Design Validation of Toric Contact Lenses in Senofilcon A with a Blue-Blocking Chromophore

Protocol CR-6521

Version: 3.0

Date: 01 June 2023

Investigational Products: The test product will be rotationally stabilized astigmatic soft contact lenses in senofilcon A with a chromophore to block High-Energy Visible Light (HEVL). The control lens will be the ACUVUE® OASYS 1 Day for Astigmatism (AO1DfA) contact lenses.

Keywords: Astigmatism, toric contact lenses, senofilcon A, [redacted] chromophore, High-Energy Visible Light, dispensing, daily wear, daily disposable, ocular physiology, lens fit, rotational performance, logMAR visual acuity, CLUE Vision, CLUE Comfort, CLUE Handling, situational visual performance, ACUVUE® OASYS 1-Day for Astigmatism, Single use Eye-Cept® Rewetting Drops, LacriPure Saline Solution, ScleralFil Preservative Free Saline Solution.

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

This clinical trial will be conducted in compliance with ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good clinical practice,[1] and the Declaration of Helsinki.[2]

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Design Validation of Toric Contact Lenses in Senofilcon A with a Blue-Blocking Chromophore
Protocol Number: CR-6521
Version: 3.0
Date: 01 June 2023

SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

The Medica! Monitor must be notified by the clinical institution/site by e-mail or telephone within 24 how-s of leaming of a Serious Adverse Event. The Medica! Monitor may be contacted dw-ing business how-s for adverse event questions. General study related questions should be directed towards yow- ass igned clinical research associate.

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

AUTHORIZED SIGNATURES

The signatures below constitutes the approval of this protocol and the attachments and provide the necessa1y assmances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulato1y requirements and applicable U.S. federa! regulations,[3] ISO 14155:2020,[1] and the Declaration of Helsinki.[2]

Author & Study Responsible Clinician	*See Electronic Signature Report* [redacted]	DATE
Clinical Operations Manager	*See Electronic Signature Report* [redacted]	DATE
Biostatistician	*See Electronic Signature Repo,·t* [redacted]	DATE
Biostatistician Review	*See Electronic Signature Report* [redacted]	DATE
Data Management	*See Electronic Signature Repo,·t* [redacted]	DATE
Medica! Safety Officer	*See Electronic Signatw·e Repo,·t* [redacted]	DATE
Approver	*See Electronic Signature Report* [redacted]	DATE

CHANGE IDSTORY

Version	Originator	Description of Change(s) and Section Numbe s Affected	Justification for Change	Date
1.0	[redacted]	Original Protocol.	N/A	21 December, 2022
2.0	[redacted]	Updated Protocol Management lens build protocol numbers in section 6.1.	Test lenses are being remade under new Protocol Management build protocol. Additional over-labelling Protocol Management protocol was created for a subset of the control lenses.	20 January, 2023
3.0	[redacted]	Section 7.1 Time and Events Table: Removed the 'x' from Distance HLHC visual acuity using ETDRS charts at Visit 3 as this is not applicable. Updated biostatistician reviewer to current on signature page.	Accmacy Accmacy	01 Jun, 2023

SYNOPSIS

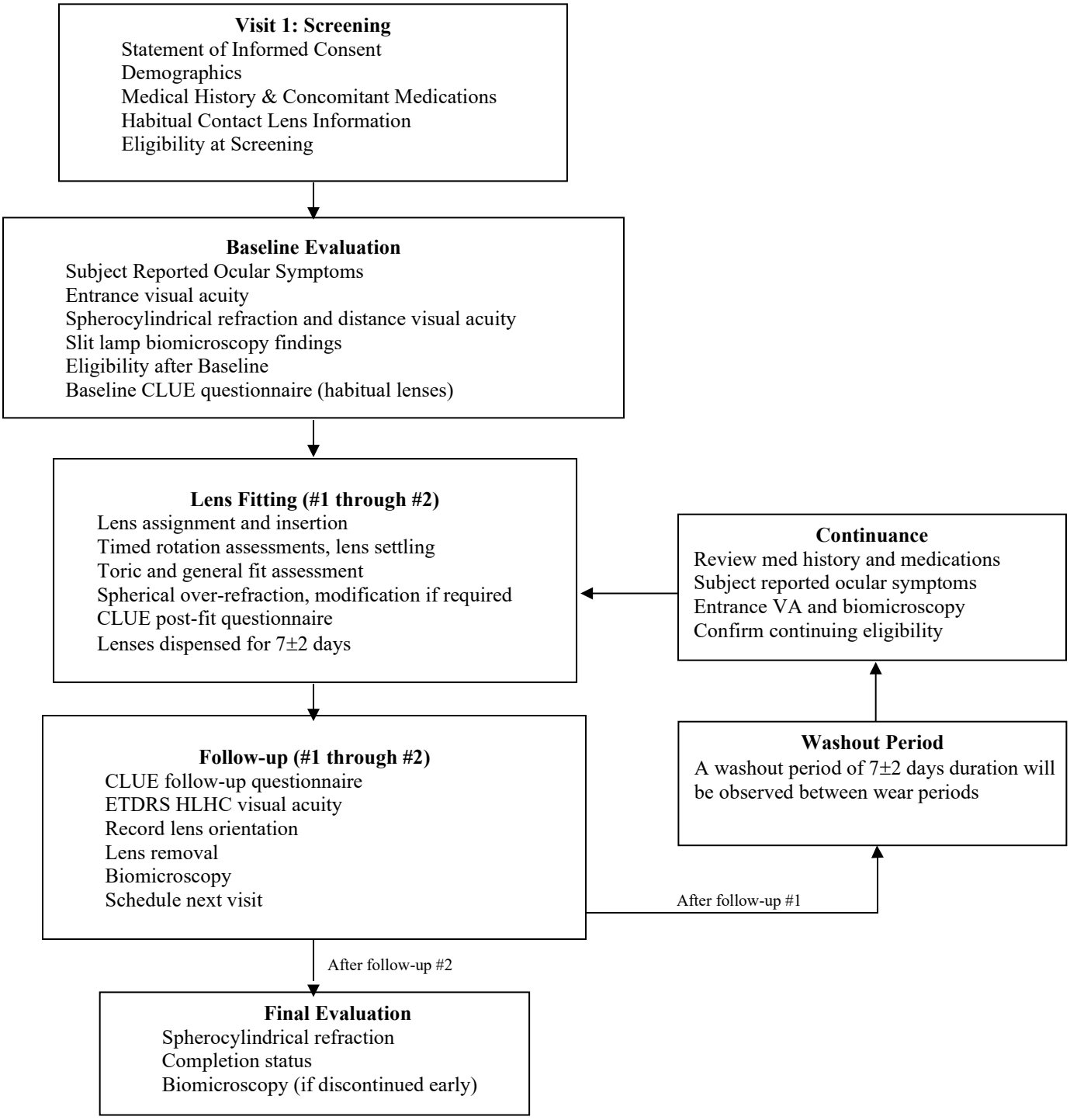
Protocol Title	Design Validation of Toric Contact Lenses in Senofilcon A with a Blue-Blocking Chromophore
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Design validation Design control phase: Confirmatory phase, phase 3
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor.
Test Article(s)	Investigational Products: The test product will be rotationally stabilized astigmatic soft contact lenses in senofilcon A with a chromophore to block High-Energy Visible Light (HEVL). Approved Products: The control product will be ACUVUE® OASYS 1-Day for Astigmatism (AO1DfA) contact lenses.
Wear and Replacement Schedules	Wear Schedule: Daily wear Replacement Schedule: Daily disposable
Objectives	The primary objectives of this study are to demonstrate that the investigational toric contact lenses in senofilcon A with a blue-blocking chromophore meet the design validation requirements related to visual acuity, eye health, fit acceptance, and subjective vision. The secondary objectives of this study are to demonstrate that the investigational toric contact lenses in senofilcon A with a blue-blocking chromophore meet the market preference requirements related to subjective handling and comfort. An exploratory objective of this study is to evaluate the subjective response to specific situational visual performance questions regarding vision while driving and during digital device use for the test lenses compared to the control lenses.
Study Endpoints	Primary endpoints: • Grade 3 or higher biomicroscopy findings related to study lens wear (Yes/No) • Acceptable lens fit (Yes/No) • Monocular, High-Luminance, High-Contrast (HLHC) distance Visual Acuity (VA) (logMAR) • Absolute lens orientation ≤ 10° (Yes/No) • Lens rotational stability with blinks ≤ 5° (Yes/No) • CLUE Vision score Secondary endpoints: • CLUE Handling score • CLUE Comfort score Exploratory endpoints: • Ability to see comfortably while driving during the day [redacted] • My vision was clear enough to allow me to drive at night [redacted] • Reduction in the feeling of tired eyes from using a computer or other digital device [redacted]

Study Design	This will be a 4-visit, randomized, controlled, single-masked, bilateral wear, dispensing, 2-treament, 2-sequence, 2-period crossover study. Each subject will be randomized into one of two unique sequences to wear two different study lenses one at a time over two wear periods (test followed by control or control followed by test). During each wear period the lenses will be worn bilaterally for approximately one week (7±2 days) in a daily disposable modality. Subjective comfort, vision and handling will be assessed using the CLUE questionnaire at fitting and follow-up visits for each wear period. HLHC monocular VA will be assessed at the follow-up evaluation using ETDRS charts. There will be a washout period of approximately one week (7±2 days) between wear periods. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	This study will have an enrollment target of approximately 180 subjects, with a target of at least 165 to complete (assuming a dropout rate of 10%).
Study Duration	Total study duration including the enrollment period is anticipated to be approximately 10 weeks.
Anticipated Study Population	Subjects will be habitual bilateral soft contact lens wearers with bilateral astigmatism who are between 18 and 39 years of age (inclusive).
Eligibility Criteria - Inclusion	Potential subjects must satisfy of all the following criteria to be enrolled in the study. 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 18 and 39 years of age (inclusive) at the time of screening. 4. Habitually wear soft contact lenses in both eyes in a daily or daily disposable wear modality (i.e., not extended wear modality). Habitual wearer is defined as a minimum of 6 hours per day, for a minimum of 2 days per week during the past four weeks. 5. Possess a wearable pair of spectacles that provide correction for distance vision. Inclusion Criteria at Baseline Evaluation The subject must: 6. In both eyes, have refractive error suitable for correction with the toric contact lens powers available in this study: a. Sphere powers (DS) -1.50 through -4.00 in 0.25 steps b. Cylinder powers (DC) -0.75 and -1.25 c. Axes (°) 170, 180, 10, 80, 90, 100 7. Have best corrected monocular distance visual acuity of 20/30 or better in each eye.

Eligibility Criteria – Exclusion	Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria following Screening The subject must not: 1. Be currently pregnant or lactating. 2. Be diabetic. 3. Be currently using any ocular medications or have an ocular infection of any type. 4. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g. rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1 for additional details regarding excluded systemic medications. 5. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g. SynergEyes, SoftPerm) within the past 6 months. 6. Be currently wearing monovision or multifocal contact lenses. 7. Be currently wearing lenses in an extended wear modality. 8. Have a history of strabismus or amblyopia. 9. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site. 10. Have participated in a contact lens or lens care product clinical trial within 7 days prior to study enrollment. Exclusion Criteria following Baseline Evaluation The subject must not: 11. Have clinically significant (grade 3 or higher on the FDA grading scale) slit lamp findings (e.g., corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection) or other corneal or ocular disease or abnormalities that contraindicate contact lens wear or may otherwise compromise study endpoints (including entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, moderate or above corneal distortion, herpetic keratitis). 12. Have fluctuations in vision due to clinically significant dry eye or other ocular conditions. 13. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, PRK, LASIK, iridotomy, retinal laser photocoagulation, etc.).
Disallowed Medications/Interventions	Subjects will not be eligible to enroll if they are taking any ocular medications, or any systemic medications that would normally contraindicate contact lens wear or may otherwise compromise study endpoints. See section 9.1 for details regarding disallowed systemic medications.

Measurements and Procedures	Key procedures associated with the endpoints for this study will include: - Measurement of HLHC VA using ETDRS charts - Examination of the anterior segment using a slit lamp biomicroscope and grading findings using the FDA grading scale - Assessment of general lens fitting characteristics (centration, movement, push-up test) - Assessment of lens orientation and rotational stability using a slit lamp biomicroscope - Overseeing completion of subjective questionnaires
Microbiology or Other Laboratory Testing	Not applicable for this study.
Study Termination	The occurrence of an Unanticipated Adverse Device Effect (UADE) or Serious Adverse Event (SAE) for which a causal relationship to a test article cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Lens cases, fluorescein strips and preservative-free rewetting drops / artificial tears will be supplied for use as needed.
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS, ACRONYMS AND DEFINITIONS OF TERMS

ADE	Adverse Device Effect
ADHD	Attention Deficit Hyperactivity Disorder
AE	Adverse Event/Adverse Experience
AO1DfA	ACUVUE OASYS® 1-DAY with HydraLuxe™ TECHNOLOGY for ASTIGMATISM
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COVID-19	Coronavirus Disease 2019
COM	Clinical Operations Manager
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICH	The 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
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

1. INTRODUCTION AND BACKGROUND

High Energy Visible Light (HEVL) may be generally defined as the visible region of the electromagnetic spectrum with wavelengths shorter than 500 nm. Due to Rayleigh scattering, light within this range of

wavelengths is scattered more than light of longer wavelengths, thus filtering these shorter wavelengths may result in increased visual contrast when looking at distant objects. At approximately 435 nm, visible light has enough energy to damage the retinal pigment epithelium and has been linked to macular degeneration. Additionally, the retinal receptors responsible for photoentrainment (entrainment of the circadian rhythm in response to patterns of light and dark) are maximally sensitive to light at approximately 480 nm.

Ophthalmic lenses that block High Energy Visible Light (HEVL) may offer improved vision through enhanced chromatic contrast sensitivity. Such lenses may also provide greater retinal protection than regular lenses without spectral filtering. This study will evaluate the clinical performance of a daily disposable, toric lens design incorporating a HEVL-blocking chromophore [redacted]

1.1. Name and Descriptions of Investigational Products

The test lens in this study will be a toric contact lens design in senofilcon A containing a HEVL-blocking chromophore [redacted] ACUVUE® OASYS 1-Day for Astigmatism (AO1DfA) contact lenses will be evaluated as a control lens.

Further details about the test and control articles are given in section 6 of this protocol.

1.2. Intended Use of Investigational Products

The intended use of the investigational products is the correction of myopic astigmatism. Study lenses will be worn bilaterally in a daily wear, daily disposable modality for at least 8 hours per day and 5 days per week over a wear period of 7±2 days. Two wear periods will be completed in total, with a washout period of 7±2 days between the wear periods.

1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. For the most comprehensive nonclinical information regarding the test and control designs refer to the latest version of the Investigator's Brochure.[4]

1.4. Summary of Known Risks and Benefits to Human Subjects

The anticipated clinical benefit of the investigational lenses will be the correction of refractive error. No adverse device effects are anticipated. The risks associated with use of the investigational lenses are considered to be the same as those for other marketed soft contact lens worn in the same modality (i.e., daily disposable wear). No additional risks associated with participation in this investigation are anticipated.

Comprehensive risk and benefit information regarding the test design and the AO1DfA control lens are included in the latest versions of the Investigator's Brochure[4] and the AO1DfA package insert (Appendix C), respectively.

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

Prototype toric lens designs featuring the [redacted] chromophore have previously been evaluated in several JJVC-sponsored clinical trials. Safety data from these trials suggest the investigational lenses have a safety profile equivalent to currently marketed soft contact lens products; a review of literature references and prior clinical data related to the test designs is given in the Investigator's Brochure.[4]

For further details regarding the AO1DfA control lens, refer to the AO1DfA package insert (Appendix C).

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective:

The objective of this study is to demonstrate that the investigational lens meets the validation requirements related to objective and subjective vision, eye health, fit acceptance, toric rotation, and rotational stability.

Secondary Objective:
The secondary objective of this study is to demonstrate that the investigational lens meets the user needs with respect to subjective lens handling and comfort.

Exploratory Objective
An exploratory objective of this study is to evaluate the subjective response to specific situational visual performance questions regarding vision while driving and during digital device use for the test lenses compared to the control lenses.

2.2. Endpoints

Primary Safety Endpoints:

Slit Lamp Findings (SLF)
SLFs (Grade 3 or higher) related to study lens wear will be assessed for each eye at all study visits (scheduled and unscheduled). SLFs will be evaluated and graded using the FDA Grading scale from 0 to 4, where Grade 0 represents the absence of findings and 1 to 4 representing successively worse findings. The percentage of eyes with Grade 3 or higher SLF will be analyzed and will include corneal infiltrates. See [redacted] in Appendix D for more details on the collection of SLFs.

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

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

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

Primary Efficacy Endpoints:

Visual Acuity (logMAR)
Visual acuity (VA) will be assessed monocularly at the 1-week follow-up evaluation under high-luminance high-contrast (HLHC) conditions at a test distance of 4 meters using ETDRS Charts. See [redacted] in Appendix D for details regarding the collection of visual acuity.

Toric Lens Orientation
Toric lens orientation (scribe mark position relative to 6 o'clock) will be assessed for each eye at 1, 3 and at least 15 minutes after lens insertion at the fitting visit, and at the 1-week follow-up visit. However, lens orientation at least 15 minutes after lens insertion at the fitting visit is the primary endpoint. Lens orientation is a binary response where Y=1 if the absolute lens orientation is $\leq 10°$ and Y=0 otherwise. See [redacted] in Appendix D for details regarding the collection of absolute toric lens orientation.

