
	Do not use if package is damaged
	Package Opening Icon
<b>L</b>	"Low" near ADD
<b>M</b>	"Medium" near ADD
<b>H</b>	"High" near ADD

Visit [www.acuvue.com/guides](http://www.acuvue.com/guides) for additional information about symbols.

**DESCRIPTION**

ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lenses are soft (hydrophilic) contact lenses available as multifocal lenses. The lenses are made of a silicone hydrogel material (senofilcon A) containing an internal wetting agent, visibility tint, and UV absorbing monomers.

The transmittance characteristics for these lenses are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 315 nm to 380 nm for the entire power range.

## **Lens Properties:**

The physical/optical properties of the lens are:

- Specific Gravity (calculated): 0.98 – 1.12
- Refractive Index: 1.42

- Light Transmittance:  $\geq 89\%$  minimum
- Surface Character: Hydrophilic
- Water Content: 38%
- Oxygen Permeability (Dk):

### VALUE

$103 \times 10^{-11}$  (cm<sup>2</sup>/sec) (ml O<sub>2</sub>/ml x mm Hg) at 35°C

$122 \times 10^{-11}$  (cm<sup>2</sup>/sec) (ml O<sub>2</sub>/ml x mm Hg) at 35°C

### METHOD

Fatt (boundary corrected, edge corrected)

Fatt (boundary corrected, non- edge corrected)

## Lens Parameters Ranges:

The ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lenses are hemispherical or hemitoric shells of the following dimensions:

- Diameter (DIA) : 12.0 mm to 15.0 mm
- Center Thickness: varies with power
- Base Curve (BC): 7.85 mm to 10.00 mm
- Spherical Power (D): -20.00D to +20.00D
- Multifocal ADD Power Range: +0.25D to +4.00D

Each lens is supplied in a foil-sealed plastic package containing borate buffered saline solution with methyl ether cellulose.

## AVAILABLE LENS PARAMETERS

The ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lenses are hemispherical shells of the following dimensions:

**Diameter:** 14.3 mm

**Center Thickness:** Minus Lens - varies with power (e.g. -4.00D: 0.070 mm)  
Plus Lens - varies with power (e.g. +4.00D: 0.168 mm)

**Base Curve:**

8.4 mm

**Powers:**

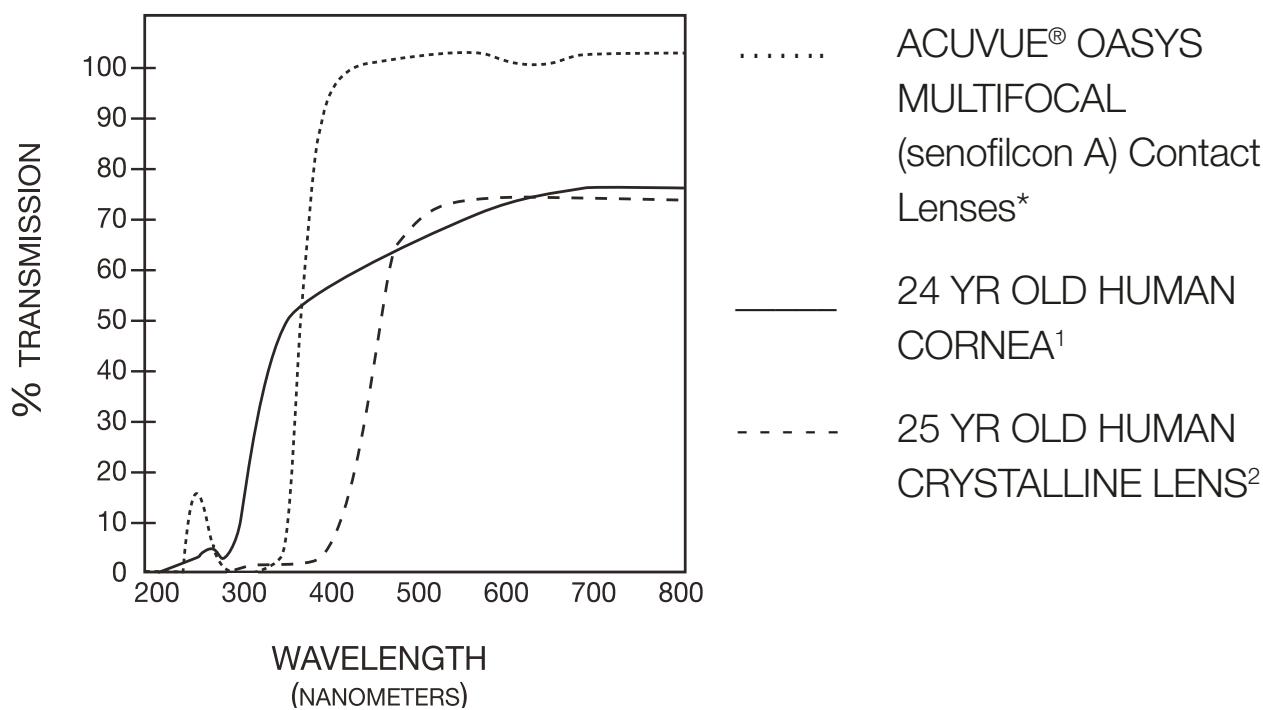
-9.00D to +6.00D (in 0.25D increments)

**ADD Powers:**

+1.25 (LOW), +1.75 (MID), +2.50 (HIGH)

## TRANSMITTANCE CURVE

ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lenses vs. 24 yr. old human cornea vs. 25 yr. old human crystalline lens.



\*The data was obtained from measurements taken through the central 3-5 mm portion for the thinnest marketed lens (-1.00D lens, 0.070 mm center thickness).

<sup>1</sup> Lerman, S., Radiant Energy and the Eye, MacMillan, New York, 1980, p.58, figure 2-21.

<sup>2</sup> Waxler, M. Hitchins, V.M., Optical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p.19, figure 5.

## ACTIONS

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

When hydrated and placed on the cornea for therapeutic use, the contact lens acts as a bandage to protect the cornea.

These lenses contain a UV Blocker to help protect against transmission of harmful UV radiation to the cornea and into the eye. The light transmittance characteristics are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 315 nm to 380 nm for the entire power range.

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

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

## INDICATIONS (USES)

ACUVUE® OASYS MULTIFOCAL (senofilcon A) Contact Lenses are indicated for the correction of vision in presbyopic people with non-diseased eyes who are either presbyopic or are

presbyopic and are also nearsighted (myopic) or farsighted (hyperopic) and may have 0.75D or less of astigmatism.

Eye Care Professionals may prescribe the lenses either for single use, disposable wear or frequent/planned replacement wear with cleaning, disinfection and scheduled replacement (see “Replacement Schedule”). When prescribed for single use disposable wear, no cleaning or disinfection is required. Lenses should be discarded upon removal. When prescribed for frequent/planned replacement wear, the lenses may be disinfected using a chemical disinfection system only.

These lenses are intended for daily wear for up to 14 days (2 weeks) and extended wear for up to 6 nights/7 days of continuous wear. It is recommended that the contact lens wearer first be evaluated on a daily wear schedule. If successful, then a gradual introduction of extended wear can be followed as determined by the prescribing Eye Care Professional.

These lenses are also indicated for therapeutic use as a bandage lens for the following acute and chronic ocular conditions:

- For corneal protection in lid and corneal abnormalities such as entropion, trichiasis, tarsal scars, and recurrent corneal erosion. In addition, they are indicated for protection where sutures or ocular structure malformation, degeneration or paralysis may result in the need to protect the cornea from exposure or repeated irritation.
- For corneal pain relief in conditions such as bullous keratopathy, epithelial erosion and abrasion, filamentary keratitis, and post-keratoplasty.
- For use as a barrier during the healing process of epithelial defects such as chronic epithelial defects, corneal ulcer, neurotrophic and neuroparalytic keratitis, and chemical burns.

- For post-surgical conditions where bandage lens use is indicated such as post refractive surgery, lamellar grafts, corneal flaps, and additional ocular surgical conditions.
- For structural stability and protection in piggy back lens fitting where the cornea and associated surfaces are too irregular to allow for corneal rigid gas permeable (RGP) lenses to be fit. In addition, the use of the lens can prevent irritation and abrasions in conditions where there are elevation differences in the host/graph junction or scar tissue.

Lenses prescribed for therapeutic use may be worn for daily or extended wearing periods.

## CONTRAINDICATIONS (REASONS NOT TO USE)

When prescribing contact lens wear for REFRACTIVE AMETROPIA USE, **DO NOT USE** these lenses when any of the following conditions exist:

- Acute or subacute inflammation or infection of the anterior chamber of the eye.
- Any eye disease, injury or abnormality that affects the cornea, conjunctiva or eyelids.
- Severe insufficiency of lacrimal secretion (dry eye).
- Corneal hypoesthesia (reduced corneal sensitivity).
- Any systemic disease that may affect the eye or be exaggerated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa that may be induced or exaggerated by wearing contact lenses or use of contact lens solutions.
- Ocular irritation due to allergic reactions which may be caused by use of contact lens solutions (i.e., cleaning and disinfecting solutions, rewetting drops, etc.) that contain chemicals or preservatives (such as mercury, Thimerosal,

etc.) to which some people may develop an allergic response.

- Any active corneal infection (bacterial, fungal, protozoal or viral).
- If eyes become red or irritated.

For THERAPEUTIC USE, the Eye Care Professional may prescribe these lenses to aid in the healing process of certain ocular conditions, which may include those cited above.

