Evaluation of Delefilcon A and Senofilcon A Daily Disposable Toric Soft Contact Lenses Over One Week of Wear

Protocol CR-6594

Version: 2.0

Date: 13 February 2025

Test Articles:

Control product: Alcon DAILIES TOTAL1® for Astigmatism Daily Contact Lenses (DT1fA).
Test product: ACUVUE® OASYS MAX 1-Day Contact Lenses for ASTIGMATISM (AOM1DfA).

Commercially Available Product Lots: Alcon DAILIES TOTAL1® for Astigmatism Daily Contact Lenses (DT1fA). The Test product (AOM1DfA) has regulatory approval but is not yet commercially available.

Keywords: Astigmatism, toric contact lenses, ACUVUE® OASYS MAX 1-Day for ASTIGMATISM, senofilcon A, Alcon DAILIES TOTAL1® for Astigmatism, delefilcon A, daily wear, daily disposable, dispensing, Single use Eye-Cept® Rewetting Drops, LacriPure Saline Solution, ScleralFil Preservative Free Saline Solution, subjective comfort, overall opinion.

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

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

Confidentiality Statement:

PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Evaluation of Delefilcon A and Senofilcon A Daily Disposable Toric Soft Contact Lenses Over One Week of Wear
Protocol Number: CR-6594
Version: 2.0
Date: 13 February 2025

SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

[redacted]

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

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

AUTHORIZED SIGNATURES

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

Author & Study Responsible Clinician	*See Electronic Signature Report* [redacted]	DATE
Clinical Operations Manager	*See Electronic Signature Report* [redacted]	DATE
Biostatistician	*See Electronic Signature Report* [redacted]	DATE
Data Management	*See Electronic Signature Report* [redacted]	DATE
Medical Safety Officer	*See Electronic Signature Report* [redacted]	DATE
Medical Monitor	*See Electronic Signature Report* [redacted]	DATE
Platform Lead/Project Lead/Director	*See Electronic Signature Report* [redacted]	DATE

[redacted]

SYNOPSIS

Protocol Title	Evaluation of Delefilcon A and Senofilcon A Daily Disposable Toric Soft Contact Lenses Over One Week of Wear
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Claims (Control product is commercially available, Test product has regulatory approval however is not yet commercially available) Design control phase: Phase 4
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor.
Test Article(s)	Approved Products: Test product: ACUVUE® OASYS MAX 1-Day for ASTIGMATISM (AOM1DfA). Control product: Alcon DAILIES TOTAL1® for Astigmatism Contact Lenses (DT1fA).
Wear and Replacement Schedules	Wear Schedule: Daily wear Replacement Schedule: Daily disposable
Objectives	Primary Objective: The primary objective of this study is to compare the Test lens to the Control lens with respect to long lasting comfort following approximately 1 week of lens wear. Secondary Objectives: The secondary objectives of this study are to compare the Test lens to the Control lens with respect to overall opinion and comfort at the end of the day following approximately 1 week of lens wear. Other Objectives: Other objectives of this study include the evaluation of lens orientation after lens insertion and following lens settling, distance Snellen VA, the incidence of slit lamp findings and adverse events.
Study Endpoints	Primary Efficacy Endpoint: • Long Lasting Comfort Co-Secondary Efficacy Endpoints: • Overall Opinion • End-of-Day Comfort Other Efficacy Endpoints: • Lens orientation at 1 minute and 3 minutes following insertion • Post-settling lens orientation • Distance Snellen visual acuity (VA) • Study Lens Preference Other Safety Endpoints: • Incidence of Slit lamp findings (SLFs) • Adverse events

Study Design	This is a prospective, multi-site, 4-visit, bilateral, dispensing, randomized, controlled, double-masked, 2×2 crossover study. Eligible subjects will be randomly assigned to one of two lens wear sequences (Test/Control or Control/Test). Each lens will be worn for a period of 7(±2) days. There will be a 7(±2) days washout period between study lens wear periods. There will be a total of 4 visits: Visit 1: Screening, baseline evaluation and lens fit #1 Visit 2: Follow-up evaluation #1 (for first lens dispensed) Visit 3: Continuance, lens fit #2 Visit 4: Follow-up evaluation #2 (for second lens dispensed) See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations Figure 1).
Sample Size	This study will have an enrollment and randomization target of approximately 132 subjects, with a target of at least 120 to complete (assuming a dropout rate of approximately 10%). The study will be conducted at up to 12 clinical sites in the United States. Eligible subjects will be randomized to one of two wear sequences (Test/Control or Control/Test) in a 1:1 ratio.
Study Duration	The total study duration (timeframe between anticipated First Subject First Visit (FSFV) and anticipated Last Subject Last Visit (LSLV)) is anticipated to be approximately 10 weeks. The maximum duration of participation for any given subject will be approximately 27 days.
Anticipated Study Population	Subjects will be habitual soft contact lens wearers with bilateral astigmatism who are between 18 and 39 years of age (inclusive).
Eligibility Criteria - Inclusion	Potential subjects must satisfy of all the following criteria to be enrolled in the study. Inclusion Criteria following Screening The subject must: 1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Be between 18 and 39 (inclusive) years of age at the time of screening. 4. By self-report, habitually wear soft contact lenses in both eyes in a daily reusable or daily disposable wear modality (i.e., not extended wear modality). Habitual wear is defined as a minimum of 6 hours of wear per day, for a minimum of 2 days per week during the past four weeks. 5. Possess a wearable pair of spectacles that provide correction for distance vision. Inclusion Criteria at Baseline Evaluation The subject must: 6. In both eyes, have refractive error suitable for correction with the range of toric contact lens powers available in this study: 6.1 Sphere powers (DS) -1.50 through -4.00 (inclusive) in 0.25 steps 6.2 Cylinder powers (DC) -0.75 and -1.25 6.3 Axes (°) 170, 180, 10, 80, 90 and 100 7. Have best corrected monocular 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. Be diabetic. 3. Be currently using any ocular medications or have any ocular infection of any type. 4. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g., rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1 for additional details regarding excluded systemic medications. 5. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g., SynergEyes, SoftPerm) within the past 6 months. 6. Be currently wearing monovision or multifocal contact lenses. 7. Be currently wearing lenses in an extended wear modality. 8. Have a history of strabismus or amblyopia. 9. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site. 10. Have participated in a contact lens or lens care product clinical trial within 7 days prior to study enrollment. Exclusion Criteria at Baseline Evaluation The subject must not: 11. Have clinically significant (grade 3 or higher on the FDA grading scale) slit lamp findings (e.g., corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection) or other corneal or ocular disease or abnormalities that contraindicate contact lens wear or may otherwise compromise study endpoints (including entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, moderate or above corneal distortion, herpetic keratitis). 12. Have fluctuations in vision due to clinically significant dry eye or other ocular conditions. 13. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, PRK, LASIK, iridotomy, retinal laser photocoagulation, etc.).
Disallowed Medications/Interventions	Subjects will not be eligible to enroll if they are taking any ocular medications, or any systemic medications that would normally contraindicate contact lens wear or may otherwise compromise study endpoints. See section 9.1 for details regarding disallowed systemic medications.

Measurements and Procedures	The key procedures associated with the endpoints for this study will be: - Fitting of toric soft contact lenses - Overseeing completion of PRO questionnaires - Measuring toric lens orientation and rotational stability using a slit lamp biomicroscope with a beam axis dial - Measuring visual acuity - Examining the anterior segment using a slit lamp biomicroscope and grading findings using the FDA grading scale
Microbiology or Other Laboratory Testing	Not applicable.
Study Termination	The occurrence of an Unanticipated Adverse Device Effect (UADE), Unanticipated Serious Adverse Device Effect (USADE), or Serious Adverse Event (SAE) for which a causal relationship to a test article cannot be ruled out, may result in stopping further dispensing of the investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Lens cases, fluorescein strips and preservative-free rewetting drops / artificial tears will be supplied for use as needed.
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.
External Organization(s)	The external organization(s) involved in this study will be listed in the Trial Master File.

