# Johnson & Johnson Vision

## Clinical Study Protocol

# Evaluating the impact of JJVC senofilcon A – based contact lens with new UV-blocker on day and night driving performance

**Protocol CR-5830**

**Version:** 3.0, Amendment 2.0

**Date:** 14 SEP 2017

Investigational Products: senofilcon A contact lens containing new UV-blocker.

Key Words: ACUVUE OASYS, senofilcon A, daily wear, non-dispensing, day and night driving performance, closed-road driving circuit

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

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## PROTOCOL TITLE, NUMBER, VERSION

Title: Evaluating the impact of JJVC senofilcon A – based contact lens with new UV-blocker on day and night driving performance
Protocol Number: CR-5830
Version: 3.0
Date: 14 SEP 2017

## SPONSOR NAME AND ADDRESS

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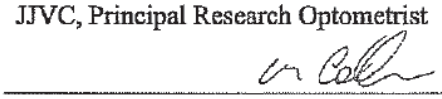
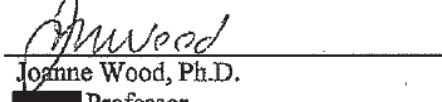
The Medical Monitor must be notified by the clinical institution/site by e-mail, fax, or telephone within 24 hours of learning of a Serious Adverse Event. The Medical Monitor may be contacted during business hours for adverse event questions. General study related questions should be directed towards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

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

## AUTHORIZED SIGNATURES

The signature below constitutes the approval of this protocol and the attachments, and provides the necessary assurances that this trial will be conducted according to all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements and applicable U.S. federal regulations, ICH guidelines, ISO 14155 and the Declaration of Helsinki.

| | | |
|---|---|---|
| Author | See Electronic Signature Report<br>John R. Buch, O.D., M.S.<br>JJVC, Principal Research Optometrist | DATE |
| Co-Author |  <br>Michael Collins, PhD.<br>[redacted] Professor | September 19, 2017<br>DATE |
| Co-Author |  <br>Joanne Wood, Ph.D.<br>[redacted] Professor | Sept 19th, 2017<br>DATE |
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| Reviewer | See Electronic Signature Report<br>Tom Karkkainen, O.D., M.S.<br>JJVC, Sr. Principal Research Optometrist | DATE |
| Independent Review |  <br>Stacy Balk, Ph.D.<br>[redacted] Human Factors Program Manager, Sr. Research Scientist | September 18, 2017<br>DATE |
| Approver | See Electronic Signature Report<br>Zohra Fadli, Ph.D.<br>JJVC, Platform Senior Manager | DATE |

## CHANGE HISTORY

| Version | Originator | Description of Change(s) and Section Number(s) Affected | Date |
|---|---|---|---|
| 1.0 | John R. Buch | Final protocol | 15 JUN 2017 |
| 2.0 | John R. Buch | Updated questions in Appendix A: Patient Reported Outcomes (Study Questionnaires)<br>Minor correction in the Sample Size Justification and Primary Analysis sections<br>Medical Monitor has changed and contact information has been updated | 22 JUN 2017 |
| 3.0 | John R. Buch | S2.2.3: Clarified language surrounding the questionnaire content. Added reference to 2016 CLUE article.<br>Age range updated throughout piece to 20-49 instead of 18-49 due to Australian law for an Open driver's license. | 14 SEP 2017 |

**SYNOPSIS**

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| Protocol Title | Evaluating the impact of JJVC senofilcon A – based contact lens with new UV-blocker on day and night driving performance |
| Sponsor | JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256 |
| Clinical Phase | Development phase, phase 2b |
| Trial Registration | This study will be registered on ClinicalTrials.gov by the Sponsor. |
| Test Article(s) | Investigational Products:<br>• JJVC senofilcon A-based contact lens with new UV-blocker (Test)<br>Predicate Devices:<br>• ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS (Control 1)<br>• ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS worn with Plano Transitions® XTRActive™ – Gray Spectacles (Control 2)<br>Note: for all test conditions the participants will wear the same spectacle frame. For the Test lens and Control 1 lens, the frame will have no spectacle lenses to standardize the experimental methodology for all test conditions. |
| Wear and Replacement Schedules | Wear Schedule: daily wear, single use.<br>Replacement Schedule: Single use. Contact lenses will only be worn during the fitting assessment in the research laboratory and during the closed-road driving assessments (between 1-3 hours of lens wear per session). |

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| Objectives | The objective of this study is to evaluate the effect of JJVC senofilcon A – based contact lens with new UV-blocker on vision and driving performance in both daytime and nighttime lighting under real world driving conditions. This will be achieved through field-based driving studies on a closed-road driving circuit at night and during the day. Quantitative methods will be used to assess vision and driving performance under a range of challenging conditions and appropriate masking, order of testing, randomization and control conditions will be used. |
| Study Endpoints | Primary endpoint: Overall driving performance score.<br><br>Secondary endpoint(s):<br><br>• Low luminance high contrast distance visual acuity distance visual acuity (~1 lux)<br>• Low luminance (~1 lux) contrast threshold<br>• Road sign recognition (percentage)<br>• Percentage of hazards avoidance<br>• Pedestrian recognition distance<br><br>Other Endpoints: Subjective assessment of vision and night driving using a questionnaire, course lap time (in seconds), pupil size, binocular distance visual acuity under high luminance and high/low contrast. |
| Study Design | This is a bilateral, non-dispensing, randomized, partially-masked (subject), four visits, single site,3-period by 3-treatment crossover study. There are 3 levels of randomization in this study. (1) Driving time (Day and Night) (2) Study Lens (Test, Control 1 and Control 2) and (3) driving route (Route 1, Route 2 and Route 3). Hazard and pedestrian locations will be randomized between each route.<br><br>There will be a total of 4 visits:<br><br>1. Visit 1: Screening, preliminary contact lens fit<br>2. Visit 2: Laboratory based measures of binocular visual performance (test and control items)<br>3. Visit 3: Closed circuit on road driving assessment (day or night time based on randomization)<br>4. Visit 4: Closed circuit on road driving assessment (day or night time based on randomization)<br><br>See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations. |

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| Sample Size | Twenty-eight (28) eligible subjects will be enrolled and 24 are targeted to complete the study |
| Study Duration | Three months are allotted from first subject first visit (FSFV) to last subject last visit (LSLV).<br>Per subject:<br>• Visits 1-4 completed within 8 weeks accounting for weather and access to the driving track<br>• Visits 1, 2 and 3 will be separated by at least 24 hours<br>• Visits 3 and 4 will be separated by at least one week |
| Anticipated Study Population | Habitual soft contact lens wearers aged between 20-49 years (of any ethnicity) |
| Inclusion Criteria | Potential subjects must satisfy all of the following criteria to be enrolled in the study:<br>1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form<br>2. Appear able and willing to adhere to the instructions set forth in this clinical protocol<br>3. Between 20 and 49 (inclusive) years of age at the time of screening<br>4. Presbyopic subjects must be habitual wearers of distance vision correction in both eyes.<br>5. The subject's vertex corrected spherical equivalent distance refraction must be in the range of -1.00 through -6.00 D (inclusive) in each eye.<br>6. The subject's refractive cylinder must be ≤ 1.00 D in each eye.<br>7. Have spherocylindrical best corrected visual acuity of 20/20 or better in each eye<br>8. Be a current soft contact lens wearer in both eyes, defined as at least 5 days per week and 6 hours per day averaged over the past 30 days.<br>9. Hold a current Open driver's license<br>10. Be a regular driver (at least once per week)<br>11. Have at least one year of driving experience |

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| Exclusion Criteria | Potential subjects who meet any of the following criteria will be excluded from participating in the study:<br>1. Currently pregnant or lactating<br>2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study<br>3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear, pupil size or accommodation<br>4. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion<br>5. History of binocular vision abnormality or strabismus<br>6. Any current use of ocular medication<br>7. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.)<br>8. Any grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA slit lamp biomicroscopy scale<br>9. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear<br>10. Employee of clinical site (e.g., Investigator, Coordinator, Technician) |
| Disallowed Medications/Interventions | Concomitant medications will be documented during screening and prior to enrollment. Disallowed medications for this study include the use of any medication which might interfere with contact lens wear, alter pupil size or affect accommodation. |

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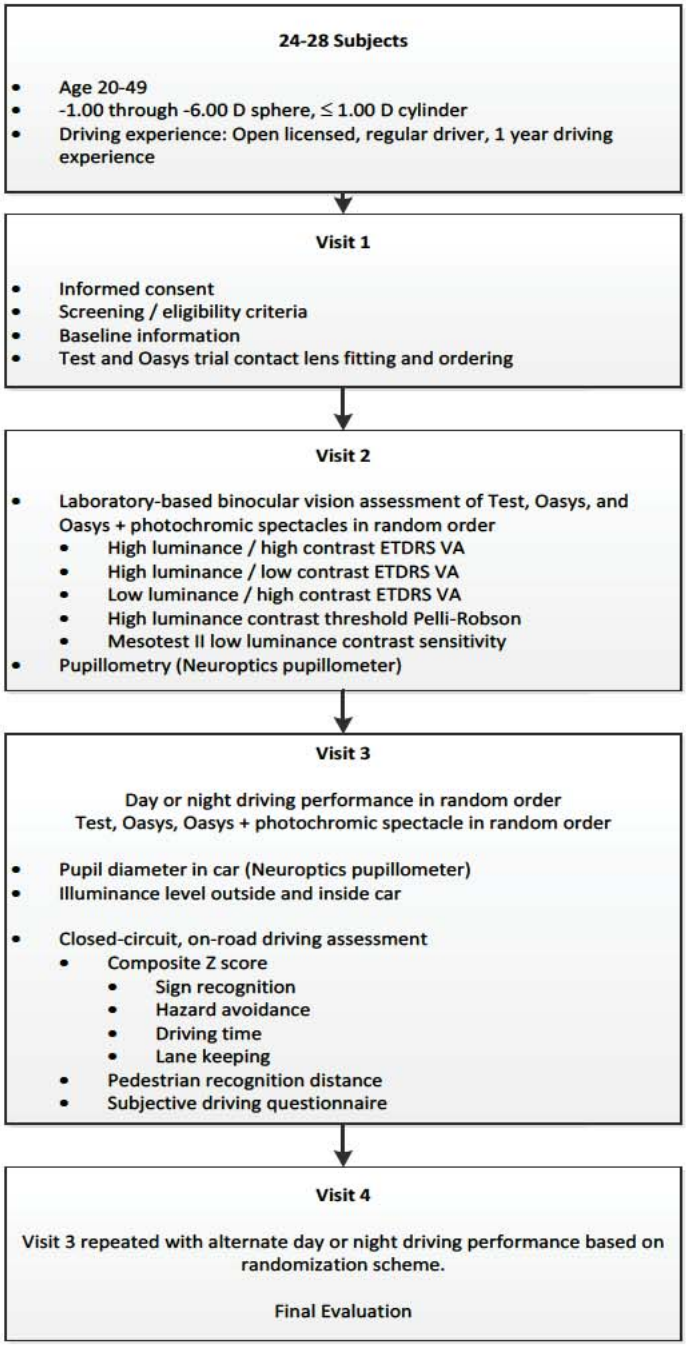
| Measurements and Procedures | The key measurements and procedures associated with the study endpoints are:<br><br>Measures of on road driving performance during day and night times for each of the test and control items. These measures include:<br><br>1. Sign recognition (percentage)<br>2. Hazard avoidance<br>3. Driving lap time<br>4. The composite Z score<br>5. Pedestrian recognition distance<br>6. Subjective questionnaire responses<br>7. Lane keeping<br><br>Other key measurements include laboratory based measures of binocular visual performance including:<br><br>1. High luminance (~500 lux) high contrast (90%) logMAR distance visual acuity<br>2. High luminance (~500 lux) low contrast (10%) logMAR distance visual acuity<br>3. Low luminance (~1 lux) high contrast (90%) logMAR distance visual acuity<br>4. High luminance (~500 lux) contrast threshold (Pelli Robson chart)<br>5. Low luminance (~1 lux) contrast threshold with and without glare (Mesotest II instrument by Oculus, Germany) |
| Microbiology or Other Laboratory Testing | None |
| Study Termination | The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled. |
| Ancillary Supplies/ Study-Specific Materials | Lens Plus OcuPure saline solution |
| Principal Investigator(s) and Study Institution(s)/Site(s) | A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File. |

Figure 1: Study Flowchart



## COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

| | |
|---|---|
| ADD | Plus Power Required for Near Use |
| ADE | Adverse Device Effect |
| AE | Adverse Event/Adverse Experience |
| BCVA | Best Corrected Visual Acuity |
| BSCVA | Best Spectacle Corrected Visual Acuity |
| CFR | Code of Federal Regulations |
| CLUE | Contact Lens User Experience |
| COAS | Complete Ophthalmic Analysis System |
| COM | Clinical Operations Manager |
| CRA | Clinical Research Associate |
| CRF | Case Report Form |
| CRO | Contract Research Organization |
| CT | Center Thickness |
| CTP | Clinical Technical Procedure |
| D | Diopter |
| DMC | Data Monitoring Committee |
| eCRF | Electronic Case Report Form |
| EDC | Electronic Data Capture |
| ETDRS | Early Treatment Diabetic Retinopathy Study |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act |
| HIV | Human Immunodeficiency Virus |
| IB | Investigator's Brochure |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| IDE | Investigational Device Exemption |
| IEC | Independent Ethics Committee |
| IRB | Institutional Review Board |
| ISO | International Organization for Standardization |
| ITT | Intent-to-Treat |
| JJVC | Johnson & Johnson Vision Care, Inc. |
| LASIK | Laser-Assisted in situ Keratomileusis |
| LC | Limbus Center |
| LED | Light-emitting diode |
| LogMAR | Logarithm of Minimal Angle of Resolution |
| Lux | one lumen per square meter |
| MedDRA© | Medical Dictionary for Regulatory Activities |
| MOP | Manual of Procedures |
| NIH | National Institutes of Health |
| OD | Right Eye |
| OHRP | Office for Human Research Protections |
| OHSR | Office for Human Subjects Research |
| OS | Left Eye |
| OU | Both Eyes |

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|---|---|
| PD | Protocol Deviation |
| PHI | Protected Health Information |
| PI | Principal Investigator |
| PIG | Patient Instruction Guide |
| PQC | Product Quality Complaint |
| PRK | Photorefractive Keratectomy |
| PRO | Patient Reported Outcome |
| QA | Quality Assurance |
| QC | Quality Control |
| [redacted] | [redacted] |
| SAE | Serious Adverse Event/Serious Adverse Experience |
| SAP | Statistical Analysis Plan |
| SAS | Statistical Analysis System |
| SD | Standard Deviation |
| SOP | Standard Operating Procedure |
| UADE | Unanticipated Adverse Device Effect |
| USADE | Unanticipated Serious Adverse Device Effect |
| UV | Ultraviolet |
| VA | Visual Acuity |

## 1. INTRODUCTION AND BACKGROUND

There is limited published information regarding the visual problems experienced by normally sighted young people at night, particularly, those experienced in driving at nighttime where light levels are typically mesopic. Under mesopic conditions the pupils dilate, which degrades vision performance through increased higher order aberrations and a larger blur circle diameter on the retina. Lower illumination reduces visual acuity (VA) and contrast sensitivity[1, 2] because in mesopic conditions vision is mediated to a greater extent by rod rather than cone photoreceptors[3].

