

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

Evaluation of Daily Disposable Toric Soft Lenses Manufactured with an Alternative Hydration Process

Protocol CR-6590

Version: 1.0

Date: 13 March 2025

Test Articles:

Control: currently marketed ACUVUE® OASYS 1-Day for ASTIGMATISM (AO1DfA) lenses manufactured on 3GT legacy lines using isopropyl alcohol (IPA) as the hydration solvent.

Test Product: Investigational lenses manufactured on 4GT lines with extended mini-stack hydration using propylene glycol (PG) as the hydration solvent

Commercially Available Product Lots: currently marketed ACUVUE® OASYS 1-Day for ASTIGMATISM (AO1DfA) lenses manufactured on 3GT legacy lines using isopropyl alcohol (IPA) as the hydration solvent

Keywords: Astigmatism, ACUVUE® OASYS 1-Day for Astigmatism, senofilcon A, daily wear, daily disposable, dispensing, Single use Eye-Cept® Rewetting Drops, LacriPure Saline Solution, ScleralFil Preservative Free Saline Solution, CLUE comfort, CLUE vision, CLUE handling, logMAR visual acuity, rotation performance.

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

This clinical trial will be conducted in compliance with ISO 14155<sup>1</sup>, Declaration of Helsinki<sup>2</sup>, United States (US) Code of Federal Regulations (CFR)<sup>3</sup>, and International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP)<sup>4</sup>.

**Confidentiality Statement:**

This document contains confidential information, which should not be copied, referred to, released or published without written approval from Johnson & Johnson Vision Care, Inc. The information may not be disclosed to others except to the extent necessary to obtain Institutional Review Board/Independent Ethics Committee approval and informed consent, or as required by International, Federal and State Laws, as applicable. Persons to whom this information is disclosed must be informed that this information is privileged and confidential and that it should not be further disclosed without the written permission of Johnson & Johnson Vision Care, Inc. Any supplemental information that may be added to this document is also confidential and proprietary to Johnson & Johnson Vision Care, Inc. and must be kept in confidence in the same manner as the contents of this document.

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

Title: Evaluation of Daily Disposable Toric Soft Lenses Manufactured with an Alternative Hydration Process  
Protocol Number: CR-6590  
Version: 1.0  
Date: 13 March 2025

**SPONSOR NAME AND ADDRESS**

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

**MEDICAL MONITOR**

[REDACTED]

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

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

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**AUTHORIZED SIGNATURES**

The signatures below constitute the approval of this protocol and the attachments and provide the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements, ISO 14155<sup>1</sup> Declaration of Helsinki<sup>2</sup>, and the United States (US) Code of Federal Regulations (CFR)<sup>3</sup>, and International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP)<sup>4</sup>.

|                                         |                                                                |               |
|-----------------------------------------|----------------------------------------------------------------|---------------|
| Author & Study<br>Responsible Clinician | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Clinical Operations<br>Manager          | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Biostatistician                         | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Biostatistician Reviewer                | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Data Management                         | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Medical Safety Officer                  | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Medical Monitor                         | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |
| Platform Lead/Project<br>Lead/Director  | <i>See Electronic Signature Report</i><br>[Redacted Signature] | _____<br>DATE |

