Clinical Study Protocol
Johnson & Johnson Vision Care, Inc.

Protocol Title: Evaluation of Rotation with a Multifocal Toric Contact Lens

Protocol Number: CR-6491

Version: 1.0

Date: 02 June 2022

Test Articles: JJVC Investigational Multifocal Toric Contact Lenses manufactured in Senofilcon A (C3) material with UV/HEV filter

Key Words: Presbyopia, Multifocal, Astigmatism, Daily Wear, Daily Disposable, Non-Dispensing, senofilcon A, rotation, CLUE questionnaire

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

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION AND DATE

Protocol Title: Evaluation of Rotation with a Multifocal Toric Contact Lens
Protocol Number: CR-6491
Version: 1.0
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SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

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

Author	See Electronic Signature Page [redacted]	DATE
Clinical Operations Manager	See Electronic Signature Page [redacted]	DATE
Biostatistician	See Electronic Signature Page [redacted]	DATE
Biostatistics Reviewer	See Electronic Signature Page [redacted]	DATE
Data Management	[redacted]	DATE
Medical Safety Officer	See Electronic Signature Page [redacted]	DATE
Approver	See Electronic Signature Page [redacted]	DATE

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Justification for Change	Date
1.0	[redacted]	Original Protocol	NA	02 Jun 2022

SYNOPSIS

Protocol Title	Evaluation of Rotation with a Multifocal Toric Contact Lens
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Confirmatory Design control phase: phase 3
Trial Registration	This study will be registered on ClinicalTrials.gov based on the following: The clinical trial is evaluating a prototype contact lens with the finalized design.
Test Article	Investigational Product: JJVC Investigational Multifocal Toric Contact Lenses manufactured in Senofilcon A (C3) material with UV/HEV filter
Wear and Replacement Schedules	Wear Schedule: The lenses will be used once for a brief period within the study visit in this non-dispensing study. Replacement Schedule: Not applicable.
Objectives	Primary Objective: The primary objective of this study is to evaluate absolute rotation of the investigational multifocal toric lenses 15-minutes after insertion. Exploratory Objectives: Exploratory objectives include evaluations of absolute rotation at 1-, 3-, 7- and, 25-minutes and rotational stability with blink at 15- and 25-minutes. Additionally, initial comfort and handling scores will be assessed.
Study Endpoints	Primary endpoint: • Absolute rotation less than or equal to 10° 15-minutes after insertion Exploratory endpoints: • Summary of Rotation 1-, 3-, 7- and, 25-minutes after insertion • Rotational stability with blink 15- and 25-minutes after insertion • Comfort scores approximately 30-minutes after insertion • Handling scores approximately 30-minutes after insertion

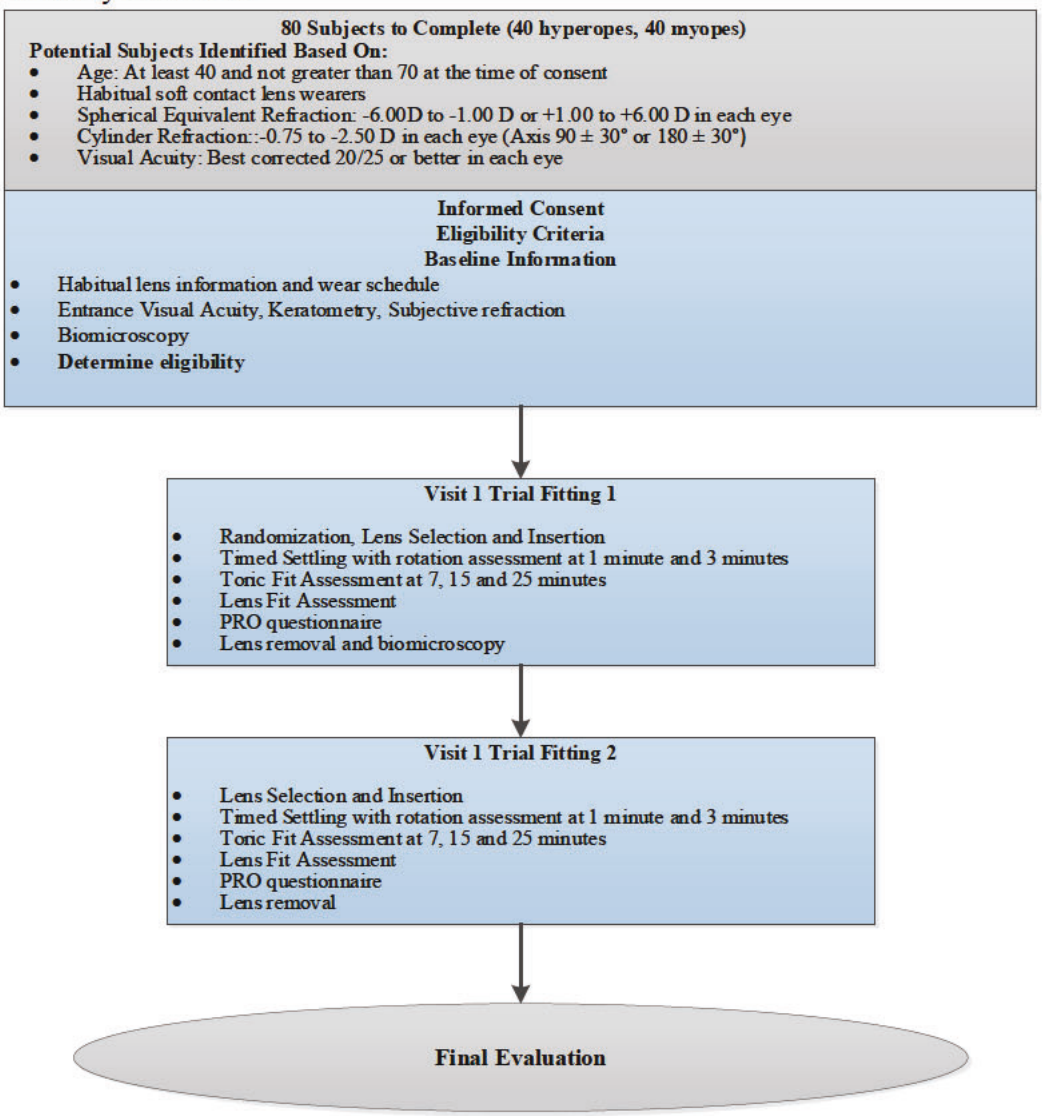
Study Design	The study is a bilateral, single-masked, single-visit, non-dispensing 2x2 crossover study. There will be eight study lens types, however, each subject will only be randomized to receive two study lens types. • Myopes with against-the-rule astigmatism will wear -3.00/-1.00 x 90 and -3.00/-1.75 x 90 • Myopes with with-the-rule astigmatism will wear -3.00/-1.00 x 180 and -3.00/-1.75 x 180 • Hyperopes with against-the-rule astigmatism will wear +3.00/-1.00 x 90 and +3.00/-1.75 x 90 • Hyperopes with with-the-rule astigmatism will wear +3.00/-1.00 x 180 and +3.00/-1.75 x 180 The two lens powers that each subject wears are unlikely to be an exact match to their refractive error (ie. They may under-correct or over-correct the sphere and/or cylinder) and will therefore provide sub-optimal vision correction during the brief wearing period while rotation and comfort are evaluated. The wear period will be approximately forty (40) minutes per lens type. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	Approximately 90 subjects who habitually wear soft contact lenses will be enrolled, with the aim that at least 80 will complete the study (40 myopes and 40 hyperopes).
Study Duration	The study will last approximately 2 months.
Anticipated Study Population	Healthy male and female volunteers in the age range of 40 to 70 with either myopia or hyperopia will be screened as per criteria outlined below. The study will aim to enroll at least 15 subjects in each of these four groups: • Myopes with against-the-rule astigmatism • Myopes with with-the-rule astigmatism • Hyperopes with against-the-rule astigmatism • Hyperopes with with-the-rule astigmatism All volunteers will have baseline measurements taken to ensure eligibility. The baseline procedures will occur after informed consent has been obtained. For a detailed list of procedures see the time and events schedule listed below.
Eligibility Criteria - Inclusion	Potential subjects must satisfy all of the following criteria to be enrolled in the study: Inclusion Criteria following Screening