"Night myopia" also contributes to the reduced acuity experienced in mesopic conditions. This phenomenon is caused by an increase in positive spherical aberration and in the retinal blur area when the pupils are dilated and by a tendency for over-accommodation for far targets (known as dark focus)[3]. As vision relies more on rod photoreceptors in mesopic/scotopic conditions, there is also a shift in the peak spectral sensitivity of the visual system towards shorter wavelengths, which induces a slight relative myopic refractive error shift.

Since any ophthalmic lens that absorbs visible wavelengths will reduce retinal illuminance, it is important to understand the impact of ophthalmic lenses on night vision. This is of particular interest when considering nighttime driving, since the lens could influence driver vision and safety. Photochromic spectacle lenses are designed so that they are relatively clear when exposed to light in the visible spectrum, but become darker when exposed to ultraviolet (UV) wavelengths and some blue wavelengths, arising from sunlight. Since car windscreens have significant UV absorption, the degree of photochromic lens darkening during daytime driving depends on the whether the side windows (or sun roof) are open/closed, the level of sunlight together with the activation spectrum of the photochromic lens. During nighttime driving, the absence of sunlight should cause a photochromic lens to shift to its un-darkened (clear) state. It appears that most automobile headlights have relatively little spectral content in the blue visible or ultraviolet wavelengths[4] and that automobile windscreens would block the vast majority of ultraviolet wavelengths that are emitted by headlights[5]. For these reasons, it is highly unlikely that a photochromic lens would be activated by ambient lighting or headlights when driving at night. On the other hand, any residual visible light absorption by the photochromic lens at night, would potentially diminish the brightness (glare) of oncoming headlights, but could also potentially reduce the visibility of low contrast objects, such as pedestrians.

Road crash fatality rates at night are 2 to 4 times higher than those for daytime driving when adjusted for distances driven[6]. These effects are even more pronounced for fatal crashes involving pedestrians, where nighttime pedestrian fatality rates are up to 7 times higher than those in the day[7]. Analyses of crash statistics clearly indicate that reduced lighting and poor visibility are the primary factors associated with these relatively high fatal crash rates, rather than other factors that vary between day and nighttime, such as driver fatigue and alcohol consumption[8,9].

This study aims to investigate the effect of senofilcon A contact lenses with new UV-blocker on vision and driving performance in both daytime and nighttime lighting under real world driving conditions. This will be achieved through field-based driving studies on a closed-road

driving circuit at night and during the day. Quantitative methods will be used to assess vision and driving performance under a range of challenging conditions and appropriate masking, order of testing randomization and control conditions will be used.

### 1.1. Name and Descriptions of Investigational Products

The investigational product is a senofilcon A-based contact lens containing a new UV-blocker (Test).

The predicate devices are:

- ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS a senofilcon A-based clear contact lens (Control 1)
- ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS worn with Plano Transitions® XTRActive™ – Gray Spectacles (Control 2)

Further details about the test articles are found in Section 6 of this protocol.

### 1.2. Intended Use of Investigational Products

- The intended use of the investigative product is for the correction of refractive error and to reduce the effects of bright lights.
- The intended use of the Control 1 product is for the correction of refractive error.
- The intended use of the Control 2 products for the correction of refractive error and to reduce the effects of bright lights.

During each experimental condition (laboratory testing and on road daytime or nighttime driving), each test and control articles will be worn bilaterally in a daily wear, daily disposable modality for 1-3 hours depending on the duration of testing.

### 1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. [redacted]

### 1.4. Summary of Known Risks and Benefits to Human Subjects

[redacted] has demonstrated a safety and efficacy profile that is non-inferior to commercial products such as ACUVUE® OASYS®. This extends into daytime and nighttime subjective questions.

[redacted]

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

Note: References relevant to the topic at hand are shown here. References cited in sections 1 and 2 are shown in section 22. [redacted]

1. Bullough JD, van Derlofske J, Dee P, Chen J and Akashi Y. (2003) An investigation of headlamp glare: intensity, spectrum and size. US Department of Transportation Report No. DOT HS 809 672.
2. Gruber, N., Mosimann, UP., Muri, RM., & Nef, T. (2013). Vision and night driving abilities of elderly drivers. Traffic Injury Prevention, 14(5), 477-485.
3. Lopez-Gil, N., Peixoto-de-Matos, SC., Thibos, LN., & Gonzalez-Meijome, JM. (2012). Shedding light on night myopia. Journal of Vision, 12(5), 1-9.
4. Moehrle, M., Soballa, M., & Korn, M. (2003). UV exposure in cars. Photodermatology Photoimmunology Photomedicine 19: 175-181.
5. National Highway Traffic Safety Administration (2005). Motor vehicle traffic crash fatality counts and injury estimates for 2004. Washington DC: US Department of Transportation, 2005.
6. Owens, DA., & Sivak, M. (1996). Differentiation of visibility and alcohol as contributors to twilight road fatalities. Human Factors: The Journal of the Human Factors and Ergonomics Society, 38, 680-689.
7. Sullivan, JM., & Flannagan, MJ. (2002). The role of ambient light level in fatal crashes: Inferences from daylight saving time transitions. Accident Analysis and Prevention, 34, 487-498.
8. Sullivan, JM., & Flannagan, MJ. (2007). Determining the potential safety benefit of improved lighting in three pedestrian crash scenarios. Accident Analysis and Prevention, 39, 638-647.
9. Wood, JM., Collins, MJ., Chaparro, A., Marszalek, R., Carberry, T., Lacherez, P., & Chu, BS. (2014). Differential effects of refractive blur on day and nighttime driving performance. Investigative Ophthalmology and Visual Science, 55(4), 2284-2289.

## 2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

### 2.1. Objectives

#### 2.1.1. Primary Objective(s)

The primary objective of this study is to evaluate the effect of JJVC senofilcon A – based contact lens with new UV-blocker on driving performance in nighttime lighting under real world driving conditions by comparison with ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR Plus.

#### 2.1.2. Secondary Objective(s)

The secondary objective is to evaluate the performance of JJVC senofilcon A – based contact lens with new UV-blocker in the following area by comparison with ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR Plus:

- Low luminance high contrast distance visual acuity;
- Low luminance (~1 lux) contrast threshold;
- Road sign recognition;
- Hazards avoidance;
- Pedestrian recognition.

#### 2.1.3. Other Objective(s)

Other objectives include the evaluation of the performance of the Test lens on vision and driving performance in daytime lighting under real world driving conditions by comparison with Control 2.

### 2.2. Endpoints

#### 2.2.1. Primary Endpoint(s)

**Overall driving performance score**

A closed road driving circuit environment will be used to evaluate the effects of the Test lens on night and day time driving performance. This approach involves driving a real vehicle on a closed road circuit (closed to all traffic except [redacted] vehicles), the driving environment can be modified to closely resemble real on-road conditions and safety can be assured. Quantitative methods will be used to assess vision and driving performance under a range of challenging conditions and appropriate masking, order of testing, randomization and control conditions will be used.

Overall driving performance score is a composite score calculated as the mean of the Z-scores of the following six driving measures: average sign recognition distance (in meters), percentage of correctly identified sign (~42 signs), percentage of hazard avoidance/detection (9 hazards), average pedestrian recognition distance (in meters), lane keeping (percentage of time inside the lane) and the inverse of driving lap time (in seconds).). Equal weighting will be assigned to each measure. Where necessary the individual Z scores will be transformed (inverted) such that positive Z scores relate to better performance than the mean. This approach captures participants' performance relative to the group as a whole across conditions and takes into consideration the fact that some tasks may be prioritized over others during driving (Wood JM.; 2002).

Overall driving performance will be calculated for each participant by test article (Test, Control 1 and Control 2) and driving time (day and night).

#### 2.2.2. Secondary Endpoint(s)

**Binocular visual performance:**

The following measurements will be used to assess the performance of the test and control products in a controlled laboratory setting which simulate a wide range of visual conditions encountered while driving.

1. High luminance (~500 lux) high contrast (90%) LogMAR distance visual acuity
2. High luminance (~500 lux) low contrast (10%) LogMAR distance visual acuity
3. Low luminance (~1 lux) high contrast (90%) LogMAR distance visual acuity
4. High luminance (~500 lux) contrast threshold (Pelli-Robson chart)
5. Low luminance (~1 lux) contrast threshold (Mesotest II instrument by Oculus, Germany)

The order of the vision tests will be randomized for each condition. The ETDRS logMAR chart will be used, which is scored on a letter by letter basis (-0.02 log units per letter correctly identified). A number of different EDTRS charts will be used to reduce potential learning effects. Letter contrast sensitivity will also be determined binocularly using the Pelli-Robson chart, scored on a letter by letter basis (0.05 log units per each letter correctly identified). The ETDRS logMAR chart and the Pelli-Robson contrast sensitivity chart are validated techniques routinely used in research to accurately quantify visual performance. Room illuminance will be controlled using dimmer switches and quantified using a lux meter.

There will be two secondary endpoints considered from binocular visual performance evaluation:

- Low luminance ~1 lux) high contrast (90%) distance visual acuity
- Low luminance (~1 lux) contrast threshold

During low luminance contrast threshold evaluation, five Landolt C targets in random orientation will be presented for each of four contrast levels 95%, 80%, 63% and 50%. Participants will be asked to correctly identify the orientation of the Landolt C. The number of correct response will be recorded for each contrast level. This entire test will be done with and without the presence of a glare source.

**Sign recognition (percentage)**

Participants will be instructed to report the identity of a percentage of the standard road signs (typically about 42 signs dependent on the route travelled) containing about 65 items of information as they drive around the circuit. We will also measure the recognition distance using the in-vehicle measurement system for one specific road sign while the participant is driving.

**Hazard avoidance:**

Participants will be required to report and avoid hitting any of nine large, low contrast grey foam “hazards” (220 cm x 80 cm x 15 cm) positioned orthogonally in the driving lane along the roadway, the locations of which will be randomized between trials.

**Pedestrian recognition distance:**

The in-vehicle measurement system will be utilized to determine the distance at which the participant (as a driver) first recognizes the presence of two pedestrians positioned at the side of the road. An experimenter will act as the pedestrian and “walk in-place” at the end of a 400 m straight section of roadway which starts and finishes at approximately the same elevation, but features a dip halfway along its length. The pedestrian will not be surrounded by any visual clutter or lighting. To reduce expectancy effects, a series of four flashing LEDs and four retro-reflective bollards will be positioned around the circuit to increase the instances of flashing

lights and retro-reflective material being presented to the driver. Figure 2 shows an example of a low contrast hazard (grey foam) in the driving lane in front of some retroreflective bollards and signage.

**Figure 2**
Example of low contrast hazards (grey foam) in driving lane

On each lap the pedestrian will walk in place as the test vehicle approaches, facing directly towards the oncoming vehicle; this allows for the inclusion of naturalistic motion and ensures the safety of the pedestrian. The pedestrian will wear biomotion reflective strips on the moveable joints, which has been shown to be a configuration that allows good discrimination between different levels of spherical blur[2].

The main dependent variable is the driver's response distance to the pedestrian which is defined as the distance from the test vehicle to the pedestrian at that moment when the response button is pressed to indicate recognition of the presence of the pedestrian at the side of the road.

#### 2.2.3. Other Endpoints

**Subjective assessment of vision and night driving using a questionnaire:**

Participants will be asked to provide subjective responses to a series of questions for the night and day driving conditions. The subject is asked to provide a rating on 5-point scale (strongly agree to strongly disagree) following the testing of each condition.

For example:

How much difficulty did you have for the following driving tasks, specifically for the drive you just completed?