## WARNINGS

**Patients should be advised of the following warnings pertaining to contact lens wear:**

**EYE PROBLEMS, INCLUDING CORNEAL ULCERS, CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION. IF THE PATIENT EXPERIENCES:**

- Eye Discomfort,
- Excessive Tearing,
- Vision Changes,
- Loss of Vision,
- Eye Redness, or
- Other Eye Problems,

**THE PATIENT SHOULD BE INSTRUCTED TO IMMEDIATELY REMOVE THE LENSES AND PROMPTLY CONTACT THE EYE CARE PROFESSIONAL.**

- When prescribed for daily wear, patients should be instructed not to wear their lenses while sleeping. Clinical studies have shown that when lenses are worn overnight, the risk of ulcerative keratitis is greater than among those who do not wear them overnight.<sup>3</sup>
- Studies have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.

- Problems with contact lenses or lens care products could result in serious injury to the eye. Patients should be cautioned that proper use and care of contact lenses and lens care products, including lens cases, are essential for the safe use of these products.
- The overall risk of ulcerative keratitis may be reduced by carefully following directions for lens care, including cleaning the lens case.

<sup>3</sup> New England Journal of Medicine, September 21, 1989; 321 (12), pp. 773-783

## **Specific Instructions for Use and Warnings:**

### **• Water Activity**

#### **Instruction for Use**

Do not expose contact lenses to water while wearing them.

#### **WARNING:**

**Water can harbor microorganisms that can lead to severe infection, vision loss, or blindness. If lenses have been submersed in water when participating in water sports or swimming in pools, hot tubs, lakes or oceans, the patient should be instructed to discard them and replace them with a new pair. The Eye Care Professional should be consulted for recommendations regarding wearing lenses during any activity involving water.**

### **• Soaking and Storing Your Lenses**

#### **Instruction for Use**

Use only fresh multi-purpose (contact lens disinfecting) solution each time the lenses are soaked (stored).

#### **WARNING:**

**Do not reuse or “top off” old solution left in the lens case since solution reuse reduces effective lens disinfection and could lead to severe infection, vision loss, or blindness.**

## **“Topping-Off” is the addition of fresh solution to solution that has been sitting in the case.**

### **• Discard Date on Multi-Purpose Solution Bottle**

#### **Instructions for Use**

- Discard any remaining solution after the recommended time period indicated on the bottle of multi-purpose solution used for disinfecting and soaking the contact lenses.
- The discard date refers to the time that the patient can safely use the contact lens care product after the bottle has been opened. It is not the same as the expiration date, which is the last date that the product is still effective before it is opened.

#### **WARNING:**

**Using multi-purpose solution beyond the discard date could result in contamination of the solution and can lead to severe infection, vision loss, or blindness.**

- **To avoid contamination, DO NOT touch tip of container to any surface. Replace cap after using.**
- **To avoid contaminating the solution, DO NOT transfer to other bottles or containers.**

### **• Rub and Rinse Time**

#### **Instruction for Use**

To adequately disinfect the lenses, the patient should rub and rinse the lenses according to the recommended lens rubbing and rinsing times in the labeling of the multi-purpose solution.

#### **WARNING:**

- **Rub and rinse lenses for the recommended amount of time to help prevent serious eye infections.**
- **Never use water, saline solution, or rewetting drops to disinfect the lenses. These solutions will not disinfect the lenses. Not using the recommended**

**disinfectant can lead to severe infection, vision loss, or blindness.**

• **Lens Case Care**

**Instructions for Use**

- Empty and clean contact lens cases with digital rubbing using fresh, sterile disinfecting solutions/contact lens cleaner. Never use water. Cleaning should be followed by rinsing with fresh, sterile disinfecting solutions (never use water) and wiping the lens cases with fresh, clean tissue is recommended. Never air-dry or recap the lens case lids after use without any additional cleaning methods. If air drying, be sure that no residual solution remains in the case before allowing it to air-dry.
- Replace the lens case according to the directions provided by the Eye Care Professional or the manufacturer's labeling that accompanies the case.
- Contact lens cases can be a source of bacterial growth.

**WARNING:**

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

## PRECAUTIONS

**Special Precautions for Eye Care Professionals:**

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect

lens performance and ocular health; including oxygen permeability, wettability, central and peripheral thickness and optic zone diameter.

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

- Patients who wear these lenses to correct presbyopia using monovision or multifocal correction may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Eye Care Professionals should instruct the patient to remove lenses immediately if the eyes become red or irritated.
- Eye Care Professionals should instruct the patient to always have a functional pair of spectacles with a current prescription available to use if the patient becomes unable to wear contact lenses, or in circumstances where contact lens wear is not advised.

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

### **Handling Precautions:**

- DO NOT use if the sterile blister package is opened or damaged.
- Always wash, rinse, and dry hands before handling lenses. It is best to put on lenses before putting on makeup.
- Carefully follow the handling, insertion, removal, cleaning, disinfecting, storing and wearing instructions in the Patient

# Instruction Guide for these lenses and those prescribed by the Eye Care Professional.

- Never use tweezers or other tools to remove lenses from the lens container. Slide the lens up the side of the bowl until it is free of the container.
- Close supervision is necessary for the Therapeutic use of these lenses. Ocular medications used during treatment with a bandage lens should be closely monitored by the Eye Care Professional. In certain ocular conditions, only the Eye Care Professional will insert and remove the lenses. In these cases, patients should be instructed not to handle the lenses themselves.

## **Lens Wearing Precautions:**

- If the lens sticks (stops moving) on the eye, follow the recommended directions in "Care for Sticking (Non-Moving) Lenses". The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. Sharing lenses greatly increases the chance of eye infections.
- If aerosol products, such as hair spray, are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.
- The patient should be advised to never rinse the lenses in water from the tap. Tap water contains many impurities that can contaminate or damage the lenses and may lead to eye infection or injury.

## **Lens Care Precautions:**

- Different solutions cannot always be used together and not all solutions are safe for use with all lenses. Use only recommended solutions.
- Do not change solution without consulting with the Eye Care Professional.
- Never use solutions recommended for conventional hard contact lenses only.
- Always use fresh, unexpired lens care solutions and lenses, and always follow directions in the package inserts for the use of contact lens solutions.
- Sterile unpreserved solutions, when used, should be discarded after the time specified in the directions.
- Do not use saliva or anything other than the recommended solutions for lubricating or wetting lenses.
- Always keep the lenses completely immersed in the recommended storage solution when the lenses are not being worn (stored). Prolonged periods of drying (e.g., exposing the lens to air for 30 minutes or more) will reduce the ability of the lens surface to return to a wettable state. If the lens surface does become dried out, discard the lens and use a new one.

## **Other Topics to Discuss with Patients:**

- Always contact the Eye Care Professional before using any medicine in the eyes.
- Certain medications, such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness may cause dryness of the eye, increased lens awareness or blurred vision. Should such conditions exist, proper remedial measures should be prescribed.

- Oral contraceptive users could develop visual changes or changes in lens tolerance when using contact lenses. Patients should be cautioned accordingly.
- Do not change lens type (e.g. brand name, etc.) or parameters (e.g. diameter, base curve, lens power, etc.) without consulting the Eye Care Professional.
- Instruct patients to always confirm the lens parameters printed on the multi-pack and on the individual lens package match their prescription. If there is a mismatch the patient should not use the product.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.

## **Who Should Know That the Patient is Wearing Contact Lenses?**

- Patients should inform all doctors (Health Care Professionals) about being a contact lens wearer.
- Patients should always inform their employer of being a contact lens wearer. Some jobs may require use of eye protection equipment or may require that the patient not wear contact lenses.

## **ADVERSE REACTIONS**

### **The patient should be informed that the following problems may occur when wearing contact lenses:**

- The eye may burn, sting and/or itch.
- There may be less comfort than when the lens was first placed on the eye.
- There may be a feeling of something in the eye (foreign body, scratched area).
- There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral

corneal ulcers, and corneal erosion. There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis and conjunctivitis, some of which are clinically acceptable in low amounts.

- There may be excessive watering, unusual eye secretions or redness of the eye.
- Poor visual acuity, blurred vision, rainbows or halos around objects, photophobia or dry eyes may also occur if the lenses are worn continuously or for too long a time.
- The patient should be instructed to conduct a simple 3-part self-examination at least once a day. They should ask themselves:
  - How do the lenses feel on my eyes?
  - How do my eyes look?
  - Have I noticed a change in my vision?

If the patient reports any problems, he or she should be instructed to IMMEDIATELY REMOVE THE LENS. If the problem or discomfort stops and the lens appears undamaged, the patient should clean and rinse the lens with a recommended soft contact lens care solution and reinsert the lens. If after reinserting the lens, the problem continues, the patient should discard the lens and place a new fresh lens on the eye. If after inserting the new lens, the problem continues, the patient should be directed to IMMEDIATELY REMOVE THE LENS AND CONTACT HIS OR HER EYE CARE PROFESSIONAL.

The patient should be instructed NOT to use a new lens as self-treatment for the problem.

The patient should be advised that when any of the above symptoms occur, a serious condition such as infection, corneal ulcer, neovascularization, or iritis may be present. He or she should be instructed [REDACTED] immediate professional

identification of the problem and prompt treatment to avoid serious eye damage.

## GENERAL FITTING GUIDELINES

### A. Patient Selection

Patients selected to wear these lenses should be chosen based on:

- Motivation to wear lenses
- Ability to follow instructions regarding lens wear care
- General health
- Ability to adequately handle and care for the lenses
- Ability to understand the risk and benefits of lens wear

Patients who do not meet the above criteria should not be provided with contact lenses.

### B. Pre-fitting Examination

Initial evaluation of the patient should begin with a thorough case history to determine if there are any contraindications to contact lens wear. During the case history, the patient's visual needs and expectations should be determined as well as an assessment of their overall ocular, physical, and mental health.