COMMONLY USED ABBREVIATIONS, ACRONYMS AND DEFINITIONS OF TERMS

ADE	Adverse Device Effect
ADHD	Attention Deficit Hyperactivity Disorder
AE	Adverse Event/Adverse Experience
AOM1DfA	ACUVUE® OASYS MAX 1-Day for ASTIGMATISM
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CI	Confidence Interval
CLUE	Contact Lens User Experience
COM	Clinical Operations Manager
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HEV	High Energy Visible
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
IB	Investigator's Brochure
ICH	The International Council for Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intention-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LASIK	Laser-Assisted in Situ Keratomileusis
OD	Right Eye
OS	Left Eye
OU	Both Eyes
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRK	Photorefractive Keratectomy
PRO	Patient Reported Outcome
QA	Quality Assurance
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
UV	Ultraviolet
VA	Visual Acuity

1. INTRODUCTION AND BACKGROUND

DAILIES TOTAL1® for Astigmatism Contact Lenses (DT1fA, delefilcon A) are single-use, daily disposable lenses indicated for the correction of astigmatism and associated ametropia in persons with non-diseased eyes. Rotational stability of the DT1fA lenses is achieved through a peri-ballast stabilization design. ACUVUE® OASYS MAX 1-Day for ASTIGMATISM (AOM1DfA, senofilcon A) are daily disposable, toric soft contact lenses featuring a blink-stabilized design. The purpose of this study is to evaluate subjective comfort, overall opinion and end of day comfort following wear of AOM1DfA relative to DT1fA as Control.

[redacted]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective:
The primary objective of this study is to compare the Test lens to the Control lens with respect to long lasting comfort following approximately 1 week of lens wear.

Secondary Objectives:
The secondary objectives of this study are to compare the Test lens to the Control lens with respect to overall opinion and comfort at the end of the day following approximately 1 week of lens wear.

Other Objectives:
Other objectives of this study include the evaluation of lens orientation after lens insertion and following lens settling, distance Snellen VA, the incidence of slit lamp findings and adverse events.

2.2. Endpoints

2.2.1 Efficacy Endpoints

Primary Efficacy Endpoint

- Long Lasting Comfort

Long lasting comfort, with respect to contact lens wear, will be assessed using the individual questionnaire item: 'I could wear these contact lenses comfortably for as long as I wanted to'. This item will utilize an agreement scale of, 1: Strongly Disagree, 2: Disagree, 3: Neither Agree nor Disagree, 4: Agree and 5: Strongly Agree. Long lasting comfort will be assessed at baseline and after 1-week of lens wear. However, data collected at the 1-week follow-up will be the primary endpoint. Subjects' responses to this questionnaire item will be dichotomized as Y=1 if a subject responds Strongly Agree or Agree and Y=0, otherwise.

Co-Secondary Efficacy Endpoints

- Overall Opinion

Overall opinion, with respect to the study contact lenses, will be evaluated using the individual questionnaire item 'Considering your experience with the study contact lenses, which statement best describes your overall opinion of these contact lenses?'. This item will utilize an excellence scale of, 1: Poor, 2: Fair, 3: Good, 4: Very Good and 5: Excellent. Overall opinion will be assessed at baseline and after 1-week of lens wear. However, data collected at the 1-week follow-up will be the primary endpoint. Subjects' responses to this questionnaire item will be dichotomized as Y=1 if a subject responds Excellent or Very good and Y=0, otherwise.

- Comfort at the End of the Day

Comfort at the end of the day, with respect to contact lens wear, will be assessed using the individual questionnaire 'These lenses were very comfortable at the end of the day'. This item will utilize an agreement scale of, 1: Strongly Disagree, 2: Disagree, 3: Neither Agree nor Disagree, 4: Agree and 5: Strongly Agree. Subjects' responses to this questionnaire item will be dichotomized as Y=1 if a subject responds Strongly Agree or Agree and Y=0, otherwise.

Other Efficacy Endpoints

- Lens orientation at 1 minute and 3 minutes following insertion

Toric lens orientation (scribe mark position relative to 6 o'clock, in degrees) will be assessed for each eye at 1-, and 3-minutes following lens insertion at the fitting visits. Subjects will insert lenses with random orientation. Lens orientation will be assessed using a slit lamp biomicroscope with a beam axis dial by aligning the beam with the scribe mark on the anterior surface of the lens.

- Post-settling lens orientation

Toric lens orientation (scribe mark position relative to 6 o'clock, in degrees) will be assessed for each eye following settling at the fitting visits, and at the 1-week follow-up visits. Lens orientation will be assessed using a slit lamp biomicroscope with a beam axis dial by aligning the beam with the scribe mark on the anterior surface of the lens.

- Distance (4m) Snellen Visual Acuity

Visual acuity (VA) will be assessed monocularly at distance (4m) using Snellen Charts at the fitting evaluation and after approximately 1-week of lens wear. The distribution of eyes (n, %) for each VA category (e.g., 20/20, 20/25, 20/30…, etc.) will be summarized by study lens and timepoint using counts and percentages.

- Study Lens Preference

Study lens preference will be evaluated using a questionnaire and will be asked at the final follow-up evaluation (visit 4). Preference will be assessed using the following wording:

"Comparing the first set of study contact lenses to the second set of study contact lenses, please describe your preferences to each of the following items":

a. Overall Comfort [redacted]
b. Overall Opinion [redacted]
c. Comfort at the end of the day [redacted]
d. Comfort throughout the day [redacted]

Preference items will utilize the following response scale 1: Strongly prefer the first set of study lenses, 2: Slightly prefer the first set of study lenses, 3: No Preference, 4: Slightly prefer the second set of study lenses and 5: Strongly prefer the second set of study lenses. The final data reported for these endpoints will be derived based on the lens wear sequences (Test/ Control or Control/Test). The final output for preference will display the following response set: 1: Strongly prefer the Test Lens, 2: Slightly prefer the Test Lens, 3: No Preference, 4: Slightly prefer the Control lens and 5: Strongly prefer the Control lens.

Subjects' responses to the preference questionnaire items will be categorized as Y=1 if a subject responds "Strongly prefer the Test lens" or "Slightly prefer the Test Lens", Y=2 if a subject responds "Strongly prefer the Control Lens" or "Slightly prefer the Control Lens", and Y=3 if a subject responds "No Preference".

2.2.2 Safety Endpoints

This study has no primary or secondary safety endpoints. The following safety endpoints are included as other endpoints of the study.

Other Safety Endpoints

- Incidence of slit lamp findings

The anterior segment of each eye of each subject will be examined using a slit lamp biomicroscope at all study visits (scheduled and unscheduled). Slit lamp findings will be graded using the FDA Grading scale given in Appendix D. Findings will be recorded using a scale from 0 to 4, where Grade 0 represents the absence of findings and 1 to 4 representing successively worse findings (i.e., Grade 1=trace, Grade 2= mild, Grade 3=moderate and Grade 4= severe).

- Adverse events

All Adverse Events (AEs) including ocular and non-ocular AEs. Details for AE will be provided through listings. Details regarding AEs and their classification are given in section 13.

2.3. Hypotheses

Primary Efficacy Hypothesis

- After approximately one week of lens wear, the "top-two-box" (two most favorable responses) response rate for the Test lens will be statistically superior to that for the Control lens with respect to long lasting contact lens comfort. Superiority of the Test lens will be demonstrated if the p-value is less than 0.025 in the one-sided test of the difference (Test minus Control) in the "top-two-box" response rate.