- Reading the street signs
- Accurately judging the distance to turn offs
- Seeing pedestrians or animals on the road side
- Seeing road hazards (low contrast bumps) on the road in time to avoid them
- Keeping in your lane

This questionnaire contains items from recently published work[12]. The daytime questionnaire will be the same as the nighttime questionnaire with the omission of the "I noticed a glare effect in dim light" question that is not applicable.

**High luminance binocular visual performance:**

This includes the following endpoints:

1. High luminance (~500 lux) high contrast (90%) logMAR distance visual acuity
2. High luminance (~500 lux) low contrast (10%) logMAR distance visual acuity
3. High luminance (~500 lux) contrast threshold (Pelli-Robson chart)

See more details in section 2.2.2 above

**Pupil diameter**

The right eye pupil diameter of each participant will be measured both in the research laboratory and in the research vehicle at the closed road circuit using a NeurOptics VIP-200 Pupillometer (Irvine, CA, USA). Three measurements will be taken and the average recorded.

In the research laboratory, the right pupil diameter of the participant will be measured with the Test and control contact lenses. Note that the measurement cannot be taken through spectacles, so the OASYS + Transitions Spectacles pupil diameter cannot be collected. The measurements will be conducted in the following conditions:

1. High luminance (~500 lux room illuminance) while viewing a distant target
2. Low luminance (~1 lux room illuminance) while viewing a distant target

The average pupil diameter of the right eye will also be determined from 3 measures obtained while participants are seated in the research vehicle at the closed road circuit for each condition of driver assessment (i.e. the test and control contact lens product under nighttime and daytime conditions).

**Lighting levels**

Ambient light levels at the driving track will be measured during each day and night driving session using custom-designed in-vehicle measurement systems. A standard location on the track will be chosen for all measurements and we will measure ambient illuminance (lux) at

the horizontal plane outside the car and will measure illuminance at the plane of the eye inside the car, with the illuminance probe facing horizontally along the road.

### 2.3. Hypotheses

#### 2.3.1. Primary Hypotheses

The Test lens will be non-inferior to the Control 1 lens with respect to overall night driving performance. A non-inferiority margin of -0.25 will be used.

#### 2.3.2. Secondary Hypotheses

1. The Test lens will be non-inferior to the Control 1 lens with respect to binocular low luminance high contrast visual acuity. A non-inferiority margin of 0.1 LogMAR will be used
2. The Test lens will be no different than the Control 1 with respect to low luminance low contrast threshold without glare.
3. The Test lens will be no different than Control 1 with respect to the percentage of roads signs correctly identified at night driving.
4. The Test lens will be no different to Control 1with respect to the average distance to correctly identify a pre-determined road sign at night driving.
5. The Test lens will be no different than the Control 1 with respect to the percentage of hazards avoidance at night driving.
6. The Test lens will be no different than the Control 1 with respect to average pedestrian recognition distance at night driving.

## 3. TARGETED STUDY POPULATION

### 3.1. General Characteristics

Participants will consist of Open licensed drivers (aged 20-49 years) with more than one year of driving experience. Participants must be regular drivers with best-corrected monocular visual acuity of 20/20 (logMAR 0.00) or better in each eye. Participants must be regular soft contact lens wearers with refractive errors within the range of available study contact lenses supplied by JJVC with uncorrected astigmatism of no more than 1.00 DC.

### 3.2. Inclusion Criteria

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

1. The subject must 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. Between 20 and 49 (inclusive) years of age at the time of screening
4. Presbyopic subjects must be habitual wearers of distance vision correction in both eyes.

5. The subject's vertex corrected spherical equivalent distance refraction must be in the range of -1.00 through -6.00 D (inclusive) in each eye
6. The subject's refractive cylinder must be ≤ 1.00 D in each eye.
7. Have spherocylindrical best corrected visual acuity of 20/20 or better in each eye
8. Be a current soft contact lens wearer in both eyes, defined as at least 5 days per week and 6 hours per day averaged over the past 30 days.
9. Hold a current Open driver's license
10. Be a regular driver (at least once per week)
11. Have at least one year of driving experience

### 3.3. Exclusion Criteria

Potential subjects who meet any of the following criteria will be excluded from participating in the study:

1. Currently pregnant or lactating
2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study
3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear, pupil size or accommodation
4. Any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion
5. History of binocular vision abnormality or strabismus
6. Any current use of ocular medication
7. Any previous, or planned (during the course of the study) ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.)
8. Any grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA slit lamp biomicroscopy scale
9. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear
10. Employee of clinical site (e.g., Investigator, Coordinator, Technician)

### 3.4. Enrollment Strategy

Study subjects will be recruited from the Institution/clinical site's subject database and/or utilizing Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approved materials.

## 4. STUDY DESIGN AND RATIONALE

### 4.1. Description of Study Design

This is a one site, 4-visit, randomized crossover, bilateral dispensing clinical trial. Approximately 28 eligible subjects will be screened and enrolled to ensure a sample size of 24 after subjects who withdraw or are lost-to-follow-up.

The study begins with an Initial Visit (Visit 1). If a subject is found to meet all eligibility criteria, he/she will be scheduled for the next visit; otherwise, the subject will be deemed ineligible for this study.

At Visit 2, eligible subjects will be randomized and laboratory testing will be conducted on all test articles in a random order based on the randomization scheme. Subjective assessment of driving performance in both daytime and nighttime will be performed in a random order, based on the randomization scheme, in two different visits at Visit 3 and Visit 4. Unscheduled follow-up visits may occur during the study. The planned duration of lens wear is for the experimental procedures only (between 1-3 hours during visits 2-4). Participants will not have access to test articles at study closure.

### 4.2. Study Design Rationale

Crossover designs are a well-established study design in which subjects are exposed to multiple treatments during different time periods. This design was considered to reduce the influence of potential confounding factors such as age, gender, vision correction and driving performance. A washout period of 20 minutes or more between driving assessments is built in from the 15-minute lens settling time and the 5-minute acclimation inside the car. This will help reduce any potential carry-over effect. Since subjects will be performing the same task repeatedly driving track conditions are randomized for each test article in order to further reduce any potential bias.

### 4.3. Enrollment Target and Study Duration

- Approximately 28 subjects will be recruited for screening, with a target sample size of 24 subjects to complete the study
- Study enrollment is defined as the execution of informed consent
- The study will involve 4 visits and the study duration will be approximately 3 months, with an enrollment period of 1 month. Each subject will complete the study within 8 weeks, depending on weather and access to the driving track. Visits 1-3 will be separated by at least 24 hours, while visits 3-4 will be separated by at least 1 week.

4.4. **Site Selection**

[redacted] It is used extensively by Queensland University of Technology (QUT) researchers/experimenters in previous vision and driving studies. The center represents rural roads that include hills, bends, curves, intersections, lengthy straight sections and standard road signs and driving lane markings. [redacted]

## 5. TEST ARTICLE ALLOCATION AND MASKING

5.1. **Test Article Allocation**

Participants will wear all study lenses in a bilateral fashion. There will be three levels of randomization in this study: (1) Sequence of driving time (Day and Night) (2) Sequence of lens wear (Test, Control1 and Control2) and (3) Driving Route (A, B, C). Hazard and pedestrian locations will be randomized for each driving route.

Subjects will be first randomly assigned to one of two possible driving time sequences (Day/Night and Night/Day) using a 2x2 crossover design. Within each driving time (Day and Night) subjects will be randomly assigned to one of six possible lens wear sequences using a 3x3 Williams crossover design:

Table 1: 3x3 Williams design

| Sequence | Period1 | Period 2 | Period 3 |
|---|---|---|---|
| 1 | Test | Control 1 | Control 2 |
| 2 | Test | Control 2 | Control 1 |
| 3 | Control 1 | Test | Control 2 |
| 4 | Control 1 | Control 2 | Test |
| 5 | Control 2 | Test | Control 1 |
| 6 | Control 2 | Control 1 | Test |

This design is balanced with respect to first carry-over effect as every treatment follows every other treatment the same number of times.

Within each time and lens type combination subjects will be randomized to a driving route (Route1, Route2 and Route3) to further reduce the potential for treatment bias. The randomization scheme will be generated using the PROC PLAN procedure form SAS Software Version 9.4 or higher (SAS Institute, Cary, NC). The study site must follow the randomization scheme provided and complete enrollment according to the randomization list and not pre-select or assign subjects.

### 5.2. **Masking**

Every effort will be made to mask both the subject and the investigator, in order reduce potential bias where possible. Subjects will be masked to the identity of the investigational product when only a contact lens correction is worn. However, if subjects perceive a change in light levels during Test contact lens wear, they may become aware of the product being tested.

Subjects will also be aware of the test condition when the ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS is worn with Transitions® XTRActive™ – Gray Spectacles (Control 2) as the other test conditions will involve contact lens wear with a spectacle frame without spectacle lenses.

Investigators involved in the on-road driving data collection (clinical personnel within the vehicle) will be partially-masked as to the identity of the investigational product (i.e. another investigator will fit the contact lenses prior to the driving assessment).

### 5.3. **Procedures for Maintaining and Breaking Randomization Codes**

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

## 6. STUDY INTERVENTION

### 6.1. **Identity of Test Articles**

The following contact lenses will be used in this study:

Table 2: Test Articles

| | Test | Control 1 | Control 2 |
|---|---|---|---|
| Name | Senofilcon A-based contact lens with new UV-blocker (worn with spectacle frame without lenses) | ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS (worn with spectacle frame without lenses) | ACUVUE® OASYS® Brand Contact Lenses with HYDRACLEAR® PLUS worn Transitions® XTRActive™ – Gray Spectacles |
| Manufacturer | JJVC | JJVC | JJVC / TOI |

| | Test | Control 1 | Control 2 |
|---|---|---|---|
| Compass Protocol(s) and/or Lot Number or Other Identifier | [redacted] | Commercial ACUVUE OASYS | Commercial ACUVUE OASYS and plano Transitions spectacles |
| Lens Material | Senofilcon A | Senofilcon A | Senofilcon A XTRActive |
| Nominal Base Curve @ 22 °C | 8.4 | 8.4 | 8.4 |
| Nominal Diameter @ 22 °C | 14.0 | 14.0 | 14.0 |
| Nominal Distance Powers (D) | -1.00 through -6.00 | -1.00 through -6.00 | -1.00 through -6.00 |
| Oxygen Permeability (Dk) | ~ 103 | ~ 103 | ~ 103 |
| Modality in Current Study | Daily wear | Daily wear | Daily wear |
| Replacement Frequency | Single use | Single use | Single use |
| Packaging Form (vial, blister, etc.) | Blister | Blister | Blister |
| Other distinguishing items | NA | NA | See spectacle table below |

Approximately 30 Test lenses per sku will be needed for Visits 1, 2, 3 and 4. Since OASYS will be worn twice at each of these visits, approximately 60 control lenses per sku will be needed. Additional lenses may be shipped to cover any lenses lost, damaged, or heavy concentration on a particular power.

Examples of the spectacle frames are shown. The polycarbonate lenses will be 0.00 D in power and will contain the XTRActive photochromic agent from Transitions Optical Inc. The lenses will not contain an anti-reflective coating for a more valid comparison to the contact lenses. Half of the frames will have no lenses whatsoever and will be worn during the Test and OASYS trials to keep frame awareness the same as during the OASYS + photochromic spectacle trial.

| Small unisex frames<br>• 2 with 0.00 D XTRActive lenses<br>• 2 with no lenses | Medium unisex frames<br>• 2 with 0.00 D XTRActive lenses<br>• 2 with no lenses | Large unisex frames<br>• 2 with 0.00 D XTRActive lenses<br>• 2 with no lenses |
|---|---|---|
|  |  |  |

### 6.2. Ancillary Supplies/Products

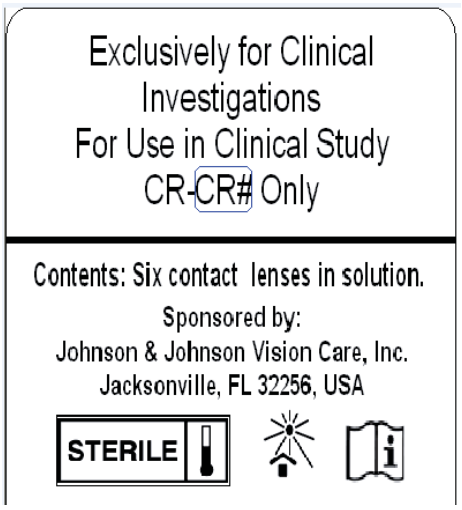
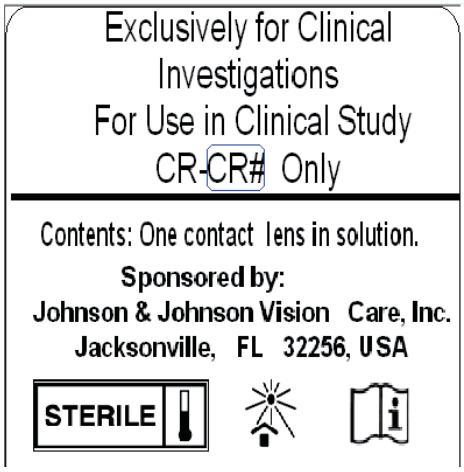
This is a non-dispensing study. No contact lens care solutions are required. The use of Lens Plus OcuPure saline solution for rinsing the lenses and the use of preservative-free rewetting drops is permitted as needed.

### 6.3. Administration of Test Articles

Test articles will be worn by the subjects for the duration of the testing sessions. Subjects must meet all eligibility requirements set forth in this clinical protocol to be fit with the lenses.