Rotational Stability
Rotational stability will be assessed for each eye at least 15 minutes after lens insertion at the fitting visit, and at the 1-week follow-up visit. However, rotational stability assessed at least 15 minutes after lens insertion at the fitting visit is the primary endpoint. Rotational stability is a binary response where Y=1 if the lens stability with blinks is $\leq 5°$ and Y=0 otherwise. See [redacted] in Appendix D for details regarding the collection of lens stability with blinks.

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

Secondary Endpoints
- CLUE Handling score at follow-up
- CLUE Comfort score at follow-up

Exploratory Endpoints
- Ability to see comfortably while driving during the day [redacted]
- My vision was clear enough to allow me to drive at night [redacted]
- Reduction in the feeling of tired eyes from using a computer or other digital device [redacted]

2.3. Hypotheses

Co-Primary Safety Hypotheses:

1. The percentage of eyes with one or more clinically significant, study-lens related, slit-lamp findings (Grade 3 or 4) following wear of the test lenses will be less than 5%.

2. At least 80% of lens fits will be acceptable at the dispensing visit.

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

Co-Primary Efficacy Hypotheses:

1. After approximately 1-week of wear, the mean monocular, high-luminance, high-contrast distance visual acuity for the test lens will be lower than 0.00 logMAR (equivalent to 20/20 Snellen visual acuity).

2. Following lens settling (at least 15 minutes) at the dispensing visit, at least 80% of lens fits will have absolute rotation less than or equal to 10 degrees.

3. Following lens settling (at least 15 minutes) at the dispensing visit, at least 80% of lens fits will have lens rotational stability with blink less than or equal to 5 degrees.

4. After approximately 1 week of wear, the mean overall CLUE™ Vision score for the test lens will be statistically greater than 62 points.

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

Secondary Hypotheses:
1. After approximately 1 week of wear, the mean overall CLUE™ Handling score for the test lens will be greater than 61 points with 95% statistical confidence.

2. After approximately 1 week of wear, the mean overall CLUE™ Comfort score for the test lens will be greater than 58 points with 95% statistical confidence.

Exploratory Hypotheses:

1. After approximately 1 week of wear, the test lens will be non-inferior to the control lens with respect to at least one of the following subjective questionnaire items asked at the follow-up visit:
    a. Ability to see comfortably while driving during the day
    b. My vision was clear enough to allow me to drive at night
    c. Reduction in the feeling of tired eyes from using a computer or other digital device

A non-inferiority margin of 10% will be used.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

The target population for this study will be healthy adult soft contact lens wearers between 18 and 39 years of age with binocular myopic astigmatism.

3.2. Inclusion Criteria

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

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 18 and 39 years of age (inclusive) at the time of screening.
4. Habitually wear soft contact lenses in both eyes in a daily or daily disposable wear modality (i.e., not extended wear modality). Habitual wearer is defined as a minimum of 6 hours per day, for a minimum of 2 days per week during the past four weeks.
5. Possess a wearable pair of spectacles that provide correction for distance vision.

Inclusion Criteria at Baseline Evaluation

6. In both eyes, have refractive error suitable for correction with the toric contact lens powers available in this study:
    a. Sphere powers (DS) -1.50 through -4.00 in 0.25 steps
    b. Cylinder powers (DC) -0.75 and -1.25
    c. Axes (°) 170, 180, 10, 80, 90, 100
7. Have best corrected monocular distance visual acuity of 20/30 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. Be diabetic.
3. Be currently using any ocular medications or have an ocular infection of any type.
4. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g. rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1 for additional details regarding excluded systemic medications.
5. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g. SynergEyes, SoftPerm) within the past 6 months.

6. Be currently wearing monovision or multifocal contact lenses.
7. Be currently wearing lenses in an extended wear modality.
8. Have a history of strabismus or amblyopia.
9. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site.
10. Have participated in a contact lens or lens care product clinical trial within 7 days prior to study enrollment.

Exclusion Criteria at Baseline Evaluation
The subject must not:

11. Have clinically significant (grade 3 or higher on the FDA grading scale) slit lamp findings (e.g., corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection) or other corneal or ocular disease or abnormalities that contraindicate contact lens wear or may otherwise compromise study endpoints (including entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, moderate or above corneal distortion, herpetic keratitis).
12. Have fluctuations in vision due to clinically significant dry eye or other ocular conditions.
13. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, PRK, LASIK, iridotomy, retinal laser photocoagulation, etc.).

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 will be a 4-visit, randomized, controlled, single-masked, bilateral wear, dispensing, 2-treatment, 2-sequence, 2-period crossover study.

At the initial visit (Visit 1), eligible subjects will be randomized into one of two unique sequences to wear two different study lenses one at a time over two wear periods (test/control or control/test). Subjects will wear each study lens type in a daily wear, daily disposable modality for approximately 1-week. Subjects will be advised to wear the study lenses for a minimum of 8 hours per day for at least 5 days during each wear period. Subjective comfort, vision and handling will be assessed using the CLUE questionnaire at both fitting and follow-up visits for each wear period. Monocular HLHC VA will be assessed at the follow-up evaluation using ETDRS charts. There will be a washout period of 7±2 days duration between wear periods. Subjects will not have access to the study lenses following completion of the protocol.

Unscheduled visits may be conducted, if appropriate, and lost or damaged lenses may be replaced when necessary.

4.2. Study Design Rationale

The primary objective of this study is to evaluate the clinical performance of the test lenses against predefined targets specified in the Customer Requirements Document, based on historical performance of the ACUVUE® OASYS 1-Day for Astigmatism contact lenses.[6] While the co-primary, safety, efficacy and secondary hypotheses will be tested for the test lenses only, a two-treatment by two-period crossover design was chosen for this study. This was considered the optimal design as it will address the primary, secondary and exploratory objectives as well as provide clinical data for the control lens. The rationale for collecting data on a marketed product is to the monitor the clinical performance, as the lenses for this study will be manufactured from the Flexible Manufacturing Platform (FMP), which is not the distributional line utilized for the Control lens (AO1Dfa). Moreover, this is only the second study where lenses from the FMP line are being evaluated.

Though the primary hypothesis is to test only the investigational study lens, the study design is not anticipated to have an impact on subjects' visual acuity, toric lens orientation, rotational stability, lens fit or SLFs since these endpoints are objective in nature, there will be a 1-week washout period between study lenses, and different EDTRS charts will be utilized for each eye (left vs. right) to help reduce potential for optotype memorization during collection of visual acuity.

However, there is a potential risk of carryover effect in all data collected from this study design, however, this is a greater risk for subjective responses than objective ones, i.e., CLUE vision scores. If a sequence effect is observed in the statistical model, then the primary hypothesis will be tested on data from the first period only.

4.3. Enrollment Target and Study Duration

This study will have an enrollment target of approximately 180 subjects, with a target of at least 165 to complete. The study will be conducted at up to 14 clinical sites, where the enrollment target for each site will be approximately 10 to 20 subjects. A subject will be considered enrolled upon signing of the informed consent form.

At Visit 1, eligible subjects will be randomized to one of two lens wear sequences. There will be 4 visits in total per subject; total study duration including the enrollment period is expected to be approximately 10 weeks. Subjects who are discontinued prior to the final evaluation may be replaced at the discretion of the study sponsor. The investigation will end at the time that the study data is hard locked.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn bilaterally in a randomized fashion using a 2x2 crossover design with 2 lens types and 2 periods. At Visit 1, eligible subjects will be randomized to one of two unique lens wear sequences using a computer-generated randomization scheme provided by the study biostatistician. Permuted block randomization will be used to avoid bias in the assignment of subjects to treatment, and to enhance the validity of statistical comparisons across treatment groups. Each block will contain two different lens trial sequences. 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).[7]

The study site must follow the randomization scheme provided and complete enrollment per the randomization scheme and not pre-select or assign subjects. Randomization will be performed at Visit 1 prior to the first lens fitting. The following must have occurred prior to randomization:

- Informed consent must have been obtained.
- The subject must have met all eligibility criteria.
- The subject's screening and baseline information must have 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.
2. Investigator or designee will record the subject's number on the appropriate line of the randomization (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

To reduce the potential for bias, this will be a single-masked trial; subjects will not be aware of the identity of the assigned lenses, however, due to the difference in appearance of the test lenses containing the [redacted]

chromophore, it is expected that subjects will be able to visually differentiate between the test and control designs. The identity (i.e., brand and type) ofthe studylenses will bemasked by having the blister packs labeled with the study number, lot number, sphere power, cylinder power, axis, expiration date and randomization code. Investigators, site staff and sponsor personnel (including the medical monitor) will be aware of the identity of the test and control lenses.

5.3. Procedures for Maintaining and Breaking the Masking

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

6. STUDY INTERVENTION

6.1. Identi ty of Te st Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

	Test	Contrnl
Test Atticle Fonu	Sofi contact lens	
Design/ Description	TRAlOO and TRA200 series toric contact lens with HEVL-blocking chromo hore	AOlD fA
Desi◇ Name	TRAlXX and TRA2XX	AOlD fA
Manufacturer	Johnson & Johnson Vision Care, Ine.	
Packaging Form	Blister packaging in sterile packing solution	
Packaging Solution	Optimized Borate Buffer (OBB) solution	
Lens Material	senofilcon A (C3) with [redacted] chromophore	senofilcon A (C3)
Sphere Powers (DS)	-1.50 to -4.00 in 0.25 ste s	
Cylinder Powers (DC)	-0.75, -1.25	
Cylinder Axes (°)	10, 80, 90, 100, 170, 180	
Nominal Water Content %	38	
Nominal Base Curve mm	8.5	
Lens Diameter (mm)	14.3	
Fiducial marks	6 and 12 o'clock fiducial lines	
Dk (Fatt method, boundary coITected , edge COITected , x10-11 [cm2 /sec] [ml Oi/ ml x mm Hᵖ at 35°C	103	
Modality in Ct11Tent Stud	Daily wear	
Replacement Frequency in CulTent Study	Daily disposable	
[redacted]	[redacted]	[redacted]

1n total, both test and control lenses will be available in 132 unique lens powers (11 sphere powers x 2 cylinder powers x 6 axes).

For each study lens design (test and control), the total number of test lenses to be used in this study (not including lenses that are replaced due to droppage, loss or damage) is expected to be approximately 2520 lenses (target enrollment of 180 subjects x 2 eyes per subject x 7 days per wear period).

6.2. Ancillary Supplies/Products

The following solutionswill be used in this study:

Table 2: Ancillary Supplies

	Non-Preserved Rewetting Droos		
Solution Name/Description	Single use Eye-Cept® Rewett.ing Drops	LacriPure Saline Solution	ScleralFil Preservative Free Saline Solution
Manufacturer	Optics Laboratory	Menicon	Bausch & Lomb
Preservative	None	None	None

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 aiticles will be dispensed to subjects meeting all eligibility requirements, including any dispensing requirements set fo1ih in this clinical protocol. Subjects will be dispensed an adequate supply of test a1ticles to complete the study. Lost or datnaged 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 primaiy packaging. The test aiticle will be over-labeled to mask the subject to the identity of the lens. The sample study label is shown below:

Prima1y Packaggi.'-'—

CAUTON: INVESIIGAIIONAL DEVICE
UMTED BY U.S. LAW
TO INVESTIGAIONAL USE
EXCLUSVIELY FOR
CUNICAL INVESTIGATIONS

Cnm:Onecontact nsi1sokitim.

STE RI LE

LOT ABC123
SPH -1.00
CYL-0.75 AXIS 180
EXP 2025/12/31
CR-6521 RC A

Secondaiy Packaging

Sponsored By/Parrairre par:

Johnson & Johnsoo V'ision care, Ine.
7500 Centurion Parkway
Jacksonvile, FL 32256, USA

Conten1s/Contenu:

Contact Lenses in Solution
Lentes cornéennes dans u esolulion

6.5. . Storage Conditions

Test a1ticles will be maintained at ambient temperatures at the clinical site. Test a1ticles must be kept under secure conditions.

6.6. Collection and Storage of Samples

No samples will be collected as pati of thestudy procedures.

When possible, any lens or test aiticle associatedwith 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 retum to *JN C* .

6.7. Accountability of Test A11icles

JNC will provide the Investigator with sufficient quantitie s 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 ait icles 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 retumed to the Investigator unused, including expired or malfunctioning product.
3. The number and reason forunplanned replacements.

The Investigator will collect all unused test articles from the subjects at the end of the subject's pa1ticipation. Subject retumed unused test articles must be separated from the clinical study invent01y of un-dispensed test articles and must be labeled with the subject number and date of retum. Following final reconciliation of test articles by the monitor, the Investigator or monitor will retum all unused test a1ticles to *JN C* .

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

[redacted]

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Infonnation	Visit 1 Screening, Baseline, LensFitting #1	Visit 2 Follow-up #1	Visit 3 Continuance, Lens Fitting #2	Visit 4 Follow-up #2, Final Evaluation
Time Point	Day0	7 ±2 days following Visit 1	7 ±2 days following Visit 2	7 ± 2 days following Visit 3
Minimum lens wear time immediately prior to visit	Mustwear habitual lenses	1 hour (study lenses)	No reauirement	1 hour (study lenses)
Estimated Visit Duration	2.5 hours	1.5 hours	1.5 hours	1.5 hours
Statement of info1med consent	x			
Demographic s	x			
Medica! histo1y/concomitant medications	x	x	x	x
Habitual contact lens info1mation	x			
Habitual lens wear time	x			
Eligibilitv at Screening	x			
Subiect reoorted ocular svmotollIS	x	x	x	x
Baseline PRO ouestionnaire	x			
Entrance visual acuitv	x	x	x	x

Visit Infon nation	Visit 1 Screening, Baseline, Lens Fitting #1	Visit 2 Follow-up #1	Visit 3 Continuance, Lens Fitting #2	Visit 4 Follow-up #2, Final Evaluation
Time Point	Day 0	7 ±2 days following Visit 1	7 ±2 days following Visit 2	7 ± 2 days following Visit 3
Minimum lens wear time inunediatelv orior to visit	Mustwear habitual lenses	1 hour (study lenses)	No reauirement	1 hour (study lenses)
Estimated Visit Duration	2.5 hours	1.5 hours	1.5 hours	1.5 hours
Remove habitual lenses	x		x	
Subjective Sphero-Cylindrical Refraction	x			x
Slit Lamp Biomicroscoov	x	x	x	x
Eligibility at Baseline	x			
Iris color	x			
Lens Selection	x		x	
Lens insertion and timed rotation assessments	x		x	
Lens settling	x		x	
Toric fit assessment	x		x	
General fit assessment	x		x	
Soherical over-refraction	x		x	
Lens modification *(if* necessarv)	x		x	
Post-fit PRO auestionnaire	x		x	
Additional samples of toric lens orientation foerformed tv.•ice)	x	x	x	x
Exit visual acuitv	x		x	
Disoensiniz criteria	x		x	
Disoensiniz instructions	x		x	
Schedule next visit	x	x	x	
Wear time and comoliance		x	x	x
Collect unwom lenses		x	x	x
Follow-uo PRO auestionnaire		x	x	x
Distance HLHC visual acuity using ETDRS cha1t s		x		x
Toric lens orientation		x	x	x
Lens removal		x	x	x
Continuance			x	
Subiect comoletion status				x

7.2. Detailed Study Procedure

VISIT 1

Subjects must wear their habitual contact lenses to this visit.