Co-Secondary Efficacy Hypotheses

- After approximately one week of lens wear, the "top-two-box" (two most favorable responses) response rate for the Test lens will be statistically superior to that for the Control lens with respect to overall opinion. Superiority of the Test lens will be demonstrated if the p-value is less than 0.025 in the one-sided test of the difference (Test minus Control) in the "top-two-box" response rate.

- After approximately one week of lens wear, the "top-two-box" (two most favorable responses) response rate for the Test lens will be statistically superior to that for the Control lens with respect to comfort and the end of the day. Superiority of the Test lens will be demonstrated if the p-value is less than 0.025 in the one-sided test of the difference (Test minus Control) in the "top-two-box" response rate.

Exploratory Efficacy Hypotheses

- After approximately 1-week of wear, the "top-two-box" response rate (proportion of subjects whose response is one of the two most favorable responses) for the Test lens will be statistically superior to that for the Control lens with respect to at least one of the following preference questionnaire items:
    a) Overall Comfort [redacted]
    b) Overall Opinion [redacted]
    c) Comfort at the end of the day [redacted]
    d) Comfort throughout the day [redacted]

2.4. Criteria of Study Success

This study will be considered successful if all primary and secondary hypotheses are demonstrated.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

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

3.2. Inclusion Criteria

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

Inclusion Criteria following Screening
The subject must:

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

Inclusion Criteria at Baseline Evaluation
The subject must:

6. In both eyes, have refractive error suitable for correction with the range of toric contact lens powers available in this study:
   6.1 Sphere powers (DS) -1.50 through -4.00 (inclusive) in 0.25 steps
   6.2 Cylinder powers (DC) -0.75 and -1.25
   6.3 Axes (°) 170, 180, 10, 80, 90 and 100
7. Have best corrected monocular 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. Be diabetic.
3. Be currently using any ocular medications or have any ocular infection of any type.
4. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g., rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1 for additional details regarding excluded systemic medications.
5. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g., SynergEyes, SoftPerm) within the past 6 months.
6. Be currently wearing monovision or multifocal contact lenses.
7. Be currently wearing lenses in an extended wear modality.
8. Have a history of strabismus or amblyopia.
9. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site.
10. Have participated in a contact lens or lens care product clinical trial within 7 days prior to study enrollment.

Exclusion Criteria at Baseline Evaluation
The subject must not:

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

[redacted]

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

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

At the initial visit (Visit 1), eligible subjects will be randomized into one of two unique sequences of lens wear (Test/Control or Control/Test). Subject deemed ineligible will be exited from the study.

Subjects will wear each study lens (Test lens and Control lens) in a daily disposable modality for approximately one week (7±2 days). There will be a washout period of approximately one week (7±2 days) between study lens wear periods. Subjects will not have access to the study lenses following completion of the protocol.

Subjects will be advised to wear the study lenses for a minimum of 8 hours per day for at least 5 days during each wear period. Unscheduled visits may be conducted, as appropriate. Lost or damaged lenses may be replaced when necessary.

[redacted]

4.3. Enrollment Target and Study Duration

This study will have an enrollment target of approximately 132 subjects, with a target of at least 120 to complete. The study will be conducted at up to 12 clinical sites in the United States, where the enrollment target for each site will be approximately 11 subjects. A list of principal investigators, clinical sites, and institutions will be kept in the study Trial Master File. A subject will be considered enrolled upon signing of the informed consent form.

There will be 4 visits in total per subject. The total study duration including the enrollment period is expected to be approximately 10 weeks. The maximum duration of participation for any given subject will be approximately 27 days. Subjects who are discontinued prior to the final evaluation may be replaced at the discretion of the study sponsor. The investigation will end at the time that the study data is hard locked.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

Randomization will be used to minimize bias in the assignment to interventional products, to increase the likelihood that known and unknown subject attributes (e.g., demographic and baseline characteristics) are evenly balanced across intervention arms, and to enhance the validity of statistical comparisons across interventions. The study lenses will be worn bilaterally. Subjects will be randomized to one of two unique lens wear sequences based on a 2x2 crossover design.

A computer-generated randomization scheme will be used to randomly assign subjects to one of two unique sequences of lens wear using an allocation ratio of 1:1. [redacted]

The assignment of subjects will be performed at the first visit prior to the first lens fitting. Clinical sites must follow the randomization scheme provided and not pre-select subjects. The following must have occurred prior to randomization:

- Informed consent must have been obtained
- The subject must have met all inclusion and exclusion criteria
- The subject history and baseline information must have been collected

[redacted]

5.2. Masking

Masking will be used to mitigate the risk of bias. This will be a double-masked trial; subjects, investigators and clinical site personnel will not be made aware of the identity of the assigned lenses. While every effort will be made to maintain masking of study investigators, due to differences in the lens designs, it is possible that investigators may be able to determine the identity of the Test and Control articles while conducting study procedures. The study sponsor and project team will also be masked to the identity of the assigned lenses.

5.3. Procedures for Maintaining and Breaking the Masking

Every attempt will be made to keep the clinical trial personnel involved in the study (e.g., data management, project biostatistician, and clinical operations) unaware of the identity of the assigned study lenses. The identity of the study lenses will be masked by having the blister packs labeled with the study number, lot number, sphere power, cylinder power, axis, expiration date, and randomization code. During study execution, only the independent unmasked biostatistician generating the lens fitting schedule will have access to the decode information that allows matching of the randomization codes to the test articles. The medical monitor will also have access to the decode information in case breaking the mask is necessary for the urgent medical treatment of a subject. All personnel involved in the study will be unmasked once the study database is locked.

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

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

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

	Test	Control
Test Article Form	Soft contact lens	
Brand and Product Name	ACUVUE® OASYS MAX 1-Day for ASTIGMATISM (AOM1DfA)	DAILIES TOTAL1® for Astigmatism (DT1fA)
Manufacturer	Johnson & Johnson Vision Care, Inc.	Alcon Laboratories, Inc.
Packaging Form	Blister packaging in sterile packing solution	
Packaging Solution	Optimized Borate Buffer (OBB) solution	Phosphate buffered saline solution with wetting agents
Lens Material	senofilcon A	delefilcon A
Sphere Powers (DS)	-1.50 to -4.00 in 0.25 steps	
Cylinder Powers (DC)	-0.75, -1.25	
Cylinder Axes (°)	10, 80, 90, 100, 170, 180	
Nominal Water Content (%)	38%	33%
Nominal Base Curve (mm)	8.5	8.6
Nominal Lens Diameter (mm)	14.3	14.5
Fiducial marks	6 and 12 o'clock fiducial lines	6 o'clock scribe mark
Oxygen Permeability (Dk)	103 x 10^{-11} (cm^2/sec) (ml O_2/mL x mm Hg) at 35°C (Fatt method, boundary corrected, edge corrected)	140 barrer units, measured at 35 °C (intrinsic Dk - Coulometric method)
Wear Modality	Daily wear	
Replacement Frequency	Daily disposable	
[redacted]	[redacted]	[redacted]

*All lens powers except sphere -2.25 / cylinder -1.25 / axis 180
**Only lens power sphere -2.25 / cylinder -1.25 / axis 180

Test and control lenses will be available in 132 unique lens powers (11 sphere powers × 2 cylinder powers × 6 axes).

The total number of test lenses to be used in this study (not including lenses that are replaced due to droppage, loss or damage) is expected to be approximately 1848 lenses (target enrollment of 132 subjects × 2 eyes per subject × 7-day average wear period). Test and control lenses will be worn in a 1:1 ratio, thus the number of control lenses to be used is expected to be approximately the same (1848 lenses).