### 6.4. Packaging and Labeling

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

| Control Lens Label | Test Lens Label |
|---|---|
|  |  |

### 6.5. Storage Conditions

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

### 6.6. Collection and Storage of Samples

No samples will be collected as part of the study procedures. When possible, any lens or test article associated with an Adverse Events and/or a Product Quality Complaint must be retained and stored in a glass vial with moderate solution pending directions from the sponsor for potential return to JJVC.

### 6.7. Accountability of Test Articles

JJVC will provide the Investigator with sufficient quantities of study articles and supplies to complete the investigation. The Investigator is asked to retain all lens shipment documentation for the test article accountability records.

Test article must be kept in a locked storage cabinet, accessible only to those assigned by the Investigator for dispensing. The Investigator may delegate this activity to authorized study site personnel listed on the Site Delegation Log. All test articles must be accounted. This includes:

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

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

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

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

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

## 7. STUDY EVALUATIONS

### 7.1. Time and Event Schedule

Table 3: Time and Events

| Visit Information | Visit 1 Screening, Contact lens fit | Visit 2 Laboratory measurements | Visit 3 Closed track day/night time driving | Visit 4 Closed track day/night time driving |
|---|---|---|---|---|
| Time Point | Day 1 | > 24 hours after Visit 1 | > 24 hours after Visit 2 | > 1 week after Visit 3 |
| Estimated Visit Duration | 1 hour | 1.5 hours | 2.5 hours | 2.5 hours |
| Statement of Informed Consent | X | | | |
| Demographics | X | | | |
| Medical History/Concomitant Medications | X | | | |
| Inclusion/Exclusion Criteria | X | | | |
| Habitual Contact Lens Information | X | | | |
| Compliance and Subject Reported Ocular Symptoms and Adverse Event Review | X | | | |
| Entrance Snellen Distance Visual Acuity | X | X | | |
| Subjective Sphero-Cylindrical Refraction | X | | | |
| Subjective Best Sphere Refraction | X | | | |
| Slit Lamp Classification Scale | X | X | | |
| Lens Insertion & Settling | X | X | X | X |
| Lens Fit Assessment | X | X | | |
| Order required lenses | X | | | |
| Visual acuity measurements | X | X | | |

| Visit Information | Visit 1 Screening, Contact lens fit | Visit 2 Laboratory measurements | Visit 3 Closed track day/night time driving | Visit 4 Closed track day/night time driving |
|---|---|---|---|---|
| Time Point | Day 1 | > 24 hours after Visit 1 | > 24 hours after Visit 2 | > 1 week after Visit 3 |
| Estimated Visit Duration | 1 hour | 1.5 hours | 2.5 hours | 2.5 hours |
| Contrast sensitivity measurements | | X | | |
| Pupillometry | | X | X | X |
| Post lens wear slit lamp evaluation | X | X | | |
| Measurement of illuminance levels | | | X | X |
| On road driving assessment | | | X | X |
| Subjective driving questionnaires | | | X | X |
| Study completion | | | | X |

7.2. **Detailed Study Procedures**

**VISIT 1**

| Visit 1: Screening | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.1 | Statement of Informed Consent | Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form.<br>**Note**: The subject must be provided a signed copy of this document. | [redacted] |
| 1.2 | Demographics | Record the subject's date of birth, gender, race and ethnicity. | |
| 1.3 | Medical History and Concomitant Medications | Questions regarding the subjects' medical history and concomitant medications. | |
| 1.4 | Habitual Lenses | Questions regarding the subject's habitual lens type and parameters. | |
| 1.5 | Iris Color | The investigator will record the subject's iris color based on the scale provided. | Appendix E |

| Visit 1: Screening | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.6 | Eligibility after Screening | All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible. | |

| Visit 1: Baseline | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.7 | Entrance Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br><br>EDC: record logMAR acuity | |
| 1.8 | Subjective Sphero-cylindrical Refraction | Complete subjective spherocylindrical refraction and record the resultant distance logMAR visual acuity (OD, OS and OU) to the nearest letter. | [redacted] |
| 1.9 | Subjective Best Sphere Refraction | Perform subjective best sphere refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance logMAR visual acuity (OD, OS, OU) to the nearest letter.<br><br>**Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leave the red chart sharper. | [redacted] |

| Visit 1: Baseline | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.10 | Slit Lamp Findings | FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility.<br><br>If any of these slit lamp findings are grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to determine eligibility. If discontinued a final examination must be completed.<br><br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 1.11 | Eligibility after Baseline | All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible. | |

| Visit 1: Trial Lens Fitting 1 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.12 | Lens Selection | Select the trial contact lens based on the randomization scheme.<br><br>Select the trial contact lens power based on subjective best sphere refraction. | |
| 1.13 | Lens Insertion | The Investigator or the subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable. | |
| 1.14 | Lens Settling | Allow the study lenses to settle for a minimum of 15 minutes. A Patient Instruction Guide will be provided to the subject. | |

| Visit 1: Trial Lens Fitting 1 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.15 | Subjective Best Sphere Over Refraction | Perform subjective best sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance logMAR visual acuity to the nearest letter (OD, OS, OU).<br><br>**Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leave the red chart sharper. | [redacted] |
| 1.16 | Lens Power Modification (if applicable) | Adjust the lens power if the subject's best sphere over-refraction is not plano.<br><br>For each power modification, repeat steps (1.13 - 1.16).<br><br>One power modification is allowed. | |
| 1.17 | Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with the study contact lenses in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br><br>EDC: record logMAR acuity | |
| 1.18 | Subjective Lens Fit Assessment | Subjective Assessment of the Lens Fit. If the fit is graded as unacceptable based on the criteria below, then the subject is discontinued from the study and will be replaced.<br><br>1. Limbal exposure in any gaze<br>2. Edge lift<br>3. Insufficient and/or excessive movement in all three movement categories | [redacted] |

| Visit 1: Trial Lens Fitting 1 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.19 | Continuance | For the subject to continue in the study, they must meet all three of the following criteria:<br>1. Visual acuity is 0.1 logMAR (20/25) or better OD and OS<br>2. The lens fit is acceptable OD and OS<br>3. Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject. | |
| 1.20 | Lens removal | The study lens will be removed and discarded. | |

| Visit 1: Trial Lens Fitting 2 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.21 | Lens Selection | Select the alternate trial contact lens based on the randomization scheme.<br>Select the trial contact lens power based on subjective best sphere refraction. | |
| 1.22 | Lens Insertion | The Investigator or the subject inserts the study lenses. Record the time of lens insertion.<br>Check for lens damage under the slit lamp before proceeding with lens settling.<br>Replace damaged lenses if applicable. | |
| 1.23 | Lens Settling | Allow the study lenses to settle for a minimum of 15 minutes. | |

| Visit 1: Trial Lens Fitting 2 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.24 | Subjective Best Sphere Over Refraction | Perform subjective best sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance logMAR visual acuity to the nearest letter (OD, OS, OU).<br><br>**Note**: The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leave the red chart sharper. | [redacted] |
| 1.25 | Lens Power Modification (if applicable) | Adjust the lens power if the subject's best sphere over-refraction is not plano.<br><br>For each power modification, repeat steps (1.21 - 1.24).<br><br>One power modification is allowed. | |
| 1.26 | Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with the study contact lenses in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br><br>EDC: record logMAR acuity | |
| 1.27 | Subjective Lens Fit Assessment | Subjective Assessment of the Lens Fit. If the fit is graded as unacceptable based on the criteria below, then the subject is discontinued from the study and will be replaced.<br><br>1. Limbal exposure in any gaze<br>2. Edge lift<br>3. Insufficient and/or excessive movement in all three movement categories | [redacted] |

| Visit 1: Trial Lens Fitting 2 | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.28 | Continuance | For the subject to continue in the study, they must meet all three of the following criteria:<br>1. Visual acuity is 0.1 logMAR (20/25) or better OD and OS<br>2. The lens fit is acceptable OD and OS<br>3. Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject. | |
| 1.29 | Lens Removal | The study lens will be removed and discarded. | |
| 1.30 | Exit Slit Lamp Biomicroscopy | FDA Slit Lamp Classification Scale will be used to grade the findings.<br>If any of these slit lamp findings are grade 3 or higher, the subject is classified as having an adverse event. Adverse events shall be documented and followed until resolved, at which time they will be terminated from the study.<br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 1.31 | Exit Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |

**VISIT 2**

| Visit 2: Laboratory measures of vision performance | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.1. | Adverse Events and Concomitant Medications Review | Review the subject's concomitant medications and record any changes from the previous study visit.<br>Record any adverse events or medical history changes from the previous study visit. | |
| 2.2. | Entrance Visual Acuity | Record subjects' distance logMAR visual acuity, OD, OS and OU to the nearest letter with habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |
| 2.3. | Slit Lamp Findings | FDA Slit Lamp Classification Scale will be used to grade the findings.<br>If any of these slit lamp findings are grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to continue. If discontinued a final examination must be completed.<br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 2.4. | Continuance | Confirm that the entrance slit lamp findings are grade 2 or less. | |
| 2.5. | Randomization | Refer to pre-determined randomization order of testing (counter balancing) for the three test treatments. The final contact lens powers found in Visit 1 will be used.<br>• Test contact lenses with lens-less spectacle frame<br>• OASYS clear contact lenses with lens-less spectacle frame<br>• OASYS clear contact lenses worn with photochromic spectacles | |

| Visit 2: Laboratory measures of vision performance | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.6. | Lens Insertion | The Investigator or the subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable. | |
| 2.7. | Lens Settling | Allow the study lenses to settle for a minimum of 15 minutes. | |
| 2.8. | Pupillometry | Measure the right eye pupil diameter during distance fixation (3 measures) using NeurOptics Pupillometer.<br>EDC: record pupil diameters in mm (0.1 mm increments) | |
| 2.9. | Distance ETDRS LogMAR Visual Acuity | Perform binocular (OU) distance ETDRS logMAR visual acuity test at a 4-meter distance under the following conditions with the study lenses on. The charts will be rotated during testing to reduce memorization.<br>1. Bright illumination (~500 lux)<br>A. High contrast (90%) chart<br>B. Low contrast (10%) chart<br>2. Dim illumination (~1 lux)<br>A. High contrast (90%) chart | [redacted] |
| 2.10. | Contrast Sensitivity Bright Illumination | Perform binocular (OU) contrast sensitivity test under the following conditions with the study lenses on. The Pelli Robson charts will be rotated to reduce memorization.<br>1. Bright illumination (~500 lux)<br>A. Pelli-Robson chart at 3 meters<br>EDC: record log contrast sensitivity | |

| Visit 2: Laboratory measures of vision performance | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.11. | Contrast Sensitivity Dim Illumination | Perform binocular (OU) contrast sensitivity test under the following conditions with the study lenses on. The Pelli Robson charts will be rotated to reduce memorization.<br>1. Dim illumination (< ~1 lux)<br>A. Mesotest II instrument<br>B. With glare and without glare<br>C. 4 contrast levels + 5 Landolt C targets per contrast level<br>EDC: record the total targets correctly identified with glare and without glare | |
| 2.12. | Lens Removal | The study lenses will be removed and discarded. A fresh pair of lenses will be used for each trial. | |
| 2.13. | Vison and lens assessments | Repeat 2.5 to 2.12 for the other two treatment conditions | |
| 2.14. | Exit Slit Lamp Biomicroscopy | FDA Slit Lamp Classification Scale will be used to grade the findings.<br>If any of these slit lamp findings are grade 3 or higher, the subject is classified as having an adverse event. Adverse events shall be documented and followed until resolved, at which time they will be terminated from the study.<br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 2.15. | Exit Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |

**VISIT 3**

| Visit 3: Closed-circuit on-road driving performance 1 (Day/night condition based on randomization) | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.1. | Adverse Events and Concomitant Medications Review | Review the subject's concomitant medications and record any changes from the previous study visit.<br>Record any adverse events or medical history changes from the previous study visit. | |
| 3.2. | Practice Driving Lap | Perform familiarization driving lap in habitual spectacle correction in opposite direction to test laps | |
| 3.3. | Entrance Visual Acuity | Record subjects' distance logMAR visual acuity, OD, OS and OU to the nearest letter with habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |
| 3.4. | Entrance Slit Lamp Findings | FDA Slit Lamp Classification Scale will be used to grade the findings.<br>If any of these slit lamp findings are grade 3 or higher, the subject may not continue at this time, but may return up to one additional time to continue. If discontinued a final examination must be completed.<br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 3.5. | Continuance | Confirm that the entrance slit lamp findings are grade 2 or less. | |

| Visit 3: Closed-circuit on-road driving performance 1 (Day/night condition based on randomization) | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.6. | Randomization | Refer to pre-determined randomization order of testing (counter balancing) for the three test treatments. The final contact lens powers found in Visit 1 will be used.<br>• Test contact lenses (worn with spectacle frame without lenses)<br>• OASYS clear contact lenses (worn with spectacle frame without lenses)<br>• OASYS clear contact lenses (worn with photochromic spectacles) | |
| 3.7. | Lens Insertion | The Investigator or the subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable. | |
| 3.8. | Lens Settling | Allow the study lenses to settle for a minimum of 15 minutes.<br>Note: for nighttime testing, sufficient time is allowed for the subject to dark adapt. | |
| 3.9. | Pupillometry | Measure the right eye pupil diameter during distance fixation (3 measures) using NeurOptics Pupillometer while subject seated in vehicle.<br>EDC: record pupil diameters in mm (0.1 mm increments) | |
| 3.10. | Illuminance levels | Measurement of lighting level on the track outside the vehicle and at the plane of the eye in the vehicle.<br>• For daytime testing, the illuminance must be > 1000 lux.<br>• For nighttime testing, the illuminance must be < 10 lux.<br>EDC: record outside and inside illuminance in lux rounded to the nearest whole number. | |

| Visit 3: Closed-circuit on-road driving performance 1 (Day/night condition based on randomization) | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.11. | Driving assessment | Subject performs three laps of the circuit while under assessment. Measurements recorded include:<br>1. Sign recognition<br>a. EDC: record % signs correctly identified<br>b. EDC: record distance to signs in meters<br>2. Hazard avoidance<br>a. EDC: record % hazards hit<br>3. Driving time<br>a. EDC: record lap time in seconds<br>b. EDC: record the % time in wrong lane<br>4. Pedestrian recognition distance<br>a. EDC: record distance to recognition in meters<br>A composite driving Z score will be calculated afterwards using measures listed above. | |
| 3.12. | Subjective Questionnaire | Administer subjective questionnaire regarding driving task just completed. This will be a paper-administered questionnaire. | Appendix A |
| 3.13. | Lens Removal | The study lenses will be removed and discarded. A fresh pair of lenses will be used for each trial. | |
| 3.14. | Test Treatments 2 and 3 | Repeat steps 3.6 to 3.13 for the other testing treatments until all three have been completed. | |

| Visit 3: Closed-circuit on-road driving performance 1 (Day/night condition based on randomization) | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.15. | Exit Slit Lamp Findings | FDA Slit Lamp Classification Scale will be used to grade the findings.<br>If any of these slit lamp findings are grade 3 or higher, the subject is classified as having an adverse event. Adverse events shall be documented and followed until resolved, at which time they will be terminated from the study.<br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | [redacted] |
| 3.16. | Exit Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |

**VISIT 4**

| Visit 4: Closed-circuit on-road driving performance 2 (Day/night condition based on randomization) | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 4.1. | As per Visit 3 | Visit 4 follows the same procedures outlined in Visit 3, but is conducted under the opposite condition to Visit 3 (day/night). | |

**FINAL EVALUATION**

The final evaluation will ordinarily take place immediately following the last scheduled follow-up visit per the study protocol. It may also take place at any point the subject discontinues the study or is terminated from the study.

| Final Evaluation | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| F.1 | Final Exam Form | Indicate if the subject completed the study successfully. If subject discontinued from the study indicate the reason. | [redacted] |
| F.2 | Exit Visual Acuity | Record the distance logMAR visual acuity (OD, OS, and OU) to the nearest letter with their habitual correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.<br>EDC: record logMAR acuity | |

7.3. **Unscheduled Visits**

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

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

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

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

The following information will be collected during an unscheduled visit.

| Step | Procedure | Details | [redacted] |
|---|---|---|---|
| U.1 | Chief Complaints | Record the subject's chief complaints for reasons for the unscheduled visit | |
| U.2 | Change of Medical History and Concomitant Medications | Questions regarding the change of subjects' medical history and concomitant medications. | |

| Step | Procedure | Details | [redacted] |
|---|---|---|---|
| U.3 | Entrance VA | Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter. | [redacted] |
| U.4 | Subjective Sphero-cylindrical Refraction | Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU). | [redacted] |
| U.5 | Slit Lamp Biomicroscopy | FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" grade for all observations listed.<br>After the slit lamp examination, at the discretion of the Investigator, rinse the subject's eyes thoroughly with preservative-free saline. | |
| U.6 | Exit Visual Acuity | Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter with the subjects wearing the study provided spectacle glasses. | [redacted] |

### 7.4. Laboratory Procedures

Not Applicable

## 8. SUBJECTS COMPLETION/WITHDRAWAL

### 8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent;
- they are eligible;
- completed all visits through the final visit 4

### 8.2. Withdrawal/Discontinuation from the Study

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

- Subject death during the study period
- Subject withdrawal of consent

- Subject not compliant to protocol
- Subject lost to follow-up
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant)
- Subject develops significant or serious adverse events causing discontinuation of study lens wear (e.g. an event during a measurement session at any visit)
- Subjects who have experienced a Corneal Infiltrative Event (CIE)
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment)
- 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

An additional subject will be enrolled if a subject discontinues from the study prematurely.

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

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

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include: any medications that may influence the tear film, pupil size, or accommodation.

## 10. DEVIATIONS FROM THE PROTOCOL

Investigator will notify study sponsor upon identification of a protocol deviation. Major protocol deviations must be reported to the sponsor within 24 hours after discovery of the protocol deviation. The Investigator will report deviations per IRB/IEC requirements. All deviations will be tracked and corrective actions implemented as appropriate.

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

## 11. STUDY TERMINATION

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

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

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

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

Should the study be terminated (either prematurely or as scheduled), the Investigator will notify the IEC/IRB and Regulatory Authority as required by local regulatory requirements.

## 12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

Within 24 hours of site personnel becoming aware that a PQC has occurred, the PQC must be recorded in the EDC system, which will trigger an automatic email notification to the appropriate COM/CRA and Clinical QA representative. In cases where the EDC system in use

is not configured to send automatic notifications or when an EDC system is not used, the COM/CRA is responsible for notifying Clinical QA upon discovery that a PQC has occurred.

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

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

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

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

## 13. ADVERSE EVENTS

### 13.1. Definitions and Classifications

**Adverse Event (AE)** – An AE is any untoward (unwanted) medical occurrence in a patient or clinical investigation subject administered a test article, study treatment or study procedure whether or not caused by the test article, study treatment or procedure. An AE can therefore be any unfavorable or unintended sign (including an abnormal finding), symptom, or disease temporally associated with the use of the test article, study treatment, or study procedure whether or not related to the test article, study treatment, or study procedure.

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

1. Was not present prior to the study, but appeared or reappeared following initiation of the study
2. Was present prior to the study, but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event

**Serious Adverse Event (SAE)** – An SAE is any untoward medical occurrence that:

- Results in death
- Is life threatening
- Requires in-patient hospitalization or prolongation of existing hospitalization
- Results in persistent or significant disability/incapacity (e.g., a sight threatening event, a significant persistent or permanent change, impairment, damage, or disruption to the subject's body)
- Is a congenital anomaly/birth defect
- Requires intervention to prevent permanent damage (the use of the test article resulting in a condition which requires medical or surgical intervention to preclude permanent impairment of the body structure or a body function). Important medical events that may not result in death, be life-threatening, or require hospitalization may be considered an SAE when, based upon appropriate medical judgment, they may jeopardize the patient or subject and may require medical or surgical intervention to prevent one of the outcomes listed in the above definition.

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

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

**Significant Adverse Events** – Those events that are usually symptomatic and warrant discontinuation (temporary or permanent) of the test article (excluding Serious Adverse Events).

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

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

**Non-Significant Adverse Events** – Those conditions that are usually asymptomatic and usually do not warrant discontinuation (temporary or permanent) of the test article. However, the Investigator may choose to treat as a precautionary measure.

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

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

**Adverse Device Effect (ADE)** – A sub-set of AEs, and include only those adverse events that are cause by or related to the investigational device.

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

### 13.2. Assessing Adverse Events

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

- Seriousness/Classifications (see definition in Section 13.1)
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; doubtful; possible; probable; very likely - see definition in Section 13.2.1)

- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild; moderate; severe for all events - see definition in Section 13.2.2).
- Outcome – Not Recovered or Not Resolved; Recovering or Resolving; Recovered or Resolved with Sequelae; Recovered or Resolved; Death Related to Adverse Event; Unknown
- Actions Taken – None; temporarily discontinued; permanently discontinued; other action taken

#### 13.2.1 Causality Assessment

**Causality Assessment** – A determination of the relationship between an adverse event and the test article, study treatment, or study procedure. The test article, study treatment or study procedure relationship for each adverse event shall be determined by the Investigator using these explanations:

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

#### 13.2.2 Severity Assessment

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

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

### 13.3. Documentation and Follow-Up of Adverse Events

The recording and documenting of adverse events (ocular and non-ocular) begins when the subjects are exposed to the test article, study treatment or study procedure. Adverse events reported before the use of test article, start of study treatment, or study procedures will be recorded as medical history. However, if the condition deteriorates at any time during the study

it will be recorded and reported as an AE. Untoward medical events reported after the subject's exit from the study will be recorded as adverse events at the discretion of the Investigator.

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

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

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

- Adverse event (diagnosis not symptom)
- Drawings or photographs (where appropriate) that detail the finding (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, including concomitant medications prescribed, in accordance with applicable licensing requirements
- Any referral to another health care provider if needed
- Outcome, ocular damage (if any)
- Likely etiology
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event

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

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

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether or not a subject reporting with an adverse event will continue in the

study. If a subject is discontinued from the study, it will be the responsibility of the Investigator to record the reason for discontinuation. The Investigator will also document the adverse event appropriately and complete the Adverse Event /eCRF. Any subjects with ongoing adverse events related to the test article, study treatment or study procedures, as of the final study visit date should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator.

### 13.4. Reporting Adverse Events

The Investigator will notify the Sponsor of an adverse event by e-mail, facsimile, or telephone as soon as possible and no later than 24 hours from discovery for any serious /significant adverse events, and 2 days from discovery for any non-significant adverse event. In addition, a written report will be submitted by the Principal Investigator to the IEC/IRB according to their requirements (Section 13.4.2). The report will comment whether or not the adverse event was considered to be related to the test article, study treatment or study procedures.

#### 13.4.1 Reporting Adverse Events to Sponsor

**Serious/Significant Adverse Events**

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

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

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

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

**Unanticipated (Serious) Adverse Device Effect (UADE)**

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

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

**Non-Serious Adverse Events**

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

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

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

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

### 13.5. Event of Special Interest

None

### 13.6. Reporting of Pregnancy

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

## 14. STATISTICAL METHODS

This section is a general outline of the statistical methods that will be implemented in this clinical trial. More details will be included in the stand-alone Statistical Analysis Plan (SAP).

### 14.1. General Considerations

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

Summary tables (Descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables for each subject/eye by study lens type (as appropriate). Continuous variables will be summarized with descriptive statistics (n,

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

### 14.2. Sample Size Justification

The study is designed and powered to demonstrate non-inferiority of the Test lens relative to the Control 1 with respect to night driving performance score. Assuming no difference between Test and Control 1, the sample size was calculated using a non-inferiority margin of -0.25. The sample size of 24 subjects is considered sufficiently large to test for non-inferiority with a minimum power of 80% and a two sided type I error of 0.05. The plan is to enroll 28 eligible subjects with a target completion of 24 subjects. During the enrollment period, the subject dropout rate will be closely monitored, if unexpectedly high dropout rate is observed, the targeted total enrollment number will be increased accordingly in order to ensure a minimum of 24 subjects per group to complete the study.

The non-inferiority margin and sample size calculations were based on available historical data from 6 published papers between 2009 and 2015 and from an investigator initiated study (IIS) sponsored by JJVC in 2016 that examined the effect of vision condition on driving performance. The table below summarized the studies considered in the meta-analysis

After categorizing the vision condition of the study groups into a binary variable as corrected and uncorrected, a Bayesian random effect meta-regression model was conducted on the pooled data to evaluate the overall effect of uncorrected vision on driving performance. The model can be written as

$$y_{ij}|\mu_{ij} = \mu_{ij} + e_{ij}; \text{ with } e_{ij} \sim N(0, s_{ij}^2)$$
$$\mu_{ij} = \boldsymbol{X_{ij}\beta} + \delta_{ij}; \text{ with } e_{ij} \sim N(0, \sigma^2)$$

Here $y_{ij}$ is the driving performance in vision condition group *i* in study *j*, $\boldsymbol{X_{ij}}$ is a vector of covariates from the $i^{th}$ vision condition group and $j^{th}$ study and $\boldsymbol{\beta}$ is the vector of regression coefficients. The term $\delta_{ij}$ is the random effect due to the between study variation while $s_{ij}^2$ represents the within study variation (known). The regression model included vision condition (corrected vs. uncorrected) and the covariates: driving time (day, night, day & night), average age and indicator variables of whether or not cone gap perception (not used in this study), course time and hazard avoidance were included in the calculation of the driving performance composite score.

We used independent vague normal N(0,1000) priors for the regression coefficients $\boldsymbol{\beta}$, vague inverse-gamma with shape and scale parameters of 0.001for the variance parameter $\sigma^2$. The Metropolis sampler algorithm as implemented in the SAS MCMC Procedure (SAS/STAT 14.1, SAS Institute, 2015) was used to carry out parameter estimation. After a burn-in of 80,000 iterations, we run the algorithm for additional 500,000 iterations with a thinning factor of 100 to allow posterior chains of estimated parameters to converge. Convergence of the simulated chains was assessed using autocorrelation and sample trace plots.

The posterior mean difference in driving performance between corrected and uncorrected vision was estimated to be 0.579 with 95% credible interval (95% CrI) of (0.249, 0.917). The estimated variance was 0.0483 with 95% CrI of (0.0051, 0.1692).

With a sample size of 24 subjects, the estimated power for different scenarios of intra-class correlation (ICC) is shown in the table below:

**Table 5: Statistical Power by ICC**

| Intra-class correlation (ICC) | Between subject variance $\sigma^2$ | Effect size | Power (%) |
|---|---|---|---|
| .40 | 0.05 | 0.25 | 71 |
| .50 | 0.05 | 0.25 | 85 |
| .60 | 0.05 | 0.25 | 95 |

The sample size calculation was conducted using the PROC POWER Procedure (SAS/STAT 14.1, SAS Institute, 2015). The non-inferiority hypothesis testing problem of a 3x3 crossover design was formulated as a two-sample non-inferiority hypothesis testing (Peng Sun, 2010).