Visit 1: Screenimz			
Step	Procedure	Details	
1.1	Statement oflnfo1med Consent	Each subject must read, understand, and sign the Statement of Info 1med Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the info1med consent discussion must also sign the consent fonn. **Note:** The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject' s year of birth, age, gender, race, and ethnicitv.	
1.3	Medical Histo1y and Concomitant Medications	Record the subject' s medical histo1yand concomitant medications.	
1.4	Habitual Lenses	Record the subject' s habitual lens type, parameters, lens care solution, wear modality, and approximate orescriotion date.	
1.5	Habitual lens wear time.	Record the average and comfortable wear time for the subiect's habitual contact lenses.	
1.6	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "y es" and ali responses to Exclusion Criteria must be answered " no" for the subject to be considered eligible. If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy fo1ms do not need to be comoleted as oait of Final Evaluation.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.7	Subject reported ocular s toms	Record any subject reported oculai·symptoms reported with re ard to their habitual contact lenses.	
1.8	Baseline PRO questionnaire	Ask the subject to fill out the baseline questionnaire regarding their experience with their **habitual contact lenses.**	
1.9	Entrance visual acuity	Record the monoculai·distance Snellen visual acuity for each eye (OD, OS) to the nearest letter with the subject's habitual contact lens cot1'ection . Subject s must continue until at least 50% of the letters on a line are read incot1'ectl .	
1.10	Remove habitual lenses	The subject's habitual contact lenses will be removed and stored in a lens case, if required.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.11	Subjective sphero-cylindrical refraction	Conduct a full spherocylindrical bare eye subjective refraction with binocular balance and record the resultant monocular visual acuity for each eye to the nearest letter. Note: The duo-chrome test should be used for refining the monocular and binocular spherical endpoints. This test will be considered to have reached the endpoint when the targets on red and green backgrounds appear to be equally sharp. However, if the subject's response change immediately from "red" to "green" with a 0.25DS change in power, the endpoint will be the most plus power (with "red" target clearer) before this reversal.	
1.12	Slit lamp biomicroscopy	The FDA Slit Lamp Classification Scale will be used to grade findings. If any slit lamp finding is graded as 3 or worse, the visit will be discontinued; however, the subject may repeat the baseline evaluation (one time) at a later date once the condition lessens. Should the clearance of the fluorescein need to be expedited, preservative-free rewetting drops or artificial tears ma be instilled.	[redacted]
1.13	Eligibility at baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible. If subject is deemed to be ineligible after baseline, proceed to Final Evaluation.	
1.14	Iris color	The investigator will record the subject's iris color using the scale provided Appendix E.	Appendix E [redacted]

Visit 1: Lens Fittin #1			
Step	Procedure	Details	
1.15	Lens selection	Assign the study lens based on the randomization scheme. Select the fitting lens powers based on velt ex-con-ecte d subjecti ve refraction for each eye, with consideration of the following guidelines: 1. Label cylinder axis should be determined by rounding the refraction cylinder axis to the nearest 1O deg rees. Axis ending in the digit '5' should be rounded towards 180 for eyes with with-the-mle astigmatism, or towards 90 for eyes with against-the-rule astigmatism (e.g., 175 should be rounded to 180, 105 should be rounded to 100). 2. Cylinder power should be chosen based on the following table:	

<table>
<tr><td colspan="4">Visit 1: Lens Fittin #1</td></tr>
<tr><td>Step</td><td>Procedure</td><td>Details</td><td>[redacted]</td></tr>
<tr><td></td><td></td><td>
<table>
<tr><td>Ve1tex conected cylinder power (X) within the range: (DC)</td><td>Label cylinder power to be fit (DC)</td></tr>
<tr><td>-0.625 X < -1.125</td><td>-0.75</td></tr>
<tr><td>-1.125 X < -1.625</td><td>-1.25</td></tr>
</table>
3. The fitting lens spherical equivalent (SE) power (label sphere power + 1/2 of the label cylinder power) should be as close as possible to the SE of the vertex-con ected refraction. If the SE of the vertex-con ected refraction is exactly halfv.•ay betv.•een two label SE powers, the least minus label ower should be fit first.
</td><td></td></tr>
<tr><td>1.16</td><td>Right eye lens insertion</td><td>Instruct the subject to insert the right-eye lens with random orientation.
If lens is uncornfortable, inspect for datnage and remove. reinsert or re lace as necessa .</td><td>[redacted]</td></tr>
<tr><td>1.17</td><td>Timed rotation assessments during settling period</td><td>Start a stopwatch (or suitable smartphoneor tablet tirning app) as soon as the right lens is inse1ted. Record lens rotation (direction and magnitude) to the nearest degree at one (1) and three (3) minutes following insertion.
Note: All lenses in this study have scribe marks at the 6 o'clock position and rotation measurements are made relative to a ve1tical reference line.</td><td></td></tr>
<tr><td>1.18</td><td>Left eye lens insertion</td><td>Instruct the subject to insert the left-eye lens with random orientation.
If lens is uncornfortable, inspect for datnage and remove, reinsert, or re lace as necessa .</td><td>[redacted]</td></tr>
<tr><td>1.19</td><td>Timed rotation assessments during settling period</td><td>Start a stopwatch (or suitable smartphoneor tablet tirning app) as soon as the left lens is inse1ted. Record lens rotation (direction and magnitude) to the nearest degree at one (1) and three (3) minutes following inse1tion.
Note: All lenses in this study have scribe marks at the 6 o'clock position and rotation measurements are made relative to a ve1tical reference line.</td><td></td></tr>
<tr><td>1.20</td><td>Lens settling</td><td>Allow lenses to settle for a period of at least 15 minutes followin<> left lens insertion.</td><td></td></tr>
</table>

Visit 1: Lens Fittin #1			
Step	Procedure	Details	[redacted]
1.21	Toric fit assessment	Record for each eye: 1. The rotational position to the nearest degree 2. Lens stability with blinks 3. Toric fit acceptability. The toric lens fit will be designated as ' unacceptable' if either: a. The lens ABSOLUTE ROTATION is greater than 20 degrees b. The LENS STABILITY WITH BLINK is greater than 5 degrees If one or both lenses demonstrate an unacceptable toric fit, the subject will be discontinued (proceed to final evaluation .	
1.22	General lens fit assessment	The fitting characteristics of the lens in both eyes will be assessed using a slit lamp. Lens position (centration, limbal exposure, edge lift) and movement (primary and up gaze as well as push-up) will be assessed. Fit acceptability is defined as any lens that does **not** display the following general fit characteristics: • Limbal exposure (presence of clear comea) in any direction of gaze. • Edge lift. • Insufficient movement in ali three movement assessments (primary gaze, up-gaze and push-up test). • Excessive movement in prima1y gaze. If the general fit is unacceptable for either eye, the subject will be discontinued (proceed to exit evaluation .	[redacted]
1.23	Spherical over-refraction	Perfonn monocular spherical over-refraction using duo-chrome to refme the endpoint as described in step 1.11 (the final spherical endpoint may be detennined binocularly). The spherical over-refraction must be plano in both eyes to continue. If a non-plano over-refractionis found in either eye, the lens(es) must be refit with the indicated change in sphere power. If the indicated lens power is not available for either eye (e.g., outside the available SKU range), the subject will be discontinued (proceed to fmal evaluation .	[redacted]

Visit 1: Lens Fittin #1			
Step	Procedure	Details	[redacted]
1.24	Lens modification (if necessa1y)	If modification is necessary in one or both eyes, select the reason for refitting lenses: • The settled lens rotation is such that a different cylinder axis would be more appropriate (use the LARS rule to determine the replacement lens cylinder axis) • The spherical over-refraction is not plano • Other (specify reason) Repeat steps 1.16 through 1.23 for one or both eyes, as appropriate. A maximum of 2 lens modifications are allowed per eye. If, for either eye, the fit is not successful after 2 modifications, the subject will be discontinued roceed to final evaluation .	
1.25	Post-fit PRO questionnaire	Subjects will complete a PRO questionnaire regarding the initial comfo1t, vision and handling of the study lenses.	[redacted]
1.26	Additional sample of toric lens orientation (I)	Instruct the subject to leave the consulting room and walk around for at least 2 minutes. Upon their retum, measure and record the toric lens orientation for each e e to the nearest de ree.	
1.27	Additional sample of toric lens orientation 2	Repeat the previousstep once again.	
1.28	Exit visual acuity	Record the exit monocular distance Snellen visual acuity for each eye with the subject wearing the study lenses.	[redacted]
1.29	Dispensing criteria	Lenses may be dispensed if both following conditions are met: 1. The monocular distance visual acuity with the study lenses is equal to or better than 20/25 in each eye. 2. The subject indicates that the comfo1t and vision with the study lenses is acceptable. If either of these conditions is not met, the subject will be discontinued roceed to exit evaluation .	
1.30	Dispensing instructions	If the study lenses are suitable for dispensing: • Instruct the subject to wear the study lenses for at least 8 hours per day (in a daily wear / daily disposable modality) on at least 5 days of the wear period. **Subjects must not wear their habitual lenses at any time dming the dispensing period.** • Provide the subject with a copy of the Patient Instruction Guide. • Preservative-fre e rewetting drops are pe1mitted, if needed. • Dispense enough lenses for the subject to complete the wear period (i.e., up to and including their scheduled follow-up visit). At the investigator's discretion, in instances where there is a high likelihood of the subject needing replacement lenses (e.g., due to subject activities, unavailabili of su·b ect or site durin the wear	

Visit 1: Lens Fittin #1			
Step	Procedure	Details	[redacted]
		period, high likelihood ofl ens tears, etc.), one additional spare pair may be dispensed. 1n the event that a subject requires additional lenses due to loss or damage, they may retum to the clinical site for lens replacement. As much as reasonably possible, damaged lenses and packaging should be retumed to the clinical site (in solution, if possible) for shipping to the Sponsor. If lens datnage is present, complete the Product Quality Complaint Fonu, store the lens ina labeled vial with sahne and retum it to the Sponsor. • Ensure the subject is aware of the con-ect len s power for each eye (label the lenses with R and L as appropriate). • Instruct the subject to bring their habitual spectacles or contact lenses to the next visit (to wear following removal of the study lenses). • Instruct the subject to also bring any unwom study lenses to the next visit.	
1.31	Schedule next visit	Schedule the follow-up visit to occur in 7±2 days (counting the day of this visit as day O, the su bject may retum on day 5 through 9). Ensure the subject is instructed to wear the study lenses for at least 1 hour immediatel rior to attendin . the follow-u visit.	

VISIT 2

Visit 2 will occur 5 to 9 days following Visit **1.** Subjects must present to this visit wearing the study lenses in both eyes, and lenses must have been wom for at least 1 hour prior to the visit.
Subjects should bring their own habitual spectacles or contact lenses to this visit to wear following study lens removal.

Visit 2: Follow-U #1			
Step	Procedure	Details	[redacted]
2.1	Wear time and compliance	Record the subjects wearing time and comfortable wearing time. Subjects must have wom lenses for at least 8 hours on at least 5 days during the dispensing period, and for at least 1 hour prior to attending this visit.	
2.2	Collect unwom lenses	Collect any unwom study lenses that were dispensed at the revious visit.	
2.3	Review medical history and concomitant medications	Record any changes to the subject' s medical history (including adverse events) or concomitant medications.	
2.4	Subject repo1ted ocular symptoms	Record any subject repo1ted ocular symptoms in response to a verbal open-ended symptoms uestionnaire.	[redacted]

<table>
<tr><th colspan="3">Visit 2: Follow-U #1</th></tr>
<tr><th>Step</th><th>Procedure</th><th>Details</th></tr>
<tr><td>2.5</td><td>Follow-up PRO questionnaire</td><td>Subjects will complete a PRO questionnaire to assess their experience with the study lenses.
Note: at the end oj the second wear pel'iod (Visit 4: Follo w-Up #2) the PRO questionnaire ,vi/1 a/so ine/ude questions regarding lens preference bet, veen the lenses worn in thefirst and second wear eriods.</td></tr>
<tr><td>2.6</td><td>Entrance visual acuity</td><td>Record the entrance Snellen VA for each eye while wearin . the stud lenses.</td></tr>
<tr><td>2.7</td><td>Distance ETDRS visual acuity</td><td>Measure monocular distance high luminance high contrast (HLHC) visual acuity using ETDRS charts at 4 meters.
Measure each eye using the cha1t s shown in the table below·
<table>
<tr><td>Condition</td><td colspan="2">HLHC</td></tr>
<tr><td>Room illumination</td><td colspan="2">> 400 lux</td></tr>
<tr><td>Cha1t luminance</td><td colspan="2">120 - 200 cd/m^2</td></tr>
<tr><td>Eye</td><td>OD</td><td>OS</td></tr>
<tr><td>Cha1ts</td><td>HC-1
HC-2</td><td>HC-3
HC-4</td></tr>
</table>
Recorded letter-b -letter results into EDC.</td></tr>
<tr><td>2.8</td><td>Toric lens orientation</td><td>Record the toric lens orientation for each eye to the nearest de◦ -ee.</td></tr>
<tr><td>2.9</td><td>Additional sample of toric lens orientation (1)</td><td>Instrnct the subject to leave the consulting room and walk around for at least 2 minutes. Upon their retum, measure and record the toric lens orientation to the nearest de◦ -ee in each e e.</td></tr>
<tr><td>2.10</td><td>Additional sample of toric lens orientation 2</td><td>Repeat the previous step once again.</td></tr>
<tr><td>2.11</td><td>Lens removal</td><td>Remove and place both lenses into a lens case with saline solution.
Do not discard the lenses until after biomicroscopy has been com leted.</td></tr>
<tr><td>2.12</td><td>Biomicroscopy</td><td>The FDA Slit Lamp Classification Scale will be used to grade findings. If any slit lamp finding is graded as 3 or worse, the subject must be discontinued, an adverse event will be recorded, and the subject will be monitored as per the guidelines given in section 13.
Should the clearance of the fluorescein need to be expedited, preservative-free rewetting drops or a1tificial tears may be instilled.
Study lenses may be discarded if there is no reason to store them followin<> biomicrosco</td></tr>
<tr><td>2.13</td><td>Exit visual acuity</td><td>Record the exit monocular distance Snellen visual acuity for each eye with the subject wearing their habitual co!1'ection .</td></tr>
</table>

Visit 2: Follow-U #1			
Step	Procedure	Details	[redacted]
2.14	Schedule next visit	Schedule the next visit (Visit 3) to occur following a washout period of 7±2 days (counting the day of this visit as day O, the su bjec t may retum on day 5 through 9). Subjects may wear their habitual lenses during the washout eriod.	

VISIT 3

Visit 3 will occur 5 to 9 days following Visit 2. Subjects may wear their habitual contact lenses to this visit.

Visit 3: Continuance			
Ste	Procedure	Details	[redacted]
3.1	Review medical histo1y and concomitant medications	Record any changes to the subject's medical history or concomitant medications.	
3.2	Subject reported ocular symptoms	Record any subject repo1ted ocular symptoms in response to a verbal open-ended symptoms uestionnaire.	
3.3	Entrance visual acuity	Record the entrance distance Snellen visual acuity for OD and OS with the subject wearing their habitual con-ection .	
3.4	Remove habitual lenses (if wom)	If wom, the subjec t's habitual contact lenses will be removed. Lenses may be stored in a lens case, if re uired.	
3.5	Biomicroscopy	The FDA Slit Lamp Classification Scale will be used to grade findings. If any slit lamp finding is graded as 3 or worse, the subject must be discontinued, an adverse event will be recorded, and the subject will be monitored as per the guidelines given in section 13. Should the clearance of the fluorescein need to be expedited, preservative free rewetting drops or a1tificial tears ma be instilled.	
3.6	Continuance	Verify that the subject is eligible to continue in the stud .	

¥3: Lens Fitting #2

The steps followed will be the same as those listed under Visit 1: Lens Fitting #1.

VISIT 4

Visit 4 will occur 5 to 9 days following Visit 3. Subjects must present to this visit wearing the study lenses in both eyes, and lenses must have been wom for at least 1 hour prior to the visit.
Subjects should bring their own habitual spectacles or contact lenses to this visit to wear following study lens removal.

Visit 4: Follow-Up #2

The steps followed will be the same as those listed under Visit 2: Follow-Up #1, up to and including step 2.12 'Biomicroscopy' (' Exit visual acuity' and 'Schedule next visit' will not be completed here). Additionally, a Preference Questionnairewill be completed as pati ofthe Follow-UpPRO questionnaire (step 2.5).

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			
Ste	Procedure	Details	[redacted]
F.1	Subject Disposition	Indicate ifthe subjectcompleted the study successfully. If the subject is discontinued from the study, indicate the reason.	
F.2	Exit Refraction	Perfo1m bare-eye subjective spherocylindrical refraction with a phoropter and record the best-coITected distance visual acuity (OD and OS) to the nearest letter. **Note:** Thisstep is notnecessaiy if the subject was exited due to scre en failure.	[redacted]
F.3	Exit Slit Latnp Biomicroscopy (for subjects that are discontinued eai·ly)	FDA Slit Lamp Classification Scale will be used to grade the findings. If the cleai·ance of the fluore sc ein needs to be expedited, preservative-free rewetting drops or saline may be instilled. This step is not necessaiy if the subject was exited due to screen failure. **Note:** Thisstep is notnecessa1y if the subject was exited due to screen failure, or if biomicroscopy was perfo1med as patiofthe final follow-up visit procedures i.e,, immediatel rior to the final evaluation .	[redacted]

7.3. Unscheduled Visits

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

- Chief complaint prompting the visit. If the reason is an adverse event, the applicable eCRF for the adverse event must be completed and subject record completed as appropriate.
- Date and time of the visit and all procedures completed at the unscheduled visit.
- Review of adverse event and concomitant medications.
- Documentation of any test a1ticle dispensed or collected from the subject, if applicable.
- Slit lainp findings (using the Slit Lamp Classification Scale).

If the Investigator withdraws a subject from the study, the final study visit case repo1t fonns 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, retumed to pre-treatment status, stabilized, or been satisfactorily explained. If futther treatment i.e., beyond licensure is required, the subject will be refeITed to the appropriate health cai·e pro vider .

The follo wing info1mation will be collec ted during an unscheduled visit.

Unscheduled Visit			
Ste	Procedure	Details	
U.I	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, s ec the reason for the visit.	
U.2	Chief Complaints (if a licable	Record the subject' s chief complaints for reasons for the unscheduled visit.	
U.3	Adverse Events and Concomitant Medications Review (if a licable	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 a licable	Record the entrance distance visual acuity (OD, OS) to the nearest letter.	[redacted]
U.5	Subjective Sphero-cylindrical Refraction (if applicable)	Perfo1m bare-eye sub jective spherocylindrica l 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 cot1'ected distance visual acuity to the nearest letter OD, OS .	[redacted]
U.6	SlitLamp 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 dro s ma be instilled.	[redacted]
U.7	Dispensing (if applicable)	If the subject requires additional lenses to complete the wear period and is eligible to do so, provide additional lenses per the dispensing instmctions given in the detailed stud rocedures.	
u.s	Exit Visual Acuity (if a licable	Record the subject' s exit distance visual acuity (OD, OS to the nearest letter.	[redacted]

NOTE: If **the onl y rea son fo1· the unscheduled visit is that the subject requires additional test articles, only the dispensing information needs to be recorded.**

7.4. Laboratory Procedures

Not applicable.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided infonned consent.
- they are eligible.
- have not withdrawn/discontinued from the study for any reason described in section 8.2.
- completed ali visits through the final visit (visit 4).
- If ali visits were completed but an additional visit is considered necessary for subject care, follow the requirements for unscheduled visits in section .7.3.