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**SYNOPSIS**

|                                |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                    |
|--------------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Protocol Title                 | Evaluation of Daily Disposable Toric Soft Lenses Manufactured with an Alternative Hydration Process                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Sponsor                        | JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                               |
| Clinical Phase                 | Clinical trial phase:<br>Pivotal/ Design Validation<br>[REDACTED]                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                  |
| Trial Registration             | This study will be registered on ClinicalTrials.gov by the Sponsor                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                 |
| Test Article(s)                | Investigational Product (test lens): Investigational daily disposable, soft, toric lenses manufactured on 4 <sup>th</sup> Generation Technology (4GT) lines with extended mini-stack hydration using propylene glycol (PG) as the hydration solvent.<br><br>Approved Product (control lens): ACUVUE® Oasys 1-Day for Astigmatism (AO1DfA) soft contact lenses manufactured on 3 <sup>rd</sup> Generation Technology (3GT) legacy lines using isopropyl alcohol (IPA) as the hydration solvent.                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                     |
| Wear and Replacement Schedules | Wear Schedule: Daily wear<br>Replacement Schedule: Daily Disposable                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Objectives                     | Primary Objectives:<br>1. To demonstrate non-inferiority of the investigational test lens compared to the control lens related to efficacy in terms of in: <ul style="list-style-type: none"> <li>High-luminance, high-contrast (HLHC) distance mean visual acuity (VA) [REDACTED]</li> <li>Percentage of eyes achieving lens rotational stability with blinks <math>\leq 5^\circ</math> [REDACTED]</li> <li>Percentage of eyes achieving absolute rotation <math>\leq 10^\circ</math> [REDACTED]</li> </ul> 2. To demonstrate that the test lens meets the design validation requirements related to safety in terms of: <ul style="list-style-type: none"> <li>Percentage of eyes with at least one clinically significant (grade 3 or 4) slit-lamp biomicroscopy finding related to wear of the test lenses [REDACTED]</li> <li>Percentage of eyes with an acceptable lens fitting for the test lenses [REDACTED]</li> </ul><br>Secondary Objectives:<br>To evaluate the difference in subjective vision, handling and comfort scores between test and control lenses following approximately 1-week of wear measured by the Contact Lens User Experience (CLUE) questionnaire. |
| Study Endpoints                | Co-Primary efficacy endpoints: <ul style="list-style-type: none"> <li>HLHC distance VA (in logMAR) after approximately 1 week of lens wear.</li> <li>Lens rotational stability with blinks following settling at the dispensing visit.</li> <li>Absolute lens orientation following settling at the dispensing visit.</li> </ul><br>Co-Primary safety endpoints:                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                   |

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|                                  | <ul style="list-style-type: none"> <li>Grade 3 or higher slit-lamp biomicroscopy findings related to wear using the FDA grading scale.</li> <li>Acceptable lens fitting (i.e., acceptable toric and general fitting characteristics) at the dispensing visit.</li> </ul> <p>Secondary efficacy endpoints:</p> <ul style="list-style-type: none"> <li>Subjective comfort CLUE score following approximately 1 week of wear.</li> <li>Subjective vision CLUE score following approximately 1 week of wear.</li> <li>Subjective handling CLUE score following approximately 1 week of wear.</li> </ul> <p>Other safety endpoint</p> <ul style="list-style-type: none"> <li>Ocular and non-ocular adverse events (AEs)</li> </ul>                                          |
| Study Design                     | <p>This is a prospective, multi-site, dispensing, randomized, controlled, double-masked, bilateral wear, 2×2 crossover study. Each subject will be randomly assigned to one of two wear sequences (Test followed by Control lens or Control followed by Test lens). Each wear period will be 7(±2) days, with a 7(±2) day washout period between wear periods.</p> <p>There will be a total of 4 visits:<br/> Visit 1: Screening, baseline evaluation and lens fit #1<br/> Visit 2: Follow-up evaluation for first lens<br/> Visit 3: Continuance, lens fit #2<br/> Visit 4: Follow-up evaluation for second lens</p> <p>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).</p> |
| Sample Size                      | <p>This study will enroll approximately a total of 282 subjects, with a target of at least 256 to complete the study (assuming a dropout rate of approximately 10%).</p> <p>The randomization to one of the two sequences (test/control or control/test) will be in a 1:1 ratio and stratified by clinical site.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                   |
| Study Duration                   | <p>Total study duration including the enrollment period (first subject, first visit [FSFV] through last subject, last visit [LSLV]) is anticipated to be approximately 10 weeks. The maximum expected duration of participation for an individual subject will be 27 days.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                         |
| Anticipated Study Population     | <p>Subjects will be habitual soft contact lens wearers with bilateral myopic astigmatism who are between 18 and 39 years of age (inclusive).</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                       |
| eligibility Criteria - Inclusion | <p>Potential subjects must satisfy of all the following criteria to be enrolled in the study.</p> <p>Inclusion Criteria following Screening<br/> The subject must:</p> <ol style="list-style-type: none"> <li>Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.</li> <li>Appear able and willing to adhere to the instructions set forth in this clinical protocol.</li> <li>Be between 18 and 39 (inclusive) years of age at the time of screening.</li> <li>By self-report, habitually wear soft contact lenses in both eyes in a daily reusable or daily disposable wear modality (i.e. not extended wear modality). Habitual wear is defined as a minimum</li> </ol>                                     |