6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies

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

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

6.3. Administration of Test Articles

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

[redacted]

[redacted]

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

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

8.2. Withdrawal/Discontinuation from the Study

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

- Subject withdrawal of consent.
- Subject not compliant to protocol.
- Subject lost to follow-up.
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant).
- Subject develops significant or serious adverse events necessitating discontinuation of study lens wear.
- Subjects who have experienced a Corneal Infiltrative Event (CIE).
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment).
- Subject misses any study visits.
- Subject not compliant with study lens wear schedule.
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit.

For discontinued subjects, the Investigator will:

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

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

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

9.1. Systemic Medications

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

A summary of disallowed systemic medications is shown in Table 4. Subjects with a history of taking these medications will be allowed to enroll only if:

- The medications have been taken on a continual, routine basis for at least 6 months, and

- The subject has demonstrated successful contact lens wear during this time.

Or:

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

Subjects with a history of taking medications listed in Table 4 on a long-term, routine basis for less than 6 months will not be allowed to participate in the study.

Table 4: Disallowed systemic medications

Class of Drug	Common Indication(s)	Common Examples
Estrogens (not including contraceptive medication)	Menopause, osteoporosis, vaginitis	Vagifem, Estrace, Climara, Vivelle-Dot, Premarin, Minivelle, etc.
Anticholinergics	Irritable bowel syndrome, Parkinson's disease, peptic ulcer, cystitis, nasal congestion, cold symptoms, overactive bladder, COPD	Bentyl, Spiriva, Atrovent, Hyosyne, Levsin, Symax Fastab, Symax SL, Homax SL, Cogentin, Transderm Scop, etc.
Beta-blockers	Hypertension, angina, heart attack, migraine, atrial fibrillation, adrenal cancer, essential tumor, glaucoma	Toprol XL, Lopressor, Tenormin, Propranolol, Timoptic, Trandate, Inderal LA, etc.
Psychotropics	Antipsychotic (schizophrenia, mania), antidepression, antiobsessive, antianxiety, mood stabilizer, stimulants (ADHD)	Zoloft, Celexa, Prozac, Lexapro, Effexor, Cymbalta, Ativan, Xanax, Desyrel, Wellbutrin, etc.
Vitamin A analogs	Cystic acne	Isotretinoin

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

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

Or:

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

Table 5: Disallowed systemic antihistamines

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

10. DEVIATIONS FROM THE PROTOCOL

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

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

Within 24 hours after the implemented deviation, the Investigator must notify and provide the rationale to the Sponsor and, as required, to the IEC/IRB.

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

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

Protocol waivers are prohibited.

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

Table 6: Examples of major and minor protocol deviations

Deviation category	**Major deviation**	**Minor deviation**
Out-of-window visit	Visit attended > 3 days out of visit window defined in study procedures	Visit attended ≤ 3 days out of visit window defined in study procedures
Unanswered PRO questions	If questionnaire is not completed (i.e., all questions are unanswered) for any visit.	Any individual PRO questions are unanswered (i.e., left blank).
Insufficient wear of study lenses	Subject does not wear study lenses for at least 8 hours on at least 5 days of a study lens dispensing period. Subject wears their habitual lenses during any of the study lens wear periods.	Subject does not wear study lenses for at least 1 hour prior to attending a follow-up visit.

In the case of a major protocol deviation, the decision of whether or not the subject will be excluded from the Per-Protocol analysis population will be made at the time of cohort review. The list of major deviations with potential impact on the study endpoints will be flagged separately and used to define the per protocol population.

11. STUDY TERMINATION

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

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

JJVC reserves the right to terminate the study at any time for any reason and will follow the internal applicable quality review process and will notify the IEC/IRB. Additionally, the IEC/IRB reserves the right to terminate the

study if an unreasonable risk is determined. The study can be terminated by the Principal Investigator at the individual clinical site due to specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

JJVC (and the IEC/IRB 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. The sponsor may disqualify a clinical investigator if the clinical investigator has repeatedly or deliberately failed to comply with the protocol, applicable regulatory requirements, or deliberately submitted false information.

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

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

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

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

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

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

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device and whether anticipated or unanticipated."
NOTE: This definition includes events related to the investigational medical device or the comparator, and to the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.[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
- Hordeolum
- Any corneal event not explicitly defined as serious or significant adverse event, which necessitates temporary lens discontinuation < 2 weeks

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device."
NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
NOTE 3: This includes 'comparator' if the comparator is a medical device.

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

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

Unanticipated Adverse Device Effect (UADE) – A UADE is any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, the test article, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan, Investigator's Brochure or protocol, or any other unanticipated serious problem associated with the test article that relates to the rights, safety and welfare of subjects. [UADE is synonymous with USADE above from ISO 14155[1].]

13.2. Assessing Adverse Events

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

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

Causality Assessment

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

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

Severity Assessment

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

13.4. Reporting Adverse Events

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

Reporting Adverse Events to Sponsor

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

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

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

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

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

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

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

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

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

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

13.5. Event of Special Interest

None.