Preceding the initial selection of trial contact lenses, a comprehensive ocular evaluation should be performed that includes, but is not limited to, the measurement of distance and near visual acuity, distance and near refractive prescription (including determining the preferred reading distance for presbyopes), keratometry and biomicroscopic evaluation.

Based on this evaluation, if it is determined that the patient is eligible to wear these lenses, the Eye Care Professional should proceed to the appropriate lens fitting instruction outlined below.

## C. Initial Power Determination

A spectacle refraction should be performed to establish the patient's baseline refractive status and to guide in the selection of the appropriate lens power. Remember to compensate for vertex distance if the refraction is greater than  $\pm 4.00\text{D}$ .

## D. Base Curve Selection (Trial Lens Fitting)

The following trial lenses should be selected for the patient regardless of keratometry readings. However, corneal curvature measurements should be performed to establish the patient's baseline ocular status.

- **ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lens:** 8.4 mm/14.3 mm

The trial lenses should be placed on each of the patient's eyes and evaluated after the patient has adjusted to the lenses.

### 1. Criteria of a Properly Fit Lens

A properly fit lens will center and completely cover the cornea (i.e., no limbal exposure), have sufficient movement to provide tear exchange under the contact lens with the blink, and be comfortable. The lens should move freely when manipulated digitally with the lower lid, and then return to its properly centered position when released.

### 2. Criteria of a Flat Fitting Lens

A flat fitting lens may exhibit one or more of the following characteristics: decentration, incomplete corneal coverage (i.e., limbal exposure), excessive movement with the blink and/or edge standoff. If the lens is judged to be flat fitting, it should not be dispensed to the patient.

### 3. Criteria of a Steep Fitting Lens

A steep fitting lens may exhibit one or more of the following characteristics: insufficient movement with the blink, conjunctival indentation, and resistance when pushing the

lens up digitally with the lower lid. If the lens is judged to be steep fitting, it should not be dispensed to the patient.

If the initial trial base curve is judged to be flat or steep fitting, the alternate base curve, if available, should be trial fit and evaluated after the patient has adjusted to the lens. The lens should move freely when manipulated digitally with the lower lid, and then return to a properly centered position when released.

**All patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at [www.acuvue.com](http://www.acuvue.com).**

## MULTIFOCAL FITTING GUIDELINES

### A. Presbyopic Needs Assessment & Patient Education

Multifocal contact lenses may produce compromise to vision under certain circumstances and the patient should understand that they might not find their vision acceptable in specific situations (i.e., reading a menu in a dim restaurant, driving at night in rainy/foggy conditions, etc.). Therefore, caution should be exercised when the patient is wearing the correction for the first time until they are familiar with the vision provided in visually challenging environments. Occupational and environmental visual demands should be considered. If the patient requires critical visual acuity and stereopsis, it should be determined by trial whether this patient can function adequately with the ACUVUE® OASYS MULTIFOCAL (senofilcon A) Soft Contact Lens. Wear may not be optimal for such activities as:

1. Visually demanding situations such as operating potentially dangerous machinery or performing other potentially hazardous activities; and
2. Driving automobiles (e.g., driving at night). Patients who cannot pass their state driver's license requirements with these lenses should be advised to not drive with this

correction, OR may require that additional over-correction be prescribed.

These lenses are not recommended for patients who have  $-1.00\text{D}$  or greater of refractive cylinder as this level of uncorrected cylinder may lead to additional visual compromise.

These lenses are available in the following ADD powers:

- Lens “LOW” = “low” near ADD lens (Max +1.25 ADD)
- Lens “MID” = “medium” near ADD lens (Max +1.75 ADD)
- Lens “HIGH” = “high” near ADD lens (Max +2.50 ADD)

## **B. Initial Power Determination**

A spectacle refraction should be performed to establish the patient’s baseline refractive status and to guide in the selection of the appropriate lens power. Remember to compensate for vertex distance if the refraction is greater than  $\pm 4.00\text{D}$ . Determine the spherical equivalent distance prescription for a multifocal patient. Determine the eye dominance using one of the methods below:

Method 1: Determine which eye is the “sighting eye.” Have the patient point to an object at the far end of the room.

Cover one eye. If the patient is still pointing directly at the object, the eye being used is the dominant (sighting) eye.

Method 2 (preferred): Determine which eye will not accept added power. Place a  $+1.00$  hand-held trial lens in front of one eye and then the other with the distance refractive error correction is in place for both eyes while the patient is viewing the distance visual acuity chart. The eye that the patient notices the greatest reduction in vision while having the plus over it is determined to be the dominant eye.

## **C. Select the Initial Trial Lens**

1. For each eye, select the trial lens distance power that is closest to the patient’s distance spherical equivalent.

Remember to compensate for vertex distance if the refraction is greater than  $\pm 4.00\text{D}$ .

2. Select the near power of the lens based on the patients ADD range as follows:
  - ADD: +0.75 to +1.25 use a “LOW” near ADD lens on each eye
  - ADD: +1.50 to +1.75 use a “MID” near ADD lens on each eye
  - ADD: +2.00 to +2.50 use a “MID” near ADD on the dominant eye and a “HIGH” near ADD lens on the non-dominant eye
3. Allow the lenses to settle for a minimum 10 minutes.
4. Assess distance and near vision binocularly and monocularly.
5. Demonstrate the vision under various lighting conditions (normal and decreased illumination) and at distance, intermediate and near.
6. Make adjustments in power as necessary based on the distance over-refraction. The use of hand held trial lenses is recommended. Check the impact on distance and near vision.
7. If vision is still unacceptable, make adjustments in power as necessary (see **“Multifocal Troubleshooting”** below). If distance and near vision are acceptable, perform a slit lamp examination to assess adequate fit (centration and movement). If fit is acceptable, dispense the lenses instructing the patient to return in one week for reassessment (see PATIENT MANAGEMENT section).

## **D. Multifocal Troubleshooting**

### **Unacceptable Near Vision:**

If it has been determined that no change is required based on the over-refraction then add +0.25 D to the spherical power of the non-dominant eye.

## Unacceptable Distance Vision:

If it has been determined that no change is required based on the over-refraction then make the changes as listed below:

- If the patient is wearing two “LOW” ADD lenses, change the dominant eye to a ACUVUE® OASYS (senofilcon A) Soft Contact Lens sphere lens with a power equal to the spherical equivalent distance prescription.
- If the patient is wearing two “MID” ADD lenses, change the ADD power in the dominant eye to the “LOW” ADD power.
- If the patient is wearing a “MID” ADD lens in the dominant eye and a “HIGH” ADD lens in the non-dominant eye, change the non-dominant eye to a “MID” ADD lens and add +0.25D to the distance power.

Once the changes have been made for the troubleshooting repeat steps 3-6 in section C above (**“Select the Initial Trial Lens”**) to assess if the vision is acceptable.

## E. Adaptation

Visually demanding situations should be avoided during the initial wearing period. A patient may at first experience some mild blurred vision, dizziness, headaches and a feeling of slight imbalance. You should explain the adaptational symptoms to the patient. These symptoms may last for a brief minute or for several weeks. The longer these symptoms persist, the poorer the prognosis for successful adaptation.

To help in the adaptation process, the patient can be advised to first use the lenses in a comfortable familiar environment such as in the home.

Some patients feel that automobile driving performance may not be optimal during the adaptation process. This is particularly true when driving at night. Before driving a motor vehicle, it may be recommended that the patient be a

passenger first to make sure that their vision is satisfactory for operating an automobile. During the first several weeks of wear (when adaptation is occurring), it may be advisable for the patient to only drive during optimal driving conditions. After adaptation and success with these activities, the patient should be able to drive under other conditions with caution.

**All patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at [www.acuvue.com](http://www.acuvue.com).**

## PATIENT MANAGEMENT

- PROVIDE THE PATIENT WITH A COPY OF THE PATIENT INSTRUCTION GUIDE FOR THESE LENSES. REVIEW THESE INSTRUCTIONS WITH THE PATIENT SO THAT HE OR SHE CLEARLY UNDERSTANDS THE PRESCRIBED WEARING AND REPLACEMENT SCHEDULE (DAILY DISPOSABLE, EXTENDED WEAR, OR FREQUENT REPLACEMENT).
- Recommend an appropriate cleaning and disinfecting system and provide the patient with instructions regarding proper lens care. Chemical or hydrogen peroxide disinfection is recommended.
- Schedule a follow-up examination.

## WEARING SCHEDULE

The wearing schedule should be determined by the Eye Care Professional. Regular checkups, as determined by the Eye Care Professional, are also extremely important.

### For Daily Wear:

Patients tend to over wear the lenses initially. The Eye Care Professional should emphasize the importance of adhering to the initial maximum wearing schedule. Maximum wearing time should be determined by the Eye Care Professional based upon the patient's physiological eye condition, because

individual response to contact lenses varies.

The maximum suggested wearing time for these lenses is:

DAY	HOURS
1	6-8
2	8-10
3	10-12
4	12-14
5 and after	all waking hours

### **For Extended Wear:**

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

These lenses are intended for extended wear up to 6 nights/7 days of continuous wear. Not all patients can achieve the maximum wear time.

### **For Therapeutic Lens Wear:**

Close supervision by the Eye Care Professional is necessary. These lenses can be worn for extended wear for up to 6 nights/7 days of continuous wear. The Eye Care Professional should determine the appropriate wearing time and provide specific instructions to the patient regarding lens care, insertion, and removal.

## REPLACEMENT SCHEDULE

### **For Lenses Prescribed for Frequent Replacement:**

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

### **For Lenses Prescribed for Single Use Disposable Wear:**

These lenses are indicated for single use disposable wear and should be discarded upon removal.

## LENS CARE DIRECTIONS

### For Lenses Prescribed for Frequent Replacement Wear:

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

### For Lenses Prescribed for Single Use Disposable Wear:

The Eye Care Professional should review with the patient that no cleaning or disinfection is needed with disposable lenses. Patients should always dispose of lenses when they are removed and have replacement lenses or spectacles available.