	The subject must: 1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Be at least 40 and not more than 70 years of age at the time of screening. 4. Own a wearable pair of spectacles with distance vision correction. 5. Be an adapted soft contact lens wearer in both eyes (i.e. has worn lenses a minimum of 2 days per week for at least 8 hours per wear day, for the past four weeks). Inclusion Criteria at Baseline The subject must: 6. Have distance spherical equivalent refraction in the range of either –1.00 D to -6.00 D or +1.00 to +6.00 D in each eye. 7. Have distance cylinder refraction in the range of -0.75 to -2.50 D in each eye, with the axis being in the range of either 90 ± 30° or 180 ± 30°. 8. Have best corrected distance visual acuity of 20/25 or better in each eye.
Eligibility Criteria - Exclusion	Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria following Screening The subject must not: 1. Be currently pregnant or lactating. 2. Have any active or ongoing ocular or systemic allergies that may interfere with contact lens wear. 3. Have any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis). 4. Use systemic medications that may interfere with contact lens wear or cause blurred vision. See section 9.1 for additional details regarding excluded systemic medications.

	5. Currently use ocular medication with the exception of rewetting drops. 6. Have any known hypersensitivity or allergic reaction to single use preservative free rewetting drops, or sodium fluorescein. 7. Have had any previous ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, cataract surgery, retinal surgery, etc.). 8. Have a history of amblyopia or strabismus. 9. Have a history of herpetic keratitis. 10. Have a history of irregular cornea. 11. Have a history of pathological dry eye. 12. Have participated in any contact lens or lens care product clinical trial within 14 days prior to study enrollment. 13. Be an employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician). Exclusion Criteria at Baseline The subject must not: 14. Have clinically significant (Grade 3 or greater) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear. 15. Have entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions. 16. Have any current ocular infection or inflammation. 17. Have any other ocular abnormality that may interfere with contact lens wear
Disallowed Medications/Interventions	Use of any prescription or over-the-counter (OTC) medications that may affect contact lens wear. See section 9.1 for details regarding disallowed systemic medications.
Measurements and Procedures	The key measurements are contact lens rotation assessment, requiring the availability of a slit lamp biomicroscope with an adjustable beam orientation and axis dial, or an eyepiece reticle with axis protractor. Subjective questionnaire responses will be recorded by computer-based direct data entry.
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, may result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Rewetting drops for optional use during lens wear. Stopwatches will be provided to the site for use during visits.
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS, ACRONYMS AND DEFINITIONS OF TERMS

ADD	Plus Power Required For Near Use
ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager

COVID-19	Coronavirus Disease 2019
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
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
PD	Protocol Deviation
PHI	Protected Health Information
PI	Principal Investigator
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRO	Patient Reported Outcome
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect

VA Visual Acuity

1. INTRODUCTION AND BACKGROUND

Johnson & Johnson Vision launched their most recent multifocal contact lens called ACUVUE® OASYS MULTIFOCAL in March, 2021. The lens is recommended for presbyopes who have up to -0.75 D of refractive cylinder. There is a considerable population of presbyopic patients who have greater than -0.75 D of cylinder, in one or both eyes. Currently there are a limited number of soft toric multifocal lenses available. This study will evaluate the performance of prototype daily disposable multifocal toric lenses with a similar optical design to ACUVUE® OASYS MULTIFOCAL which are manufactured in senofilcon A (C3) material with an added high energy visible (HEV) light filter.

1.1. Name and Descriptions of Investigational Products

Test Article: JJVC Investigational Multifocal Toric Contact Lenses manufactured in Senofilcon A (C3) material with UV/HEV filter
Refer to Table 2 in Section 6.1 the protocol.

1.2. Intended Use of Investigational Products

The Investigational Test lens is indicated for daily wear for the optical correction of refractive ametropia (myopia, hyperopia) and presbyopia in phakic or aphakic persons with non-diseased eyes who may need up to +2.50 D of ADD power and have astigmatism in the range of -0.75 D to -2.50 D. In this study, the lenses will be used in a population of presbyopes with spherical equivalent refraction in the range of +1.00 D to +6.00 D or -1.00 D to -6.00 D, and -0.75 D to -2.50 D of cylinder with axis within 90°±30° or 180 ± 30° (see Section 3.2). In this non-dispensing study, study lenses will be available in eight lens powers, and each subject will wear two powers that are unlikely to be an exact match to their refractive error, since vision is not being evaluated.

1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. For the most comprehensive nonclinical information regarding JJVC Multifocal Toric Contact Lenses manufactured in senofilcon A material refer to the latest version of the CR-6491 Investigator's Brochure.[5]

1.4. Summary of Known Risks and Benefits to Human Subjects

For the most comprehensive risk and benefit information regarding JJVC Multifocal Toric Contact Lenses manufactured in senofilcon A material refer to the latest version of the CR-6491 Investigator's Brochure and Informed Consent.[5]

As each study participant will wear two contact lens powers that may over-correct or under-correct the sphere and/or cylinder, there is a risk that they may experience blurred vision, headaches or nausea during wear. It is recommended that subjects remain seated in the examination chair if they experience blurred vision due to the lens power being dissimilar to

their refractive needs. Subjects will need to be monitored by research staff during the brief period of lens wear due to this potential mismatch between the lens power and their refraction. If subjects experience unacceptable headaches or nausea during study lens wear, the lenses should be removed and the subject will need to be discontinued from the study.

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

Investigational multifocal toric lenses with similar designs and materials have been evaluated in three other clinical studies prior to this study. A summary of these studies is shown below, and relevant safety information for these studies is included in the CR-6491 Investigator's Brochure.