13.6. Reporting of Pregnancy

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

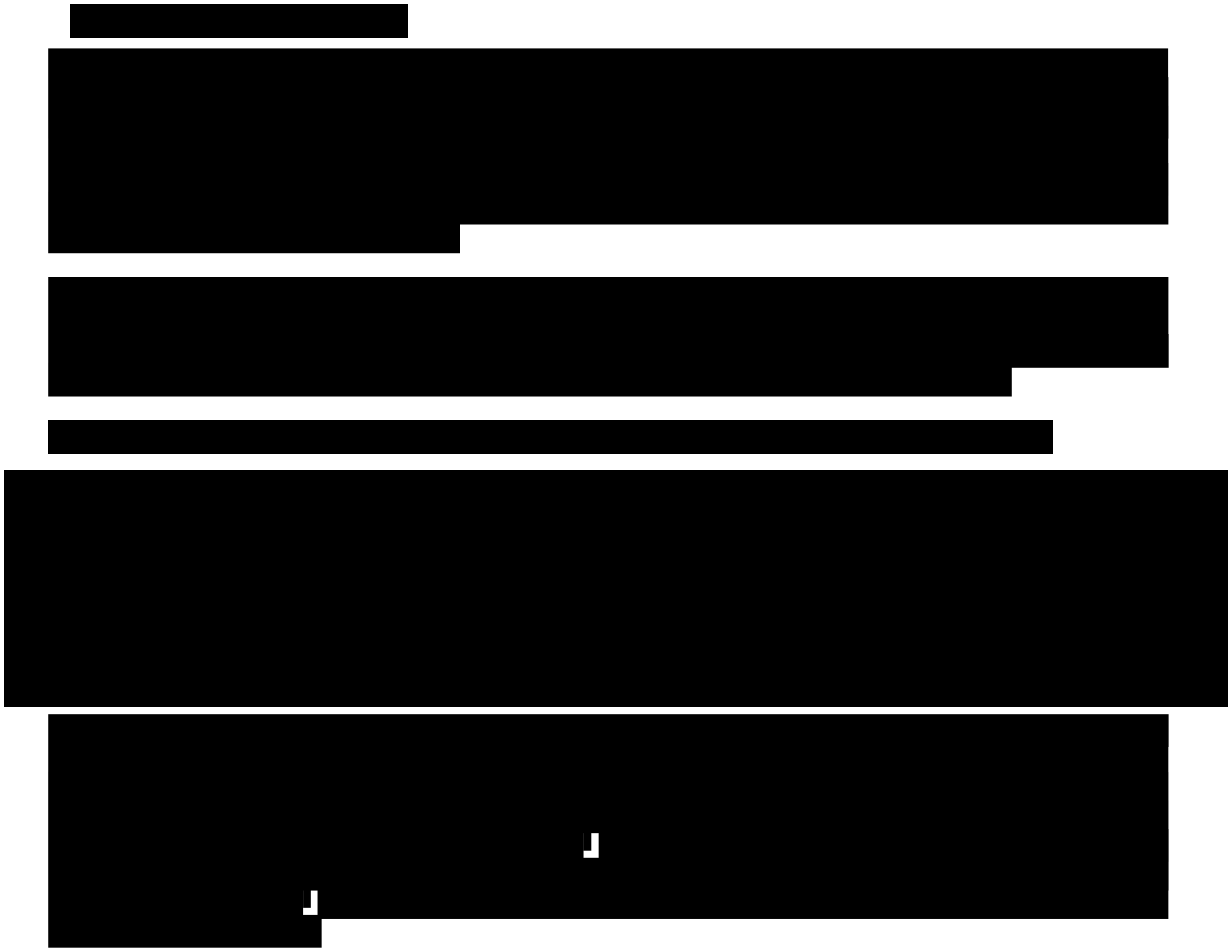
14. STATISTICAL METHODS

14.1. General Considerations

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

Data manipulation, statistical summaries and statistical analyses will be performed using the Statistical Analysis System (SAS) software Version 9.4 or higher (SAS Institute, Cary, NC).[6]

Descriptive statistics will be reported for all key variables as appropriate. Continuous data will be summarized descriptively by sample size (n), mean, standard deviation (SD), median, minimum (Min) and maximum (Max). Categorical data will be summarized descriptively by frequency count (n) and percentage (%) of subjects or eyes within each category level. Summary tables will be presented by event (Baseline, Fitting, 1-Week follow-up, Unscheduled and Final Evaluations) and study lens type as applicable, for the analysis set of interest. The denominator for all percentages will be the number of subjects (or eyes, as applicable) with available data in the lens group under consideration. Unscheduled visits will be summarized separately and will be excluded from the primary and co-secondary efficacy analyses.



[redacted]

14.3. Analysis Populations

Intention-to-Treat (ITT) Population:
Intention-to-treat population will include all randomized subjects. Subjects will be analyzed as per planned randomized treatment.

Safety Population:
All subjects who are administered any study lenses. Subjects will be analyzed as per actual treatment received.

Per-Protocol Population:
All subjects that complete the study who do not have any of the selected major protocol deviations that may affect the assessment of primary or co-secondary efficacy endpoints as determined by the trial cohort review prior to database lock. Justification for the exclusion of subjects with protocol deviations from the per-protocol population set will be documented in a memo.

14.4. Level of Statistical Significance

The type I error rate of the trial will be controlled at 1-sided 0.025 level. The primary efficacy hypothesis and co-secondary hypotheses will be tested using a 1-sided type I error of 0.025 for each hypothesis. The primary hypothesis must demonstrate statistical superiority to test the co-secondary hypotheses. All study hypotheses (primary and co-secondary) are required to demonstrate statistical superiority to satisfy the study objectives. As all hypotheses are required to be statistically significant no adjustment for multiple secondary hypotheses was necessary.

14.1. Missing Data Handling Rules

No imputation of missing values will be used; all analyses will be based on observed case data.

[redacted]

[redacted]

14.3. Safety Endpoints Analyses

Safety endpoints will be summarized for the safety population using observed case data without imputation of missing values. This study has no primary or secondary safety endpoints. The endpoints listed below will be analyzed as other safety endpoints.

Other Safety Endpoints

Incidence of Slit lamp findings
Descriptive table will be provided for slit lamp findings, summarized by finding and grade.

Adverse events

All Adverse Events reported during this study will be provided in a listing. This listing will include subject demographic information, treatment information (associated with the time of the reported AE), AE type (ocular or non-ocular), seriousness / classification, causality or relatedness, adverse severity, outcome, actions taken and the associated start and end date / time for each AE.

[redacted]

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

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

No external data sources will be included in this study.

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

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

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

15.2. Subject Record

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

- subject identification
- eligibility
- study identification
- study discussion
- provision of and date of informed consent
- visit dates
- results of safety and efficacy parameters as required by the protocol
- a record of all adverse events
- follow-up of adverse events
- medical history and concomitant medication
- test article receipt/dispensing/return records

- date of study completion
- reason for early discontinuation of test article or withdrawal from the study, if applicable

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

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

15.3. Trial Registration on ClinicalTrials.gov

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

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

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

16.2. Confidentiality of Information

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

16.3. Data Quality Assurance

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

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

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

16.4. Data Monitoring Committee (DMC)

Not applicable.

17. CLINICAL MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

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

18.2. Investigator Responsibility

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

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

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

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

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

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

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

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

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

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

18.4. Informed Consent

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

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

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

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA)[9] and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

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

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

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

19. STUDY RECORD RETENTION

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

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

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

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

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

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

[redacted]

[redacted]

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Alcon DAILIES TOTAL1® for Astigmatism (delefilcon A) soft contact lenses for Daily Disposable Wear.

Alcon	Package Insert for Alcon DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lenses for daily disposable wear	W900409251

IMPORTANT: This package insert is effective as of May 2020 and applicable to the delefilcon A contact lenses described below. Please read carefully and keep this information for future use.
This package insert is intended for the Eye Care Professional, but should be made available to patients upon request. The Eye Care Professional should provide the patient with appropriate instructions that pertain to the patient's prescribed lenses. Alcon also recommends that patients receive a copy of the **Patient Instruction Booklet** for their prescribed lenses. Copies of this package insert and the **Patient Instruction Booklet** are available without charge from Alcon by calling Customer Service at 1-800-241-5999 or download from our website at www.alcon.com.

℞ only

CAUTION: Federal law (United States) restricts this device to sale by or on the order of a licensed Eye Care Professional.

PRODUCT DESCRIPTION

DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lenses are made of a lens material that is approximately 33% water and 67% (delefilcon A) polymer, a silicone containing hydrogel with added phosphatidylcholine. The core lens material containing 33% water transitions through a water gradient to a hydrogel surface layer that exceeds 80% water. Lenses contain the color additive copper phthalocyanine, and have a light blue-green tint that makes them easier to see when handling. This package insert applies to DAILIES TOTAL1™ for Astigmatism lenses with light absorbing chromophores (as identified in 'Contents' statement on carton labeling). Benzotriazole UV and UV-Vis absorbing monomers are used to block UV radiation and reduce transmittance of high energy visible light (HEVL) wavelengths in the range from 380 nm to 450 nm*.

Lens Properties

- Refractive Index (hydrated): 1.42
- Light Transmittance: 90% ± 5% for average over 380 to 780 nm
- HEVL Transmittance: ≤ 80%T at 420 nm (refer to Figure 1 for transmittance profile)*
- UV Transmittance: τUVB < 1.0 % (average percent transmittance over 280 nm to 315 nm)
  τUVA < 10.0 % (average percent transmittance over 315 nm to 380 nm)
- Oxygen Permeability (Dk): 140 barrer units, measured at 35 °C (intrinsic Dk - Coulometric method)
- Water Content: 33% by weight in normal saline

Lens Parameters

- Diameter Range: 13.0 to 15.0 mm
- Power Range: -20.00 to +20.00 D
- Base Curve Range: 8.0 to 9.2 mm

Lens Parameters Available[1]

DAILIES TOTAL1™ for Astigmatism (delefilcon A)

- Chord Diameter: 14.5 mm
- Center Thickness: 0.11 mm @ -3.00 D (varies with power)
- Base Curve: 8.6 mm
- Sphere Power: +4.00 to -6.00 D (0.25 D steps); -6.50 to -8.00 D (0.50 D steps)
- Cylinder Power: -0.75 D, -1.25 D, -1.75 D, -2.25 D
- Axis: 10° to 180°, in 10° steps

ACTIONS

When hydrated and placed on the cornea, DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lenses act as a refracting medium to focus light rays on the retina.