### Care for a Sticking (Non-Moving) Lens

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

## EMERGENCIES

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

## HOW SUPPLIED

Each sterile lens is supplied in a foil-sealed plastic package containing buffered saline solution with methyl ether cellulose. The plastic package is marked with the following:

- ACUVUE® OASYS MULTIFOCAL : base curve, power, diameter, ADD, lot number, and expiration date

## REPORTING OF ADVERSE REACTIONS

All serious adverse experiences and adverse reactions observed in patients wearing these lenses or experienced with the lenses should be reported to:

Johnson & Johnson Vision Care, Inc.  
7500 Centurion Parkway  
Jacksonville, FL 32256  
USA  
Tel: 1-800-843-2020  
**www.acuvue.com**

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7500 Centurion Parkway  
Jacksonville, FL 32256  
USA  
Tel: 1-800-843-2020  
**www.acuvue.com**



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**Clinical Study Protocol**  
**Johnson & Johnson Vision Care, Inc.**

**APPENDIX D:**

Determination of Near Addition  
Lens Fitting Characteristics  
Subject Reported Ocular Symptoms/Problems  
Determination of Distance Spherocylindrical Refractions  
Biomicroscopy Scale  
Distance and Near Visual Acuity Evaluation

**Clinical Study Protocol  
Johnson & Johnson Vision Care, Inc.**

**DETERMINATION OF NEAR ADDITION**

**Title:** Determination of Near Addition

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 5

**Title:** Determination of Near Addition

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 5

**Title:** Determination of Near Addition

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

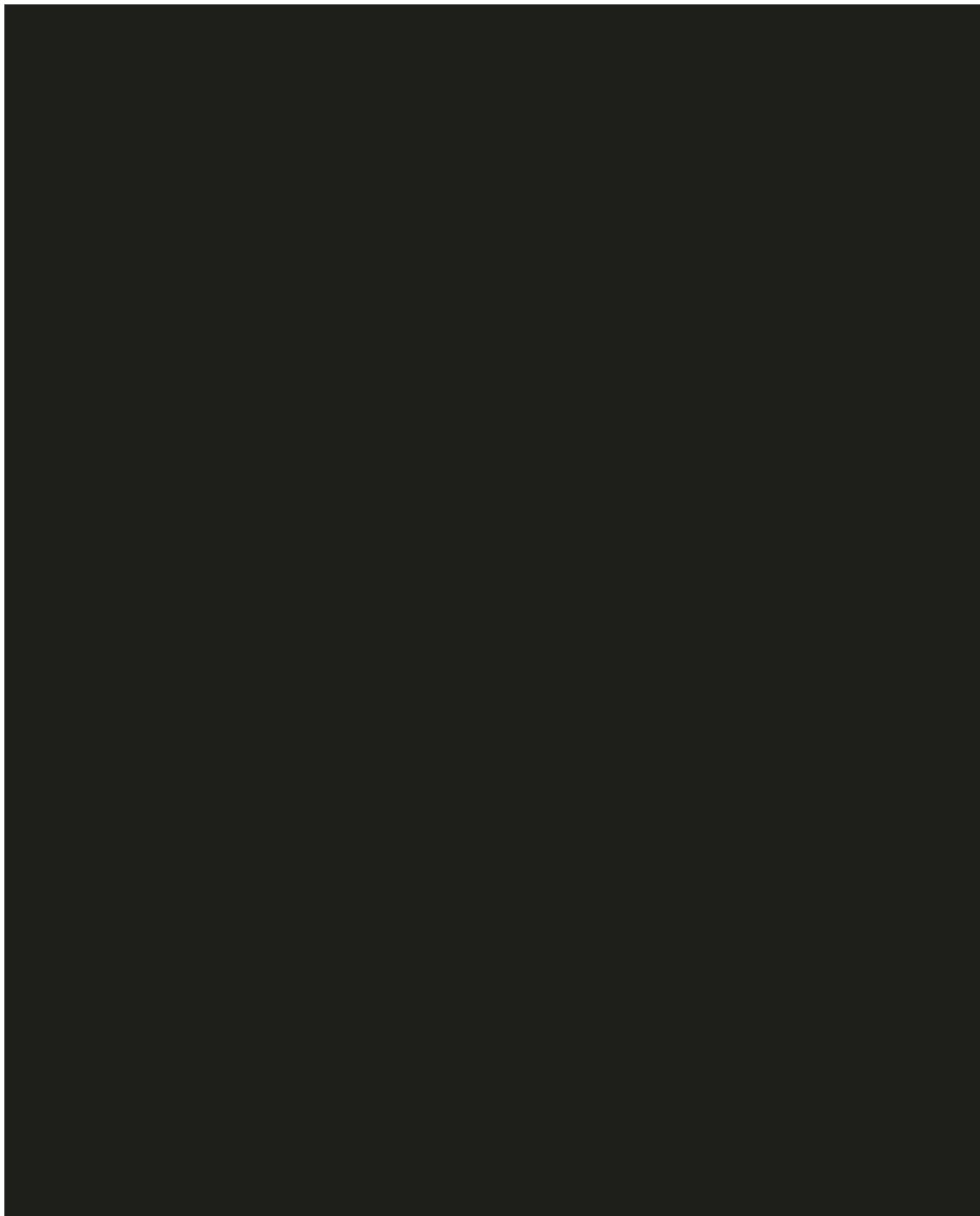
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**Document Number:** [REDACTED]

**Revision Number:** 5

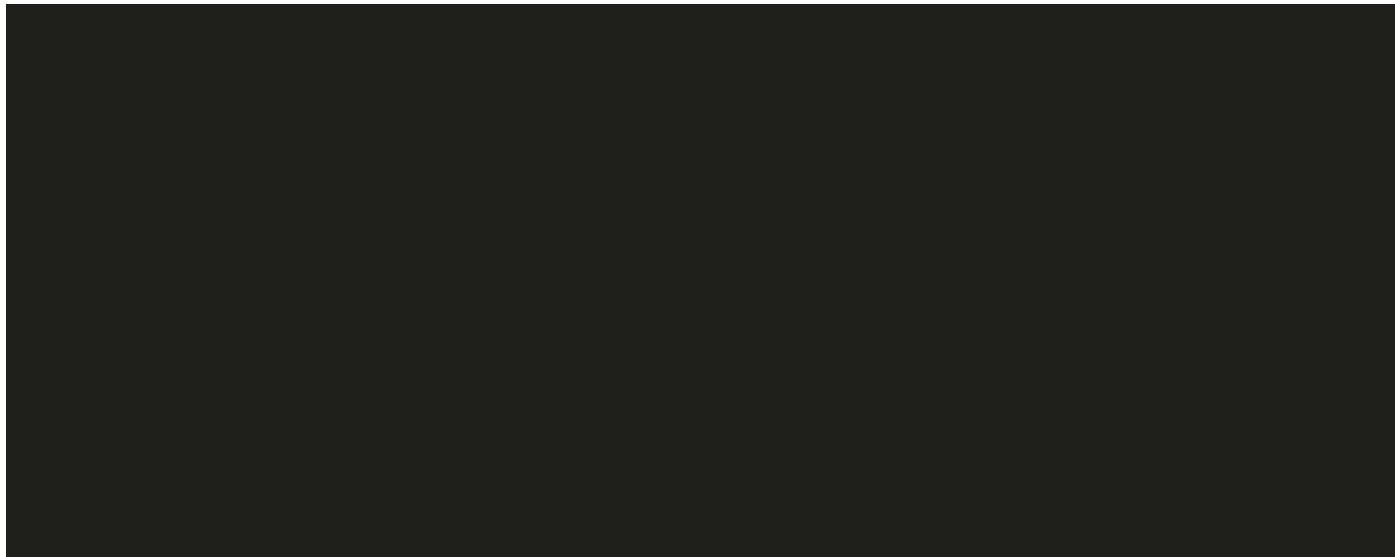


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**Document Number:** [REDACTED]

**Revision Number:** 5



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Johnson & Johnson Vision Care, Inc.**