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|----------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
|                                  | <p>of 6 hours of wear per day, for a minimum of 2 days per week during the last 30 days.</p> <p>5. Possess a wearable pair of spectacles that provide correction for distance vision.</p> <p>Inclusion Criteria at Baseline Evaluation<br/> The subject must:</p> <p>6. In both eyes, have astigmatic refractive error suitable for correction with the toric contact lens powers available in this study:</p> <p>a. Sphere powers (DS) -1.50 through -4.00 (inclusive) in 0.25 steps</p> <p>b. Cylinder powers (DC) -0.75 and -1.25</p> <p>c. Axes (°) 170, 180, 10, 80, 90, 100</p> <p>7. Have best corrected monocular distance visual acuity of 20/30 or better in each eye.</p>                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                              |
| Eligibility Criteria – Exclusion | <p>Potential subjects who meet any of the following criteria will be excluded from participating in the study:</p> <p>Exclusion Criteria following Screening<br/> The subject must not:</p> <ol style="list-style-type: none"> <li>1. Be currently pregnant or lactating.</li> <li>2. Be diabetic.</li> <li>3. Be currently using any ocular medications or have an ocular infection of any type.</li> <li>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.</li> <li>5. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g. SynergEyes, SoftPerm) within the past 6 months.</li> <li>6. Be currently wearing monovision or multifocal contact lenses.</li> <li>7. Be currently wearing lenses in an extended wear modality.</li> <li>8. Have a history of strabismus or amblyopia.</li> <li>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.</li> <li>10. Have participated in a contact lens or lens care product clinical trial within 7 days prior to study enrollment.</li> </ol> <p>Exclusion Criteria at Baseline Evaluation<br/> The subject must not:</p> <p>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,</p> |

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|                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
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|                                                            | <p>glaucoma, history of recurrent corneal erosions, aphakia, moderate or above corneal distortion, herpetic keratitis).</p> <p>12. Have fluctuations in vision due to clinically significant dry eye or other ocular conditions.</p> <p>13. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, Photorefractive Keratectomy [PRK], Laser-Assisted in Situ Keratomileusis [LASIK], iridotomy, retinal laser photocoagulation, etc.).</p>             |
| 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.                                                                                                                                                                                                                        |
|                                                            |                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                |
| Microbiology or Other Laboratory Testing                   | None                                                                                                                                                                                                                                                                                                                                                                                                                                                                                                           |
| Study Termination                                          | The occurrence of an Unanticipated Adverse Device Effect (UADE), Unanticipated Serious Adverse Device Effect (USADE), or Serious Adverse Event (SAE) for which a causal relationship to a test article cannot be ruled out, may result in stopping further dispensing of the 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.                                                                                                                                                                                                                                                                                                                                            |
| External Organization(s)                                   | The external organization(s) involved in this study will be listed in the Trial Master File.                                                                                                                                                                                                                                                                                                                                                                                                                   |



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**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                                                       |
| CI                                                                                | Confidence Interval                                                               |
| CLUE                                                                              | Contact Lens User Experience                                                      |
| COM                                                                               | Clinical Operations Manager                                                       |
| CRA                                                                               | Clinical Research Associate                                                       |
| CRF                                                                               | Case Report Form                                                                  |
| CRO                                                                               | Contract Research Organization                                                    |
|  |  |
| D                                                                                 | Diopter                                                                           |
| DMC                                                                               | Data Monitoring Committee                                                         |
| eCRF                                                                              | Electronic Case Report Form                                                       |
| EDC                                                                               | Electronic Data Capture                                                           |
| ESD                                                                               | Eyelid Stabilized Design                                                          |
| ETDRS                                                                             | Early Treatment Diabetic Retinopathy Study                                        |
| FDA                                                                               | Food and Drug Administration                                                      |
| GCP                                                                               | Good Clinical Practice                                                            |
| HEV                                                                               | High Energy Visible                                                               |
| HIPAA                                                                             | Health Insurance Portability and Accountability Act                               |
| HIV                                                                               | Human Immunodeficiency Virus                                                      |
| IB                                                                                | Investigator's Brochure                                                           |
| ICH                                                                               | International Council for Harmonization                                           |
| IEC                                                                               | Independent Ethics Committee                                                      |
| IRB                                                                               | Institutional Review Board                                                        |
| ISO                                                                               | International Organization for Standardization                                    |
| ITT                                                                               | Intention-to-Treat                                                                |
| JJVC                                                                              | Johnson & Johnson Vision Care, Inc.                                               |
| LASIK                                                                             | Laser-Assisted in Situ Keratomileusis                                             |
| 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                                       |
| UV                                                                                | Ultraviolet                                                                       |
| VA                                                                                | Visual Acuity                                                                     |

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**1. INTRODUCTION AND BACKGROUND**

The Acuvue Oasys 1-Day for Astigmatism (AO1DfA) lens is a daily wear, daily disposable toric soft contact lens manufactured in senofilcon A. This lens is currently produced with isopropyl alcohol (IPA) hydration, whereas the spherical counterpart to this lens (ACUVUE® OASYS 1-Day Contact Lenses) is manufactured with propylene glycol (PG) hydration.