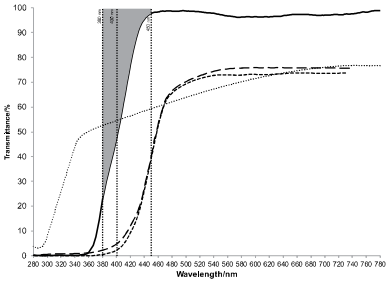
The lenses contain a combination of UV and UV-Vis blocking monomers to help protect against transmission of harmful UV radiation to the cornea and into the eye. For example, a lens with 0.09 mm center thickness (-3.00 D, thinnest projected parameter) blocks 97% of UVA radiation, and 99% UVB radiation average across the spectrum. The lenses reduce high energy visible light (HEVL) radiation reaching the back of the eye by about 33% in the range from 380 nm to 450 nm*. See Figure 1 for the transmittance profile of delefilcon A lenses with light absorbing chromophores (-3.00 D, thinnest projected parameter). The radiation transmittance will be further reduced with increasing lens thickness.

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

NOTE: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV-Blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV-Blocking contact lenses reduces the risk of developing cataracts or other eye disorders. High energy visible light filtering provided by delefilcon A soft contact lenses with light absorbing chromophores is additive to the natural crystalline lens. There is no demonstrated clinical benefit to a 33% reduction in visible light at wavelengths below 450 nm. The Eye Care Professional should be consulted for more information.

Figure 1 illustrates the transmittance of a lens with 0.09 mm center thickness (-3.00 D, thinnest projected parameter), a human cornea, a human lens, and the combined filtration effect of the contact lens and the human lens on retinal exposure. The shaded regions of the graph represent the integrated attenuation transmittance percentages of the delefilcon A lenses with light absorbing chromophores (-3.00 D, thinnest projected parameter) in the high energy visible light region (380 nm to 450 nm). The overall light attenuation over this region is 33%*, with 65% attenuation over the region from 380 nm to 400 nm, and 21% attenuation over the region from 400 nm to 450 nm. This represents the filtration of the contact lens through the central 6 mm portion for a lens with 0.09 mm center thickness (-3.00 D, thinnest projected parameter). Filtration would increase for contact lens powers with higher center thickness.

Wavelength	Percent integrated attenuation transmittance of high energy visible light*
380 nm to 400 nm	65%
400 nm to 450 nm	21%
380 nm to 450 nm	33%



—— Delefilcon A with light absorbing chromophores: Contact lens with 0.09 mm center thickness measured through central 6 mm portion for the thinnest marketed lens (-3.00 D, thinnest projected parameter).

····· Human Cornea from a 24 year old person as described in Lerman S., Radiant Energy and the Eye, MacMillian, New York, 1980, p.58, Figure 2-21.

– – – Human crystalline lens from a 25 year old person as described in Waxler M., Hitchins V.M., Optical Radiation and Visual Health, CRC Press, Boca Raton, Florida, 1986, p. 19, Figure 5.

---- Combined filtering effect of the contact lens and the natural crystalline lens on retinal exposure.

Figure 1: ***Transmittance of a** DAILIES TOTAL1™ for Astigmatism **(delefilcon A) Contact Lens versus a Human Cornea and a Human Crystalline Lens***

INDICATIONS (Uses)

DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes with up to 6.00 diopters (D) of astigmatism.

The lenses are to be used for single use, daily disposable wear (less than 24 hours while awake) only. The lenses are not intended to be cleaned or disinfected and should be discarded after a single use.

CONTRAINDICATIONS (Reasons Not to Use)

DO NOT use delefilcon A soft contact lenses when any of the following exists:

- Microbial infection of the eye
- Inflammation or infection of the anterior chamber of the eye
- Any active disease, injury, or abnormality affecting the cornea, conjunctiva, or eyelids that may be exacerbated by contact lens wear
- Inadequate tear film (dry eye) that interferes with contact lens wear
- Reduced corneal sensitivity (corneal hypoesthesia)
- If eyes become red or irritated
- Use of any medication that is contraindicated or interferes with contact lens wear, including certain eye medications
- Any systemic disease which may be exacerbated by or interferes with safe contact lens wear, handling, or care
- Allergic reactions of the ocular surfaces or adnexa that may be caused by or exacerbated by the wearing of contact lenses
- Patient history of recurring eye or eyelid infections, adverse effects associated with contact lens wear, intolerance, or abnormal ocular response to contact lens wear

WARNINGS

Advise patients of the following warnings pertaining to contact lens wear:

- Problems with contact lenses and lens care products could result in serious injury to the eye. It is essential that patients follow their Eye Care Professional's directions and all labeling instructions for proper use of lenses and lens care products. **Eye problems, including corneal ulcers, can develop rapidly and lead to loss of vision.**
- If a patient experiences eye discomfort, foreign body sensation, excessive tearing, vision changes, or redness of the eye, the patient should be instructed to immediately remove lenses and promptly contact his or her Eye Care Professional. It is recommended that contact lens wearers see their Eye Care Professional regularly as directed.
- Studies have shown that contact lens wearers who smoke have a greater risk of suffering ulcerative keratitis than among those who are nonsmokers. [2,3]
- Daily wear lenses are not indicated for overnight wear, and patients should be instructed not to wear lenses while sleeping. Clinical study results[2] have shown that the risk of ulcerative keratitis is greater for daily wear users who wear their lenses overnight (outside the approved indication) compared to those who do not wear them overnight.
- Non-sterile liquids (i.e., tap water, distilled water, homemade saline solution, or saliva) should not be used as a substitute for any component in the lens care process. The use of tap and distilled water has been associated with *Acanthamoeba* keratitis, a corneal infection that is resistant to treatment and cure.

PRECAUTIONS

To prevent damage to the eyes or to the contact lenses, the following precautions should be taken:

Special Precautions for the Eye Care Professional

The following patients may not be suitable candidates and/or may experience a higher rate of adverse effects associated with contact lens wear:

- **Patients with a history of non-compliance with contact lens care and disinfection regimen, wearing restrictions, wearing schedule or follow-up visit schedule.**
- **Patients who are unable or unwilling to understand or comply with any directions, warnings, precautions, or restrictions. Contributing factors may include but are not limited to age, infirmity, other mental or physical conditions, and adverse working or living conditions.**
- **Patients with diabetes may have reduced corneal sensitivity. As a result, they are more prone to corneal injury and will not heal as quickly or completely as non-diabetics.**

Note regarding lens designs and parameters:

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

The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction. Therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully evaluated on initial dispensing and monitored on an ongoing basis by the prescribing Eye Care Professional.

Note the following precautions during initial dispensing and subsequent visits:

- Fluorescein, a yellow dye, should not be used while the lenses are on the patient's eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used, the eyes should be flushed thoroughly with sterile saline solution that is recommended for in-eye use prior to inserting lenses. Avoid dispensing saline from an aerosol can directly into the eye.
- Instruct the patient to remove the lenses immediately if the eye becomes red or irritated.
- Visual changes or changes in lens tolerance may occur during pregnancy or use of oral contraceptives. Caution patients accordingly.
- Patients who wear contact lenses to correct presbyopia may not achieve the best corrected visual acuity for either far or near vision. Vision requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Before leaving the Eye Care Professional's office, patients should be able to promptly remove their lenses or should have someone else available who can remove their lenses for them.