**LENS FITTING CHARACTERISTICS**

**Title:** Lens Fitting Characteristics

**Document Type:** [REDACTED]

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

**Title:** Lens Fitting Characteristics

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 6

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**Revision Number:** 6

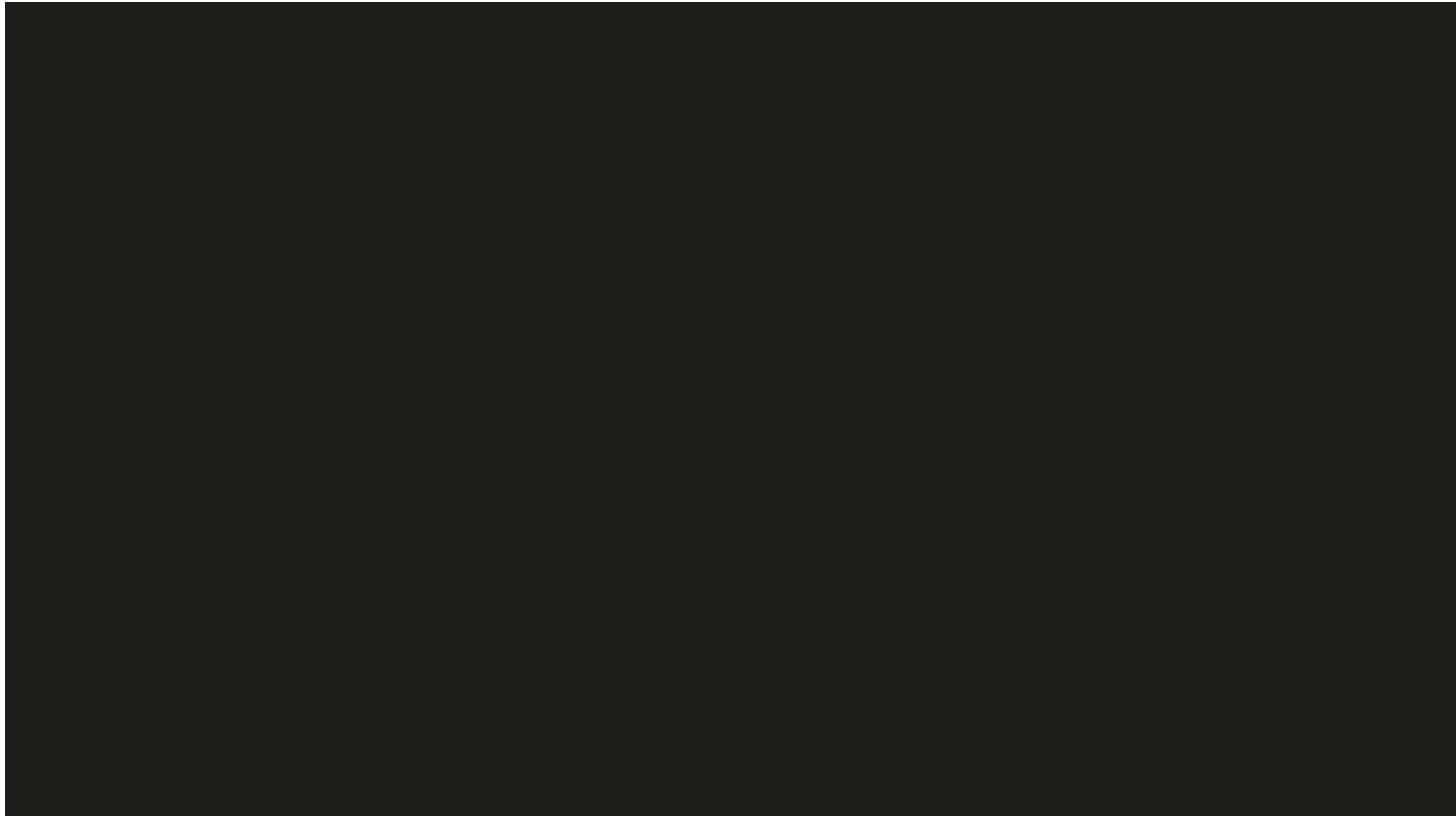


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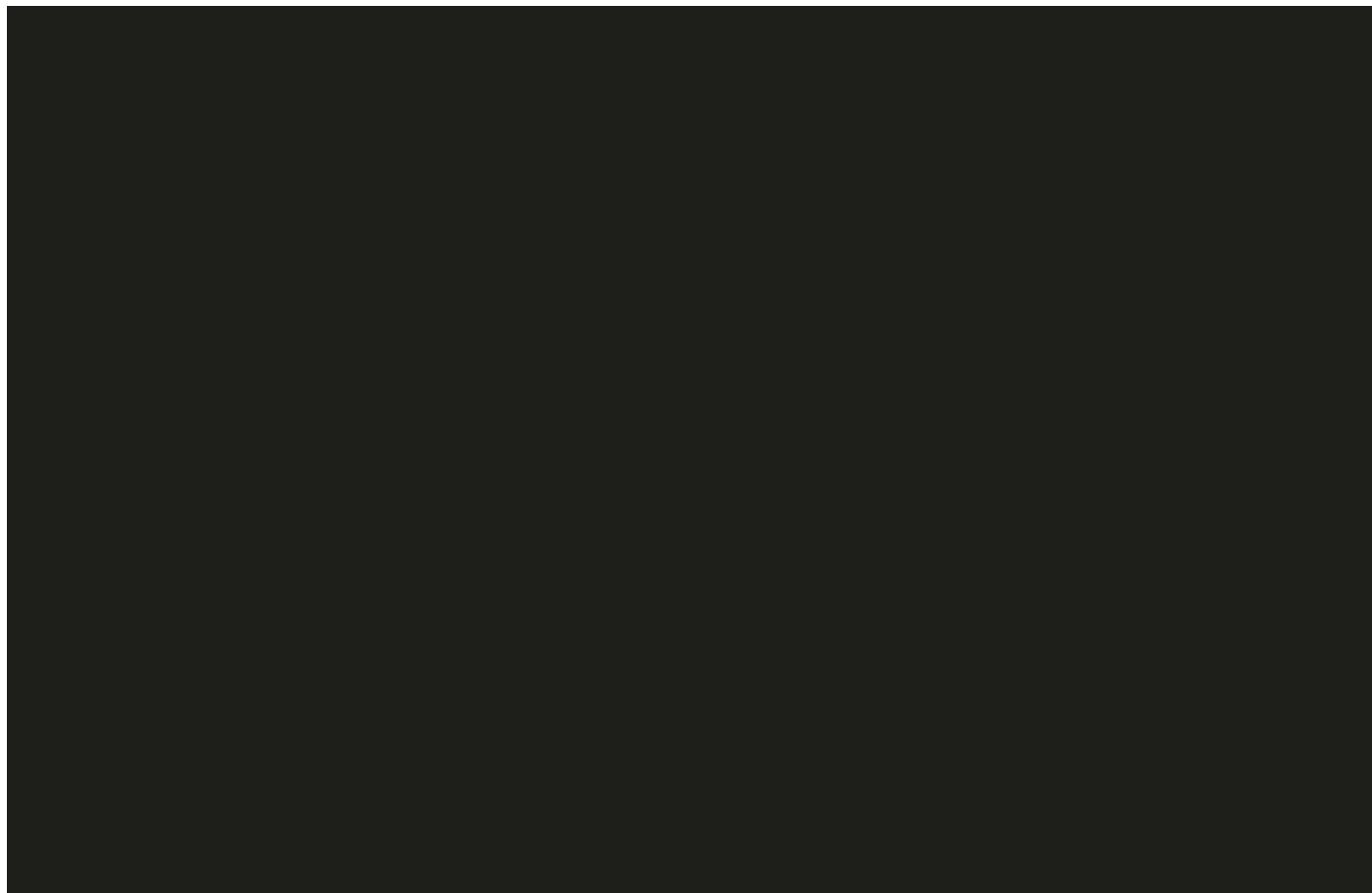


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**Revision Number:** 6



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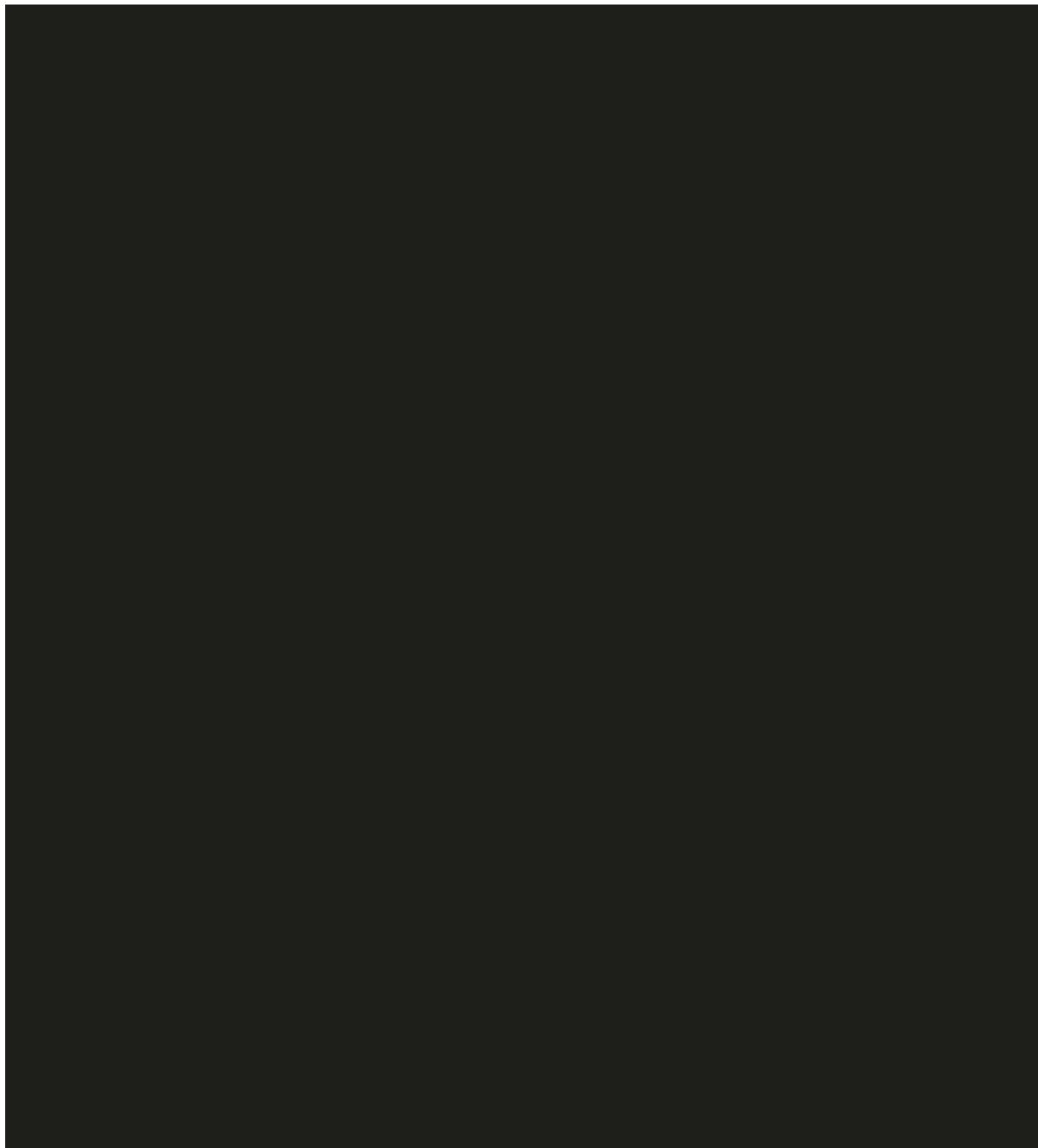
**SUBJECT REPORTED OCULAR SYMPTOMS**