[redacted] was a single-arm dispensing evaluation of multifocal toric investigational lenses in a myopic population with against-the-rule astigmatism. Lenses used in this study had a slightly different material formulation than the lenses being used in the current [redacted] study. The study lenses were worn for approximately 2 weeks (with a first follow-up visit after 6-8 days, and second follow-up visit after a further 6-8 days). Forty subjects were enrolled in the study and thirty-seven completed it. No adverse events were reported.[6,7]

[redacted] was a single-arm dispensing evaluation of multifocal toric investigational lenses in a hyperopic population with against-the-rule astigmatism. This study tested lenses with an older formulation (same as the one used in [redacted]) in comparison with a newer formulation. In the 2x3 crossover study design involving 6 visits, subjects wore one of the study lens types for approximately 2 weeks, and the other study lens type for approximately 3 weeks. Of the 35 subjects enrolled, 32 were dispensed study lenses, and 28 completed the study per protocol. Two non-significant ocular adverse events were reported. One ocular adverse event was determined to be not related to the study article or procedure. One ocular adverse event (blepharitis) was considered unlikely to be related to the study article.[6,8]

[redacted] was a bilateral, single-masked, single-arm, 4-visit dispensing study. Study participants wore the study lenses for a period of approximately three weeks. Of the 95 subjects enrolled, 86 were dispensed study lenses, and 83 completed the study per protocol. No adverse events were reported during the study.[7]

In addition to these multifocal toric studies, a series of studies have been performed on a non-toric multifocal version of the study lens. Further details of the safety profile of these related lens types are included in the Investigator's Brochure.[5]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective:
The primary objective of this study is to evaluate absolute rotation of the investigational multifocal toric contact lens 15-minutes after insertion.

Exploratory Objectives:
Exploratory objectives include evaluations of absolute rotation at 1-, 3-, 7- and, 25-minutes and rotational stability with blink at 15- and 25-minutes. Additionally, initial comfort and handling scores will be assessed.

2.2. Endpoints

Primary endpoint:
Absolute rotation ≤ 10° (Acceptable Absolute Rotation)
Absolute rotation will be assessed at 1-, 3-, 7-, 15- and 25-minutes after insertion for each subject eye. However, absolute rotation at 15-minutes will be the primary endpoint. Acceptable absolute rotation is a binary response where Y=1 if absolute rotation is less than or equal to 10° and Y=0 otherwise (absolute rotation greater than 10°). See [redacted] in Appendix D for additional details on the collection of absolute rotation.

Exploratory endpoints:
- Summary of Rotation 1-, 3-, 7- and, 25-minutes after insertion
- Rotational stability with blink 15- and 25-minutes after insertion
- Comfort scores approximately 30-minutes after insertion
- Handling scores approximately 30-minutes after insertion

Comfort and handling scores will be assessed using the Contact Lens User Experience (CLUE™) questionnaire approximately 30-minutes after lens insertion. CLUE™ is a validated patient-reported outcomes questionnaire to assess patient-experience attributes of soft, disposable contact lenses (comfort, vision, handling, and packaging) in a contact-lens wearing population in the US, ages 18-65. Derived CLUE™ scores using Item Response Theory (IRT) follow a normal distribution with a population average score of 60 (SD 20), where higher scores indicate a more favorable/positive response with a range of 0-120. A 5-point increase in an average CLUE™ score translates into 10% shift in the distribution of scores for population of soft contact lens.[9]

2.3. Hypotheses

Primary Hypothesis
1. Approximately 15-minutes after lens insertion, the percentage of lens fits with absolute rotation less than or equal to 10 degrees will be superior to 80%.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

The population to be studied will consist of adapted contact lens wearers with presbyopia, ametropia (hyperopia or myopia) and astigmatism.

3.2. Inclusion Criteria

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

Inclusion Criteria following Screening
The subject must:

1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Be at least 40 and not more than 70 years of age at the time of screening.
4. Own a wearable pair of spectacles with distance vision correction.
5. Be an adapted soft contact lens wearer in both eyes (i.e. has worn lenses a minimum of 2 days per week for at least 8 hours per wear day, for the past four weeks).

Inclusion Criteria at Baseline Evaluation
The subject must:

6. Have distance spherical equivalent refraction in the range of either –1.00 D to -6.00 D or +1.00 to +6.00 D in each eye.
7. Have distance cylinder refraction in the range of -0.75 to -2.50 D in each eye, with the axis being in the range of either 90 ± 30° or 180 ± 30°.
8. Have best corrected distance visual acuity of 20/25 or better in each eye.

3.3. Exclusion Criteria

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

Exclusion Criteria following Screening
The subject must not:

1. Be currently pregnant or lactating.
2. Have any active or ongoing ocular or systemic allergies that may interfere with contact lens wear.
3. Have any active or ongoing systemic disease, autoimmune disease, or use of medication, which may interfere with contact lens wear. This may include, but not be limited to, diabetes, hyperthyroidism, Sjögren's syndrome, xerophthalmia, acne rosacea, Stevens-Johnson syndrome, and immunosuppressive diseases or any infectious diseases (e.g. hepatitis, tuberculosis).
4. Use systemic medications that may interfere with contact lens wear or cause blurred vision. See section 9.1 for additional details regarding excluded systemic medications.
5. Currently use ocular medication with the exception of rewetting drops.
6. Have any known hypersensitivity or allergic reaction to single use preservative free rewetting drops, or sodium fluorescein.
7. Have had any previous ocular or intraocular surgery (e.g. radial keratotomy, PRK, LASIK, lid procedures, cataract surgery, retinal surgery, etc.).
8. Have a history of amblyopia or strabismus.
9. Have a history of herpetic keratitis.
10. Have a history of irregular cornea.

11. Have a history of pathological dry eye.
12. Have participated in any contact lens or lens care product clinical trial within 14 days prior to study enrollment.
13. Be an employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).

Exclusion Criteria at Baseline Evaluation
The subject must not:

14. Have clinically significant (Grade 3 or greater) corneal edema, corneal vascularization, corneal staining, tarsal abnormalities or bulbar injection, or any other corneal or ocular abnormalities which would contraindicate contact lens wear.
15. Have entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions.
16. Have any current ocular infection or inflammation.
17. Have any other ocular abnormality that may interfere with contact lens wear.

3.4. Enrollment Strategy

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

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

The study is a bilateral, single-masked, single-visit, non-dispensing 2x2 crossover study. Up to 90 (45 Hyperopes and 45 Myopes) subjects will be enrolled with the aim of 80 subjects (40 Hyperopes and 40 Myopes) to complete the study.

Eligible subjects will be randomized to receive two investigational multifocal toric lenses in a random order at the single study visit. Subjects will be fitted, and evaluations of toric and mechanical lens fit will be conducted as well as assessment of subjects' initial comfort and handling. Each lens will be worn for approximately forty (40) minutes. Lens powers fit on subjects during this study are unlikely to be an exact match to their refractive error (ie., They may under-correct or over-correct the sphere and/or cylinder) and will therefore provide sub-optimal vision correction during the brief wearing period while rotation and comfort are evaluated.