Eye Care Professionals should carefully instruct the patient to take the following care regimen and safety precautions:

Handling Precautions

- Be sure that before leaving the Eye Care Professional's office, the patient is able to promptly remove lenses or have someone else available to remove them.
- Good hygiene habits help promote safe and comfortable lens wear. Always wash, rinse, and dry hands with a lint-free towel before handling lenses.
- Carefully follow the handling, insertion, removal, cleaning, disinfecting, storing, and wearing instructions in the Patient Instruction Booklet for DAILIES TOTAL1™ for Astigmatism (delefilcon A) Soft Contact Lenses and any additional instructions provided by the Eye Care Professional.
- Note the correct lens power for each eye to prevent getting them mixed up.
- Never use tweezers or other sharp objects such as fingernails to remove lenses from the lens container.
- Always handle lenses carefully. If a lens is dropped, small particles or fibers may adhere to the lens surface, which can irritate the eye. Replace with a sterile new lens.
- Discard any lens that has become dehydrated or damaged. Replace with a sterile new lens.

Lens Wearing Precautions

- Remove the lenses before sleeping. Never exceed the prescribed wearing schedule regardless of how comfortable the lenses feel. Doing so may increase the risk of adverse effects.
- Always keep a supply of replacement lenses on hand or have back-up spectacles available, as lenses should not be reused.
- Do not share lenses with anyone as this may spread microorganisms, which could result in serious eye health problems.
- Lenses should be disposed of each day upon removal from the eye.
- The lens should move freely on the eye at all times. If the lens sticks (stops moving) on the eye, follow the recommended directions in the ***CARE FOR A STICKING, TORN, DRY, OR DECENTERED LENS*** section. If non-movement of the lens continues, consult your Eye Care Professional immediately.

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* See "Note". There is no demonstrated clinical benefit to a 33% reduction in visible light at wavelengths below 450 nm.

- REMOVE THE LENS IMMEDIATELY if your eye becomes red or irritated.
- Promptly remove the lens to avoid serious injury in the event that dust, a foreign body, or other contaminant gets between the lens and the eye.
- Avoid all harmful or irritating vapors and fumes while wearing lenses to reduce the chance of lens contamination or physical trauma to the eye.
- Eye irritation, infection, or lens damage may result if cosmetics, lotion, soap, cream, hair spray, deodorant, aerosol products, or foreign particles come in contact with lenses. If sprays are used, eyes should be kept closed until the spray has settled.
- Consult an Eye Care Professional about wearing lenses during water sports and water related activities. Contact lens exposure to non-sterile water during activities such as swimming, water skiing, and hot tubs may increase the risk of ocular infection including, but not limited to, *Acanthamoeba* keratitis.
- Never allow contact lenses to come into contact with non-sterile liquids (including tap water and saliva) as microbial contamination can occur, which may lead to permanent eye damage.
- Do not use lenses beyond the expiration date.

Solution Precautions

- Do not use saliva or any liquid other than the recommended solution for lubricating or rewetting drops with the lenses.

Other Topics to Discuss with Patients

- Periodic eye examinations are extremely important for contact lens wearers. Schedule and conduct appropriate follow-up examinations to determine ocular response. Alcon recommends that patients see their Eye Care Professional at least once each year or as recommended by the Eye Care Professional.
- Certain medications may cause dryness of the eye, increased lens awareness, lens intolerance, blurred vision, or visional changes. These include, but are not limited to, antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness. Caution patients using these medications accordingly and prescribe proper remedial measures.
- Visual changes or changes in lens tolerance may occur during pregnancy or use of oral contraceptives. Caution patients accordingly.

It is strongly recommended that patients be provided with a copy of the DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lens Patient Instruction Booklet available from Alcon. It is important that patients understand its contents prior to dispensing the lenses.

Who Should Know the Patient is Wearing Contact Lenses

- Instruct patients to inform their employers that they are wearing contact lenses. Some jobs may require the use of eye protection equipment or may prohibit the wearing of contact lenses.
- Instruct the patients to inform their health care professionals that they are wearing contact lenses, as certain medications may interfere with contact lens wear.

WATER ACTIVITIES

Do not expose contact lenses to water while wearing them.

Warning:

Water can harbor microorganisms that can lead to severe infection, vision loss or blindness. If lenses have been submersed in water when showering or swimming, discard them and replace with a new pair. Ask the Eye Care Professional for recommendations about wearing lenses during any activity involving water.

ADVERSE EFFECTS (Possible Problems)

Patients should be instructed to check their eyes regularly to make sure they look well, feel comfortable, and vision is clear.

Potentially serious complications are usually accompanied by one or more of the following signs and symptoms:

- Moderate to severe eye pain not relieved by removing the lens
- Feeling of something in the eye (foreign body sensation)
- Excessive watering or other eye secretions, including mucopurulent discharge
- Redness of the eyes
- Sensitivity to light (photophobia)
- Burning, stinging, itching or other pain associated with the eyes
- Comfort is less compared to when the lens was first placed on eye
- Reduced sharpness of vision (poor visual acuity)
- Blurred vision, rainbows, or halos around objects
- Feeling of dryness

These symptoms, if ignored, may lead to more serious complications.

WHAT TO DO IF A PROBLEM OCCURS

If any of the above signs or symptoms occur:

- IMMEDIATELY REMOVE THE LENSES.
- If the discomfort or problem stops, discard the lens and replace it with a new one.
- If the discomfort or problem continues after removing the lens(es) or upon insertion of a new lens, IMMEDIATELY remove the lens(es) and contact an Eye Care Professional for identification of the problem and prompt treatment to avoid serious eye damage.
- Eye Care Professionals should inform the patient that a serious condition such as corneal ulcer, ulcerative keratitis, infection, corneal vascularization, or iritis may be present. These conditions may progress rapidly and may lead to permanent loss of vision. Less serious reactions such as abrasions, infiltrates, and bacterial conjunctivitis must be managed and treated properly to avoid more serious complications.
- Additionally, contact lens wear may be associated with ocular changes that require consideration of discontinuation or restriction of wear. These include, but are not limited to, local or generalized corneal edema, epithelial microcysts, epithelial staining, infiltrates, neovascularization, endothelial polymegathism, tarsal papillary changes, conjunctival injection, or iritis.

CARE FOR A STICKING, TORN, DECENTERED, OR DRY LENS

Patients should be informed that it may be possible to resolve less serious problems associated with contact lens wear by following the directions below. However, if following these directions does not resolve the problem, patients should consult their Eye Care Professional immediately to avoid injury to the eye.

- **The lens should move freely on the eye at all times**. If the lens sticks (stops moving) or begins to dry on the eye, apply several drops of a recommended lubricating solution (used in accordance with package labeling). Wait until the lens begins to move freely on the eye before attempting to remove it. It is important that you wash and dry your hands thoroughly before removing the lens. If the lens continues to stick, IMMEDIATELY consult your Eye Care Professional.
- **If a lens tears in your eye**, remove the pieces carefully by pinching them as you would for normal lens removal. If the lens pieces do not seem to remove easily, do not pinch the eye tissue. Rinse with saline. If this does not help, contact the Eye Care Professional for assistance.
- **If a lens decenters on the eye**, it may be possible to re-center it by:
  - Closing your eyelids and gently massaging the lens into place, or
  - Looking in the direction of the lens and blinking gently, or
  - Gently pushing the off-centered lens onto the cornea with light finger pressure on the edge of the upper or lower eyelid.
- **Occasional dryness** may be relieved by blinking fully several times or by the use of contact lens rewetting drops that are approved for use with soft contact lenses. If dryness persists, consult your Eye Care Professional.