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 may be enrolled if a subject discontinues from the study prematurely.

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed concomitant interventions for this study include ocular medications of any kind, or any systemic medications that would normally contraindicate contact lens wear or may otherwise compromise study endpoints.

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 4. 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 4 on a long-term, routine basis for less than 6 months will not be allowed to participate in the study.

Table 4: 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	In-itable 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, Transdenn Scop, etc.
Beta-blockers	Hypetension, angina, heart attack, migraine, atrial fibrillation, andrenal cancer, essential tumor, glaucoma	Toprol XL, Lopressor, Tenonnin, Propranolol, Timoptic, Trandate, Inderal LA, etc.
Psychotropics	Antipsychotic (schizophrenia, mania), antidepression, antiobsessive, antianxiety, mood stabilizer, stimulants (ADHD)	Zoloft, Celexa, Prozac, Lexapro, Effexor, Cymbalta, Ativan, Xanax, Desyrel, Wellbutrin, etc.
Vitamin A analogs	Cystic acne	Isotretinoin
Analgesics	Urinruy tract infection	Phenazopyridine HCL

Examples of disallowed systemic antihistamines are given in Table S. Subjec ts with a hist01y oftaking 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

Or:

- They stopped taking the medication for at least 2 weeks prior to enrollment.

Table 5: 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, Zyitec, Astepro, Astelin, Optivar, Allegra, Benadryl, etc.

10. DEVIATIONSFROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. Protocol deviations must be repo1ted to the sponsor within 24 hours after discove1y of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked, and con-ective actions implemen ted as appropr iate.

If it become s necessa1y for the Investigator to implement a deviation in order to eliminate an immediate hazru·d 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 repo1t ed to IEC/IRB. This is a "Major Deviation". Deviations that contradict the info1mation contained in the Infon ned Consent/Assent fonn s will be considered Major Deviations.

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

Protocol waivers are prohibited.

Table 6 lists examples of deviations that will constitute major and minor protocol deviations for this study.

Table 6: Examples of major and minor protocol deviations

Deviation categolY	Maio r deviation	Minor deviation
Out-of-window visit	Visit attended > 3 days out of visit window defined in study procedures	Visit attended 3 days out of visit window defined III study procedures
Unanswered PRO questions	If questionnaire is not completed (i.e., all questions are unanswered) for any visit questionnaire, or more than 2 questions are unanswered for the follow-up visit CLUE auestionnaire.	Any individua! or multiple PRO questions (2 or less) are unanswered (i.e., left blank).
Insufficient wear of study lenses	Subject does not wear study lenses for at least 8 hours on at least 5 days of a study lens wear period. Subject wears their habitual lenses during any of the study lens wear periods.	Subject does not wear study lenses for at least 1 hour prior to attending a follow-up visit.

1n the case of a major protocol deviation, the decision of whether or not the subject will be excluded from the Per-Protocol analysis population will be made at the time of coho1t review.

11. STUDY TERMINATION

The occm1·ence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be rnled out, may result in stopping further dispensing of test article. 1n 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 fmiher subjects are enrolled.

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

JNC reserves the right to te1minate the study at any time for any reason. Additionally, the IEC/IRB reserves the right to tenninate the study if an unreasonable risk is dete1mined. The study can be tenninated by the Principal Investigator at the individua! clinical site due to specific clinical observations, if in their opinion, after a discussion with *JN C,* it is detennined that it would be unwise to continue at the clinical site.

JNC (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 palt of the investigation presenting the risk, will be te1minated as soon as possible.

Should the study be te1minated (either prematm·ely or as scheduled), the Investigator will notify the IEC/IRB and Regulato1yAuthority as required by local regulato1yrequirements.

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

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

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

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness).
- Who received the complaint.
- Study number.
- Clinical site information (contact name, site ID, telephone number).
- Lot number(s).
- Unique Subject Identifier(s).
- Indication of who first observed complaint (site personnel or subject).
- OD/OS indication, along with whether the lens was inserted.
- Any related AE number if applicable.
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.).
- Eye Care Provider objective (slit lamp) findings if applicable.
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return [redacted]

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

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

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated."
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.[1]

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

1. Was not present prior to the study, but appeared or reappeared following initiation of the study.
2. Was present prior to the study but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states.

NOTE: Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event.

Serious Adverse Event (SAE) – An SAE is any adverse event that led to any of the following:

- Death
- Serious deterioration in the health of the subject that resulted in any of the following:
- Life-threatening illness or injury
- Permanent or persistent impairment of a body structure or a body function
- Hospitalization or prolongation of patient hospitalization
- Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Chronic disease
- Foetal distress, foetal death or a congenital physical or mental impairment of birth defect.

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

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

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

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

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

- Asymptomatic Corneal Scar
- Any corneal event which necessitates temporary lens discontinuation > 2 weeks

Non-Significant Adverse Events – are defined as those events that are usually asymptomatic and usually do not warrant discontinuation of contact lens wear but may cause a reduction in wear time. However, the Investigator may choose to prescribe treatment as a precautionary measure.

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

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

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

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

13.2. Assessing Adverse Events

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

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

13.2.1. Causality Assessment

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

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

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

13.2.2. Severity Assessment

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

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

13.3. Documentation and Follow-Up of Adverse Events

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

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

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

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

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

- Best corrected visual acuity at the discovery of the event and upon conclusion of the event, if the AE is related to the visual system.

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

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

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

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

13.4. Reporting Adverse Events

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to their requirements (section 13.4.2). The report will comment whether the adverse event was considered to be related to the test article, study treatment or study procedures.

13.4.1. Reporting Adverse Events to Sponsor

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

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

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

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

- Notify the IEC/IRB as required by the IEC/IRB reporting procedure according to national regulations.

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

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

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

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

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

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

13.5. Event of Special Interest

None.

13.6. Reporting of Pregnancy

Subjects reporting pregnancy (by self-report) during the study will be discontinued after the event is recorded as an Adverse Event. Once discontinued, pregnant participants and their fetuses will not be monitored for study related purposes. Pregnant participants are not discontinued from contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

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

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 SAS Institute, Cary, NC)[7]. Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. For the analysis of co-primary safety endpoints, unscheduled visits will be summarized separately and will not be excluded from the statistical analysis. However, for the analysis of co-primary efficacy endpoints and secondary endpoints, unscheduled visits will be summarized separately and excluded from the statistical analysis.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics

(n, mean, standard deviation (SD), median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

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

14.2. Sample Size Justification

This study was designed and powered to test for superiority of the test lens after 1-week of lens wear with respect to the following: distance monocular HLHC visual acuity (logMAR), subjective vision scores, toric lens orientation, and rotational stability. This study was also powered to test superiority of the test lenses with respect to grade 3 or higher slit lamp findings and percentage of eyes with acceptable lens fit. Additionally, this study was also powered to test for superiority with respect to CLUE Comfort and Handling scores after 1-week of lens wear. The described alpha adjustment is also factored into these estimations of sample size and power.

The sample size for co-primary efficacy endpoints was estimated to achieve a minimum statistical power of 90% for distance monocular visual acuity (logMAR), toric lens orientation, rotational stability, and CLUE Vision scores using a 2-sided type I error rate of 5%. Co-primary safety endpoints (grade 3 or higher SLFs and acceptable lens fitting) were estimated to achieve a minimum statistical power of 99% with 95% central posterior credible interval.

A summary of historical studies utilized in the sample size calculation are summarized in Table 7 below, while Table 8 summarizes the historical data for the test lens by endpoint.

Table 7: Historical Studies Utilized for Sample Size Calculations

Study Number	Design	Study Phase	Number Enrolled	Number in Safety Population	Number in PP Population
[redacted]	2x3	Feasibility	145	144	133
	2x3	Confomation	126	26	119

PP: Per-Protocol

Table 8: Historical Data by Endpoint - Test Lens

Endpoint Type	Endpoint	Data Type	Value
*Primary Safety	Grade 3 + SLFs (Adverse Event)	Rate	0%
	Acceptable Lens Fitting		100%
**Primary Efficacy	Distance Monocular Visual Acuity (logMAR)	Mean (SD)	-0.115 (0.0769)
	Absolute Toric Rotation 10°		97.5%
	Lens Stability with Blinks 5°		100%
	CLUE Vision Scores		67.4 (19.67)
**Secondary	CLUE Handling Scores	Mean (SD)	65.4 (21.50)
	CLUE Comfort Scores		67.9 (21.50)

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

Co-Primary Safety Endpoint Sample Size Calculations:

Grade 3 or Higher Slit Lamp Findings (SLFs)

Grade 3 or Higher SLFs related to study lens wear will be converted to a binary response as $YY = 1$, if a subject eye has a clinically significant SLF, and $YY = 0$ otherwise, for analysis purposes. From the historical data there was *none or an extremely low rate* (< 1%) for clinically significant SLFs (Grade 3 or higher) for the test lens. Assuming a correlation of 0.70 between left and right eyes within the same subject, a total of 5000 replicating trials were simulated with a reference rate of 2% (worse-case scenario). Given the rare event binary outcome of slit lamp findings, each replicated sample was analyzed using a Bayesian beta-binomial model with correlated binary data (Diniz et al; 2010).[8] For each simulated trial, the upper bound of the 95% central posterior credible interval constructed for the percentage of grade 3 or higher SLFs for the test lens was compared to a margin of 5%. With the proposed sample size, at least 99% of the estimated 95% credible intervals had the upper bound below 5%.

Acceptable Lens Fitting

Acceptable lens fitting will be converted to a binary response as $YY = 1$, if a subject eye has acceptable lens fitting, and $YY = 0$ otherwise, for analysis purposes. As indicated in the historical data of these lenses there was an extremely high rate (> 99%) acceptable lens fitting for the test lens. Assuming a correlation of 0.70 between left and right eyes within the same subject, a total of 5000 replicating trials were simulated with a reference rate of 99% (worse-case scenario). Given the rare event binary outcome of Y=0 (unacceptable lens fitting), each replicated sample was analyzed using a Bayesian beta-binomial model with correlated binary data (Diniz et al; 2010).[8] For each simulated trial, the upper bound of the 95% central posterior credible interval constructed for the percentage of acceptable lens fittings for the test lens was compared to a margin of 80%. With the proposed sample size, at least 99% of the estimated 95% credible intervals had the lower bound above 80%.

Co-Primary Efficacy Endpoint Sample Size Calculations:

Distance Monocular Visual Acuity (logMAR) and CLUE Vision Scores

Sample size calculations for visual acuity and vision scores were carried out separately using one-sided, one-sample mean t-test, with a type I error rate of 5% for each hypothesis. The hypothesis regarding visual acuity was powered to 99%, while the hypothesis for CLUE Vision scores was powered to 91%. Sample size calculations were performed using the *One-Sample T-Tests for Superiority by a Margin* procedure in Power Analysis & Sample Size (PASS2021) software Version 21.0.6 (NCSS LLC, Kaysville UT).[9] Table 9 below, displays sample size estimates by endpoint.

Toric lens orientation and rotational stability

Sample size estimates for toric lens orientation and rotational stability were calculated using the same technique. Both endpoints are testing against an 80% threshold and have an event rate greater than 97%. A reference rate of 97.5% was used for toric lens orientation, while a worst-case scenario of 98% was used for rotational stability.

Toric lens orientation and rotational stability will be converted to a binary response as $YY = 1$ if a subject eye has absolute toric lens orientation ≤ 10° (rotational stability: Y=1 if a subject eye has lens stability with blinks ≤ 5°) and $YY = 0$ otherwise, for analysis purposes. As indicated historical data of these products there was an extremely high rate (> 97%) for both toric lens orientation and rotational stability for the test lens. Assuming a correlation of 0.70 between left and right eyes within the same subject, a total of 5000 replicating trials were simulated with a reference rate of 97.5% for toric rotation and 98% for rotation stability (worse-case scenario). Given the rare event binary outcome of Y=0, each replicated sample was analyzed using a Bayesian beta-binomial model with correlated binary data (Diniz et al; 2010).[8] For each simulated trial, the upper bound of the 95% central posterior credible interval constructed for the percentage of acceptable lens fittings for the test lens was compared to a margin of 80%. With the proposed sample size, at least 99% of the estimated 95% credible intervals had the lower bound above 80%.

Secondary Endpoint Sample Size Calculations:

CLUE Handling and Comfo1t Scores

Sample size calculations for handling and comfo1t scores were caITied sepa rate ly ou t using one-sided, one-sample mean t-test, with a type I eITor rate of 2.5% for each hypothesis. To preserve the overall study power, each endpoint was powered to 99%. Sample size calculations were perfo1med using the *One-Sample T-Tests for SuperiOl'i ty b y a Margin* procedure in Power Analysis & Sample Size (PASS2021) software Version 21.0.6 (NCSS LLC, Kaysville UT).[9]

Table 9 below, displays sample size estimates by endpoint. As indicated below, co-primary safety endpoints were powered ~99% individually yielding a combined power of ~98%. With respect to co-prima1y efficacy, each hypothesis, except for CLUE Vision (powered to 91%) was powered to ~99%, which provided a combine power of~88%. Therefore, the overall combined study power for co-primary safety and co-primaiy efficacy hypotheses is ~86% and is considered reasonable to suppo1t any conclusions from these analyses. Furthe1more, secondaly endpoints were powered to achieve at least 99% statistical power. This was considered to have a minimal impact on overall study power because of the multibranch gate keeping approach being implemented.

Table 9: Samole Size Estimates for Co-PrimarvSafetv. Efficacv and Secondarv End)oints

Endpoint Tvoe	Endpoint	Test Tvoe	Sample Size	Power (%)
Prima1y Safety	Grade 3 or Hillher SLFs (5%)	Statisticallv less then (5%)	100	99
	Acceptable Lens Fitting (%)	Statistically greater then (80%)	100	99
Prima1y Efficacy	Distance (4m) Monocular Visual Acuitv (lollMAR)	Superiority (0.00)	9	99
	Absolute Toric Rotation < 100	Statistically greater then (80 %)	40	99
	LensStability with Blinks 5°	Statistically greater then (80%)	100	99
	CLUE Visions Scores	Suoerioritv (62)	144	91
Seconda1y	CLUE Handling Scores	Suoerioritv (61)	135	97
	CLUE Comfo1t Scores	Suoerioritv (58)	135	97

While only a total of 144 subjects are required to complete the study based on the sample size calculations, the target enrollment is approximately 180 subjects with a target completion of at least 165 subjects. Data collected from this study may be utilized to pe1fonn a meta-analysis at a later date, therefore, the target completion for this study was increased to 165 subjects to accommodate this possibility.

14.3. Analysis Populations

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

Per-Protocol Population:
All subjects who successfully complete all visits and do not substantially deviate from the protocol as detennined by the trial coho1t review collllllittee 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 randomized subjects regardless of actual treatment and subsequent withdrawal from the study or deviation from the protocol. At least one observation should be recorded.

14.4. Level of Statistical Significance

All co-prima1ysafety, co-primary efficacy, and secondaty hypotheses will be tested using a multibranch gate keeping strntegy. Study hypotheses will be evaluated sequentially as follows:

First, co-primary safety hypotheses will be evaluated using 95% central posterior credible intervals for the probability of grade 3 or higher SLFs and acceptable lens fitting. Both hypotheses must be met in order to test co-primary efficacy hypotheses. Each co-primary efficacy hypothesis will be tested with a type I error rate of 5%. All co-primary safety and co-primary efficacy hypotheses must be met to test any secondary hypotheses. Secondary hypotheses will be tested utilizing a Bonferroni adjustment[10] with an overall two-sided family-wise type I error rate of 5% (2.5% individually).

14.5. Primary Analysis

Methodology regarding the plan for testing and/or handling statistical associations between co-primary safety and/or efficacy endpoints will be documented in the SAP.

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

Grade 3 or Higher SLF
Grade 3 of Higher SLFs will be analyzed using a Bayesian beta-binomial model with correlated binary data.[8]

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

$$P(Y = y \mid p, \rho) = (1 - \rho)BBBBBB(2, p)I_{A1} + \rho MMBBMMMNBB(p)I_{A2},$$

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

To overcome the complexity of the mixture likelihood a latent variable Z_{ii}, i = 1, 2 is introduced in the model to indicate in which component of the model the observation y_{ii}, i=1, 2, belongs to, that is,

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

The joint distribution of the augmented data (Y_{ii}, Z_{ii}), $B = 1, 2$, is given by

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

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

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

It is assumed that β_0, β_1 and ρ to be independent with a non-informative prior N(0, 1000) for β_0 and β_1, and beta(0.5, 0.5) for ρ. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC Procedure[7] will be used to estimate the posterior distributions of the parameters (β_0, β_1, ρ). Inferences will be made based on a posterior credible interval for the relevant parameters.

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

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

$$H_0: p_T \geq 5\%$$
$$H_A: p_T < 5\%,$$

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

In the case of zero clinically significant SLF, a Bayesian hierarchical model accounting for zero-event problem will be considered.[8]

A***cceptable Lens Fitting***
Lens fit acceptance will be analyzed using a Bayesian beta-binomial model with correlated binary data.[8]

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

Primary Safety Hypothesis 2:
The null and alternative hypotheses for evaluating superiority of the test lens relative to 80% are as follows:

$$HH_0: pp_T \leq 80\%$$
$$HH_{AA}: pp_T > 80\%,$$

where pp_T is the probability of event (i.e., probability of acceptable lens fitting while wearing the test lens). Based on Bayesian posterior probability distribution of the proportion pp_{TT}, superiority is interpreted as 95% probability of the test lens being statistically larger than the pre-defined threshold of 80% (i.e., $pp_T > 80$) with respect to acceptable lens fitting rate. If the lower bound of the 95% central posterior credible interval is above 80%, it can be concluded that there is 95% probability that the test lens is superior to the 80% threshold (statistically greater) based on the observed sample.