4.2. Study Design Rationale

A non-dispensing, single-visit, 2×2 bilateral crossover design was considered to be the optimal design to evaluate the primary objective of absolute rotation of the investigational lenses 15-minutes after insertion. The lens design of the investigational multifocal toric lenses in this study was modified after reviewing the results from a previous study [redacted]. Since the primary objective is to assess the absolute rotation, a limited number of lens powers were

chosen to be included in this study, as rotation and lens power are expected to be independent. Lens powers in combinations of plus and minus sphere powers (-3.00, +3.00 DS), low and high cylinder powers (-1.00, -1.75 DC), and cylinder axes (90°, 180°) were chosen to approximately represent the range of possible refractive errors. A 2x2 Crossover design is more cost effective compared to a parallel study as fewer subjects are required to achieve the same pre-specified statistical power. A washout period of 15-minutes will be used between study treatments. Due to the objective nature of the primary endpoint a washout of 15-minutes is considered sufficient to minimize any effects from the previous treatment.

4.3. Enrollment Target and Study Duration

Approximately 90 subjects who habitually wear soft contact lenses will be enrolled, with the aim that at least 80 will complete the study (40 myopes and 40 hyperopes). The study will aim to enroll at least 15 subjects in each of these four groups:

- Myopes with against-the-rule astigmatism
- Myopes with with-the-rule astigmatism
- Hyperopes with against-the-rule astigmatism
- Hyperopes with with-the-rule astigmatism

It is anticipated that 4 or 5 sites will participate, with each site targeting 20 to 28 completed subjects.
Each study subject will participate in a single visit. Study enrollment is expected to take 2 months.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn in a bilateral and random fashion using a 2×2 crossover design. A computer-generated randomization scheme will be used to randomly assign subjects to one of the two possible lens wear sequences (-1.00/-1.75 or -1.75/-1.00 DC) within each refraction and toric fit type group. See Table 1 below for additional details regarding the randomization for this study. The random scheme will be generated using the PROC PLAN procedure from Statistical Analysis System (SAS) Software Version 9.4 or higher (SAS Institute, Cary, NC).[10]

Randomization will be performed prior to the first lens fitting. The following must have occurred prior to randomization:

- Informed consent must have been obtained.
- The subject must have met all eligibility criteria.
- The subject's screening and baseline information must have been collected.

Table 1 Randomization Scheme for 2x2 Crossover by Refraction Group and Toric Fit Type

Refractive Error Group	Toric Fit Type	Sequence	Period 1	Period 2
Myope (-3.00 DS)	against-the-rule astigmatism (90° axis)	1	-1.00 DC	-1.75 DC
		2	-1.75 DC	-1.00 DC
	with-the-rule astigmatism (180° axis)	1	-1.00 DC	-1.75 DC
		2	-1.75 DC	-1.00 DC
Hyperope (+3.00 DS)	against-the-rule astigmatism (90° axis)	1	-1.00 DC	-1.75 DC
		2	-1.75 DC	-1.00 DC
	with-the-rule astigmatism (180° axis)	1	-1.00 DC	-1.75 DC
		2	-1.75 DC	-1.00 DC

5.2. Masking

Subjects will be unaware (masked) of the identity and differences between the investigational products to help reduce potential bias. Investigators and clinical site personnel involved in the data collection will not be masked as to the identity of the investigational product.

5.3. Procedures for Maintaining and Breaking the Masking

Investigators and site personnel will not be masked to the identity of the investigational lenses; therefore, these procedures are not appliable.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 2: Test Articles

	Test Lens
Name	JJVC Investigational Multifocal Toric Contact Lenses manufactured in Senofilcon A (C3) material with UV/HEV filter

	Test Lens
Manufacturer	JJVC
Lens Material	senofilcon A(C3) with chromophore
Nominal Base Curve	8.5
Nominal Diameter	14.3
Nominal Distance Powers (D)	-3.00, +3.00
Nominal Cylinder Powers (D)	-1.00, -1.75
Cylinder axes (°)	90, 180
Nominal ADD Power (D)	Mid
Water Content	38%
Oxygen Permeability (Dk)	122.0
Wear Schedule in Current Study	Daily Disposable
Replacement Frequency	Daily
Packaging Form (vial, blister, etc.)	Blister

Each subject will wear 4 lenses in this non-dispensing study, plus any additional lenses needed for replacements.

6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 3: Ancillary Supplies

	Single-Use Preservative-Free Rewetting Solutions (any of these three options may be supplied)		
Solution Name/Description	Eye-Cept® Rewetting Drops	ScleralFil® Preservative Free Saline Solution	LacriPure Saline Solution
Manufacturer	Optics Laboratory	Bausch + Lomb	Menicon
Preservative	Non-Preserved	Non-Preserved	Non-Preserved

Stopwatches will be provided to research sites to help with managing the timing of toric fit assessments and lens settling.

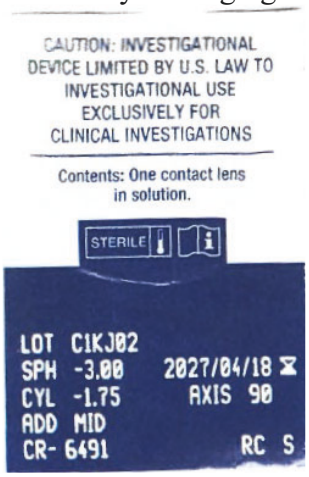
6.3. Administration of Test Articles

Test articles will be dispensed to subjects meeting all eligibility requirements, including any dispensing requirements set forth in this clinical protocol. Test articles which are lost or damaged may be replaced at the discretion of the Investigator.

6.4. Packaging and Labeling

The test articles will be packaged in blisters as the primary packaging with an investigational lens label. The test articles will be in plastic bags as the secondary packaging form. The sample study label is shown below:

Primary Packaging



Secondary Packaging

Sponsored By/Parrainé par:

Johnson & Johnson Vision Care, Inc.
7500 Centurion Parkway
Jacksonville, FL 32256, USA

Contents/Contenu:

Contact Lenses in Solution
Lentilles cornéennes dans une solution

6.5. Storage Conditions

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

6.6. Collection and Storage of Samples

When possible, any lens or test article associated with an Adverse Event and/or a Product Quality Complaint must be retained and stored in a glass vial with moderate solution pending directions from the sponsor for potential return to JJVC.

6.7. Accountability of Test Articles

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

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

1. What was dispensed for the subject for trial fitting
2. The number and reason for unplanned replacements.

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

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

[redacted]

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 4: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1 and 2
Time Point	Day 0
Estimated Visit Duration	2.5 hours
Statement of Informed Consent	X
Demographics	X
Medical History and Concomitant Medications	X
Habitual Contact Lens Information	X
Habitual Contact Lens Wear Schedule	X
Contact Lens History	X
Eligibility after Screening	X
Ocular Symptoms	X
Entrance Distance Visual Acuity	X
Keratometry / SimK	X
Subjective Sphero-cylindrical Refraction	X
Refraction Type	X
Biomicroscopy	X
Eligibility at Baseline	X
Instructions	X
Randomization	X
Lens Selection	XX
Right Lens Insertion	XX
Timed Settling for Right Lens	XX
Left Lens Insertion	XX
Timed Settling for Left Lens	XX
Toric Fit Evaluation (7, 15, 25 minutes)	XX
Lens Fit Assessment	XX
PRO questionnaire	XX
Lens removal	XX
Biomicroscopy	X
Washout period	X
Final Evaluation	X

Note: X = performed once, XX = performed twice.