As discussed above, the estimated posterior mean difference in driving performance between corrected vision (treated) and uncorrected vision (untreated) was estimated to be 0.579 with 95% credible interval (95% CrI) of (0.249, 0.917). We therefore used the lower bound of the 95% credible interval as the non-inferiority margin (~-0.25). This represents a discount of 43% from the estimated difference between corrected vision and uncorrected vision.

### 14.3. Analysis Populations

**Per-Protocol Population:**
Per-protocol population will consist of all subjects who have successfully completed all visits and did not substantially deviate from the protocol as determined by the trial cohort review committee prior to database hard lock. Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

A sensitivity analysis will be conducted on all subjects who were administered any test article excluding subjects who drop out prior to administering any test article. At least one observation should be recorded.

### 14.4. Level of Statistical Significance

All planned analysis will be conducted with an overall type I error rate of 5% for the primary and secondary hypotheses. Unless otherwise specified, all statistical tests will be 2-sided.

### 14.5. Primary Analysis

**Overall Driving Performance score**

Overall driving performance score will be analyzed using a linear mixed model; sequence of lens wear, period, lens type, first order carry-over, driving time (day or night) and the interactions between lens type by driving time and period by driving time will be included in the model as fixed effects. Age will be included as fixed covariate when appropriate. An appropriate covariance structure will be selected to model the correlation between measurements across periods within the same subject and driving time. Covariance structures that will be considered include:

- Compound Symmetry (CS)
- Heterogeneous Compound Symmetry (CSH)
- Unstructured (UN)
- Ante-dependence (ANTE(1))

For ANTE(1) structure, subject and driving time nested within subject will be included in the model as random effects. For the remaining structures only subject will be included as random effect. The covariance structure that returns the lowest Akaike Information Criteria Corrected

(AICC) will be selected as the structure that best fit the data[11]. Heterogeneous residuals covariance structures (R-side) across driving time will be considered when appropriate. The log-likelihood ratio test will be used to test for the homogeneity between the residual covariance structures. The Kenward and Roger method will be used for the denominator degree of freedom.

Comparisons between Test and Control 1 will be conducted overall across driving time and within each level of driving time. Results from the final selected model will be reported as least-square mean (LSM) differences with 95% confidence intervals.

The null and alternative hypotheses for non-inferiority of Test lens relative to Control 1 are as follows:

$$H_0: \mu_T - \mu_C \leq -0.25$$
$$H_A: \mu_T - \mu_C > -0.25,$$

where $\mu_T$ and $\mu_C$ are the means of night driving performance score for Test and Control 1, respectively. Non-inferiority of the Test relative to Control 1 will be concluded if the lower limit of the 95% confidence interval of the LSM difference between Test and Control 1, at night driving time, is greater than - 0.25.

### 14.6. Secondary Analysis

**Binocular distance visual acuity (LogMAR)**

Binocular low luminance high contrast distance visual acuity will be analyzed using a linear mixed model to test for the difference between Test and Control 1. Sequence of lens wear, period, lens type, first order carryover effect will be included in the model as fixed effects. An appropriate covariance structure will be chosen to model the residual errors between measurements within the same subject across periods. Covariance structures considered will be:

- Compound Symmetry (CS)
- Heterogeneous Compound Symmetry (CSH)
- Unstructured (UN)
- Ante-dependence (ANTE(1))

For ANTE(1) structure, subject will be included in the model as random effects. The covariance structure that returns the lowest AICC will be selected as the structure that best fit the data.

The null and alternative hypotheses for non-inferiority of Test lens relative to Control 1 are as follows:

$$H_0: \mu_T - \mu_C \geq 0.1$$
$$H_A: \mu_T - \mu_C < 0.1,$$

where $\mu_T$ - $\mu_C$ is the mean difference between Test lens and Control 1 lens. Non-inferiority of the Test lens relative to the Control 1 lens will be concluded if the upper limit of the 95% confidence interval of the LSM difference between Test and Control 1 is less than 0.1.

**Low luminance contrast threshold**

Low luminance contrast threshold will be analyzed using a Poisson generalized linear mixed model for count data. Sequence, period, lens type, first order carry-over, contrast level and the interaction contract level by lens type will be included as fixed effects and subject as random effect. An unstructured covariance matrix (UN) will be used to model the correlation between measurements from the same subject and period across contrast level. A negative binomial distribution will be considered if the data is over-dispersed.

The null and alternative hypotheses for no-difference between Test and Control 1 are as follows:

$$H_0: \lambda_T/\lambda_C = 1$$
$$H_A: \lambda_T/\lambda_C \neq 1,$$

where $\lambda_T/\lambda_C$ is the ratio of the average number of correctly identified orientation of the Landolt C. No statistical difference between Test lens and Control 1 lens will be concluded if 1 falls within the 95% confidence interval of the LSM ratio, $\lambda_T/\lambda_C$, of Test over Control 1.

**Sign Recognition and Hazard Avoidance (%)**

Proportion of correctly identified sings and proportion of hazard avoidance will be analyzed separately using a generalized linear mixed model with beta distribution and logit link function. Each model will include sequence, period, lens type, first order carry-over, driving time (day or night), and the interactions lens type by driving time and period by driving time as fixed effect factors. An unstructured covariance matrix (UN) will be used to model the correlation between measurements from the same subject across periods.

The null and alternative hypotheses for no-difference between Test and Control 1 are as follows:

$$H_0: OR = 1$$
$$H_A: OR \neq 1,$$

where OR is the odds ratio of hazard avoidance at night driving time of Test over Control 1. No statistical difference between Test and Control 1 will be concluded if 1 falls within the 95% confidence interval of the odds ratio.

**Pedestrian Distance Recognition and Road Sign Recognition**

Pedestrian distance recognition and road sign recognition distance (or log-transformed distance) will be analyzed separately using a linear mixed model; sequence of lens wear, period, lens type, first order carry-over, driving time (day or night), and the interactions between lens type by driving time and period by driving time will be included in the model as

fixed effects. Age will be included as fixed covariate when appropriate. An appropriate covariance structure will be selected to model the correlation between measurements across periods within the same subject and driving time. Covariance structures that will be considered include:

- Compound Symmetry (CS)
- Heterogeneous Compound Symmetry (CSH)
- Unstructured (UN)
- Ante-dependence (ANTE(1))

For ANTE(1) structure, subject and driving time nested within subject will be included in the model as random effects. For the remaining structures, only subject will be included as random effect. The covariance structure that returns the lowest Akaike Information Criteria Corrected (AICC) will be selected as the structure that best fit the data[11]. Heterogeneous residuals covariance structures (R-side) across driving time will be considered when appropriate. The log-likelihood ratio test will be used to test for the homogeneity between the residual covariance structures. The Kenward and Roger method will be used for the denominator degree of freedom.

Results from the final selected model will be reported as least-square mean (LSM) estimates with 95% confidence intervals.

The null and alternative hypotheses for non-inferiority of Test lens relative to Control 1 are as follows:

$$H_0: \mu_T - \mu_C = 0$$
$$H_A: \mu_T - \mu_C \neq 0,$$

where $\mu_T$ - $\mu_C$ is the mean difference of distance recognition at night driving between Test and Control 1. No statistical difference between Test and Control 1 will be concluded if 0 falls within the 95% confidence interval of the LSM difference between Test and Control 1.

### 14.7. Other Exploratory Analyses

No exploratory analysis is planned for this study. Further analysis may be conducted at the discretion of the study responsible clinician at the end of the study.

### 14.8. Interim Analysis

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

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

Missing or spurious values will not be imputed as the number of missing values is expected to be low the count of missing values will be included in the summary tables and listings. Dropout is expected to be one of the main reasons of missing data in this trial. Past soft contact lens clinical trials don't provide any evidence that subjects dropout is systematic or not at random.

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

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

## 15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

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

The data for this study will be captured on electronic case report forms (eCRFs) using an EDC system (BioClinica)). An authorized data originator will enter study data into the eCRFs using the EDC system. Data collected on equipment that is not captured in EDC will be formatted to the specification of the JJVC database manager and sent to JJVC for analysis.

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

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

The content and structure of the eCRFs are compliant with ISO14155:2011.

### 15.2. Subject Record

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

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

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

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

## 16. DATA MANAGEMENT

### 16.1. Access to Source Data/Document

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

### 16.2. Confidentiality of Information

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

### 16.3. Data Quality Assurance

Steps will be taken to ensure the accuracy and reliability of data, include the selection of qualified investigators and appropriate clinical sites and review of protocol procedures with the Principal Investigator. The Principal Investigator, in turn, must ensure that all Sub-Investigators and clinical site personnel are familiar with the protocol and all study-specific procedures and have appropriate knowledge of the study article.

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

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

## 17. MONITORING

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

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

## 18. ETHICAL AND REGULATORY ASPECTS

### 18.1. Study-Specific Design Considerations

Potential subjects 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. Only subjects who are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

### 18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP), 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$^{th}$ WMA General Assembly 2013 and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP), and applicable regulatory requirements.

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

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

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

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

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

- Protocol amendments
- Revision(s) to informed consent form and any other written materials to be provided to subjects
- If applicable, new or revised subject recruitment materials approved by the Sponsor

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

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

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

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

### 18.4. Informed Consent

Each subject must give written consent 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, current ICH and GCP guidelines, applicable regulatory requirements, and Sponsor policy.

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

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

### 18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Data Protection Act of 1998 and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

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

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

Appropriate technical and organizational measures to protect the personal data against unauthorized disclosures or access, accidental or unlawful destruction, or accidental loss or

alteration must be put in place. Sponsor personnel whose responsibilities require access to personal data agree to keep the identity of study subjects confidential

**19. STUDY RECORD RETENTION**

In compliance with the ICH/GCP guidelines, the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH/GCP Section 8, Essential Documents for the Conduct of a Clinical Trial, and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

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

**20. FINANCIAL CONSIDERATIONS**

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

Case Report Forms will be completed in real time according to the study procedures specified in the study protocol. Case Report Forms should be completed and reviewed and signed as applicable by the Investigator within 3 days of visit completion. Data queries must be addressed with complete responses within 3 days of generation. JJVC reserves the right to withhold remuneration until these activities are addressed.

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

## 21. PUBLICATION

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

## 22. REFERENCES CITED IN THIS PROTOCOL.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7. Sullivan, JM., & Flannagan, MJ. (2007). Determining the potential safety benefit of improved lighting in three pedestrian crash scenarios. Accident Analysis and Prevention, 39, 638-647.

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# APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

## APPENDIX B: PATIENT INSTRUCTION GUIDE

Patient Instruction Guide will be provided separately.

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

ACUVUE® OASYS® BRAND CONTACT LENSES WITH HYDRACLEAR® PLUS

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

**This Package Insert and Fitting Guide is intended for the Eye Care Professional, but should be made available to patients upon request.**

**The Eye Care Professional should provide the patient with the appropriate instructions that pertain to the patient's prescribed lenses. Copies are available for download at www.acuvue.com.**

# ACUVUE®

# OASYS

BRAND CONTACT LENSES

**ACUVUE OASYS® Brand Contact Lenses**

**ACUVUE OASYS® Brand Contact Lenses for ASTIGMATISM**

**ACUVUE OASYS® Brand Contact Lenses for PRESBYOPIA**

**senofilcon A Soft (hydrophilic) Contact Lenses**
**Visibility Tinted with UV Blocker**
**for Daily and Extended Wear**

℞ Only CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner.

# SYMBOLS KEY

The following symbols may appear on the label or carton:

| SYMBOL | DEFINITION |
|---|---|
|  | Consult Instructions for Use |
|  | Manufactured by or in |
|  | Date of Manufacture |
|  | Use By Date (expiration date) |
|  | Batch Code |
|  | Sterile Using Steam or Dry Heat |
| **DIA** | Diameter |
| **BC** | Base Curve |
| **D** | Diopter (lens power) |
| **CYL** | Cylinder |
| **AXIS** | Axis |
| **MAX ADD** | Near ADD |
| **LOW** | "Low" Near ADD |
| **MID** | "Medium" Near ADD |
| **HGH** | "High" Near ADD |
|  | Quality System Certification Symbol |
|  | UV-Blocking |
|  | Fee Paid for Waste Management |
|  | CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner |
|  | Lens Orientation Correct |
|  | Lens Orientation Incorrect (Lens Inside Out) |

# DESCRIPTION

The ACUVUE OASYS® Brand Contact Lenses, the ACUVUE OASYS® Brand Contact Lenses for ASTIGMATISM, and the ACUVUE OASYS® Brand Contact Lenses for PRESBYOPIA are soft (hydrophilic) contact lenses available as spherical, toric, or multifocal lenses and include HYDRACLEAR® PLUS Technology. The lenses are made of a silicone hydrogel material containing an internal wetting agent with visibility tinted UV absorbing monomer.

These lenses are tinted blue using Reactive Blue Dye #4 to make the lenses more visible for handling. A benzotriazole UV absorbing monomer is used to block UV radiation.

The transmittance characteristics are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 316 nm to 380 nm for the entire power range.