The purpose of this study is to validate the safety and efficacy of AO1DfA lenses manufactured on 4GT lines using PG hydration. Legacy AO1DfA lenses manufactured with IPA hydration will be included as a Control.

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

This study will evaluate the AO1DfA lens design produced on 4GT lines using PG hydration. AO1DfA lenses produced using the historically validated process (IPA hydration) will be evaluated as a Control. Further details about the test articles can be found in section 6.1 of this protocol.

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

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

### **2.1. Objectives**

#### **Primary Objectives:**

1. To demonstrate non-inferiority of the investigational test lens compared to the control lens with respect to:
  - High-luminance, high-contrast (HLHC) distance mean visual acuity (VA) [REDACTED]
  - Percentage of eyes achieving lens rotational stability with blinks  $\leq 5^\circ$  [REDACTED]
  - Percentage of eyes achieving absolute rotation  $\leq 10^\circ$  [REDACTED]
2. To demonstrate that the test lens meets the design validation requirements related to safety in terms of:
  - Percentage of eyes with at least one clinically significant (grade 3 or 4) slit-lamp biomicroscopy finding related to wear of the test lens [REDACTED]
  - Percentage of eyes with an acceptable lens fitting for the test lens [REDACTED]

#### **Secondary Objectives:**

To evaluate the difference in subjective vision, handling and comfort scores between test and control lenses following approximately 1-week of wear measured by the Contact Lens User Experience (CLUE™) questionnaire.

### **2.2. Endpoints**

#### **Efficacy Endpoints:**

##### **Co-Primary Efficacy Endpoints**

- Distance (4m) Monocular HLHC logMAR VA  
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.

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- 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, toric lens orientation at least 15 minutes after lens insertion at the dispensing visit is the primary endpoint. Toric lens orientation will be used to define a binary endpoint, i.e. the percentage of eyes that achieve absolute toric lens rotation  $\leq 10^\circ$ . See [REDACTED] in Appendix D for details regarding the collection of absolute toric lens orientation.
- Lens Rotational Stability with Blinks  
Rotational stability is quantified by the amount of rotation measured relative to the scribe mark from the settled position. 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 with blinks assessed at least 15 minutes after lens insertion at the dispensing visit is the primary endpoint. Lens rotational stability with blinks will be defined as a binary endpoint, the percentage of eyes that achieve rotational stability with blinks  $\leq 5^\circ$ . See [REDACTED] in Appendix D for details regarding the collection of lens rotational stability with blinks.

**Secondary Efficacy Endpoints:**

- Subjective overall Comfort scores at 1-week follow-up visit will be assessed using the CLUE questionnaire.
- Subjective Overall Quality of Vision scores at 1-week follow-up visit will be assessed using the CLUE questionnaire.
- Subjective Overall Handling scores at 1-week follow-up visit will be assessed using the CLUE questionnaire.

CLUE™ is a validated, patient-reported outcomes (PRO) 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, for wearers between 18 to 65 years of age. CLUE™ scores are derived using Item Response Theory (IRT) and 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<sup>8</sup>.

**Other Efficacy Endpoint**

Not applicable.

**Safety Endpoints**

**Co-Primary Safety Endpoints:**

- Percentage of eyes with Grade 3 or higher SLFs relating to the test lens

SLFs (Grade 3 or higher) related to study lens wear for the test lens 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.

- Percentage of eyes with acceptable lens fitting while wearing the test lens

Acceptable lens fit will be assessed at all study visits (scheduled and unscheduled) for each subject eye and used to define a binary endpoint, i.e. the percentage of eyes that achieve acceptable lens fit while wearing the test lens. 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;

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- excessive movement on blink in primary gaze.
- insufficient movement in all three of the following conditions: primary gaze, up gaze, and push up test.

See [REDACTED] and [REDACTED] in Appendix D for additional details regarding lens fit assessments.

**Secondary Safety Endpoint**

Not applicable.