In the case of all eyes have an acceptable lens fit (i.e., zero unacceptable lens fits), a Bayesian hierarchical model accounting for zero-event problem will be considered.[8] Details of this model will be provided in the stand-alone SAP.

Co-Primary Efficacy Analyses

Visual Acuity (VA)
Distance, monocular, high-luminance, high-contrast (HLHC), VA after 1 week of lens wear will be analyzed using a linear mixed model. Sequence of lens wear, lens type and period will be included in the model as fixed effects. Subject characteristics such as, gender, age and/or cylinder power may be included in the model if appropriate. Site ID and subject nested within site will be included in the model as random effects (G-side). The residual error between measurements within the same subject across study period will be modeled using an unstructured (UN) covariance structure. If the model fails to converge with a UN covariance, then a compound systemic (CS) covariance structure will be used. The Kenward and Roger Method will be used for the denominator degrees of freedom.[11] Visual Acuity scores will be estimated using 95% confidence intervals (CI) constructed for the least-square means (LSM).

Primary Efficacy Hypothesis 1:
The null and alternative hypothesis for distance monocular HLHC VA to test for superiority of test relative to the threshold 0.0 logMAR are as follows:

$$HH_{oo}: \mu\mu_{TTTTTTT} \geq 0 \text{ logMAR}$$
$$HH_{AA}: \mu\mu_{TTTTTTT} < 0 \text{ logMAR}$$

Where $\mu\mu_{TTTTTTTT}$, represents the population mean for test lens after 1-week of lens wear with respect to distance monocular HLHC VA. Superiority will be declared if the upper limit of the 95% CI is below 0.0.

Toric Lens Orientation and Rotational Stability at Least 15- Minutes Following Lens Settling

Absolute toric lens orientation (degrees) will be dichotomized as *Y=1* if the absolute lens orientation (degrees) ≤ 10° and *Y=0*, otherwise. Rotational stability will be quantified by lens stability with blinks (degrees). Lens stability will be dichotomized as *Z=1* if the lens stability with blinks (degrees) ≤ 5° and *Z=0*, otherwise.

Y and *Z* will be analyzed separately using a generalized linear mixed model with a binary distribution and the logit as the link function. Sequence of lens wear, lens type and period will be included in the model as fixed effects. Subject characteristics such as, gender, age and/or cylinder power may be included in the model if appropriate. Site ID and subject nested within site will be included in the model as random effects (G-side). The residual error between measurements within the same subject across study period will be modeled using an unstructured (UN) covariance structure. If the model fails to converge with a UN covariance, then a compound systemic (CS) covariance structure will be used. The Kenward and Roger Method will be used for the denominator degrees of freedom.[11]

Primary Efficacy Hypothesis 2:

The null and alternative hypothesis to test for superiority of absolute lens orientation ≤ 10° for the test lens relative to the threshold 80% are as follows:

$$HH_{00}: pp_{TTTTTTTT} \leq 80\%$$
$$HH_{AA}: pp_{TTTTTTTT} > 80\%$$

Where $pp_{TTTTTTTT}$, represents the population percentage for the percentage of eyes wearing the test lens with absolute lens orientation ≤ 10°. Superiority will be declared if the lower limit of the 95% CI is above 80.

Depending on the observed response rates for the percentage of subjects' eyes with absolute lens orientation ≤ 10° and the percentage of subjects' eyes with lens stability with blinks ≤ 5°, a Bayesian hierarchical model accounting for zero event problem may be considered (i.e., 0% of eyes with toric rotation >10° [or lens stability >5°]) . Details of this model will be provided in the stand-alone SAP.

Primary Efficacy Hypothesis 3:

The null and alternative hypothesis to test for superiority of lens stability with blinks ≤ 5° for the test lens relative to the threshold 80% are as follows:

$$HH_{00}: pp_{TTTTTTTT} \leq 80\%$$
$$HH_{AA}: pp_{TTTTTTTT} > 80\%$$

Where $pp_{TTTTTTTT}$, represents the population percentage for the percentage of eyes wearing the test lens with lens stability with blinks ≤ 5°. Superiority will be declared if the lower limit of the 95% CI is above 80.

CLUE Vision Scores

CLUE vision scores after 1 week of lens wear will be analyzed using a linear mixed model adjusting for baseline scores as a covariate. Sequence of lens wear, lens type and period will be included in the model as fixed effects. Subject characteristics such as, gender, age and/or cylinder power may be included in the model if appropriate. Site ID will be included in the model as a random effect (G-side). The residual error between measurements within the same subject will be modeled using an unstructured (UN) covariance structure. If the model fails to converge with a UN covariance, then a compound systemic (CS) covariance structure will be used. The Kenward and Roger Method will be used for the denominator degrees of freedom.[11] CLUE Vision Scores estimates for each study lens will be estimated using 95% confidence intervals (CI) constructed for the least-square means (LSM).

Primary Efficacy Hypothesis 4:
The null and alternative hypothesis to test for superiority of CLUE vision score for the test lens relative to the threshold 62 are as follows:

$$H_0: \mu_{TEST} \leq 62$$
$$H_A: \mu_{TEST} > 62$$

Where μ_{TEST}, represents the population mean for test lens after 1 week of lens wear with respect to CLUE vision scores. Superiority will be declared if the lower limit of the 95% CI is above 62.

14.6. Secondary Analysis

CLUE Handling and Comfort Scores
CLUE Handling and Comfort scores after 1-week of lens wear will be analyzed separately using a linear mixed model adjusting for baseline scores as a covariate. Sequence of lens wear, lens type and period will be included in the model as fixed effects. Subject characteristics such as, gender, age and/or cylinder power made be included in the model if appropriate. Site ID will be included in the model as a random effect (G-side). The residual error between measurements within the same subject will be modeled using an unstructured (UN) covariance structure. If the model fails to converge with a UN covariance, then a compound systemic (CS) covariance structure will be used. The Kenward and Roger Method will be used for the denominator degrees of freedom.[11] CLUE Handling and Comfort scores for each study lens will be estimated using 97.5% confidence intervals (CI) constructed for the least-square means (LSM).

Secondary Hypothesis 1:
The null and alternative hypothesis to test for superiority of CLUE Handling score for the test lens relative to the threshold 61 are as follows:

$$H_0: \mu_{TEST} \leq 61$$
$$H_A: \mu_{TEST} > 61$$

Where μ_{TEST}, represents the population mean for test lens after 1 week of lens wear with respect to CLUE Handling scores. Superiority will be declared if the lower limit of the 97.5% CI is above 61.

Secondary Hypothesis 2:
The null and alternative hypothesis to test for superiority of CLUE Comfort score for the test lens relative to the threshold 58 are as follows:

$$H_0: \mu_{TEST} \leq 58$$
$$H_A: \mu_{TEST} > 58$$

Where μ_{TEST}, represents the population mean for test lens after 1 week of lens wear with respect to CLUE comfort scores. Superiority will be declared if the lower limit of the 97.5% CI is above 58.

14.7. Exploratory Analysis

Ability to see comfortably while driving during the day or Reduction in the feeling of tired eyes from using a computer or other digital device
Subjective responses for exploratory endpoints will be the outcome (*aval*) defined as category one if a subject's response is 'Excellent', 'Very Good', 'Fair', or 'Poor'.

My vision was clear enough to allow me to drive at night
Subjective responses for exploratory endpoints will be the outcome (*aval*) defined as category one if a subject's response is 'Strongly Agree' or 'Agree', the outcome is defined as category two if a subject's response is 'Not Applicable', 'Strongly Disagree', 'Disagree', or 'Neither Agree nor Disagree'.

Statistical Model:
The outcome for each item will be analyzed separately using a generalized linear mixed model with a binary distribution and the logit as the link function. In each model, sequence of lens wear, period, lens type will be included as fixed effects. Site will be included as a random effect. Residual errors between measurements within the same subject will be modeled using an unstructured covariance (UN) structure. Comparisons between the test and control will be carried out using 2-sided 95% confidence intervals (CIs) constructed for the odds ratio (test over control). Non-inferiority will be concluded if a lower limit of a 95% CI is above 0.67.

Hypothesis Testing
The null and alternative hypothesis to test for non-inferiority of the test lens compared to the control lens will be conducted separately for each item as follows:

$$H_o: OR \leq 0.67$$
$$H_a: OR > 0.67$$

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.

No external data sources will be included in this study.

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

Edit checks, electronic queries, and audit trails are built into the system to ensure accurate and complete data collection. Data will be transmitted from the clinical site to a secure central database as forms are completed or

updated, ensuring information accuracy, security, and confidentiality. After the final database lock, the Investigator will be provided with Individual Patient Profiles (IPP) including the full audit trail on electronic media in PDF format for all of the study data. The IPP must be retained in the study files as a certified copy of the source data for the study.

The content and structure of the eCRFs are compliant with ISO14155:2020.[1]

15.2. Subject Record

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

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

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

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

15.3. Trial Registration on ClinicalTrials.gov

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

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, including the selection of qualified investigators and appropriate clinical sites and review of protocol procedures with the Principal Investigator. The Principal

Investigator, in turn, must ensure that all Sub-Investigators and clinical site personnel are familiar with the protocol and all study-specific procedures and have appropriate knowledge of the study article.

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

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

16.4. Data Monitoring Committee (DMC)

Not applicable.

17. CLINICAL MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

Potential subjects will be fully informed of the risks and requirements of the study, and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Subjects will only be enrolled if they are 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, according to ISO 14155:2020,[1] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[2] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with applicable regulatory requirements.

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

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

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

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

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

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

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

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

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

18.4. Informed Consent

Each subject or their representative, must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[2] and ISO 14155:2020[1] guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential subjects 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 their 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)[12] and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

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

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

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

19. STUDY RECORD RETENTION

In compliance with the ISO 14155:2020 guidelines,[1] the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ISO 14155:2020,[1] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

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

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

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

22. REFERENCES

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2. 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/
3. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR

4. Straker B.Investigator's Brochure *CR-6521 Toric lens design in senofilcon A with HEV-blocking chromophore [redacted])*. December, 2022.
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6. Straker B.Customer Requirements Document (CRD) *([redacted]) Project TRIUMPH for Astigmatism*. November 23, 2022.
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8. CAR Diniz, MH Tutia, Leite L. Bayesian analysis of a correlated binomial model. *Brazilian Journal of Probability and Statistics.* 2010;24(1).
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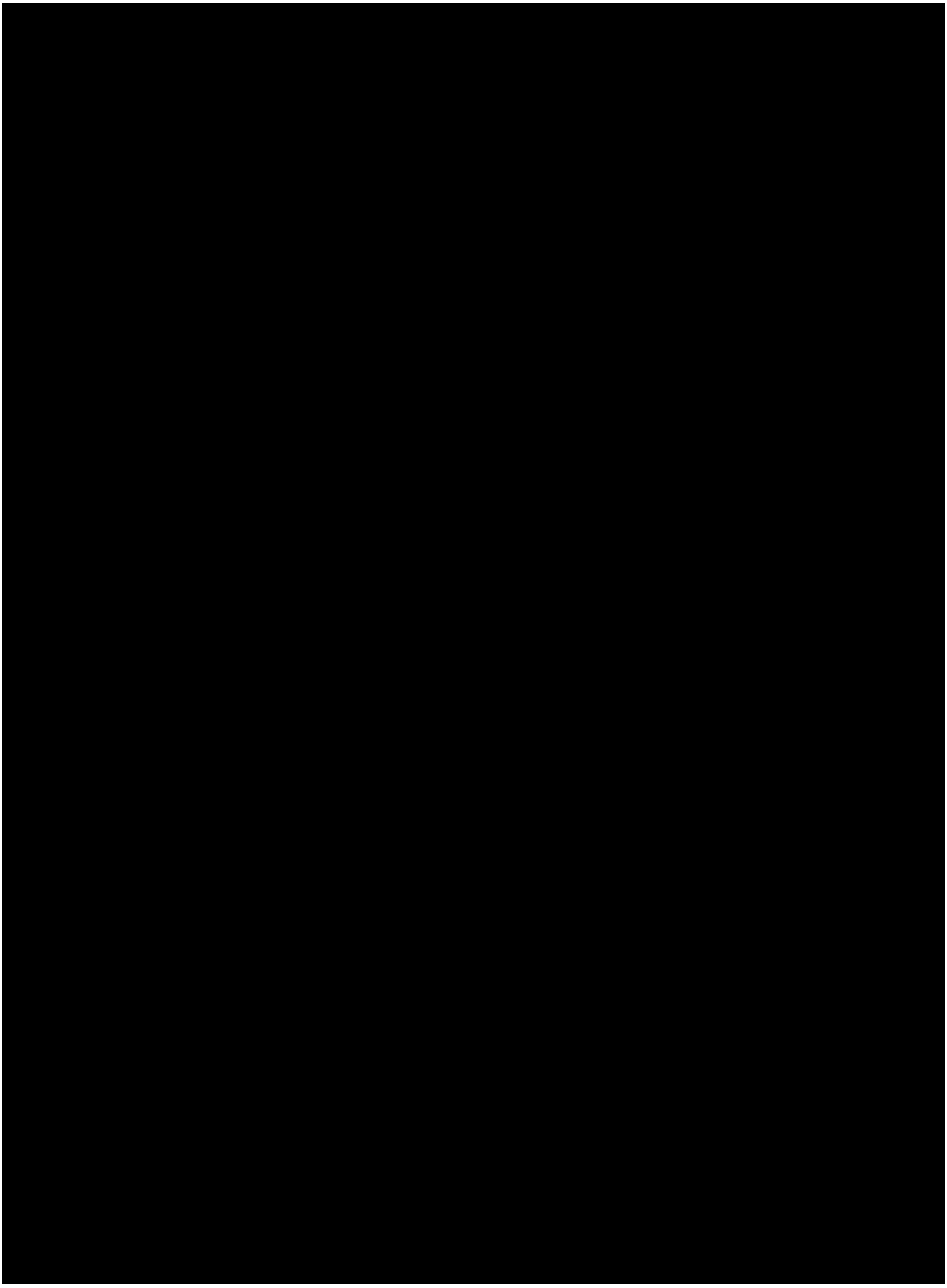
10. C B. Calculation of the insurance groups of heads. *Studies in Honour of Professor Salvatore Ortu Carboni.* 1935:13-60.
11. Kenward MG, Roger JH. Small Sample Inference for Fixed Effects from Restricted Maximum Likelihood. *Biometrics.* 1997;53(3):983.
12. Health Information Portability and Accountability Act (HIPAA), Available at: https://www.hhs.gov/hipaa/for-professionals/privacy/index.html

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

[redacted]



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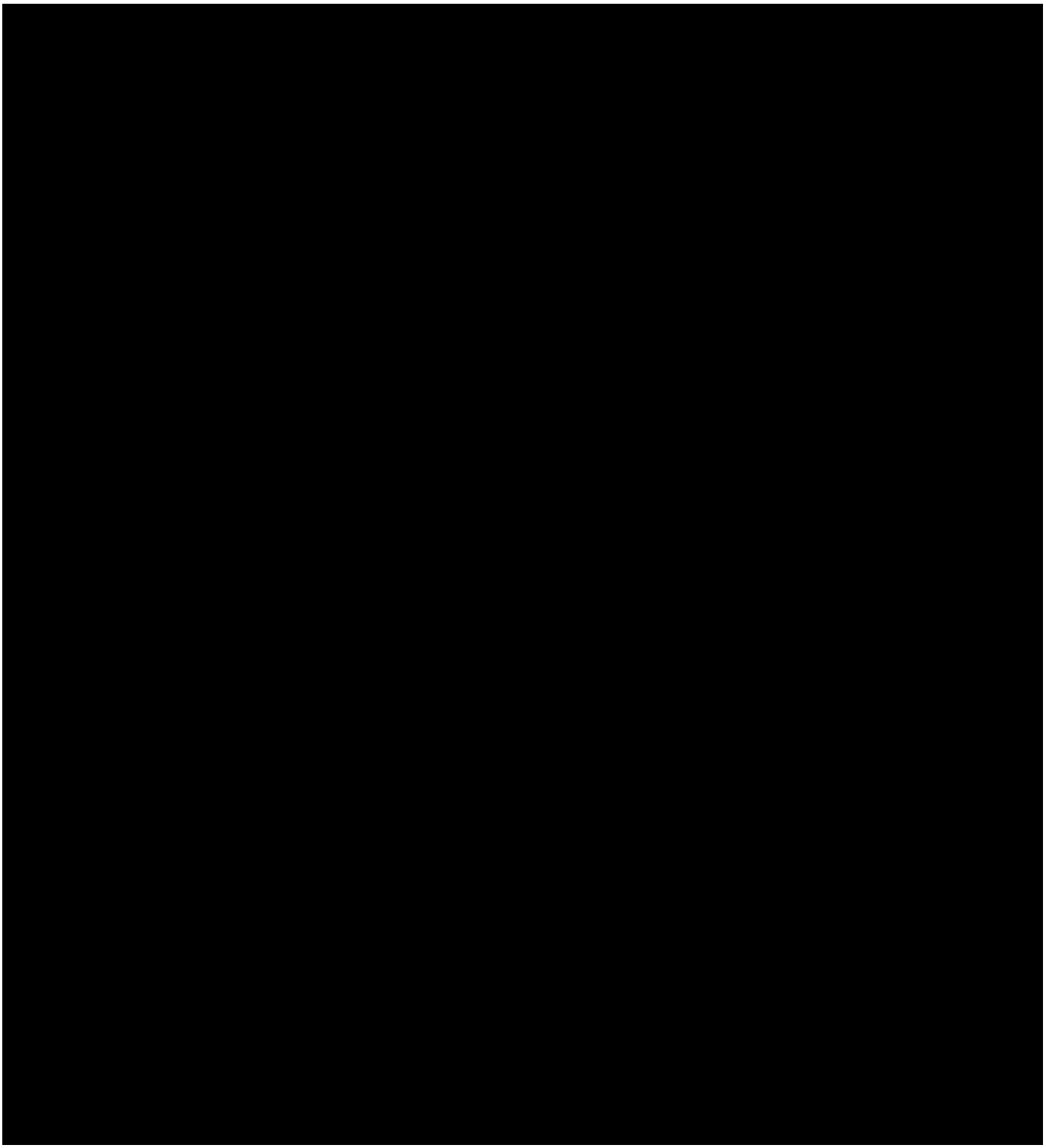