7.2. Detailed Study Procedures

VISIT 1

The subjects must present to Visit 1 wearing spectacles with distance vision correction, having not worn contact lenses on the day of the visit.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note**: The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's year of birth, age, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subject's medical history and concomitant medications.	
1.4	Habitual Contact Lens Information	Questions regarding the subject's habitual lens type and parameters.	
1.5	Habitual Contact Lens Wear Schedule	Record the duration of wearing this contact lens type and power (number of years and months). During the past four weeks, what is the minimum number of days per week that the subject has worn their lenses for at least 8 hours.	
1.6	Contact Lens History	Record the subject's correction type (i.e. monovision, multifocal, sphere with readers, etc.).	
1.7	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible. *If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.*	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.8	Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.9	Entrance Distance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, OU) to the nearest letter with the subject's habitual distance spectacle correction in place.	[redacted]
1.10	Keratometry / SimK	Keratometry/SimK will be performed OD and OS and the steep and flat dioptric power and corresponding meridians recorded.	[redacted]
1.11	Subjective Sphero-cylindrical Refraction	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity (OD, OS, OU) to the nearest letter. *Note: Best distance visual acuity with sphero-cylindrical refraction must be at least 20/25 in each eye for the subject to be eligible for the study.*	[redacted]
1.12	Refraction Type	Record whether the subject's refraction category in both eyes is: • Myopia with against-the-rule astigmatism (axis 90 ± 30°) • Myopia with with-the-rule astigmatism (axis 180 ± 30°) • Hyperopia with against-the-rule astigmatism (axis 90 ± 30°) • Hyperopia with with-the-rule astigmatism (axis 180 ± 30°) • None of the above	
1.13	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are grade 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 (biomicroscopy does not need to be repeated).	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	
1.14	Eligibility at Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible. *If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.*	
1.15	Instructions	• The subject is advised that the study contact lenses are a power that may not be a close match to their prescription, since the purpose of the study is to evaluate lens fit and comfort. • While wearing the study lenses, if the subject experiences blurry vision, they should remain seated in the exam chair. • If the subject experiences unacceptable headaches or nausea while wearing the study lenses, they should inform the study staff immediately and the lenses will be removed.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.16	Randomization	Record the randomization ID	
1.17	Lens Selection	Assign the study lens type based on the randomization scheme. • Myopes with against-the-rule astigmatism will wear -3.00/-1.00 x 90 or -3.00/-1.75 x 90 in each eye • Myopes with with-the-rule astigmatism will wear -3.00/-1.00 x 180 or -3.00/-1.75 x 180 in each eye • Hyperopes with against-the-rule astigmatism will wear +3.00/-1.00 x 90 or +3.00/-1.75 x 90 in each eye	Appendix D

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		• Hyperopes with with-the-rule astigmatism will wear +3.00/-1.00 x 180 or +3.00/-1.75 x 180 in each eye Record the test lens parameters (power and lot number).	
1.18	Right Lens Insertion	Subjects will insert the right lens themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in a labeled vial with saline for shipment back to the Sponsor. Complete the Quality Product Complaint form.	
1.19	Timed Settling for Right Lens	The investigator will start a stopwatch as soon as the right lens is inserted. **Note: All lenses in this study have toric orientation marks at the 6 and 12 o'clock positions. Rotation measurements are made relative to a vertical reference line**. At one (1) minute after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. At three (3) minutes after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree.	
1.20	Left Lens Insertion	Subjects will insert the left lens themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in a labeled vial with saline for shipment back to the Sponsor. Complete the Quality Product Complaint form.	
1.21	Timed Settling for Left Lens	The investigator will start a stopwatch as soon as the left lens is inserted. **Note: All lenses in this study have toric orientation marks at the 6 and 12 o'clock**	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		positions. Rotation measurements are made relative to a vertical reference line. At one (1) minute after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. At three (3) minutes after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree.	
1.22	Toric Fit Evaluation (7 minutes after insertion)	At approximately 7 minutes after last lens insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink • Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	[redacted]
1.23	Toric Fit Evaluation (15 minutes after insertion)	At approximately 15 minutes after last lens insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink • Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	[redacted]
1.24	Toric Fit Evaluation (25 minutes after insertion)	At approximately 25 minutes after last lens insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink	[redacted]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		• Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	
1.25	Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The lens fit is unacceptable if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	[redacted]
1.26	PRO questionnaire	Approximately 30 to 40 minutes after last lens insertion, the subject will respond to the Post-Fit PRO (CLUE Comfort, Handling) Questionnaire.	[redacted]
1.27	Lens removal	The worn lenses may be discarded.	
1.28	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]

Visit 1: Treatment 2 Lens Fitting			
Step	Procedure	Details	[redacted]
1.29	Washout period	Allow at least 15 minutes break between removal of previous lenses and the insertion of next lens type.	
1.30	Lens Selection	Assign the study lens type based on the randomization scheme. • Myopes with against-the-rule astigmatism will wear -3.00/-1.00 x 90 or -3.00/-1.75 x 90 in each eye • Myopes with with-the-rule astigmatism will wear -3.00/-1.00 x 180 or -3.00/-1.75 x 180 in each eye • Hyperopes with against-the-rule astigmatism will wear +3.00/-1.00 x 90 or +3.00/-1.75 x 90 in each eye • Hyperopes with with-the-rule astigmatism will wear +3.00/-1.00 x 180 or +3.00/-1.75 x 180 in each eye Record the test lens parameters (power and lot number).	Appendix D
1.31	Right Lens Insertion	Subjects will insert the right lens themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in a labeled vial with saline for shipment back to the Sponsor. Complete the Quality Product Complaint form.	
1.32	Timed Settling for Right Lens	The investigator will start a stopwatch as soon as the right lens is inserted. **Note: All lenses in this study have toric orientation marks at the 6 and 12 o'clock positions. Rotation measurements are made relative to a vertical reference line.** At one (1) minute after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. At three (3) minutes after insertion, record:	

Visit 1: Treatment 2 Lens Fitting			
Step	Procedure	Details	[redacted]
		• The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree.	
1.33	Left Lens Insertion	Subjects will insert the left lens themselves. If the lens is uncomfortable, inspect for damage and remove, reinsert or replace as necessary. Damaged lenses will be stored in a labeled vial with saline for shipment back to the Sponsor. Complete the Quality Product Complaint form.	
1.34	Timed Settling for Left Lens	The investigator will start a stopwatch as soon as the left lens is inserted. **Note: All lenses in this study have toric orientation marks at the 6 and 12 o'clock positions. Rotation measurements are made relative to a vertical reference line**. At one (1) minute after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. At three (3) minutes after insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree.	
1.35	Toric Fit Evaluation (7 minutes after insertion)	At approximately 7 minutes after last lens insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink • Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	[redacted]
1.36	Toric Fit Evaluation (15 minutes after insertion)	At approximately 15 minutes after last lens insertion, record:	[redacted]