**Other Safety Endpoint:**

- Ocular and non-ocular adverse events (AEs)

**2.3. Hypotheses**

Co-Primary Safety Hypotheses:

1. The percentage of eyes with at least one clinically significant slit-lamp finding (Grade 3 or 4) related to the Test lens will be statistically significantly less than 5%.
2. The percentage of eyes with an acceptable Test lens fitting, at the dispensing visit will be statistically significantly better (greater) than 80%.

Co-Primary Efficacy Hypotheses:

1. After approximately 1-week of lens wear, the mean HLHC distance (4 m) visual acuity score of the Test lens will be non-inferior compared to that of the Control lens. A non-inferiority margin of 0.05 logMAR will be used.
2. Following lens settling at the dispensing visit, the percentage of eyes with Test lens rotational stability with blink  $\leq 5^\circ$  will be non-inferior to that of the Control lens. A non-inferiority margin of 10% will be used.
3. Following lens settling at the dispensing visit, the percentage of eyes with Test lens absolute rotation  $\leq 10^\circ$  will be non-inferior to that of the Control lens. A non-inferiority margin of 10% will be used.

**2.4. Criteria of Study Success**

The test lens must demonstrate statistically significant superiority with respect to the percentage of eyes with Grade 3 or higher SLFs, and the percentage of eyes with acceptable lens fitting to satisfy the primary safety objectives.

Additionally, the test lens must demonstrate statistically significant non-inferiority compared to the control lens with respect to distance monocular HLHC logMAR VA, the percentage of eyes with rotational stability with blinks  $\leq 5^\circ$  and the percentage of eyes with absolute rotation  $\leq 10^\circ$  to satisfy the primary efficacy objectives.

**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:

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#### **Inclusion Criteria following Screening**

The subject must:

1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Be between 18 and 39 (inclusive) years of age at the time of screening.
4. By self-report, habitually wear soft contact lenses in both eyes in a daily reusable or daily disposable wear modality (i.e. not extended wear modality). Habitual wear is defined as a minimum of 6 hours of wear per day, for a minimum of 2 days per week during last 30 days.
5. Possess a wearable pair of spectacles that provide correction for distance vision.

#### **Inclusion Criteria at Baseline Evaluation**

6. In both eyes, have astigmatic refractive error suitable for correction with the toric contact lens powers available in this study:
  - a. Sphere powers (DS) -1.50 through -4.00 (inclusive) 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.

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13. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, Photorefractive Keratectomy [PRK], Laser-Assisted in Situ Keratomileusis [LASIK], iridotomy, retinal laser photocoagulation, etc.).

**4. STUDY DESIGN AND RATIONALE**

**4.1. Description of Study Design**

This is a prospective, 4-visit, multi-site, randomized, double-masked, controlled, bilateral wear, dispensing, 2×2 crossover study.

At the initial visit (Visit 1), eligible subjects will be randomized into one of two unique sequences of lens wear (Test/Control or Control/Test). Subjects will wear each study lens bilaterally for approximately 1-week (7±2 days) in a daily disposable modality. Study lenses will be worn bilaterally for a minimum of 8-hours per day for at least 5 days for each wear period. 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.

**4.3. Enrollment Target and Study Duration**

This study has an enrollment target of approximately 282 subjects. It is anticipated that approximately 282 subjects will be randomized to one of two sequences in a 1:1 ratio to achieve at least 256 subjects completing per protocol (assuming a dropout rate of approximately 10%). Subjects who drop-out early may be replaced to ensure that at least 256 subjects complete the study. The study will be conducted at up to approximately 20 clinical sites, where the enrollment target for each site will be approximately 14 subjects per site. A subject will be considered enrolled upon signing of the informed consent form.

There will be 4 visits in total per subject; total study duration is expected to be approximately 10 weeks with an enrollment period of approximately 6 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 database is locked. 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.