**Title:** **Subject Reported Ocular Symptoms/Problems**

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 4



**Clinical Study Protocol  
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**DETERMINATION OF DISTANCE SPHEROCYLINDRICAL  
REFRACTION**

**Title:**

**Determination of Distance Spherocylindrical Refractive Error**

**Document Type:**

**Document Number:**

**Revision Number: 5**

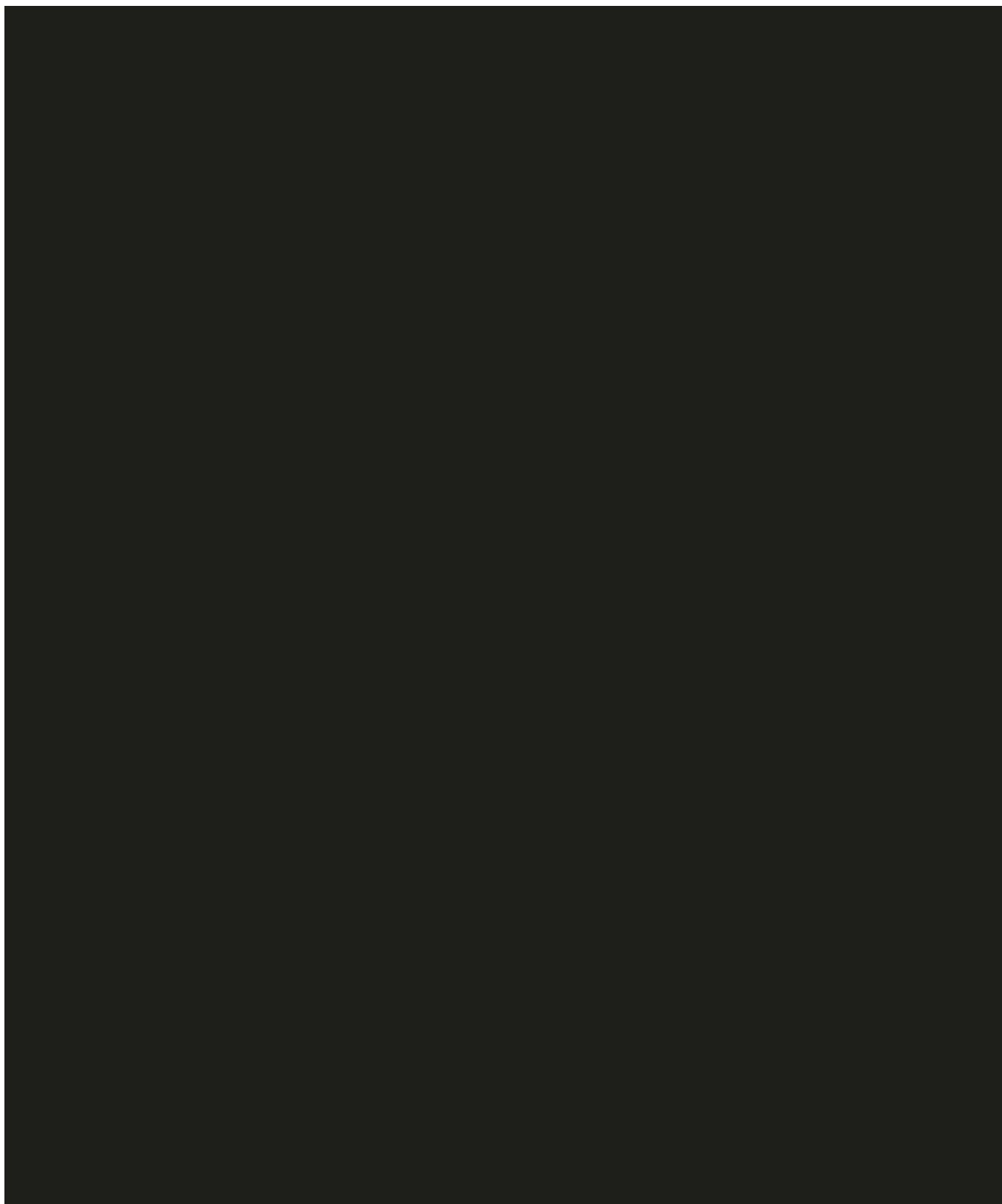
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**Determination of Distance Spherocylindrical Refractive Error**

**Document Type:**

**Document Number:**

**Revision Number: 5**



**Title:**

**Determination of Distance Spherocylindrical Refractive Error**

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**Revision Number: 5**

**Title:** Determination of Distance Spherocylindrical Refractive Error

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 5

**Title:**

**Determination of Distance Spherocylindrical Refractive Error**

**Document Type:**

**Document Number:**

**Revision Number: 5**

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**BIOMICROSCOPY SCALE**

**Clinical Study Protocol**  
**Johnson & Johnson Vision Care, Inc.**

**Title:** Biomicroscopy Scale

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 10

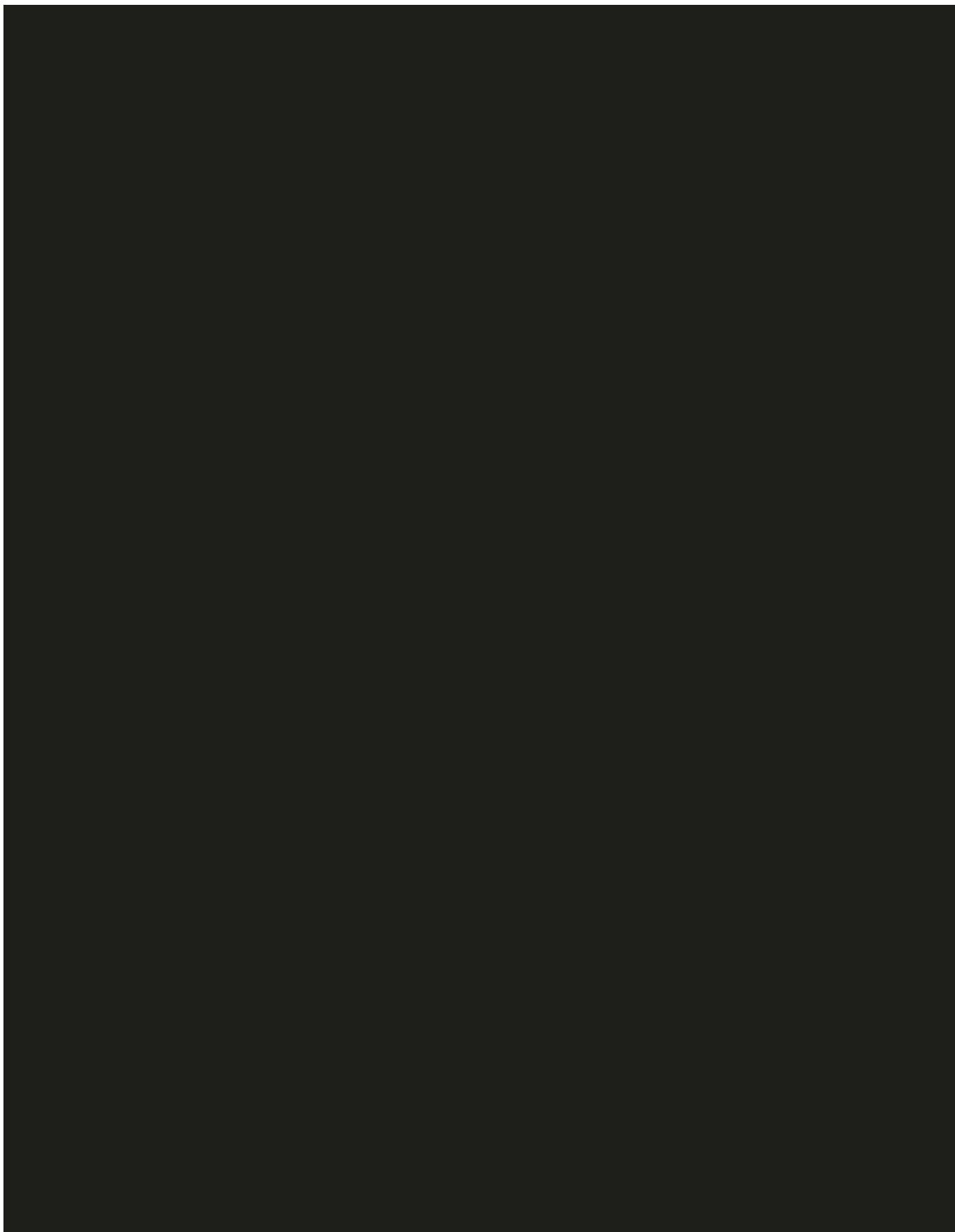
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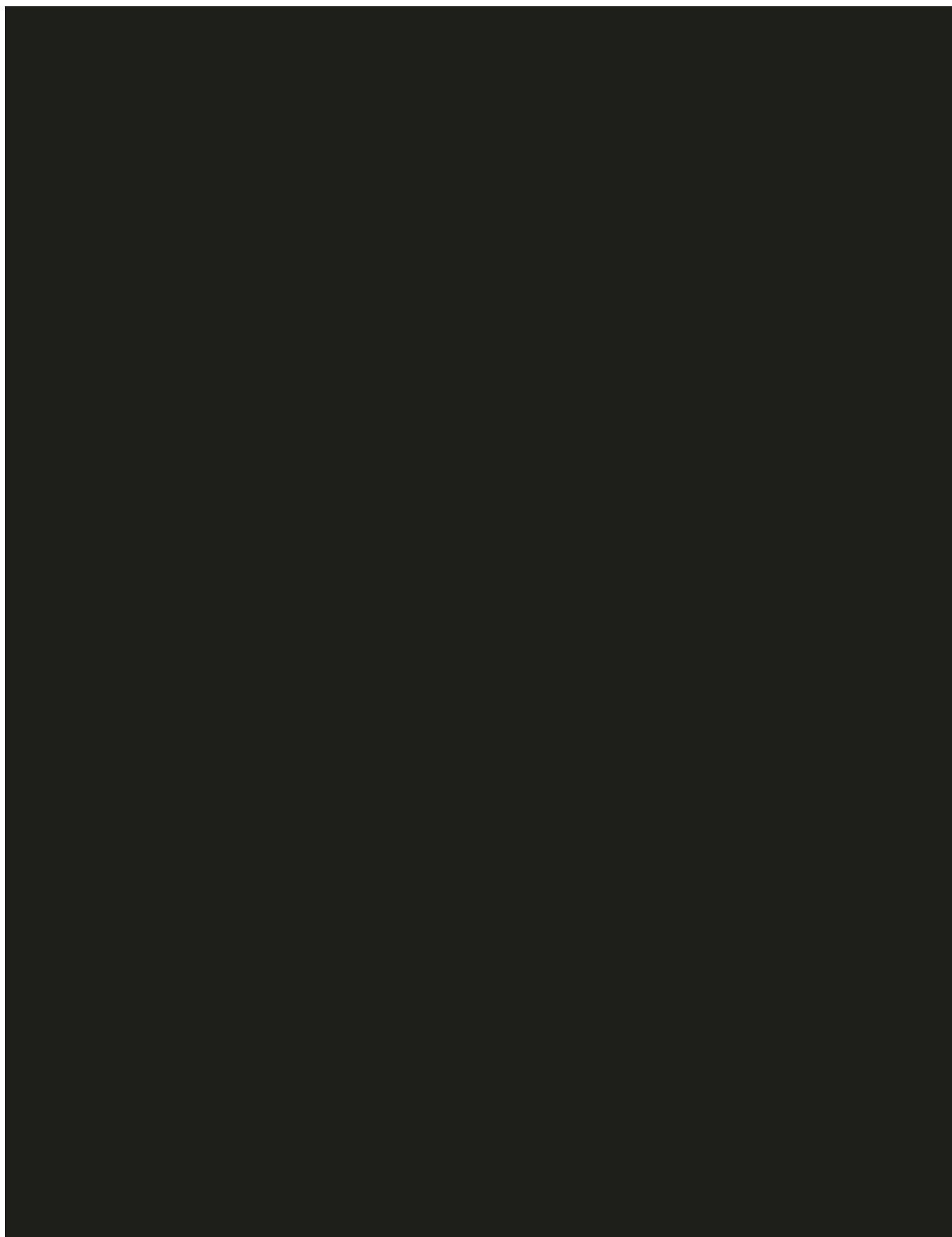
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**Revision Number:** 10