Visit 1: Treatment 2 Lens Fitting			
Step	Procedure	Details	[redacted]
		• The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink • Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	
1.37	Toric Fit Evaluation (25 minutes after insertion)	At approximately 25 minutes after last lens insertion, record: • The direction of rotation as base nasal or base temporal. The magnitude of rotation error to the nearest degree. • Lens stability with blink • Toric fit acceptable or unacceptable *Toric lens fit will be unacceptable if lenses are rotated more than 30 degrees, or lens stability is worse than 5 degrees movement with blink.* *Unacceptable toric fit is not a reason to discontinue the subject.*	[redacted]
1.38	Lens Fit Assessment	Evaluate and grade lens centration, primary gaze movement, upgaze movement and tightness (push-up test). The lens fit is unacceptable if any of the following is observed: • presence of limbal exposure (appearance of clear cornea) in any gaze • presence of edge lift • presence of unacceptable movement (excessive or insufficient) in <u>all three</u> movement categories (primary gaze, upgaze, and push-up). *If either lens is deemed unacceptable, the subject will be discontinued from the study. Remove the lenses, perform a slit-lamp evaluation, and complete the Final Evaluation form.*	[redacted]

Visit 1: Treatment 2 Lens Fitting			
Step	Procedure	Details	[redacted]
1.39	PRO questionnaire	Approximately 30 to 40 minutes after last lens insertion, the subject will respond to the Post-Fit PRO (CLUE Comfort) Questionnaire.	
1.40	Lens removal	The worn lenses may be discarded.	

FINAL EVALUATION

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

Final Evaluation			
Step	Procedure	Details	[redacted]
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study, indicate the reason.	
F.2	Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	
F.3	Subjective spherocylindrical Refraction	An optimal, binocular balanced distance sphero-cylindrical refraction will be performed. Record the refraction and distance visual acuity (OD, OS, OU) to the nearest letter.	
F.4	Exit Distance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, OU) to the nearest letter with the subject's habitual distance spectacle correction in place.	

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.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.2	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.3	Entrance VA	Record the distance Snellen visual acuity (OD, OS, OU) to the nearest letter, and the type of visual correction being worn (study lenses, habitual lenses, distance spectacles or unaided).	[redacted]
U.4	Subjective Sphero-cylindrical Refraction (if applicable)	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS).	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
U.6	Exit Visual Acuity	Record the distance Snellen visual acuity (OD, OS, OU) to the nearest letter, and the type of visual correction being worn (study lenses, habitual lenses, distance spectacles or unaided).	[redacted]

7.4. Laboratory Procedures

None

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent.
- are eligible.
- completed the study visit

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 no longer meets eligibility criteria (e.g. the subject becomes pregnant).
- Subject develops significant or serious adverse events causing discontinuation of study lens wear.
- Subjects who have experienced a Corneal Infiltrative Event (CIE).
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment).

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.
- Make arrangements for subject care, if needed, due to their study participation

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

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

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

9.1. Systemic Medications

Certain systemic medications are known to have a higher likelihood to interfere with contact lens wear, chiefly by disrupting the tear film. A summary of disallowed medications is shown in Table 5. Subjects with a history of taking these medications will be allowed to enroll only if:

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

Or

- The subject previously used these medications on a temporary basis and has ceased that medication at least 1 week prior to signing the informed consent.

Table 5: Disallowed systemic medications

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

10. DEVIATIONS FROM THE PROTOCOL

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

If it becomes necessary for the Investigator to implement a deviation in order to eliminate an immediate hazard to the trial subject, the Investigator may implement the deviation immediately without notification to the sponsor. Within 24 hours after the implemented

deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, the IEC/IRB.

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

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

Protocol waivers are prohibited.

11. STUDY TERMINATION

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

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

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

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

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

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

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

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

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

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness).
- Who received the complaint.
- Study number.
- Clinical site information (contact name, site ID, telephone number).
- Lot number(s).
- Unique Subject Identifier(s).
- Indication of who first observed complaint (site personnel or subject).
- OD/OS indication, along with whether the lens was inserted.
- Any related AE number if applicable.
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.).

- Eye Care Provider objective (slit lamp) findings if applicable.
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return [redacted]

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

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

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device."
NOTE: This definition includes events related to the investigational medical device or the comparator, and to the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.[1]

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

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

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

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

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

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

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

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

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

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

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

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

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

- Non-significant Infiltrative Event (NSIE)
- Contact Lens Papillary Conjunctivitis (CLPC)
- Superficial Punctate Keratitis (SPK)
- Conjunctivitis: Bacterial, Viral, Allergic

- Blepharitis
- Meibomianitis
- Contact Dermatitis
- Localized Allergic Reactions
- Any corneal event not explicitly defined as serious or significant adverse event, which necessitates temporary lens discontinuation < 2 weeks

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device."
NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.[9]

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

13.2. Assessing Adverse Events

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

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

13.2.1. Causality Assessment

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

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

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

13.2.2. Severity Assessment

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

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

13.3. Documentation and Follow-Up of Adverse Events

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

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

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

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

- Adverse event (diagnosis not symptom).

- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.).
- Date the clinical site was notified.
- Date and time of onset.
- Date and time of resolution.
- Adverse event classification, severity, and relationship to test articles, as applicable.
- Treatment regimen instituted (where appropriate), including concomitant medications prescribed, in accordance with applicable licensing requirements.
- Any referral to another health care provider if needed.
- Outcome, ocular damage (if any).
- Likely etiology.
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event, if the AE is related to the visual system.

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

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

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

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

13.4. Reporting Adverse Events

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

13.4.1. Reporting Adverse Events to Sponsor

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

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

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

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

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

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

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

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

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

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

13.5. Event of Special Interest

None

13.6. Reporting of Pregnancy

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

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below.

All data summaries and statistical analyses will be performed using the Statistical Analysis System (SAS) software Version 9.4 or higher (SAS Institute, Cary, NC).[11] Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. Unscheduled visits will be summarized.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation [SD], median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data. Summary tables will be summarized by timepoint, group and lens.

14.2. Sample Size Justification

This study was designed and powered to test that the percentage of lens fit with absolute rotation for both study lenses is superior to 80% 15-minutes after insertion. The sample size

was calculated using a 2-sided type I error rate of 5% with at least 80% statistical power. Historical data from [redacted] and [redacted] was both utilized in estimation of the sample size.[7,12] Table 6 below provides details regarding each clinical study and Table 7 summarizes the absolute rotation for each study and lens for all lens fits (including any modifications).

Table 6 Summary of Historical Clinical Studies

Study ID	Design	Population	Age Range (years)	Number Enrolled	Number Dispensed	Number Completed
[redacted]	Single arm	Hyperopes + Myopes	40 to 70	95	86	84
[redacted]	2x2 crossover	Myopes	18 to 39	103	98	93

Table 7 Summary of Absolute Rotation by Lens – 15-Minutes After Insertion

	AOfA N=202	Aurora A		
		Hyperopes N=114	Myopes N=136	Total N=250
Absolute rotation n(%)				
0 to 5	174 (86.1)	85 (74.6)	96 (70.6)	181 (72.4)
>5 to 10	19 (9.4)	14 (12.3)	21 (15.4)	35 (14.0)
>10 to 15	8 (4.0)	7 (6.1)	11 (8.1)	18 (7.2)
>15	1 (0.5)	8 (7.0)	8 (5.9)	16 (6.4)
Total	202	114	136	250
Absolute rotation < 10° n(%)				
Yes	193 (95.6)	99 (86.8)	117 (86.0)	216 (86.4)
No	9 (4.5)	15 (13.2)	19 (14.0)	34 (13.6)
Total	202	114	136	250

N=Number of lens fits.