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## 6. STUDY INTERVENTION

### 6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

|                                                                                                                                               | Test                                                                | Control                                              |
|-----------------------------------------------------------------------------------------------------------------------------------------------|---------------------------------------------------------------------|------------------------------------------------------|
| Test Article Form                                                                                                                             | Soft contact lens                                                   |                                                      |
| Design / Description                                                                                                                          | Investigational lenses manufactured on 4GT lines using PG hydration | AO1DfA manufactured on 3GT lines using IPA hydration |
| Manufacturer                                                                                                                                  | Johnson & Johnson Vision Care, Inc.                                 |                                                      |
| Packaging Form                                                                                                                                | Blister packaging in sterile packing solution                       |                                                      |
| Packaging Solution                                                                                                                            | Optimized Borate Buffer (OBB) solution                              |                                                      |
| Lens Material                                                                                                                                 | senofilcon A                                                        |                                                      |
| Sphere Powers (DS)                                                                                                                            | -1.50 to -4.00 in 0.25 steps                                        |                                                      |
| Cylinder Powers (DC)                                                                                                                          | -0.75, -1.25                                                        |                                                      |
| Cylinder Axes (°)                                                                                                                             | 10, 80, 90, 100, 170, 180                                           |                                                      |
| Nominal Water Content (%)                                                                                                                     | 41                                                                  |                                                      |
| Nominal Base Curve (mm)                                                                                                                       | 8.5                                                                 |                                                      |
| Lens Diameter (mm)                                                                                                                            | 14.3                                                                |                                                      |
| Fiducial marks                                                                                                                                | 6 and 12 o'clock fiducial lines                                     |                                                      |
| Dk (Fatt method, boundary corrected, edge corrected, $\times 10^{-11}$ [cm <sup>2</sup> /sec] [ml O <sub>2</sub> /ml $\times$ mm Hg] at 35°C) | 103                                                                 |                                                      |
| Modality in Current Study                                                                                                                     | Daily wear                                                          |                                                      |
| Replacement Frequency in Current Study                                                                                                        | Daily disposable                                                    |                                                      |
|                                                                                                                                               |                                                                     |                                                      |

In total, both test and control lenses will be available in 131 unique lens powers (11 sphere powers  $\times$  2 cylinder powers  $\times$  6 axes).

The total number of test lenses to be used in this study (not including lenses that are replaced due to dropage, loss or damage) is expected to be approximately 3,948 lenses (target enrollment of 282 subjects  $\times$  2 eyes per subject  $\times$  7-day wear period). Test and control lenses will be worn in a 1:1 ratio, thus the number of control lenses to be used is expected to be approximately the same (3,948 lenses).

### 6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies

|                           | Non-Preserved Rewetting Drops / Multipurpose Lens Care Solution |                           |                                              |
|---------------------------|-----------------------------------------------------------------|---------------------------|----------------------------------------------|
| Solution Name/Description | Single use Eye-Cept <sup>®</sup> Rewetting Drops                | LacriPure Saline Solution | ScleralFil Preservative Free Saline Solution |

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

■ [REDACTED]

[REDACTED]

[REDACTED]

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[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

[REDACTED]

























  
  


## **8. SUBJECTS COMPLETION/WITHDRAWAL**

### **8.1. Completion Criteria**

Subjects are considered to have completed the study if they:

- provided informed consent.
- they are eligible.
- have not withdrawn/discontinued from the study for any reason described in section 8.2.
- completed all visits through the final visit (*visit 4*).
- If all 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 not meeting the minimum wear time per period as specified in the protocol.
- 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

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If subjects are prematurely discontinued, subject enrollment may continue to meet the intended sample size. Subjects who are discontinued may be replaced at the sponsor's discretion. In cases where a subject is lost to follow-up, every possible effort must be made to contact the subject and determine the reason for discontinuation/withdrawal. The measures taken to follow up must be documented including two written attempts and a certified letter (or equivalent) as the final attempt.

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

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include 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                                   | Irritable bowel syndrome, Parkinson's disease, peptic ulcer, cystitis, nasal congestion, cold symptoms, overactive bladder, COPD | Bentyl, Spiriva, Atrovent, Hyosyne, Levsin, Symax Fastab, Symax SL, Homax SL, Cogentin, Transderm Scop, etc. |
| Beta-blockers                                      | Hypertension, angina, heart attack, migraine, atrial fibrillation, adrenal cancer, essential tumor, glaucoma                     | Toprol XL, Lopressor, Tenormin, Propranolol, Timoptic, Trandate, Inderal LA, etc.                            |
| Psychotropics                                      | Antipsychotic (schizophrenia, mania), antidepression, antiobsessive, antianxiety, mood stabilizer, stimulants (ADHD)             | Zoloft, Celexa, Prozac, Lexapro, Effexor, Cymbalta, Ativan, Xanax, Desyrel, Wellbutrin, etc.                 |
| Vitamin A analogs                                  | Cystic acne                                                                                                                      | Isotretinoin                                                                                                 |

Examples of disallowed systemic antihistamines are given in Table 5. Subjects with a history of taking systemic antihistamines will be allowed to enroll only if:

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

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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, Zyrtec, Astepro, Astelin, Optivar, Allegra, Benadryl, etc. |

## 10. DEVIATIONS FROM THE PROTOCOL

Investigator shall not deviate from the protocol. Investigator will notify study sponsor upon identification of a protocol deviation. Protocol deviations must be reported to the sponsor within 24 hours after discovery of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked, and corrective actions implemented as appropriate.