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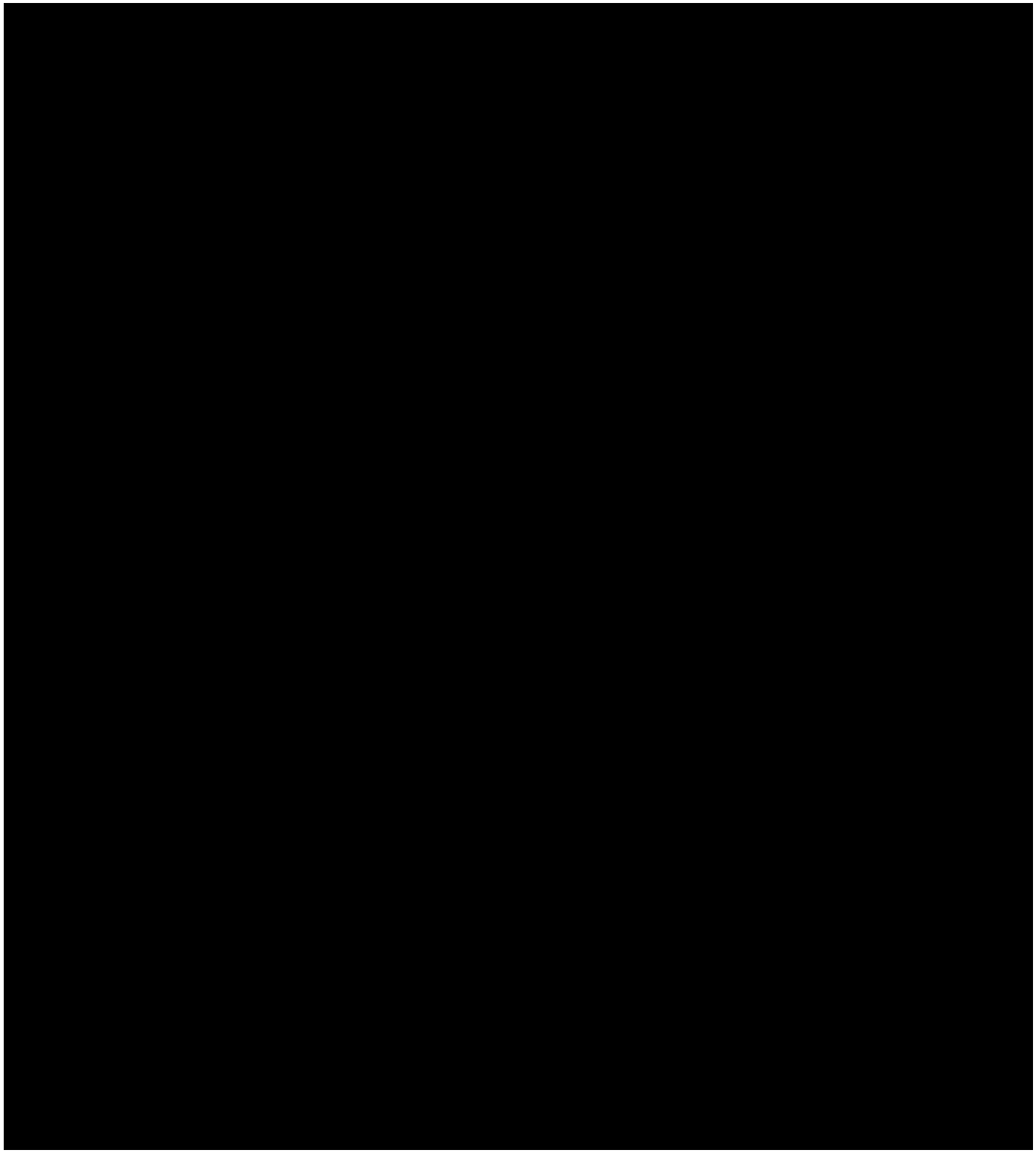

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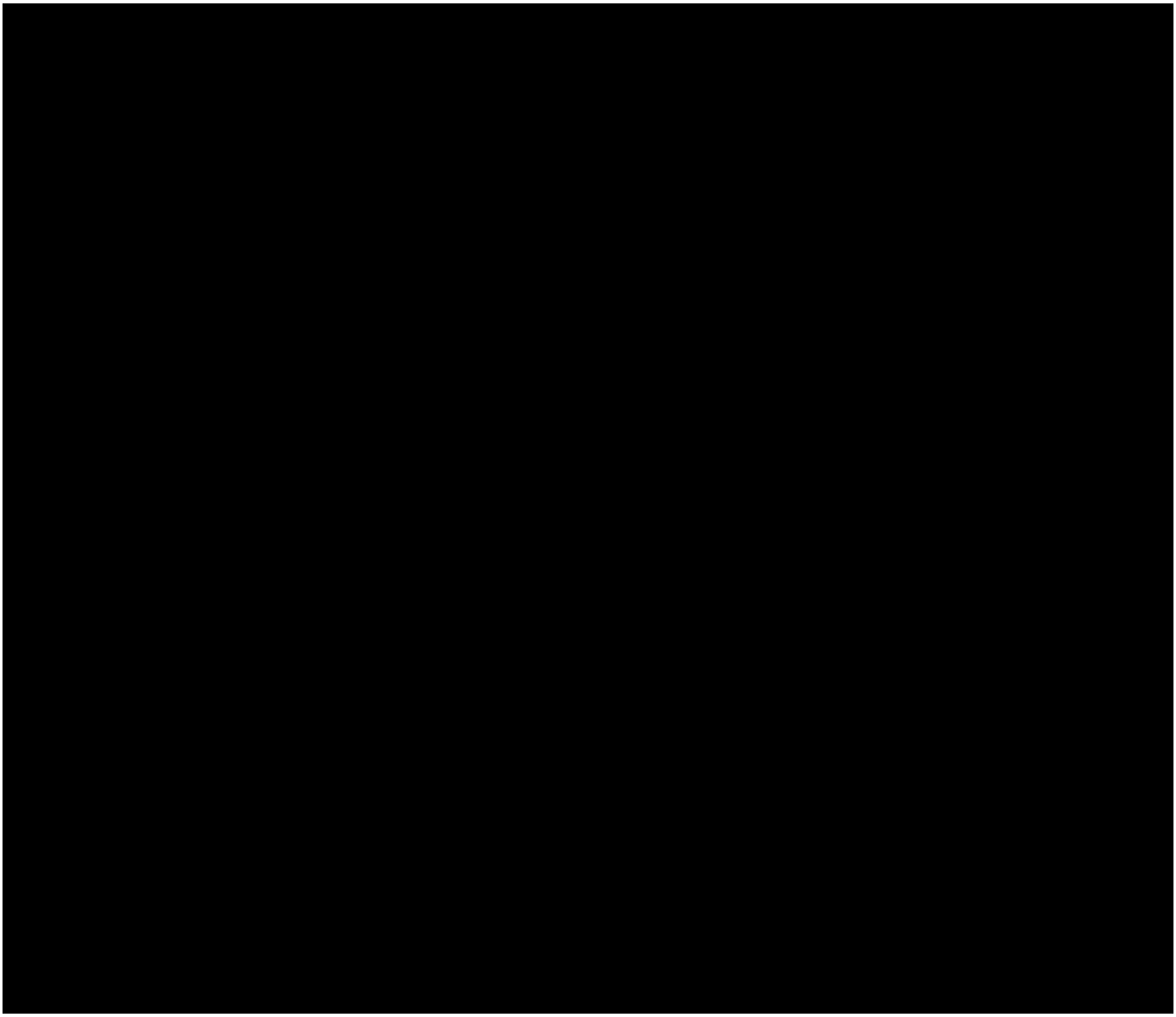


[redacted]

APPENDIX B: PATIENT INSTRUCTION GUIDE

A patient instruction guide (PIG) will be provided separately

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

IMPORTANT: Please read carefully and keep thls infonnation tor future use.

This Package Insert and Frtting Guide is intended tor the EyeCareProfesslona,lbutshoukl **be made** avallable to patients upon request

The Eye Care Professional should provide the patient wlthtlle appropriate Instructions thatpertaln to the patient's prescribed lenses. Copies are available tor download at www.acuvue.com.

ACUVUE '8 Qq ys H; draluxe™

ACUVUE OASYS Brand Contact Lenses 1-Day withHydraluxe™ Technology

ACUVUE OASYS•Brand Contact Lenses 1-Day wlthHydraluxe"' Technology tor ASTIGMATISM

senofilcon ASofi (hydrophilic) Contact Lenses
VlslbllIty TInted wlthUV Blocker
tor Daily Disposable Wear

f""D""iw.7 CAUTION U.S. Federa!law restricts this d8\lice to sale by or on the order ofa licensed practtiioner.

SYMBOLS KEY

The following symbols may appear on the label or carton:

SYMBOL	
ffi]	Consult Instructions for Use
.I	Manufactured by or in
d	Date of Manufacture
	Use By Date (expiration date)
I LOTI	Batch Code
STERILE a	Sterile Using Steam or Dry Heat
®	Single-Use
DIA	Diameter
BC	Base Curve
D	Diopter (lens power)
CYL	Cylinder
AXIS	Axis
CE 0086	Quality System Certification Symbol
@ UV Blocking	UV-Blocking
e)	Fee Paid for Waste Management
IJcOnfy	CAUTION: U.S. Federa! law restricts this device to sale by or on the order of a licensed practitioner
e	Lens Orientation Correct
x x	Lens Orientation Incorrect (Lens Inside Out)

DESCRIPTION

ACUVUE OASYS® Brand Contact Lenses 1-Day and ACUVUE OASYS® Brand Contact Lenses 1-Day for ASTIGMATISM are soft (hydrophilic) contact lenses made with Hydraluxe™ Technology. They are available as spherical or toric lenses respectively.

These lenses are made of a silicone hydrogel material containing an internal wetting agent, visibility tint, and UV absorbing monomer and are tinted blue using Reactive Blue Dye #4 to make the lenses more visible for handling.

A benzotriazole UV absorbing monomer is used to block UV radiation. 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 316 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 Transmission: 85% minimum
- Surface Character: Hydrophilic
- Water Content: 38%
- Oxygen Permeability:

VALUE	METHOD
122 x 10^{-11} (cm^2/sec) (ml O/ ml x mm Hg) at 35°C	Fatt (boundary corrected, non-edge corrected)
103 x 10^{-11} (cm^2/sec) (ml O/ ml x mm Hg) at 35°C	Fatt (boundary corrected, edge corrected)

Lens Parameters:

- Diameter Range: 12.0 mm to 15.0 mm
- Center Thickness: varies with power
- Base Curve Range: 7.85 mm to 10.00 mm
- Spherical Power Range: -20.000 to +20.000
- Cylinder Power Range: -0.250 to -10.000
- Axis Range: 2.5° to 180°

AVAILABLE LENS PARAMETERS

ACUVUE OASYS® Brand 1-0ay with Hydraluxe™ Technology are hemispherical shells of the following dimensions:

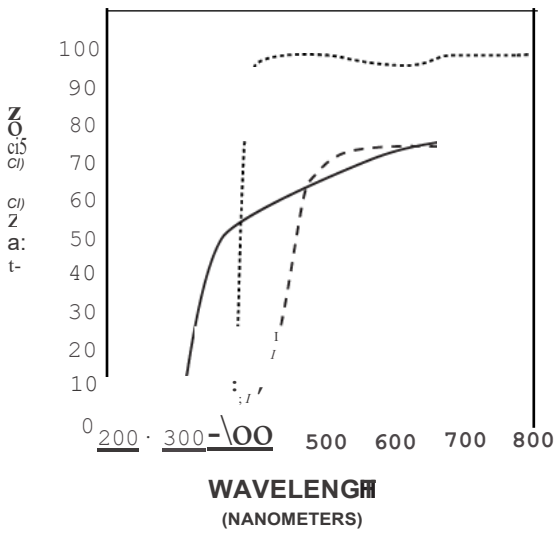
Diameter:	14.3 mm
Center Thickness:	0.085 mm to 0.221 mm (varies with power)
Base Curve:	8.5 mm, 9.0 mm
Powers:	-0.500 to -6.000 (in 0.250 increments) -6 .50 0 to -12.000 (in 0.500 increments) +0.500 to +6.000 (in 0.250 increments) +6.500 to +8.000 (in 0.50D increments)

ACUVUE OASYS® Brand 1-0ay with Hydraluxe™ Technology *tor* ASTIGMATISM are hemitoric shells of the following dimensions:

Diameter:	14.3 mm
Center Thickness:	0.075 mm to 0.172 mm (varies with power)
Base Curve:	8.5 mm
Powers:	+0.00D to -6.00D (in 0.25D increments) Cylinders: -0.75D, -1.25D, -1.75D, -2.25D* Axis: 10° to 180° in 10° increments *-2.250 cylinder is available in 10°, 20°, 70°, 80°, 90°, 100°, 110°, 160°, 170°, 180° axes only. +0.25D to +4.00D (in 0.25D increments) -6.50D to -9.00D (in 0.50D increments) Cylinders: -0.75D, -1.25D, -1.75D Axis: 10°, 20°, 70°, 80°, 90°, 100°, 110°, 160°, 170°, 180°

TRANSMITTANCE CURVES

ACUVUE OASYS® 1-Day with Hydraluxe™ Technology (senoflicon A) Visibility Tinted with UV Blocker vs. 24 yr. old human cornea and 25 yr. old human crystalline lens.



ACUVUE OASYS® 1-Day with Hydraluxe™ Technology (senofilcon A)*

24 YR. OLD HUMAN CORNEA[1]

25 YR. OLD HUMAN CRYSTALLINE LENS[2]

* The data was obtained from measurements taken through the central 3-5 mm portion for the thinnest marketed lens (-9.00D lens, 0.075 mm center thickness).

[1] Le rman, S., Radiant Energy and the Eye, MacMillan, New York, 1980, p. 58, figure 2-21

[2] Waxler, M., Hitchins, V.M., Op tical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p. 19, figure 5

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

ACTIONS

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

The 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 316 nm to 380 nm for the entire power range.

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-Blockingcontact 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® Brand Contact Lenses 1-Day with Hydraluxe™ Technology are indicated for daily disposable wear for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

ACUVUE OASYS® Brand Contact Lenses 1-Day with Hydraluxe™ Technology for ASTIGMATISM are indicated for daily disposable wear for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 0.50D to 3.00D of astigmatism.

These lenses contain a UV Blocker to help protect against transmission of harmful UV radiation to the cornea and into the eye.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE these contact 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., rewetting drops) 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 vira!).
- If eyes become red or irritated.

WARNINGS

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

EYE PROBLEM$, 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 lenses while sleeping. Clinical studies have shown that the risk of serious adverse reactions is increased when lenses are worn overnight, and that the risk of ulcerative keratitis is greater for

extended wear contact lens users than for daily wear users.[3]

- 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 are essential for the sate use of these products.
- The overall risk of ulcerative keratitis may be reduced by carefully following directions for lens care.

[3] New England Journal of Medicine, September 21, 1989; 321 (12), pp. 773 -783

Specif ic Instruct ions for Use and Warnings:

- **Water Activity**

  Instructions 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.

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 mono-vision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.
- Eye Care Professionals should instruct the patient to remove the lenses immediately if the eyes become red or irritated.

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

Handling Precautions:

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove the lenses or should have someone else available who can remove the lenses for him or her.
- DO NOT use if the sterile blister package is opened or damaged.
- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup. Water-based cosmetics are less likely to damage lenses than oil-based products.
- DO NOT touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, and wearing instructions in the "Patient Instruction Guide" for the prescribed

wearing schedule and those prescribed by the Eye Care Professional.

- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.

Lens Wearing Precautions:

- If the lens sticks (stops moving) on the eye, follow the recommended directions in "Care for a Sticking (Non-Moving) Lens." The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. They have been prescribed to fit their eyes and to correct their vision to the degree necessary. 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.
- Always discard lenses worn as prescribed by the Eye Care Professional.

Lens Care Precautions:

- The patient should be informed that no cleaning or disinfection is needed when lenses are worn for daily disposable wear. Patients should always dispose of lenses when removed and have spare lenses or spectacles available.