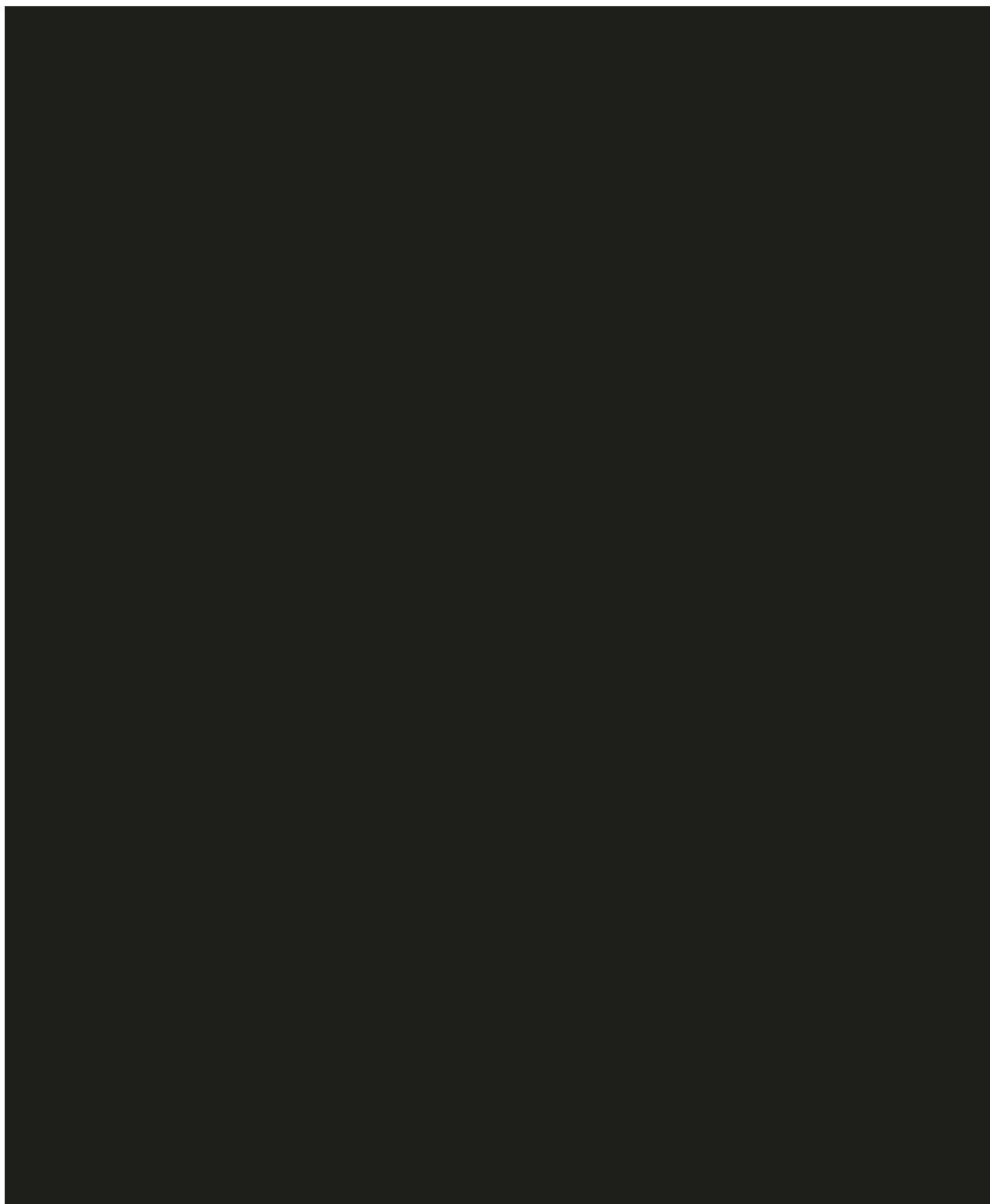
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**Johnson & Johnson Vision Care, Inc.**

**Title:** Biomicroscopy Scale

**Document Type:** [REDACTED]

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**Revision Number:** 10



**Clinical Study Protocol**  
**Johnson & Johnson Vision Care, Inc.**

**Title:** Biomicroscopy Scale

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number: 10**



**Clinical Study Protocol  
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**DISTANCE AND NEAR SNELLEN VISUAL ACUITY EVALUATION**