EMERGENCIES

If chemicals of any kind (household products, gardening solutions, laboratory chemicals, etc.) are splashed into the eyes:

- Flush eyes immediately with fresh saline solution or tap water.
- Remove and discard lenses and immediately contact the Eye Care Professional or visit a hospital emergency room without delay.

ADVERSE EFFECT REPORTING

If a patient experiences any serious adverse effects associated with the use of delefilcon A contact lenses, please notify: **Alcon Medical Affairs in the USA at 1-800-757-9780**.

FITTING GUIDE AND PATIENT BOOKLET

Conventional methods of fitting contact lenses apply to DAILIES TOTAL1™ for Astigmatism (delefilcon A) contact lenses. For a detailed description of the fitting techniques, refer to the DAILIES TOTAL1™ for Astigmatism (delefilcon A) soft contact lens Professional Fitting and Information Guide for more information. Both the Professional Fitting and Information Guide and a Patient Instruction Booklet are available free of charge from:

Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099, USA
or by calling Alcon Customer Service in the USA at:
1-800-241-5999

LENS WEAR AND REPLACEMENT SCHEDULE

Daily Wear (less than 24 hours, while awake)

- Normal daily wear of lenses assumes a minimum of 6 hours of non-lens wear per 24-hour period; however, optimum individual wearing schedules will vary.
- The maximum daily wearing time should be determined by the Eye Care Professional based upon the patient's physiological eye condition because individual responses to contact lenses vary.
- Daily wear patients may initially over-wear the lenses. Avoid this tendency by stressing the importance of adhering to a proper initial wearing schedule. For patients who are new to daily wear, gradually increasing scheduled wearing time may allow ocular tissues to more easily adapt to contact lens wear.

Lens Replacement

- Delefilcon A contact lenses are intended to be worn once (daily disposable wear) and then discarded at the end of each wearing period. The patient should be instructed to start the next wearing period with a fresh new lens.

LENS HANDLING INSTRUCTIONS

- Always wash and rinse hands thoroughly and dry completely with a clean, lint -free towel before handling contact lenses.
- Note the correct lens power for each eye to avoid getting them mixed up.
- Do not use if blister package is damaged or not sealed completely. This may result in product contamination, which can lead to a serious eye infection.
- Shake the blister pack (containing a fresh new lens) gently prior to opening.
- Remove the lens from the blister pack by carefully pouring it onto the palm of the hand.
- Ensure that the lens is right side out.
- Inspect the lenses prior to insertion. Do not insert damaged or unclean lenses.

Lens Insertion Instructions

- Wash and rinse hands thoroughly and dry completely with a clean, lint-free towel.
- Place a lens on the tip of your clean and dry right or left index finger. Place the middle finger of the same hand close to lower eyelashes and pull down the lower eyelid.
- Use the fingers of the other hand to lift the upper eyelid.
- Place the lens directly on the eye (cornea) and gently roll finger away from the lens.
- Look down and slowly release the lower lid.
- Look straight ahead and slowly release the upper lid.
- Blink gently.

Lens Removal Instructions

- Wash and rinse hands thoroughly, and dry completely with a clean, lint-free towel.
- Blink fully several times.
- While looking up, use the tip of the finger to slide the lens down onto the white part of the eye.
- Remove the lens by pinching gently between thumb and forefinger. Do not pinch the eye tissue.
- If the lens is difficult to grasp, dry fingers once more and try again. Do not use rewetting drops in this instance.
- Never use tweezers or other sharp objects such as fingernails to remove lenses from your eyes.

LENS CARE DIRECTIONS

- To help avoid serious eye injury from contamination, the Eye Care Professional should review the following instructions with the patient:
- Cleaning and disinfection of daily disposable lenses is not recommended. The patient should be reminded to have replacement lenses or back-up spectacles available at all times.
- Do not use saliva, tap water, homemade saline solution, distilled water, or anything other than the recommended rewetting drops or lubricants indicated for use with soft lenses.

DISPOSAL AND RECYCLING

Dispose of contact lenses and the blister pack lidding in the waste bin, not down the toilet or sink. The carton packaging and the polypropylene (PP) plastic shell of the blister pack should be placed in the waste bin or recycled according to local waste management guidance.

IN OFFICE USE OF TRIAL LENSES

Eye Care Professionals should educate contact lens technicians concerning proper use of trial lenses. Each contact lens is shipped sterile in a blister pack containing phosphate buffered saline solution. Hands should be thoroughly washed, rinsed, and dried with a lint-free towel prior to handling a lens. In order to ensure sterility, the blister pack should not be opened until immediately prior to use. For fitting and diagnostic purposes, the lenses should be disposed of after a single use and not be re-used from patient to patient.

HOW SUPPLIED

Each lens is packaged in a foil-sealed plastic blister pack containing phosphate buffered saline solution with approximately 0.3% of polymeric wetting agents consisting of copolymers of polyamidoamine and poly(acrylamide-acrylic) acid and is steam sterilized The package is marked with the base curve, diameter, dioptric power, cylinder axis and power (where applicable), ADD power (where applicable), manufacturing lot number, date of manufacture, and expiration date. Lenses are supplied in cartons containing up to 90 individually sealed contact lenses.

The following may appear on labels or cartons:

Symbol / Abbreviation	Description
BC	Base Curve
DIA	Diameter
PWR	Power
D	Diopter
L	Left
R	Right
CYL AXIS	Cylinder power and axis
UV	Ultra-violet
UVA	Ultra-violet A
UVB	Ultra-violet B
UV-Vis	Ultra-violet and Visible
HEVL	High Energy Visible Light (blue light)
	Packaging waste license sign
2	Do not re-use
LOT	Batch code
EXP	Use-by date (Expiry date)
	Single sterile barrier system
STERILE	Sterilized using steam
CE	European conformity mark
en	English (example of two letter code for the language)
	Caution
	Consult instructions for use
	Do not use if blister package is damaged
	DO NOT DISPOSE LENSES IN TOILET OR SINK
	Manufacturer
	Date of manufacture
MD	Medical device
EC REP	Authorized representative in the European Community
Rx only	CAUTION: Federal (United States) law restricts this device to sale by or on the order of a licensed eye care professional

Manufacturer:
Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099, USA

Date: August 2021

U.S. Pat.: www.alconpatents.com

[1] Check for actual product availability which may change over time.
[2] Cutter GR, Chalmers RL, Roseman M. The Clinical Presentation, Prevalence, and Risk Factors of Focal Corneal Infiltrates in Soft Contact Lens Wearers. *The CLAO Journal.* Jan 1996; 22 (1): 30-37.
[3] Schein OD, Glynn RJ, Poggio EC, Seddon JM, Kenyon KR. The Relative Risk of Ulcerative Keratitis Among Users of Daily-Wear and Extended-Wear Soft Contact Lenses. *The New England Journal of Medicine.* 1989; 321(12):773-783.

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6594 Evaluation of Delefilcon A and Senofilcon A Daily Disposable Toric Soft Contact Lenses Over One Week of Wear

Version and Date: 2.0 13 February 2025

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

I agree to conduct this study according to ISO 14155,[1] Declaration of Helsinki,[2] United States (US) Code of Federal Regulations (CFR), [3] the International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP),[4] and the pertinent individual country laws/regulations, and to comply with its obligations, subject to ethical and safety considerations. I, as the Principal Investigator, am responsible for ensuring that all clinical site personnel, including Sub-Investigators, adhere to all regulations and GCP guidelines regarding clinical trials during and after study completion.

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

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

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

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

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

Principal Investigator:	_____	_____
	Signature	Date
	_____	
	Name and Professional Position (Printed)	
Institution/Site:	_____	
	Institution/Site Name	
_____	_____	_____
	Institution/Site Address	