If it becomes necessary for the Investigator to implement a deviation in order to eliminate an immediate hazard to the trial subject, the Investigator may implement the deviation immediately without notification to the sponsor. Within 24 hours after the implemented deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, to the IEC/IRB.

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

Minor deviations have no substantive effect on subject 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 category                | Major 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 in study procedures                      |
| Unanswered PRO questions          | If 2 or more questions are unanswered for any visit.                                                    | Any 1 PRO question is 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 does not wear study lenses for at least 1 hour prior to attending a follow-up visit. |

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|  |                                                                                |  |
|--|--------------------------------------------------------------------------------|--|
|  | Subject wears their habitual lenses during any of the study lens wear periods. |  |
|--|--------------------------------------------------------------------------------|--|

In 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 cohort review. The list of major deviations with potential impact on the primary endpoint(s) will be flagged separately and used to define the per protocol population.

## **11. STUDY TERMINATION**

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

The occurrence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be ruled out, may result in stopping further dispensing of test article. In the event of a USADE or SAE, the Sponsor may unmask the treatment regimen for the subject(s) and will discuss this with the Investigator before any further subjects are enrolled.

The Sponsor will determine when a study will be stopped. The Principal Investigator always has the discretion to initiate stopping the study based on subject safety or if information indicates the study's results are compromised.

JJVC reserves the right to terminate the study at any time for any reason and will follow the internal applicable quality review process and will notify the IEC/IRB. Additionally, the IEC/IRB reserves the right to terminate the study if an unreasonable risk is determined. The study can be terminated by the Principal Investigator at the individual clinical site due to specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

JJVC (and the IEC/IRB, if applicable) will evaluate all adverse events. If it is determined that an adverse event presents an unreasonable risk, the investigation, or that part of the investigation presenting the risk, will be terminated as soon as possible.

Should the study be terminated (either prematurely or as scheduled), the Investigator will notify the IEC/IRB and Regulatory Authority as required by local regulatory requirements. Sponsor may disqualify a clinical investigator if the clinical investigator has repeatedly or deliberately failed to comply with the protocol, applicable regulatory requirements, or deliberately submitted false information.

## **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:

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- 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 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.<sup>1</sup>

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

1. Was not present prior to the study, but appeared or reappeared following initiation of the study.

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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

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- Blepharitis
- Meibomianitis
- Contact Dermatitis
- Localized Allergic Reactions
- Hordeolum
- 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.

NOTE 3: This includes ‘comparator’ if the comparator is a medical device.

**Serious Adverse Device Effect (SADE)** - Any adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

**Unanticipated Serious Adverse Device Effect (USADE):** serious adverse device effect (SADE) which by its nature, incidence, severity or outcome has not been identified in the current risk assessment. [USADE is synonymous with UADE below from the United States (US) Code of Federal Regulations (CFR)<sup>3</sup>.]

NOTE 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

**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. [UADE is synonymous with USADE above from ISO 14155<sup>1</sup>.]

### **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).
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild, moderate, or severe - see definition).
- 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.

**Causality Assessment** – A determination of the relationship between an adverse event and the test article, study treatment, or the study procedures. The test article, study treatment, or study procedures 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.

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- 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.

**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.

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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 subject 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 EDC System, e-mail, 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 13.2). The report will comment whether the adverse event was considered to be related to the test article, study treatment or study procedures.

#### **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 EDC System, 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.

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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.

#### **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 subject and their fetuses will not be monitored for study related purposes. Pregnant subjects 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 for key analyses to be implemented in this clinical trial is outlined below. All details will be included in the stand-alone Statistical Analysis Plan (SAP). The SAP will be developed and finalized prior to database lock.

Data manipulation, statistical summaries and statistical analyses will be performed using the SAS Software Version 9.4 or higher (SAS Institute, Cary, NC)<sup>10,11</sup>.

. Continuous data will be summarized descriptively by sample size (n), mean, standard deviation (SD), median, minimum (Min) and maximum (Max). Categorical data will be summarized descriptively by frequency count (n) and percentage (%) of subjects or eyes within each category level. Summary tables will be presented over time (Baseline, Fitting, 1-Week follow-up, Unscheduled and Final Evaluations) and study lens type as applicable. The denominator for all percentages will be the number of subjects (or eyes, as applicable) with available data in the lens group under consideration.