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 tor motion sickness may cause dryness *ot* the eye, increased lens awareness, or blurred vision. Should such conditions exist, proper remedial measures should be prescribed. Depending on the severity, this could include the use *ot* lubricating drops that are indicated tor use with soft contact lenses or the temporary discontinuance of contact lens wear while such medication is being used.
- Oral contraceptive users could develop visual changes or changes in lens tolerance when using contact lenses. Patients should be cautioned accordingly.
- 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 tollow-up schedule.

Who Should Know That the Patient is Wearing Contact Lenses?

- Patients should intorm all doctors (Health Care Protessionals) 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 comtort than when the lens was first placed on the eye.
- There may be a teeling *ot* something in the eye (foreign body, scratched area).
- There may be the potential tor some temporary impairment due to

peripheral infiltrates, peripheral corneal ulcers, or 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, 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 to seek 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 hande and care for the tenses
- Ability to understand the risk and benefits of tens wear

Patients v.i1o do not meet the above criteria should not be proVided with oontact tenses.

B. Pre-fitting Examination

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

Preceding the inijiaJ selection of trial oontact lenses, a comprehensive ocular evalualion should be pertormed that includes, but is not li ed to, the measurement of distance and near visual acuity distance and near refractille prescription (including determining the preferred reading distance tor presbyopes), keratometry, and biomicroscopic evaluation.

Based on this evaluation, ii It is determined thal the patient is eigible to wear these lenses, the Eye Care Professional should proceed to the tens fitting instl\Jctions as outlined below.

C . Initial Power Determination

Aspectacle retraction should be per1ormed to establish the palient's baseline relractlve status and to g1.1de in the selection of the appropriate lens power. Remember to compensate tor vertex distance if there fraction is greater than :t4.00D.

D. Base Curve Selection (Trial Lens Frtting)

The following tlial lenses should be selected tor patients regardless o! kera-tometry readings. However, corneal curvatll'8 measurements shoutl be pertormed to establish the patient's baseline ocular status.

- ACUVUE OASYS® 1-Day: 8.5 mm/14.3 mm
- ACUVUE OASYS® 1-Day for ASTIGMATISM: 8.5 mm/14.3 mm

The trial lens 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. If resistance is encountered when pushing the lens up, the lens is fitting tightly and should not be dispensed to the patient.

E. Final Lens Power (Spherical)

A spherical over-refraction should be performed to determine the final lens power after the lens fit is judged acceptable. The spherical over-refraction should be combined with the trial lens power to determine the final lens prescription. The patient should experience good visual acuity with the correct lens power unless there is excessive residual astigmatism

Example 1	
Oiagnostic lens:	-2.000
Spherical over-refraction:	-0.250
Final lens power :	-2.250

Example 2	
Oiagnostic lens:	-2.000
Spherical over-refraction:	+0.250
Final lens power:	-1.750

If vision is acceptable, perform a slit lamp examination to assess adequate fit (centration and movement). If the fit is acceptable, dispense the lenses and instruct the patient to return in one week for reassessment (see dispensing and follow up information in **PATIENT MANAGEMENT).**

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.

TORIC FITTING GUIDELINES

Although most aspects of the fitting procedure are identical for all types of soft contact lenses, including toric lenses, there are some additional steps and/or rules to follow to assure the proper fit of toric lenses.

The only new steps you must follow in prescribing ACUVUE OASYS® 1-Day for ASTIGMATISM are that you must determine the stability, repeatability, and drift angle of the lens axis so that you can prescribe the correct lens axis for the patient.

A. How to Determine Lens Cylinder and Axis Orientation

1. Locate the Orientation Marks

To help determine the proper orientation of the toric lens, you'll find two primary marks approximately 1 mm from the lens edge representing the vertical position on opposite ends of the lens at 6 and 12 o'clock (Fig. 1). Because of the lens' ballasting system, either mark can represent the vertical position - there is no "top" and "bottom" as in a prism-ballasted lens. You don't need to view both marks to assess orientation; simply look for the 6 o'clock mark as you would with a prism-ballasted lens.

Figure 1

You'll need a slit lamp biomicroscope with a 1 to 2 mm parallelepiped beam to highlight the marks when the lens is fitted to the eye. There are a number of techniques you can use to improve the visibility of the 6 o'clock mark. Using a parallelepiped beam and medium magnification (10x or 15x), slowly pan down the lens, looking just below the direct illumination at the retroilluminated area. Backlighting the mark this way should make it more visible. Sometimes manipulating the lower lid may be necessary to uncover the mark.

2. Observe Lens Rotation and Stability

Observe the position and stability of the "bottom" mark. It usually stabilizes at the 6 o'clock position. If it does, calculation of the lens power will be straightforward. The 6 o'clock position is not a "must"; however, the absolute requirement is that the axis position be stable and repeatable.

The mark may stabilize somewhat left or right (drift) of the vertical meridian and still enable you to fit a toric lens for that eye, as long as the lens always returns to the same "drift axis" position after settling. The deviation can be compensated for in the final prescription. Your objective is to ensure that whatever position the initial lens assumes near 6 o'clock, this position must be stable and repeatable. With full eye movement or heavy blink, you may see the marks swing away, but they must return quickly to the original stable position. If the lens does not return quickly, you may need to select a different lens.

3. Assessing Rotation

Imagine the eye as a clock dial and every hour represents a 30° interval. If the orientation mark of the initial lens stabilizes somewhat left or right of the vertical position, the final lens will orient on the eye with the same deviation. You can use an axis reticule in the slit lamp or use a line-scribed lens in a spectacle trial frame to measure or estimate the "drift angle" of the cylinder axis.

To compensate for this "drift", measure or estimate the "drift", then add or subtract it from the refractive axis to determine the correct cylinder axis. Use the LARS (Left Add, Right Subtract) method to determine which direction to compensate.

B. Final Lens Power

When the diagnostic lens has its axis aligned in the same meridian as the patient's refractive axis, a spherocylindrical over-refraction may be performed and visual acuity determined. However, in the case of crossed axes, such as when the diagnostic lens axis is different from the spectacle cylinder axis, it is not advisable to perform a full spherocylindrical over-refraction because of the difficulty in computing the resultant power. A spherical over-refraction without cylinder refraction may be performed.

If the required cylinder correction falls between two available cylinder powers, it is recommended to prescribe the lower cylinder power lens. See below for instructions on how to determine the final lens power.

1. For the Sphere

If sphere alone or combined sphere and cylinder Rx > ±4.00D, compensate for vertex distance. If sphere alone or combined sphere and cylinder Rx ≤ ±4.00D, vertex compensation is not necessary.

2. For the Cylinder

Adjust the axis by the drift angle using the LARS method. Choose a cylinder that is ≤ 0.50D from the refractive cylinder.

3. Case Examples

Example 1

Manifest (spectacle) refraction:
O.D. -2.50D / -1.25D x 180° 20/20
O.S. -2.00D / -1.00D x 180° 20/20

Choose a diagnostic lens for each eye with axis 180°. Place the lens on each eye and allow a minimum of 3 minutes for it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable.

Check the orientation of the axis mark. If the bottom axis mark is in the 6 o'clock position on both eyes, choose the appropriate cylinder as listed previously. If the lens has not yet stabilized, recheck until stable.

Here is the Rx Prescribed:
O.D. -2.50D / -1.25D x 180°
O.S. -2.00D / -0.75D x 180°

Example 2
Manifest (spectacle) refraction :
0 .0. -3.000 / -1.000 x 90° 20/20
O.S. -4.75 0 *I* - 2.00 0 x 90° 20/20

Choose diagnostic lenses of -3.000 / -0.750 x 90° for the right eye and -4.500 / -1.750 x 90° for the left eye, the nearest lenses available to the spherical power, cylinder power, and axis needed. For the left eye, since the manifest refraction called for -4.750, compensating for vertex distance the sphere is reduced by 0.250 to -4.500. The cylinder power will be -1.750 . Place the lens on each eye and allow a minimum of 3 minutes for it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable.

Right Eye

The orientation mark on the right lens rotates left trom the 6 o'clock position by 10° and remains stable in this position. Compensation for this rotation should be done as follows:

Compensate the 10° axis drift by adding it to the manifest refraction axis.

Here is the Rx Prescribed:
0 .0. -3.000 / -0.750 x 100°

Left Eye

The orientation mark on the left lens rotates right trom the 6 o'clock position by 10° and remains stable in this position.

Compensate for the 10° axis drift by subtracting it from the manifest refraction axis.

Here is the Rx Prescribed:
O.S. -4.500 *I* - 1 .75 0 x 80°

If vision is 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 dispensing and follow-up information in PATIENT MANAGEMENT).

Ali patients should be supplied with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.

MONOVISION FITTING GUIDELINES

A. Patient Selection

1. Monovision Needs Assessment

For a good prognosis, the patient should have adequately corrected distance and near visual acuity in each eye. The amblyopic patient or the patient with significant astigmatism (greater than 1.00D) in one eye may not be a good candidate for monovision correction with these lenses.

Occupational and environmental visual demands should be considered. If the patient requires critical vision (visual acuity and stereopsis), it should be determined by trial whether this patient can function adequately with monovision correction. Monovision contact lens wear may not be optimal for activities such as:

- visually demanding situations such as operating potentially dangerous machinery or performing other potentially hazardous activities; and
- driving automobiles (e.g., driving at night). Patients who cannot meet state driver's licensing requirements with monovision correction should be advised to not drive with this correction, OR may require that additional over-correction be prescribed.

2. Patient Education

AII p atients do not function equally well with monovision correction. Patients may not perform as well for certain tasks with this correction as they have with spectacles (multifocal, bifocal, trifocal, readers, progressives). Each patient should understand that monovision, as well as other presbyopic alternatives, can create a vision compromise that may reduce visual acuity and depth perception for distance and near tasks. 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 visuallychallenging environments (e.g., reading a menu in a dim restaurant, driving at night in rainy/foggy conditions, etc.). During the fitting process, it is necessary for the patient to realize the disadvantages as well as the advantages of clear near vision and straight ahead and upward gaze that monovision contact lenses provide.

B. Eye Selection

1. Ocular Preference Determination Methods

Generally, the non-dom inant eye is corrected for near vision. The following two methods for eye dominance can be used.

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: Determine which eye will accept the added power with the least reduction in vision. Place a hand-held trial lens equal to the spectacle near ADD in front of one eye and then the other while the distance refractive error correction is in place for both eyes. Determine whether the patient functions best with the near ADD lens over the right or left eye.

2. Other Eye Selection Methods

Other methods include the "Refractive Error Method " and the "Visual Demands Method."

Refractive Error Method

For anisometropic correction, it is generally best to fit the more hyperopic (less myop ic) eye for distance and the more myopic (less hyperopic) eye for near.

Visual Demands Method

Consider the patient's occupation during the eye selection process to determine the critical vision requirements. If a patient's gaze for near tasks is usually in one direction, correct the eye on that side for near.

Example: A secretary who places copy to the left side of the desk will function best with the near lens on the left eye.

C. Special Fitting Characteristics

1. Unilateral Vision Correction

There are circumstances where only one contact lens is required. As an example, an emmetropic patient would only require a near lens, whereas a bilateral myope would require corrective lenses on

both eyes.

Examples:

A presbyopic emmetropic patient who requires a +1.75D ADD would have a +1.75D lens on the near eye and the other eye left without correction.

A presbyopic patient requiring a +1.50D ADD who is -2.50D myopic in the right eye and -1.50D myopic in the left eye may have the right eye corrected for distance and the left uncorrected for near.

2. Near ADD Determination

Always prescribe the lens power for the near eye that provides optimal near acuity at the midpoint of the patient's habitual reading distance. However, when more than one power provides optimal reading performance, prescribe the least plus (most minus) of the powers.

3. Trial Lens Fitting

A trial fitting is performed in the office to allow the patient to experience monovision correction. Lenses are fit according to the GENERAL FITTING GUIDELINES for base curve selection described in this Package Insert.

Case history and standard clinical evaluation procedure should be used to determine the prognosis. Determine the distance correction and the near correction. Next determine the near ADD. With trial lenses of the proper power in place, observe the reaction to this mode of correction.

Allow the lenses to settle for about 20 minutes with the correct power lenses in place. Walk across the room and have the patient look at you. Assess the patient's reaction to distance vision under these circumstances. Then have the patient look at familiar near objects such as a watch face or fingernails. Again assess the reaction. As the patient continues to look around the room at both near and distance objects, observe the reactions. Only after these vision tests are completed should the patient be asked to read print. Evaluate the patient's reaction to large print (e.g., typewritten copy) at first and then graduate to newsprint and finally smaller type sizes.

After the patient's performance under the above conditions is completed, tests of visual acuity and reading ability under

conditions of moderately dim illumination should be attempted.

An initial unfavorable response in the office, while indicative of a guarded prognosis, should not immediately rule out a more extensive trial under the usual conditions in which a patient functions.

4. 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.

D. Other Suggestions

The success of the monovision technique may be further improved by having the patient follow the suggestions below:

- Have a third contact lens (distance power) to use when critical distance viewing is needed.
- Have a third contact lens (near power) to use when critical near viewing is needed.
- Having supplemental spectacles to wear over the monovision contact lenses for specific visual tasks may improve the success of monovision correction. This is particularly applicable for those patients who cannot meet state driver's licensing requirements with monovision correction.
- Make use of proper illumination when carrying out visual tasks.

Monovision fitting success can be improved by the following suggestions:

- Reverse the distance and near eyes if a patient is having trouble adapting.
- Refine the lens powers if there is trouble with adaptation. Accurate lens power is critical tor presbyopic patients.
- Emphasize the benefits of clear near vision and straight ahead and upward gaze with monovision.

The decision to fit a patient with monovision correction is most appropriately left to the Eye Care Professional in conjunction with the patient after carefully considering the patient's needs.

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.

PATIENT MANAGEMENT

Dispensing Visit

Each sterile lens is supplied ina foil-sealed plastic package containing buffered saline solution with methyl ether cellulose. To remove the lens trom the container, peel back the foil seal, place a finger on the lens, and slide the lens up the side of the bowl of the lens package until it is free of the container.

- Evaluate the physical fit and visual acuity of the lens on each eye.
- Teach the patient how to apply and remove his or her lenses.
- Explain daily disposable lens wear and schedule a follow-up examination.
- **Provide the patient with a copy of the PATIENT INSTRUCTION GUIDE for these lenses. Copies are available for download at www.acuvue.com.**

  REVIEW THESE INSTRUCTIONS WITH THE PATIENT SO THAT HE OR SHE CLEARLY UNDERSTANDS THE PRESCRIBED WEARING AND REPLACEMENT SCHEDULES.

Follow-Up Examinations

Follow-up care (necessary to ensure continued successful contact lens wear) should include routine periodic progress examinations, management of specific problems, if any, and a review with the patient of the wear schedule, daily disposable modality, and proper lens handling procedures.

Recommended Follow-up Examination Schedule (complications and specific problems should be managed on an individual patient basis):

1. One week from the initial lens dispensing to patient
2. One month post-dispensing
3. Every three to six months thereafter

NOTE: Preferably, at the follow-up visits, lenses should be worn for at least six hours.

Recommended Procedures for Follow-up Visits:

1. Solicit and record patient's symptoms, if any.
2. Measure visual acuity monocularly and binocularly at distance and near with the contact lenses.
3. Perform an over-refraction at distance and near to check for residual refractive error.
4. With the biomicroscope, judge the lens fitting characteristics (as described in the **GENERAL FITTING GUIDELINES**) and evaluate the lens surface for deposits and damage.
5. Following lens removal, examine the cornea and conjunctiva with the biomicroscope and fluorescein (unless contraindicated).
   - The presence of vertical corneal striae in the posterior central cornea and/or corneal neovascularization is indicative of excessive corneal edema.
   - The presence of corneal staining and/or limbal-conjunctival hyperemia can be indicative of an unclean lens, a reaction to solution preservatives, excessive lens wear and/or a poorly fitting lens.
   - Papillary conjunctival changes may be indicative of an unclean and/or damaged lens.
6. Periodically perform keratometry and spectacle refractions. The values should be recorded and compared to the baseline measurements.

If any observations are abnormal, use professional judgment to alleviate the problem and restore the eye to optimal conditions. If

the criteria for successful fit are not satisfied during any follow-up examinations, repeat the patient's trial fitting procedure and refit the patient.

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.

Patients tend to overwear 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 individua! 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 atter	all waking hours

REPLACEMENT SCHEDULE

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

LENS CARE DIRECTIONS

When lenses are prescribed for daily disposable wear, the Eye Care Professional should previde the patient with appropriate and adequate warnings and instructions for daily disposable lens wear at the time they are dispensed.

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

Basic Instructions

- Always wash, rinse, and dry hands before handling contact lenses.
- Do not use saliva or anything other than the recommended solutions for lubricating or rewetting lenses. Do not put lenses in the mouth.
- Eye Care Professionals may recommend a lubricating/rewetting solution which can be used to wet (lubricate) lenses while they are being worn to make them more comfortable.