Based on the results from [redacted], the lens design was modified to improve the absolute rotation. The changes implemented into the lens design are more closely aligned with the Acuvue Oasys for Astigmatism lens design utilized in [redacted]. However, as indicated in Table 5, [redacted] enrolled non-presbyopic myopic subjects only. In general, presbyopic subjects have been found to more contact lens rotation compared to non-presbyopic subjects, therefore,

results from both studies were considered when choosing different scenarios of reference rates.[7,12]

Shown in Table 6 above, [redacted] had rates of 86% and 96%, respectively. Therefore, different scenarios used for the sample size and power calculations were chosen within that range. Furthermore, taking into consideration that this study will enroll subjects aged 40 to 70, more conservative rates of 88%, 89% and 90% were used.[7,12]

Sample size estimates were carried out using Monte Carlo methods. A total of 2000 boot-strap samples were simulated using different scenarios for the reference rate for event Y and interclass correlations of 0.80 to model the covariance between the left and right eyes within the same treatment, and 0.50 to model both the covariance between treatments within the same eye as well as between eyes and treatments. Each boot-strap sample was analyzed using a generalized linear mixed model with a binary distribution and the logit and the link function. Lens was included as the only fixed effect. Errors between measurements within the same subject and period were modeled using a variance component covariance structure (VC). The Kenward and Roger Method was used for the denominator degrees of freedom.[13] The percentage of lens fits with absolute rotation less than 10° was constructed using 95% confidence intervals for the least-square mean. Success for each boot-strap sample was declared if the lower limit of the 95% CI was above 80%. Table 8 below displays the number of subjects required to test superiority for the primary hypothesis for each study lens.

While subjects will wear the study lenses in a random order data collected during evaluations in period 2 are not expected to be influenced by the lenses worn during period 1 since a wash-out 15 -minutes will be utilized between study lenses and, subjects' absolute rotation depends on the study lens on eye at that moment of data collection.

Table 8 Statistical Power for 80 Subjects to complete by Reference Rate

	Reference Rate		
	88%	**89%**	**90%**
Statistical Power (%)	87.7	95.1	98.3

Up to 90 subjects (45 Hyperopes and 45 Myopes) will be enrolled with the target of 80 subjects (40 Hyperopes and 40 Myopes) to complete the study. Since this is a single-visit, non-dispensing study, a high rate (> 10%) of subject drop-out is not expected to occur. However, subject drop-out rate will be monitored. If an unexpectedly high dropout rate is observed, then enrollment maybe be increased to ensure the minimum number of subjects required to test the primary hypothesis complete the study.

14.3. Analysis Populations

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

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

Intent-to-Treat (ITT) Population:
All randomized subjects regardless of actual treatment and subsequent withdrawal from study or deviation from protocol. At least one observation should be recorded.

14.4. Level of Statistical Significance

The primary analyses will be conducted with a 2-sided type I error rate of 5%.

14.5. Primary Analysis

The primary analysis will be conducted on the ITT population.

Absolute Rotation ≤10°
Absolute rotation data collected 15-minutes after insertion will be dichotomized as Y=1 if the absolute rotation is less than 10° and Y=0 otherwise for the purpose of analysis. Y will be analyzed using a generalized linear mixed model with a binary distribution and the logit as the link function. Sequence of lens wear, period and lens type will be included in the model as fixed effects. Other characteristics such as age may be included as covariates in the model. Site and subject will be included as random effects (G-side). The covariance measurements within the same subject (between eyes) across study periods will be modeled using an unstructured (UN) covariance structure. The Kenward and Roger method[7] will be used for the denominator degrees of freedom. If none of the fixed effects are significant, the percentage of lens fits with absolute rotation less than 10° will be estimated by combining data from both lenses using 2-sided 95% confidence intervals.

The Model:
Let y_{ijklmn} denote the absolute rotation for the n^{th} eye from the m^{th} subject at the l^{th} site assigned to the k^{th} sequence during the j^{th} period for the i^{th} lens (i=1,2,; j=1,2; k=1, 2,; l=1…,$l_m n = 1,2$). The likelihood will be constructed as follows:

$$logit(y_{ijklmn}) = \beta_0 + \beta_1 Lens_{i[j,k]} + \beta_2 Period_j + \beta_3 Sequence_k + \delta_l + \gamma_{l_m} + \varepsilon_{ijklmn}$$

Where:

- β_0: Intercept

- $Lens_i$: $Lens_i$=1 if Lens='-1.00DC'; otherwise $Lens_i$=0
- $Period_j$: $Period_j$=1 if period=1; otherwise $Period_j$=0
- $Sequence_k$: $Sequence_k$=1 if sequence=-1.00/-1.75; otherwise $Sequence_k$=0
- δ_l: effect of the l^{th} site, a random effect
- γ_{l_m}: effect of the m^{th} subject from the l^{th} site, a random effect
- ε_{ijklmn}: Random error associated between eyes (left and right) for the m^{th} subject from the l^{th} site assigned to the k^{th} sequence during the j^{th} period for the i^{th} lens

Assume δ_l, γ_{l_m} and ε_{ijklmn} are independent and

- $\delta_k \sim N(0, \sigma^2_{site})$
- $\gamma_{l_m} \sim N(0, \sigma^2_{subject(site)})$
- $\begin{bmatrix} \varepsilon_{ijklm\_Left} \\ \varepsilon_{ijklm\_Right} \end{bmatrix} = \left(\begin{bmatrix} 0 \\ 0 \end{bmatrix}, \begin{bmatrix} \sigma^2_{11} & \sigma^2_{12} \\ \sigma^2_{21} & \sigma^2_{22} \end{bmatrix} \right)$

Primary Hypothesis

The null and alternative hypothesis to test for superiority are as follows:

$$H_o: P_T \leq 80\%$$
$$H_A: P_T > 80\%$$

Where P_T is the probability of the event (i.e., the probability of having absolute rotation less than 10° 15-minutes after insertion). Superiority will be concluded if the lower limit of the 95% confidence interval is above 80%(i.e., P(p_{Test}> 80%) ≥ 0.975).

14.6. Secondary Analysis

Not applicable.

14.7. Other Exploratory Analyses

Exploratory endpoints will be descriptively summarized.

14.8. Interim Analysis

No interim analysis will be conducted on this study.

14.9. Procedure for Handling Missing Data and Drop-Outs

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

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

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

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

15.2. Subject Record

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

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

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

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

15.3. Trial Registration on ClinicalTrials.gov

This study will be registered on ClinicalTrials.gov based on the following: The purpose of the study is for design confirmation, not feasibility.

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

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

16.2. Confidentiality of Information

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

16.3. Data Quality Assurance

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

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

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

16.4. Data Monitoring Committee (DMC)

Not applicable.

17. CLINICAL MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

Potential subjects will be fully informed of the risks and requirements of the study and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. 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),[2] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this

standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] 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),[2] and applicable regulatory requirements.