Unscheduled visits will be summarized separately and will be excluded from the statistical analysis of efficacy endpoints. However, unscheduled visits will be included in the analysis of safety endpoints.

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**14.3. Analysis Populations**

**Intention-to-Treat (ITT) Population:**

The intention-to-treat population will include all randomized subjects. Subjects will be analyzed as per planned randomized treatment.

**Safety Population:**

All subjects who are administered any investigational product. Subjects will be analyzed as per treatment received.

**Per-Protocol Population:**

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

**14.4. Level of Statistical Significance**

The Type I error rate of the trial will be controlled at 1-sided 0.025 level. As all co-primary safety and efficacy hypothesis tests must show statistical significance simultaneously to meet the statistical success criteria and the study objectives, no multiplicity adjustment of the Type I error rate is required.

**14.5. Missing Data Handling Rules**

Missing values will not be imputed, and all analyses and summaries will be performed using observed case data. The count of missing values will be included in the summary tables and listings.

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## **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 a Siteo EDC system. An authorized data originator will enter study data into the eCRFs using the EDC system. Data collected on equipment that is not captured in EDC will be formatted to the specification of the JJVC database manager and sent to JJVC for analysis.

External data sources for this study include: Not Applicable

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

Edit checks, electronic queries, and audit trails are built into the system to ensure accurate and complete data collection. Data will be transmitted from the clinical site to a secure central database as forms are completed or updated, ensuring information accuracy, security, and confidentiality. After the final database lock, the Investigator will be provided with Individual Patient Profiles (IPP) including the full audit trail on electronic media in PDF format for all of the study data. The IPP must be retained in the study files as a certified copy of the source data for the study.

The content and structure of the eCRFs are compliant with ISO14155.<sup>1</sup>

### **15.2. Subject Record**

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

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

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

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

### **15.3. Trial Registration on ClinicalTrials.gov**

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

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## **16. DATA MANAGEMENT**

### **16.1. Access to Source Data/Document**

The Investigator/Institution will permit trial-related monitoring, audits, IEC/IRB review and regulatory inspection(s) by providing direct access to source data/documents. Should the clinical site be contacted for an audit by an IEC/IRB or regulatory authority, JJVC must be contacted and notified in writing within 24 hours.

### **16.2. Confidentiality of Information**

Information concerning the investigational product and patent application processes, scientific data or other pertinent information is confidential and remains the property of JJVC. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJVC will use information developed in this clinical study in connection with the development of the investigational product and therefore may disclose it as required to other clinical investigators and to regulatory agencies. In order to allow the use of the information derived from this clinical study, the Investigator understands that he/she has an obligation to provide complete test results and all data developed during this study to the Sponsor.

### **16.3. Data Quality Assurance**

Steps will be taken to ensure the accuracy and reliability of data, 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.
- Ensuring the maintenance and calibration of equipment used per standard equipment requirements.

## **18. ETHICAL AND REGULATORY ASPECTS**

### **18.1. Study-Specific Design Considerations**

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

### **18.2. Investigator Responsibility**

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, according to ISO 14155<sup>1</sup> and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64<sup>th</sup> WMA General Assembly 2013<sup>2</sup> 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

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- 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,<sup>2</sup> and ISO 14155<sup>1</sup> guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential 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)<sup>15</sup> in the United States 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:

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

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

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

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:

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

**21. PUBLICATION**

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

[REDACTED]





















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**APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)**  
**ACUVUE® OASYS 1-Day for ASTIGMATISM**







































































































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

Protocol Number and Title: CR-6590 Evaluation of Daily Disposable Toric Soft Lenses Manufactured with an Alternative Hydration Process

Version and Date: 1.0 13 March 2025

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

I agree to conduct this study according to ISO 14155<sup>1</sup>, Declaration of Helsinki<sup>2</sup>, United States (US) Code of Federal Regulations (CFR)<sup>3</sup>, and International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP)<sup>4</sup> 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 subjects.

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

I confirm I am licensed, registered, or certified to provide optometric care to subjects in the state or Country of Study Conduct.

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

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

Principal  
Investigator:

\_\_\_\_\_  
Signature

\_\_\_\_\_  
Date

\_\_\_\_\_  
Name and Professional Position (Printed)

Institution/Site:

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Institution/Site Name

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Institution/Site Address