Care for a Sticking (Non-Moving) Lens

If the lens sticks (stops moving), the patient should be instructed to apply a few drops of the recommended lubricating or rewetting solution directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement of the lens continues after a few minutes, the patient should immediately consult 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 UV-blocking 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® 1-Day: base curve, power, diameter, lot number, and expiration date
- ACUVUE OASYS® 1-Day for ASTIGMATISM: base curve, power, diameter, cylinder, axis, lot number, and expiration date

REPORTING OF ADVERSE REACTIONS

AII seriousadverse experiences and adverse reactionsobserved in patients wearing these lenses or experienced with these lensesshould be reported to:

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

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

Revision date: 09/16
Revision number: AO-03-16-13

APPENDIX D: [redacted]

- [redacted] LENS FITTING CHARACTERISTICS
- [redacted] SUBJECT REPORTED OCULAR SYMPTOMS
- [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS
- [redacted] BIOMICROSCOPY SCALE
- [redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION
- [redacted] TORIC FIT EVALUATION
- [redacted] ETDRS DISTANCE VISUAL ACUITY MEASURMENT PROCEDURE
- [redacted] PATIENT REPORTED OUTCOMES
- [redacted] LENS INSERTION AND REMOVAL
- [redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

[redacted] **LENS FITTING CHARACTERISTICS**

[redacted]

[redacted]

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[redacted]

[redacted]

[redacted] **SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS**

[redacted]

[redacted] **DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIVE ERROR**

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[redacted] **BIOMICROSCOPY SCALE**

Title: **Biomicroscopy Scale**

Document Type: [redacted]

Document Number: [redacted] Revision Number: 10

[redacted]

[redacted]

[redacted]

[redacted]

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[redacted]

Title: **Biomicroscopy Scale**

DocumentT **ype:** [redacted]

Document Number: [redacted] **Revision Number: 10**

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

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Title ----------Distance and Near Snellen Visual Acuity Evaluation
Document Type: [redacted]

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

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[redacted]

[redacted] **TORIC FIT EVALUATION**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **PATIENT REPORTED OUTCOMES**

[redacted]

[redacted] **LENS INSERTION AND REMOVAL**

[redacted]

[redacted]

[redacted]

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[redacted] **VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING**

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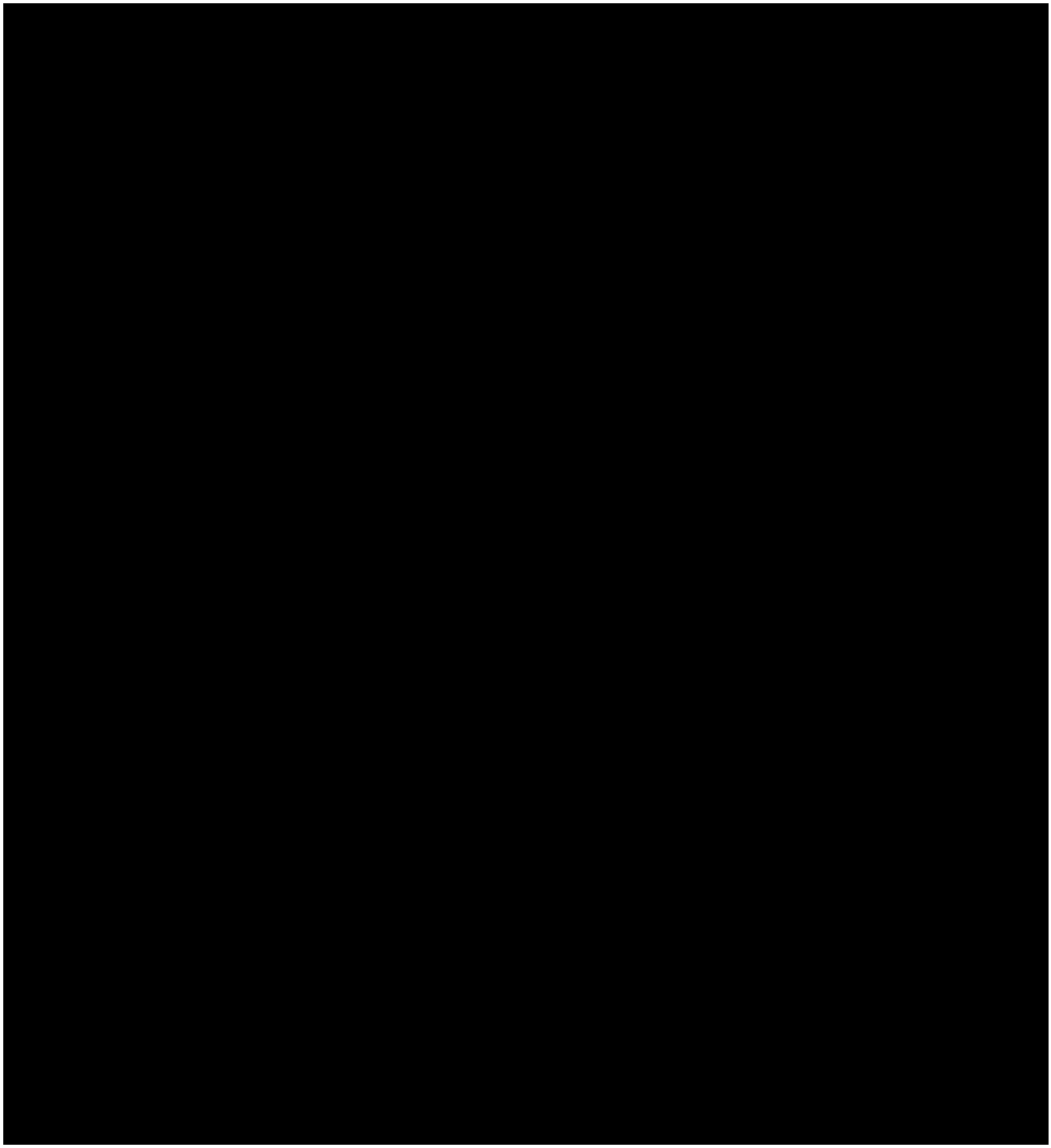

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APPENDIX E: IRIS COLOR SCALE

APPENDIX F: [redacted] GUIDELINES FOR COVID-19 RISK MITIGATION

1.0 PURPOSE

The pmpose of this document is to provide guidelines for the re-opening or initiation of clinical study sites participating in Johnson & Johnson Vision Care, fuc. (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 fustrnction 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 countr y by countr y basis subject to local health authot·ity guidance.

3.0 DEFINITIONS

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

American Optometric Association (AOA): The Ame1-ican Op tometi-ic Ass ocia tion, 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 Optometiy (O.D.), optometi-ic profe ss iona ls, and optometiy students. Doctor of Optometiy 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 Optometiy have extensive, ongoing ti·aining to examine , diagnose , treat and manage ocular disorders, diseases and injw-ies and systemic diseases that manifest in the eye. The American Optometi-ic Association is a federation of state, student, and anned forces optometric associations. Through these affiliations, the AOA serves members consisting of optometi-ists, students of optometiy , paraop tome ti·icassistants and technicians. The AOA and its affiliates work to provide the public with quality vision andeye care.

Centers fot· Disease Control and Prevention (CDC): The Centers for Disease Conti·ol and Prevention is a national public health institute in the United States. It isa United States federa! agency, under the Department of Health and Human Services, and is headqua1tered in Atlanta, Georgia.

COVID-19: CwTent outbreak of respirato1ydisease caused by a novel coronavirns. The virns has be.en named "S ARS-CoV-2" and the disease it causes has been named " Coronavirns Disease 2019" (COVID-19).

Clinical Study: Volunta1y research studies conducted in people and designed to answer specific questions about the safety or effectiveness of drngs, vaccines, other therapies, or new ways of using existing ti·eatinents. May also be called clinical trials, studies, research, ti·ials, or protocols.

Clinical Study Site: Location where a clinical study is conducted, such as a doctor's office, university, or laborato1y. 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 fuvestigator is the responsible leader of the team and may be called the P1-incipal fu vestigat or.

C linical Op era tion s Manager (COM): The Johnson & Johnson Vision Care (JJVCI) individua! responsible for the overall management of a clinical ti-ial.

Monitor: An individual designated to oversee the progress of a clinical study and ensure that it is conducted, recorded, and repo1ted in accordance with the protocol, Standard Operating Procedures (SOPs), Good Clinical Practice (GCP), and applicable regulatory requirements.

Medica! 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 evaluationof medica! safety data arising from any source throughout the product life cycle.

4.0 GUIDANCE FOR STUDY DOCUMENTS

1n alignment with recent health authority guidance, JJVCI is providing recollllllendations for study-related management in the event of disruption to the conduct of the clinical study. This guidance does not supersede any local or govemment 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 paiticipant'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 pande1nic, the additional risks listed below need to be considered for study paiticipants and study personnel:

4I I Additional Risks Related to the COVID-19 Pandernic:

- The possible transrnission 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 cai·e profes sional s 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 healthcai·e professionals who 1night be transmi tting the virus, even if they do not have symptoms.
- Potential disruptions to the study may be necessaiy due to current or future pandernic-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. 1n this event, ali assessments that can be conducted virtually will be completed by the investigator to deterrnine 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 paiticipation ina study, he/she will be discontinued from the study and followed until COVID-19 Adverse Event (AE) resolution.

To help minirnize the above potential risks, JJVCI recollllllend reviewing/complying with local, state, and govemmental guidance for COVID-19 risks.

JJVCI will provide the following study specific documents with language pe1taining to COVID-19 risks:

4.1.I Info1med Consent:

Will include info1mation conceming 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:

[redacted]

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

It is important to note that this study will be conducted, at least in palt, during the COVID-19 pandemic. As such, additional risks associated with the infection with COVID-19 exist for you. This is palticulady 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-te1mserious health consequences. In severe cases, this may result in hospitalization ancl/or dea th. Based on cun-ent 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 undedying medica! 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 confo1mance to guidance from the CDC, local health depa1tments, 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 pe1mitted to continue in-office study follow-up visits, but you will receive instmctions and your condition will be monitored by the doctor ancl/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 JNCI 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 govemmental guidance's for COVID-19 risk mitigation.

I have read the suggested guidance provided by JNCI 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, govemmental 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.

S.O G UIDANCE FOR REMOTE SUBJECT VISITS

Potential dismptions to the study may be necessary due to cmTent 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 concems 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:

[redacted]

Procedure	Details
Subject Repo1ted Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire regarding the test a1ticle 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 ofhow-s per day dw-ing weekdays and weekends, and number of days per week). Confinn 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 moming and takes off in the evening, the number of days per week lenses were wom, 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 dw-ing the telephone consultation, a subject states he/she wishes to discontinue participating in the study, instrnct the subject to stop wearing the study lenses and schedule the subject to retum to the clinic for a Final Evaluation at the at earliest possible time. Subjects should retum 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 repo1t fonns should capture specific info1mation 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 Coronavirns Disease 2019 (COVID-19) pandemic may have an impact on the conduct of this clinical study due to, for example, self-isolation/quarantineby participants and study-site personnel; travel restrictions/limited access to public places, including Optometty Clinics; and changes in clinic procedures required to address the COVID-19 challenge.

Eve1y 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 perfo1med to the extent possible remotely/vittually 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, pait icipants will be interviewed to collect safety data. Key efficacy endpoint assessments should be perfo1med if required and as feasible.

Modifications to protocol-required assessments may bepennitted via COVID-19 Appendix after consultation with the paiticipant, investigator, and the sponsor. Missed assessments/visits will be captured in the clinical tt·ial management system for protocol deviations. Intenuptions of test alt icle wear or discontinuations of study interventions and withdrawal from the study should be documented with the prefix "COVID-19-related" in the case repo1t f01m (CRF).

[redacted]

The spon sor will con tinue 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 "SuspectedCOVID-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 repo1t.

COVID-19 screening procedures that may be mandated by local healthcare systems do not need to be repo1ted as an amendmen t to the protocol even if done during clinical study visits.

6.1 Monitorin g Vi sit s

When on-site monitoring by the sponsor is not feasible, the sponsor' s site monitor will contact the study site to schedule remote visits. 1n 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 prut of standard process. When conditions pennit, all parties involved in this clinical trial should communicate relevant infonnation in a timely manner so that all relevant pa1ties remain sufficiently infonned.

6.1.1 Study SiteInitiation:

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 Teains orsimilarsoftwai·eas well as utilize online traini
tud site training will be documented utilizin . Site Initiation Report — — — —
per Study Site Initiation [redacted]

- On-site visits may be consideredwhen, 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 governnientalpolicies for COVID-19 Risk Mitigation, including social distancing, wearing of PPE, etc. as applicable for the locationof the study site.

6.1.2 Interim Monitoring Visits (if applicable):

During the period that this Work Instrnction is in effect, Interim Monitoring On-site visits will be kept to a minimum and include only those tasks that the CRA cannot pe1fonn remotely (e.g., source document verification, test a1ticle reconciliation , etc.).

To ensure da.ta integrity during the conduct of ali JJVC studies, clinical study teams will follow the study specific Clinical Monitoring Plan [redacted]

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

[redacted]

6.1.3 Study SiteClosure:

Duringthe period that this Work Instrnction is in effect, the dura.tion ofthe Study Site Closure Visit will be limited to ta.sks tha t the CRA cannot perfonn remotely (e.g., source document verifica.tion, test article final reconcilia.tion and retum, etc.).

[redacted]

A t ta c hm e nt A: S tud y S ite Co rr es pond e n ce

XXXX XX, 2020

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

Dear <<Principal Investigator>> and Study Team,

Coronavirns (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 ctmently working on or considering pa1ticipation 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 govemmental guidelines for COVID-19 risk mitigation.

Informed Consent:

- Will include infonnation conceming the study-associated risks related to the COVID-19 pandemic in bold font and/or boxed on the first page of tlie Info1med 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 tlie pandemic.

We want to encourage the need for open lines of communication about potential challenges you may foresee as the result of the cun-ent C OVID- 19 situa tion . 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 con-es pondenc e.

[redacted]

Att achment B: COVID-19 Risk Control Checklist

Study Number
SiteNumber
Principal Investigator (PI) Name

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

PI Initials	General Site Safetv Plannin2 Measures
	Si‹ma2e within site describin2 Risk Control methods
	Social Distancin2 oractices thro,w: hout site (waitin2 rooms lobbv. exam rooms. etc.)
	Non-contact thermometer available to assess temoeratures of staff and oatients
	Trainin2 on oatient flow and ohvsical distancin2 in waitin2 room
	Establish lon2er time frame betwe en oatien t annoin tments to reduce oersons 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 tirnes during interactions with subjects (e.g., putting on and removing without self-contamination)

PI Initials	Site StaffDailv Safetv Measures
	As pati of routine practice, site staff should regulai·ly monitor themselves for fever and symptoms of COVID-19 including temperature checks
	Any staff member (including non-study clinic staff and Investigators) showing signs ofbeing sick or testing positive for COVID-19 must not be pennitted to work on activity that may expose study related staff and subject and the Sponsor shall be informed **NOTE: Inform JJVC in 24 hours of any COVID-19 cases and all potential exposure during the clinical study.**
	Ensure that all staff wear a mask Gloves should be reauired when working directlv with oatients and changed between each oatient
	Have staff thoroughly wash hands for at least 20 seconds or use an alcohol-based hand sanitizer when thev airive before and after each oatient before eating and after using the bathroom.
	Cleaning and disinfection procedures for exam rooms and instnunents or equipment between oatients with 2loves.
	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 fainily member have had contact with another person with confumed COVID-19 in the past 14 days. Patients exhibiting signs ofbeing sick shouldbe rescheduled when their symptoms resolve.
	Instrnct patients that companions should remain outside of the facility and not accompany the patient into the facility unless they are a parent/guardianof the patient or if they are a trne cai·egiver and need to assist the oatient
	Request the patient to call or text the office upon an ival so entrance to and movement through facility can be coordinated by site staff

[redacted]

PI Initials	Patienst Entering the site:
	T em pera ture checks utilizing a non-contact thennometer for all patients and companions entering the site.
	All oatients and comoanions must wear cloth or disoosable 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 obiects in (e.g. toys, reading materials, etc.) should be removed or cleaned regulady.

I ce1tify that I have read and agree to implement all the listed COVID-19 Risk Control Measures required for the conduct of Johnson & Johnson Vision Care studies.

Principal Investigator Signature and Date

[redacted]

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/coronavims/2019-ncov/hcp/using-ppe.html

- l&R Training
  ACUVUE® Len sAssis t: https: // www.acuvue.com/lensassist

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

- ln-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.coronavims.gov hk/eng/index.html

- Resumption of optical services in England: Letter from Matt Neligan and Poonam Shruma
  https://www.england nhs.uk/coronavims/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/coronavims/wp-content/uploads/sites/52/2020/04/C0127-optical-letter-l -april-2020.pdf

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

- The Collegeof Optometrists COVID-19: College updates
  https://www.college-optometrists.org/the-college/media-hub/news-listing/coronavims-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

- Infection prevention and control for COVID-19: Interim guidance for outpatient andambulato1y cru·e s etting s . (2020 , May 23 May). Retrieved from Govemment of Canada: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavims-infection/guidance-documents/interim-guidance- outpatient-ambulato1y-care-settings html

- Info1mation for Members On Coronavims (COVID-19). (n.d.). Retrieved from Canadian Association Of Optometrists: https://opto.ca/sites/default/files/resources/documents/info1mation_for_members_on_coronavims.pdf

- Coronavims (COVID-19) resources for health professionals, including aged care providers, pathology providers and health care managers. (2020, September 24). Retrieved from Australian Govemment Department of Health: https://www health.gov.au/resources/collections/coronavims-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 Govemment Depa11ment 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 Optometiy Austi·alia: https://www.optometiy.org.au/practice-professional-support/coronavims-covid-19-what-optometrists-need- to-know/covid-19-clinical-advice/infection-conti·ol-guidelines-and-advice/

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6521 Design Validation of Toric Contact Lenses in Senofilcon A with a Blue-Blocking Chromophore

Version and Date: 3.0 01 June 2023

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

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

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

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

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

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

Principal Investigator: _____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site: _____

Institution/Site Name

_____

Institution/Site Address