**Lens Properties:**

- Specific Gravity (calculated): 0.98 – 1.12
- Refractive Index: 1.42
- Light Transmittance: 85% minimum
- Surface Character: Hydrophilic
- Water Content: 38%
- Oxygen Permeability:

| **VALUE** | **METHOD** |
|---|---|
| 103 x $10^{-11}$ ($cm^2$/sec) (ml $O_2$/ml x mm Hg) @ 35°C | Fatt (boundary corrected, edge corrected) |
| 122 x $10^{-11}$ ($cm^2$/sec) (ml $O_2$/ml x mm Hg) @ 35°C | Fatt (boundary corrected, non-edge corrected) |

**Lens Parameters:**

- Diameter Range: 12.0 mm to 15.0 mm
- Center Thickness: varies with power
- Base Curve Range: 7.85 mm to 10.00 mm
- Spherical Power Range: Daily Wear: -20.00D to +20.00D
  Extended Wear: -20.00D to +14.00D
- Multifocal ADD Power Range: +0.25D to +4.00D
- Cylinder Power Range: -0.25D to -10.00D
- Axis Range: 2.5° to 180°

# AVAILABLE LENS PARAMETERS

The ACUVUE OASYS® Brand Contact Lenses are hemispherical shells of the following dimensions:

| | |
|---|---|
| **Diameter:** | 14.0 mm |
| **Center Thickness:** | Minus Lens - varies with power (e.g. -4.00D: 0.070 mm)<br>Plus Lens - varies with power (e.g. +4.00D: 0.168 mm) |
| **Base Curve:** | 8.4 mm, 8.8 mm |
| **Powers:** | -0.50D to -6.00D (in 0.25D increments)<br>-6.50D to -12.00D (in 0.50D increments)<br>+0.50D to +6.00D (in 0.25D increments)<br>+6.50D to +8.00D (in 0.50D increments) |

The ACUVUE OASYS® Brand Contact Lenses for ASTIGMATISM are hemitoric shells of the following dimensions:

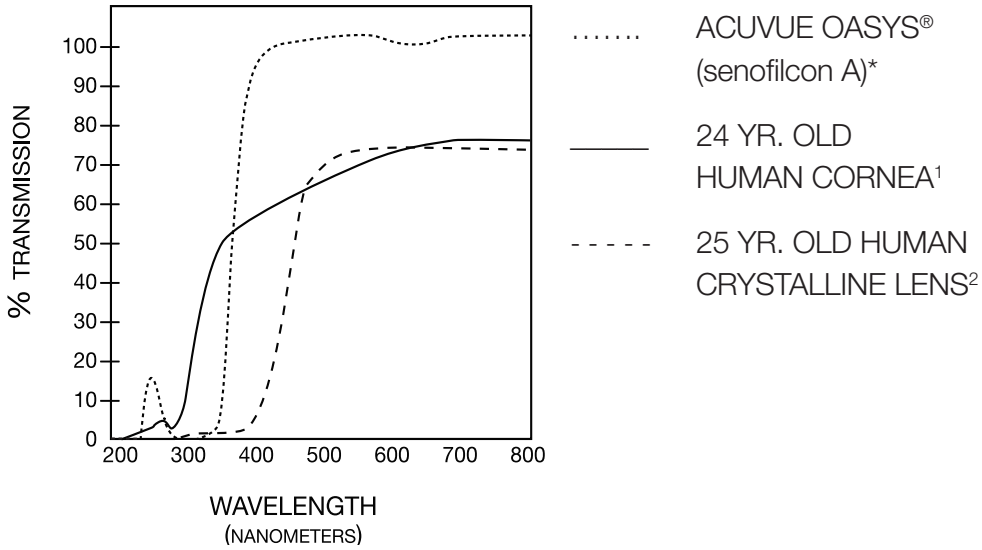
| | |
|---|---|
| **Diameter:** | 14.5 mm |
| **Center Thickness:** | Minus Lens - varies with power (e.g. -4.00D: 0.080 mm)<br>Plus Lens - varies with power (e.g. +4.00D: 0.172 mm) |
| **Base Curve:** | 8.6 mm |
| **Powers:** | plano to -6.00D (in 0.25D increments)<br>-6.50D to -9.00D (in 0.50D increments)<br>+0.25D to +6.00D (in 0.25D increments)<br>Cylinder: -0.75D, -1.25D, -1.75D, -2.25D, -2.75D<br>Axis: 10° to 180° (in 10° increments) |

The ACUVUE OASYS® Brand Contact Lenses for PRESBYOPIA are hemispherical shells of the following dimensions:

| | |
|---|---|
| **Diameter:** | 14.3 mm |
| **Center Thickness:** | Minus Lens - varies with power (e.g. -4.00D: 0.070 mm)<br>Plus Lens - varies with power (e.g. +4.00D: 0.168 mm) |
| **Base Curve:** | 8.4 mm |
| **Powers:** | -9.00D to +6.00D (in 0.25D increments) |
| **ADD Powers:** | +1.25 (LOW), +1.75 (MID), +2.50 (HGH) |

# TRANSMITTANCE CURVE

ACUVUE OASYS® Brand Contact Lenses vs. 24 yr. old human cornea vs. 25 yr. old human crystalline lens




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

1. Lerman, S., Radiant Energy and the Eye, MacMillan, New York, 1980, p.58, figure 2-21
2. Waxler, M., Hitchins, V.M., Optical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p.19, figure 5

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

# ACTIONS

In its hydrated state, the contact lens, when placed on the cornea, acts as a refracting medium to focus light rays on the retina. When hydrated and placed on the cornea for therapeutic use, the contact lens acts as a bandage to protect the cornea.

The transmittance characteristics are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 316 nm to 380 nm for the entire power range.

**NOTE: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-Blocking contact lenses help provide protection against harmful UV radiation.**

**However, clinical studies have not been done to demonstrate that wearing UV-Blocking contact lenses reduces the risk of developing cataracts or other eye disorders. The Eye Care Professional should be consulted for more information.**

# INDICATIONS (USES)

The ACUVUE OASYS® Brand Contact Lens is indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who have 1.00D or less of astigmatism.

The ACUVUE OASYS® Brand Contact Lens for ASTIGMATISM is indicated for the optical correction of visual acuity in phakic or aphakic persons with non-diseased eyes that are hyperopic or myopic and may have 10.00D or less of astigmatism.

The ACUVUE OASYS® Brand Contact Lens for PRESBYOPIA is indicated for the optical correction of distance and near vision in presbyopic, phakic or aphakic persons with non-diseased eyes who may have 0.75D or less of astigmatism.

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

Eye Care Professionals may prescribe the lenses either for single-use disposable wear or frequent/planned replacement wear with cleaning, disinfection and scheduled replacement (see “REPLACEMENT SCHEDULE”). When prescribed for frequent/planned replacement wear, the lenses may be cleaned and disinfected using a chemical disinfection system only.

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

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

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

surgical conditions.

- For structural stability and protection in piggy back lens fitting where the cornea and associated surfaces are too irregular to allow for corneal rigid gas permeable (RGP) lenses to be fit. In addition, the use of the lens can prevent irritation and abrasions in conditions where there are elevation differences in the host/graph junction or scar tissue.

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

## CONTRAINDICATIONS (REASONS NOT TO USE)

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

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

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

## WARNINGS

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

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

- **Eye Discomfort,**
- **Excessive Tearing,**

- **Vision Changes,**
- **Loss of Vision,**
- **Eye Redness,**
- **Or Other Eye Problems,**

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

- When prescribed for daily wear, patients should be instructed not to wear lenses while sleeping. Clinical studies have shown that the risk of serious adverse reactions is increased when lenses are worn overnight, and that the risk of ulcerative keratitis is greater for extended wear contact lens users than for daily wear users.[3]
- Studies have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.
- Problems with contact lenses or lens care products could result in serious injury to the eye. Patients should be cautioned that proper use and care of contact lenses and lens care products, including lens cases, are essential for the safe use of these products.
- The overall risk of ulcerative keratitis may be reduced by carefully following directions for lens care, including cleaning the lens case.

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

**Specific Instructions for Use and Warnings:**

- **Water Activity**

  **Instructions for Use**

  Do not expose contact lenses to water while wearing them.

  **WARNING:**

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

- **Soaking and Storing Your Lenses**

  **Instructions for Use**

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

  **WARNING:**

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

"Topping-Off" is the addition of fresh solution to solution that has been sitting the case.

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

  **Instructions for Use**

  – Discard any remaining solution after the recommended time period indicated on the bottle of multi-purpose solution used for disinfecting and soaking the contact lenses.

  – The Discard Date refers to the time that the patient can safely use contact lens care product after the bottle has been opened. It is not the same as the expiration date, which is the last date that the product is still effective before it is opened.

  **WARNING:**

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

  – To avoid contamination, DO NOT touch tip of container to any surface. Replace cap after using.

  – To avoid contaminating the solution, DO NOT transfer to other bottles or containers.

- **Rub and Rinse Time**

  **Instructions for Use**

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

  **WARNING:**

  – Rub and rinse lenses for the recommended amount of time to help prevent serious eye infections.

  – Never use water, saline solution, or rewetting drops to disinfect the lenses. These solutions will not disinfect the lenses. Not using the recommended disinfectant can lead to severe infection, vision loss, or blindness.

- **Lens Case Care**

  **Instructions for Use**

  – Empty and clean contact lens cases with digital rubbing using fresh, sterile disinfecting solutions/contact lens cleaner. Never use water. Cleaning should be followed by rinsing with fresh, sterile disinfecting solutions (never use water) and wiping the lens cases with fresh, clean tissue is recommended. Never air dry or recap the lens case lids after use without any additional cleaning methods. If air drying, be sure that no residual solution remains in the case before allowing it to air dry.

  – Replace the lens case according to the directions provided by the Eye Care Professional or the manufacturer's labeling that accompanies the case.

– Contact lens cases can be a source of bacterial growth.

**WARNING:**

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

# PRECAUTIONS

**Special Precautions for Eye Care Professionals:**

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.

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

- Patients who wear these lenses to correct presbyopia using monovision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.

- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.

- Eye Care Professionals should instruct the patient to remove lenses immediately if the eyes become red or irritated.

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

**Handling Precautions:**

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove the lenses or should have someone else available who can remove the lenses for him or her.

- DO NOT use if the sterile blister package is opened or damaged.

- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It

is best to put on lenses before putting on makeup. Water-based cosmetics are less likely to damage lenses than oil-based products.

- DO NOT touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, and wearing instructions in the Patient Instruction Guide for these lenses and those prescribed by the Eye Care Professional.
- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.
- Close supervision is necessary for the Therapeutic use of these lenses. Ocular medications used during treatment with a bandage lens should be closely monitored by the Eye Care Professional. In certain ocular conditions, only the Eye Care Professional will insert and remove the lenses. In these cases, patients should be instructed not to handle the lenses themselves.

**Lens Wearing Precautions:**

- If the lens sticks (stops moving) on the eye, follow the recommended directions in “Care for Sticking (Non-Moving) Lenses”. The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. They have been prescribed to fit their eyes and to correct their vision to the degree necessary. Sharing lenses greatly increases the chance of eye infections.
- If aerosol products, such as hair spray, are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.

**Lens Care Precautions:**

- Different solutions cannot always be used together and not all solutions are safe for use with all lenses. Use only recommended solutions.
- Never use solutions recommended for conventional hard contact lenses only.
- Chemical disinfection solutions should not be used with heat unless

specifically indicated on product labeling for use in both heat and chemical disinfection.

- Always use fresh, unexpired lens care solutions and lenses.
- Do not change solution without consulting with your Eye Care Professional.
- Always follow directions in the package inserts for the use of contact lens solutions.
- Use only a chemical (not heat) lens care system. Use of a heat (thermal) care system can damage these lenses.
- Sterile unpreserved solutions, when used, should be discarded after the time specified in the directions.
- Do not use saliva or anything other than the recommended solutions for lubricating or wetting lenses.
- Always keep the lenses completely immersed in the recommended storage solution when the lenses are not being worn (stored). Prolonged periods of drying will reduce the ability of the lens surface to return to a wettable state. Follow the lens care directions in "Care For A Dried Out (Dehydrated) Lens" if lens surface does become dried out.

**Other Topics to Discuss with Patients:**

- Always contact the Eye Care Professional before using any medicine in the eyes.
- Certain medications, such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness may cause dryness of the eye, increased lens awareness, or blurred vision. Should such conditions exist, proper remedial measures should be prescribed. Depending on the severity, this could include the use of lubricating drops that are indicated for use with soft contact lenses or the temporary discontinuance of contact lens wear while such medication is being used.
- Oral contraceptive users could develop visual changes or changes in lens tolerance when using contact lenses. Patients should be cautioned accordingly.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.

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

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

# ADVERSE REACTIONS

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

- The eye may burn, sting and/or itch.
- There may be less comfort than when the lens was first placed on the eye.
- There may be a feeling of something in the eye (foreign body, scratched area).
- There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral corneal ulcers, and corneal erosion. There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis and conjunctivitis, some of which are clinically acceptable in low amounts.
- There may be excessive watering, unusual eye secretions or redness of the eye.
- Poor visual acuity, blurred vision, rainbows or halos around objects, photophobia, or dry eyes may also occur if the lenses are worn continuously or for too long a time.
- The patient should be instructed to conduct a simple 3-part self-examination at least once a day. They should ask themselves:
  - How do the lenses feel on my eyes?
  - How do my eyes look?
  - Have I noticed a change in my vision?

If the patient reports any problems, he or she should be instructed to IMMEDIATELY REMOVE THE LENS. If the problem or discomfort stops, the patient should discard the lens and place a new fresh lens on the eye.

If after inserting the new lens, the problem continues, the patient should be directed to IMMEDIATELY REMOVE THE LENS AND CONTACT HIS OR HER EYE CARE PROFESSIONAL.