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

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

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

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

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

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

- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

For protocol revisions that increase subject risk, the revisions and applicable informed consent form revisions must be submitted promptly to the IEC/IRB for review and approval before implementation of the change(s).
At least once a year, the IEC/IRB will review and reapprove this clinical study. This request should be documented in writing.

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

18.4. Informed Consent

Each subject or their representative, must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and ISO 14155:2020[1] guidelines, applicable regulatory requirements, and Sponsor Policy.

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential 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.

Each subject for this study will complete an assent and a parent or legal guardian must give written informed consent according to local requirements after the nature of the study has been fully explained. The assent and consent forms must be signed before performance of any study-related activity. The assent and consent forms that are used must be approved by both the Sponsor and by the reviewing IEC/IRB. The assent and informed consent forms should be in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH[2] and GCP guidelines, applicable regulatory requirements, and Sponsor policy. Before entry into the study or pre-screening, the Investigator or an authorized member of the clinical site personnel must explain to the potential subject and parent and/or legal guardian the aims, methods, reasonably anticipated benefits, and potential hazards of the study or pre-screening, and any discomfort it may entail. Subjects and parent and/or legal guardian will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the subject will receive.

Finally, they will be told that the Investigator will maintain a subject identification register for the purposes of long-term follow-up if needed and that their records may be accessed by health authorities and authorized Sponsor personnel without violating the confidentiality of the subject, to the extent permitted by the applicable law(s) or regulations. By signing the assent and informed consent form, the subject is authorizing such access and agrees to be contacted after study completion by health authorities and authorized Sponsor personnel for the purpose of obtaining consent for additional safety evaluations if needed.

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) in the United States and other applicable personal data protection and security laws and regulations.[14] 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,[2] 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[2] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

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

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

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

22. REFERENCES

1. ISO 14155:2020: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice.
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. http://www.wma.net/en/30publications/10policies/b3/index.html.
4. United States (US) Code of Federal Regulations (CFR). . https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
5. Franklin R, *Investigator Brochure CR-6491* [redacted] *JJVC Investigational Multifocal Toric Contact Lenses manufactured in Senofilcon A (C3) material with UV blocker/HEV filter*. May 19, 2022
6. Franklin R, *Clinical Study Report* [redacted] *Pilot Evaluation of a Silicone Hydrogel Daily Disposable Toric Multifocal Contact Lens*. March 15, 2021
7. Franklin R, *Clinical Study Report* [redacted] *Evaluation of Daily Disposable Silicone Hydrogel Multifocal Toric Contact Lenses*. March 04, 2022
8. Franklin R, *Clinical Study Report* [redacted] *Evaluation of Silicone Hydrogel Multifocal Toric Contact Lenses in a Hyperopic Population*. October 20, 2021
9. Wirth RJ, Edwards MC, Henderson M, Henderson T, Olivares G, Houts CR. Development of the Contact Lens User Experience: CLUE Scales. *Optom Vis Sci.* 2016;93(8):801-808.
10. *SAS Institute Inc: SAS® 9.4 Statements: Reference, Third Edition.* Cary, NC SAS Institute Inc; 2014.
11. SAS Institute Inc: SAS® 9.4 Statements: Reference TEC, NC: SAS Institute Inc; 2014.
12. Straker B, *Clinical Study Report* [redacted] *Evaluation of Subjective Vision, Comfort and Handling of Toric Lenses with RTY-1 Chromophore*. May 01, 2020

13. Kenward MG, Roger JH. Small Sample Inference for Fixed Effects from Restricted Maximum Likelihood. *Biometrics.* 1997;53(3):983.
14. Health Information Portability and Accountability Act (HIPAA). https://www.hhs.gov/hipaa/for-professionals/privacy/index.html

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

[redacted]

APPENDIX B: PATIENT INSTRUCTION GUIDE

The patient instruction guide (PIG) will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Not Applicable, as this study uses Investigational Products

APPENDIX D: [redacted]

- [redacted] LENS FITTING CHARACTERISTICS
- [redacted] SUBJECT REPORTED OCULAR SYMPTOMS
- [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS
- [redacted] BIOMICROSCOPY SCALE
- [redacted] KERATOMETRY
- [redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION
- [redacted] TORIC FIT EVALUATION
- [redacted] PATIENT REPORTED OUTCOMES

[redacted] LENS FITTING CHARACTERISTICS

Title: Lens Fitting Characteristics

Document Type: [redacted]

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] SUBJECT REPORTED OCULAR SYMPTOMS

[redacted]

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

Title: Determination of Distance Spherocylindrical Refractive Error

Document Type: [redacted]

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **BIOMICROSCOPY SCALE**

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

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

[redacted]

[redacted] **KERATOMETRY**

Title: Keratometry Procedure
Document Type: [redacted]
Document Number: [redacted] **Revision Number:** 03

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION

Title: Distance and Near Snellen Visual Acuity Evaluation

Document Type: [redacted]

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] TORIC FIT EVALUATION

Title: Toric Fit Evaluation

Document Type: [redacted]

Document Number: [redacted] **Revision Number:** 7

[redacted]

[redacted]

[redacted]

[redacted]

APPENDIX E: GUIDELINES FOR COVID-19 RISK MITIGATION

1.0 PURPOSE

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

2.0 SCOPE

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

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

3.0 DEFINITIONS

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

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

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

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

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

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

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

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

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

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

4.0 GUIDANCE FOR STUDY DOCUMENTS

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

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

4.1 Additional Risks Related to the COVID-19 Pandemic:

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

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

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

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

4.1.1 Informed Consent:

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

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

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

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

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

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

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

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

4.1.3 Protocol Compliance Investigator(s) Signature Page:

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

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

4.1.4 Study Site Initiation Training Slides:

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

5.0 GUIDANCE FOR REMOTE SUBJECT VISITS

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

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

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

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

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

6.0 STUDY CONDUCT DURING PANDEMIC

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

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

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

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

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

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

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

6.1 Monitoring Visits

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

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

6.1.1 Study Site Initiation:

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

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

6.1.2 Interim Monitoring Visits (if applicable):

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

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

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

6.1.3 Study Site Closure:

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

Attachment A: Study Site Correspondence

XXXX XX, 2020

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

Dear <<Principal Investigator>> and Study Team,

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

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

Protocol:

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

Protocol Signature Page:

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

Informed Consent:

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

COVID-19 Risk Control Checklist for Clinical Studies:

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

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

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

Please file this letter in your site file study correspondence.

Attachment B: COVID-19 Risk Control Checklist

Study Number
Site Number
Principal Investigator (PI) Name

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

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

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

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

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

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

Principal Investigator Signature and Date

RESOURCE LINKS

US Resource Links

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

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

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

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

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

OUS Resource Links

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

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

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

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

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

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

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6491 Evaluation of Rotation with a Multifocal Toric Contact Lens

Version and Date: 1.0, 02 June 2022

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

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

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

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

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

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

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

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

Principal Investigator:

_____ _____
Signature Date

_____
Name and Professional Position (Printed)

Institution/Site:

_____
Institution/Site Name

_____
Institution/Site Address