**Title:** Distance and Near Snellen Visual Acuity Evaluation

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 5

**Title:** Distance and Near Snellen Visual Acuity Evaluation

**Document Type:** [REDACTED]

**Document Number:** [REDACTED]

**Revision Number:** 5

**Title:** Distance and Near Snellen Visual Acuity Evaluation

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**Revision Number:** 5



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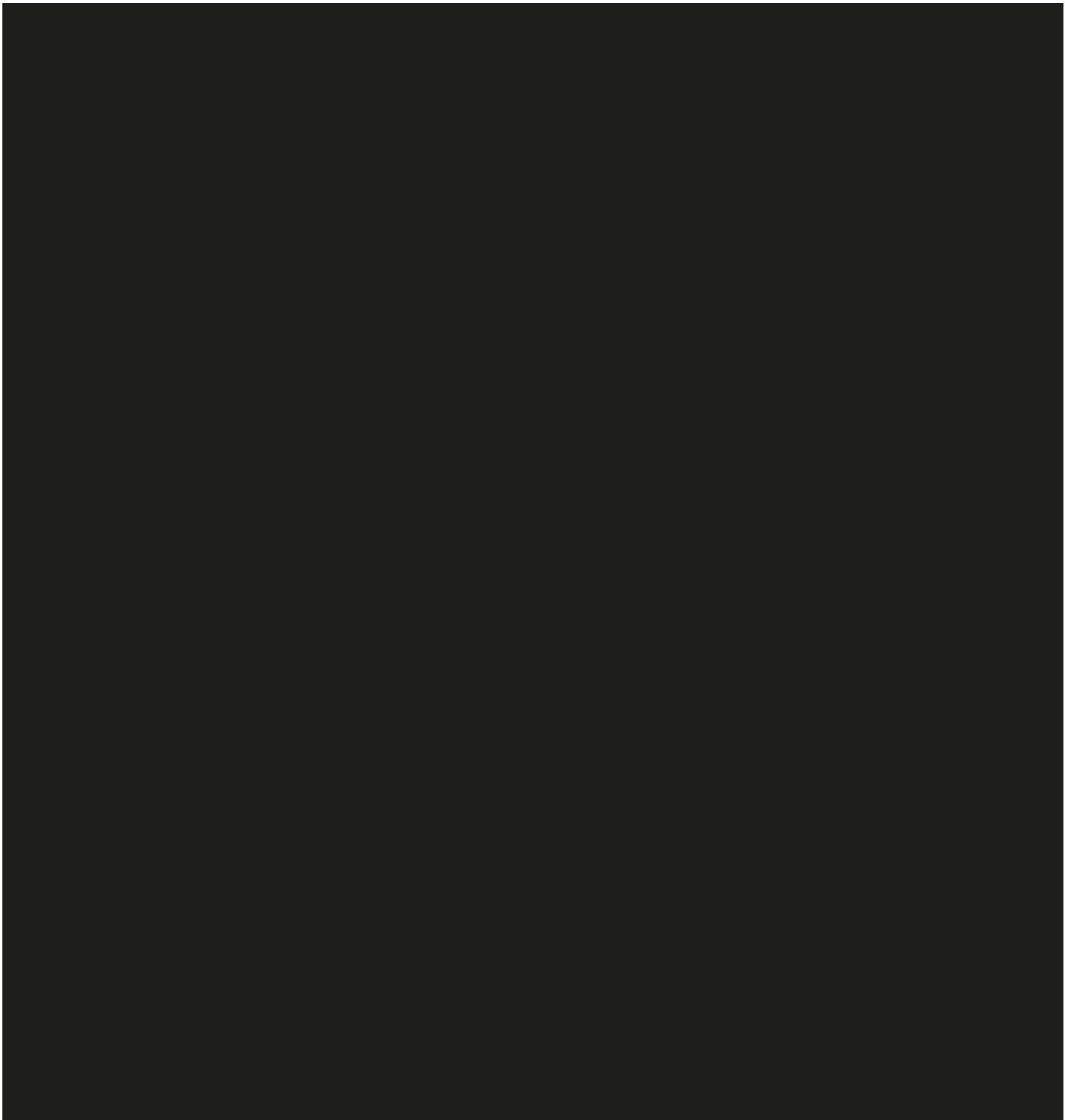
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**Clinical Study Protocol  
Johnson & Johnson Vision Care, Inc.**

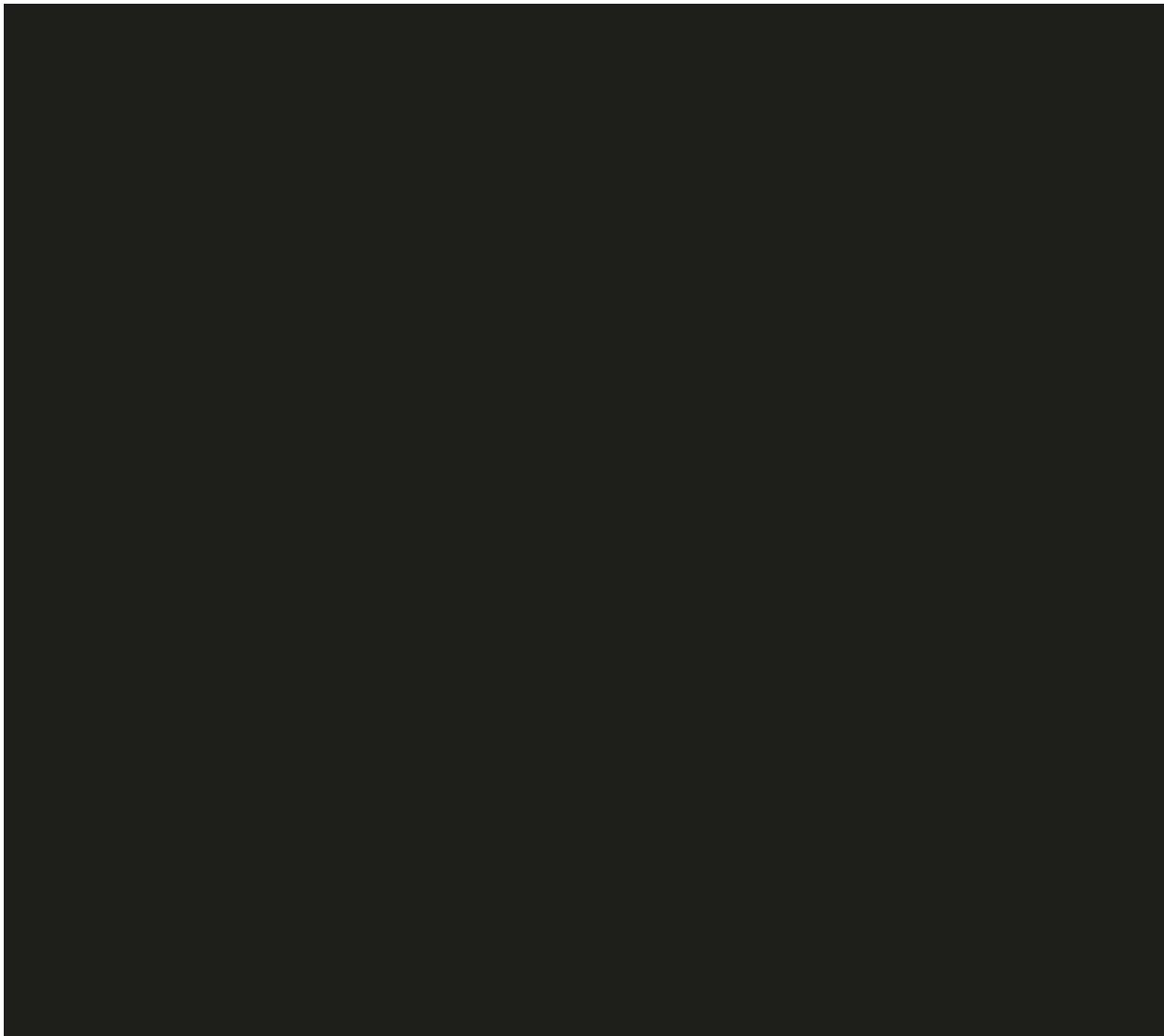
**APPENDIX E: OCULAR DOMINANCE**



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**APPENDIX F: IRIS COLOR SCALE**

**Clinical Study Protocol**  
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**APPENDIX G: TEST AND CONTROL LENS FITTING GUIDE**

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**APPENDIX H: PSYCHOPHYSICAL TESTING**



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**APPENDIX I: GUIDELINES FOR COVID-19 RISK MITIGATION**

# Clinical Study Protocol

## Johnson & Johnson Vision Care, Inc.

Title:

Document Type:

Document Number:

## Guidelines for COVID-19 Risk Mitigation

Revision Number: 5

### 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.

**Clinical Study Protocol**  
**Johnson & Johnson Vision Care, Inc.**

**Title:**

**Document Type:**

**Document Number:**

**Guidelines for COVID-19 Risk Mitigation**

**Revision Number: 5**

**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:

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Title:

Guidelines for COVID-19 Risk Mitigation

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## 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:

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<b>Procedure</b>	<b>Details</b>
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 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).

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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 (Form Control No. [REDACTED] [REDACTED]) per Study Site Initiation (Form Control No. [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 (Form Control No. [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.

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**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.).

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**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.

**Clinical Study Protocol****Johnson & Johnson Vision Care, Inc.****Title:****Guidelines for COVID-19 Risk Mitigation****Document Type:****Document Number:****Revision Number: 5****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 Vision 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 <b>NOTE: Inform JJVC in 24 hours of any COVID-19 cases and all potential exposure during the clinical study.</b>
	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

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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.

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Principal Investigator Signature and Date

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**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](https://opto.ca/sites/default/files/resources/documents/infection_control_guidelines_2016.pdf)
- Infection prevention and control for COVID-19: Interim guidance for outpatient and ambulatory care settings. (2020, May 23 May). Retrieved from Government of Canada: <https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/interim-guidance-outpatient-ambulatory-care-settings.html>

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- Information for Members On Coronavirus (COVID-19). (n.d.). Retrieved from Canadian Association Of Optometrists:  
[https://opto.ca/sites/default/files/resources/documents/information\\_for\\_members\\_on\\_coronavirus.pdf](https://opto.ca/sites/default/files/resources/documents/information_for_members_on_coronavirus.pdf)
- Coronavirus (COVID-19) resources for health professionals, including aged care providers, pathology providers and health care managers. (2020, September 24). Retrieved from Australian Government Department of Health:  
<https://www.health.gov.au/resources/collections/coronavirus-covid-19-resources-for-health-professionals-including-aged-care-providers-pathology-providers-and-health-care-managers>
- Environmental Cleaning and Disinfection Principles for COVID-19. (n.d.). Retrieved from Australian Government Department of Health:  
<https://www.health.gov.au/sites/default/files/documents/2020/03/environmental-cleaning-and-disinfection-principles-for-covid-19.pdf>
- Infection control guidelines and advice. (n.d.). Retrieved from Optometry Australia :  
<https://www.optometry.org.au/practice-professional-support/coronavirus-covid-19-what-optometrists-need-to-know/covid-19-clinical-advice/infection-control-guidelines-and-advice/>

# **Clinical Study Protocol**

## **Johnson & Johnson Vision Care, Inc.**

### **PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE**

Protocol Number and Title: CR-6391 Evaluation of Multifocal Contact Lens Designs with and without an HEV-Blocker on Visual Function

Version and Date: 4.0 12 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,<sup>1</sup> GCP and ICH guidelines,<sup>2</sup> the Declaration of Helsinki,<sup>3</sup> United States (US) Code of Federal Regulations (CFR),<sup>4</sup> 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<sup>2</sup> 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<sup>2</sup> 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 JJCPI 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:

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Signature

---

Date

---

Name and Professional Position (Printed)

Institution/Site:

---

Institution/Site Name

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Institution/Site Address