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

The patient should be advised that when any of the above symptoms occur, a serious condition such as infection, corneal ulcer, neovascularization or iritis may be present. He or she should be instructed to seek immediate professional identification of the problem and prompt treatment to avoid serious eye damage.

# GENERAL FITTING GUIDELINES

**A. Patient Selection:**

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

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

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

**B. Pre-fitting Examination:**

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

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

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

**C. Initial Power Determination**

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

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

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

- **ACUVUE OASYS®**: 8.4 mm/14.0 mm
- **ACUVUE OASYS® for ASTIGMATISM:** 8.6 mm/14.5 mm
- **ACUVUE OASYS® for PRESBYOPIA:** 8.4 mm/14.3 mm

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

1. Criteria of a Properly Fit Lens

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

2. Criteria of a Flat Fitting Lens

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

3. Criteria of a Steep Fitting Lens

A steep fitting lens may exhibit one or more of the following characteristics: insufficient movement with the blink, conjunctival indentation, and resistance when pushing the lens up digitally with the lower lid. If the lens is judged to be steep fitting, it should not be dispensed to the patient.

If the initial trial base curve is judged to be flat or steep fitting, the alternate base curve, if available, should be trial fit and evaluated after the patient has adjusted to the lens. The lens should move freely when manipulated digitally with lower lid, and then return to a properly centered position when released. If resistance is encountered when pushing the lens up, the lens is fitting tightly and should not be dispensed to the patient.

**E. Final Lens Power (Spherical)**

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

| Example 1 | |
|---|---|
| Diagnostic lens: | -2.00D |
| Spherical over-refraction: | -0.25D |
| Final lens power: | -2.25D |

| Example 2 | |
|---|---|
| Diagnostic lens: | -2.00D |
| Spherical over-refraction: | +0.25D |
| Final lens power: | -1.75D |

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

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

# TORIC FITTING GUIDELINES

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

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

## A. How to Determine Lens Cylinder and Axis Orientation

1. Locate the Orientation Marks

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

**Figure 1**

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

2. Observe Lens Rotation and Stability

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

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

**Assessing Rotation**

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

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

## B. How to Determine the Final Lens Power

When the diagnostic lens has its axis aligned in the same meridian as the patient’s refractive axis, a spherocylindrical over-refraction may be performed and visual acuity determined. However, in the case of crossed axes, such as when the diagnostic lens axis is different from the patient’s refractive axis, it is not advisable to over-refract because of the difficulty in computing the resultant power. In fitting contact lenses, it is customary to prescribe the full power in the sphere. In the cylinder, however, any lens rotation is visually disturbing to the patient, so it’s more practical to prescribe as weak a cylinder as possible.
So, here is how to determine the final lens power.

**For the Sphere:**

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

**For the Cylinder:**

Adjust the axis by the drift angle using LARS. Choose a cylinder that is ≤ 0.25D from the refractive cylinder.

**Case Examples:**

**Example 1**
Manifest (spectacle) refraction:
O.D. –2.50 -1.25 x 180 20/20
O.S. –2.00 -1.00 x 180 20/20
Choose a diagnostic lens for each eye with an axis as close to 180° as possible. Place the lens on each eye and allow a minimum of 3 minutes for

it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable.

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

Here is the Rx Prescribed:

O.D. -2.50 -1.25 x 180
O.S. –2.00 -0.75 x 180

**Example 2**

Manifest (spectacle) refraction:
O.D. –3.00 -1.00 x 90 20/20
O.S. –4.75 -2.00 x 90 20/20

Choose diagnostic lenses of –3.00 –0.75 x 90 for the right eye and –4.50 -1.75 x 90 for the left eye, the nearest lenses available to the spherical power and axis needed. Place the lens on each eye and allow a minimum of 3 minutes for it to equilibrate, based on the patient's initial response to the lens. If the lens has not yet stabilized, recheck until stable. The orientation mark on the right lens rotates left from the 6 o'clock position by 10°.

The fitting indicates the following:

**Right Eye:**
Compensate the 10° axis drift by adding it to the manifest refraction axis. Here is the Rx prescribed:
O.D. –3.00 –0.75 x 100

**Left Eye**
The lens on the left eye shows good centration, movement and a consistent tendency for the mark to drift right by 10° from the 6 o'clock position following a forced blink. Since the manifest refraction called for a power of –4.75D, adjust for the vertex distance and reduce the sphere by 0.25D and prescribe the –1.75D cylinder. Compensate for the 10° axis drift by subtracting it from the manifest refraction.

Here is the Rx Prescribed:

O.S. –4.50 –1.75 x 80

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

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

# MULTIFOCAL FITTING GUIDELINES

## A. Presbyopic Needs Assessment & Patient Education

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

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

These lenses are not recommended for patients who have –1.00D or greater of refractive cylinder as this level of uncorrected cylinder may lead to additional visual compromise.

These lenses are available in the following ADD powers:

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

## B. Fitting Instructions

### 1. Determine the following:

- Eye dominance (the methods described in MONOVISION FITTING GUIDELINES may be used)
- Spherical equivalent distance prescription (vertex corrected if necessary and rounded to less minus if between powers)
- Near ADD

### 2. Select the initial trial lens as follows:

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

- Select the near power of the lens based on the patient's ADD range as follows:

  ADD: +0.75 to +1.25 use a “LOW” near ADD lens on each eye

  ADD: +1.50 to +1.75 use a “MID” near ADD lens on each eye

  ADD: +2.00 to +2.50 use a “HGH” near ADD lens on each eye

**3. Allow the lens to settle for a minimum 10 minutes.**

**4. Assess distance and near vision binocularly and monocularly.**

- Demonstrate the vision under various lighting conditions (normal and decreased illumination) and at distance, intermediate and near.
- Make adjustments in power as necessary (see Multifocal Troubleshooting below). The use of hand-held trial lenses is recommended.
- If distance and near vision are acceptable, perform a slit lamp examination to assess adequate fit (centration and movement). If fit is acceptable, dispense the lenses instructing the patient to return in one week for reassessment (see dispensing and follow-up information in PATIENT MANAGEMENT).

## C. Multifocal Troubleshooting

**Unacceptable Near Vision:**
Determine the amount of additional plus, or less minus, over one or both eyes that is acceptable, while checking the effect on distance and near vision. If vision is still not acceptable, change the non-dominant eye to the next highest ADD power.

**Unacceptable Distance Vision:**
Determine the amount of additional minus, or less plus, over one or both eyes that is acceptable while checking the effect on distance and near vision. If vision is still not acceptable, change the dominant eye to the next lowest ADD power. If the patient is wearing two low ADD lenses, change the dominant eye to a sphere lens with a power equal to the spherical equivalent distance prescription.

**Unacceptable Distance and Near Vision:**
Determine the amount of additional plus and/or minus over one or both eyes that is acceptable while checking the effect on distance and near vision. If additional plus and/or minus is not required, change the lens power in the dominant eye to the next lowest ADD power and the lens power in the non-dominant eye to the next highest ADD power, if applicable.

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

# MONOVISION FITTING GUIDELINES

## A. Patient Selection

### Monovision Needs Assessment

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

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

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

### Patient Education

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

## B. Eye Selection

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

### 1. Ocular Preference Determination Methods

Method 1: Determine which eye is the “sighting eye.” Have the patient point to an object at the far end of the room. Cover one eye. If the patient is still pointing directly at the object, the eye being used is the dominant (sighting) eye.

Method 2: Determine which eye will accept the added power with the least reduction in vision. Place a hand-held trial lens equal to the spectacle near ADD in front of one eye and then the other while the distance refractive error correction is in place for both eyes. Determine whether the patient functions best with the near ADD lens over the right or left eye.

Other methods include the refractive error method and the visual demands method.

**2. Refractive Error Method**
For anisometropic correction, it is generally best to fit the more hyperopic (less myopic) eye for distance and the more myopic (less hyperopic) eye for near.

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

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

## C. Special Fitting Characteristics

**1. Unilateral Lens Correction**
There are circumstances where only one contact lens is required. As an example, an emmetropic patient would only require a near lens while a bilateral myope may only require a distance lens.

Example: A presbyopic emmetropic patient who requires a +1.75D ADD would have a +1.75D lens on the near eye and the other eye left without a lens. A presbyopic patient requiring a +1.50D ADD who is –2.50D myopic in the right eye and –1.50D myopic in the left eye may have the right eye corrected for distance and the left uncorrected for near.

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

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

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

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

After the patient's performance under the above conditions is completed, tests of visual acuity and reading ability under conditions of moderately dim illumination should be attempted.

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

**4. Adaptation**

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

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

Some patients feel that automobile driving performance may not be optimal during the adaptation process. This is particularly true when driving at night. Before driving a motor vehicle, it may be recommended that the patient be a passenger first to make sure that their vision is satisfactory for operating an automobile. During the first several weeks of wear (when adaptation is occurring), it may be advisable for the patient to only drive during optimal driving conditions. After adaptation and success with these activities, the patient should be able to drive under other conditions with caution.

## D. Other Suggestions

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

- Have a third contact lens (distance power) to use when critical distance viewing is needed.
- Have a third contact lens (near power) to use when critical near viewing is needed.
- Having supplemental spectacles to wear over the monovision contact lenses

for specific visual tasks may improve the success of monovision correction. This is particularly applicable for those patients who cannot pass state drivers licensing requirements with monovision correction.

- Make use of proper illumination when carrying out visual tasks.

Monovision fitting success can be improved by the following suggestions:

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

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

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

# PATIENT MANAGEMENT

### Dispensing Visit

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

### Follow-up Examinations

- Follow-up care (necessary to ensure continued successful contact lens wear) should include routine periodic progress examinations, management of specific problems, if any, and a review with the patient of the wear schedule, lens replacement schedule, and proper lens care and handling procedures.
- Recommended Follow-up Examination Schedule (complications and specific problems should be managed on an individual patient basis):
  1. One week from the initial lens dispensing to patient
  2. One month post-dispensing
  3. Every three to six months thereafter

NOTE: More frequent or additional follow-up visits may be recommended for patients on an extended wear schedule.

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

**If any observations are abnormal, use professional judgment to alleviate the problem and restore the eye to optimal conditions. If the criteria for successful fit are not satisfied during any follow-up examinations, repeat the patient's trial fitting procedure and refit the patient.**

## WEARING SCHEDULE

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

**For Daily Wear:**

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

The maximum suggested wearing time for these lenses is:

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

**For Extended Wear:**

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

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

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

## REPLACEMENT SCHEDULE

**For Lenses Prescribed for Frequent Replacement:**

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

**For Lenses Prescribed for Disposable Wear:**

When prescribed for disposable wear, the replacement schedule should be determined by the Eye Care Professional based upon the patient's history and their ocular examination, as well as the practitioner's experience and clinical judgment.

Once removed, it is recommended that the lens remain out of the eye for a period of rest of overnight or longer and be discarded in accordance with the prescribed wearing schedule. The Eye Care Professional should examine the patient during the early stages of extended wear.

# LENS CARE DIRECTIONS

When lenses are dispensed, the Eye Care Professional should provide the patient with appropriate and adequate warnings and instructions in accordance with the individual patient's lens type and wearing schedule. The Eye Care Professional should recommend an appropriate care system tailored to the patient's individual requirements.

For complete information concerning contact lens handling, care, cleaning, disinfecting and storage, refer to the Patient Instruction Guide for these lenses. Copies are available for download at www.acuvue.com.

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

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

**For Lenses Prescribed for Disposable Wear:**

The Eye Care Professional should review with patients that no cleaning or disinfection is needed with disposable lenses. Patients should always dispose of lenses when they are removed and have replacement lenses or spectacles available. Lenses should only be cleaned, rinsed, and disinfected on an emergency basis when replacement lenses or spectacles are not available.

**Care for a Dried Out (Dehydrated) Lens**

If the frequent replacement lens is off the eye and exposed to air from 30 minutes to 1 hour or more, its surface will become dry and gradually become non-wetting. If this should occur, discard the lens and use a new one.

**Care for Sticking (Non-Moving) Lenses**

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

# EMERGENCIES

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

## HOW SUPPLIED

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

- **ACUVUE OASYS®:** base curve, power, diameter, lot number, and expiration date
- **ACUVUE OASYS® for ASTIGMATISM:** base curve, power, diameter, cylinder, axis, lot number, and expiration date
- **ACUVUE OASYS® for PRESBYOPIA:** base curve, power, diameter, ADD, lot number, and expiration date

## REPORTING OF ADVERSE REACTIONS

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

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



In Canada: Johnson & Johnson Vision Care, division of Johnson & Johnson, Inc.
In USA: Johnson & Johnson Vision Care, Inc.
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Revision number: AO-06-15-01

## APPENDIX D: CLINICAL TECHNICAL PROCEDURES [redacted]

[redacted] Lens Fitting Characteristics

[redacted] Determination of Distance Spherocylindrical Refractions

[redacted] Biomicroscopy Scale

[redacted] Distance and Near Visual Acuity Evaluation

[redacted] Distance LogMAR Visual Acuity Measurement Procedure

## [redacted] LENS FITTING CHARACTERISTICS

## [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted] **BIOMICROSCOPY SCALE**

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

# [redacted] DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE

## APPENDIX E: IRIS COLOR SCALE

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

Protocol Number and Title: CR-5830, "Evaluating the impact of JJVC senofilcon A – based contact lens with new UV-blocker on day and night driving performance"

Version and Date: v3.0 14 SEP 2017

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

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

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

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

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

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

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

Principal Investigator:

_____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site: _____

Institution/Site Name

_____

Institution/Site Address