NCT06864858

Johnson & Johnson Vision

STATISTICAL ANALYSIS PLAN

Protocol CR-6571

Clinical Evaluation of Two Cosmetic Contact Lenses

Etafilcon A with PVP with cosmetic pattern (Investigational Product)

Version: 1.0

Date: 7 May 2025

[redacted]

[redacted]

Compliance: The study described in this document was performed according to the principles of Good Clinical Practice (GCP).

Confidentiality Statement
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[redacted]

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ABBREVIATIONS

AE	adverse event
CI	confidence interval
CRF	case report form
CSR	Clinical Study Report
eCRF	electronic case report form
FDA	Food and Drug Administration
HLHC	High Luminance High Contrast
ICH	International Conference on Harmonization
ITT	Intention-to-Treat
PI	principal investigator
PP	Per-Protocol
SAE	serious adverse event
SAP	Statistical Analysis Plan
SD	standard deviation

[redacted]

[redacted]

[redacted]

5. STUDY ENDPOINTS

5.1. Efficacy Endpoints

5.1.1. Primary Efficacy Endpoints

Visual Acuity (LogMAR)

Monocular distance (4m) VA under high-luminance high contrast (HLHC) will be measured post-lens fitting using ETDRS Charts. The mean VA is a continuous endpoint.

5.1.2. Secondary Efficacy Endpoints

Not Applicable.

5.2. Safety Endpoints

5.2.1. Primary Safety Endpoint

Not applicable.

5.2.2. Secondary Safety Endpoint

Not applicable.

5.2.3. Other Safety Endpoints

Mechanical Lens fit

Lens fitting will be assessed in each eye using a slit-lamp post lens fitting. Lens fitting characteristics to be reported:

- Lens Centration Grade
- Decentered Direction
- Limbal Exposure Grade
- Edge Lift (Present or Absent)
- Primary Gaze Movement Grade
- Upgaze Movement Grade
- Lens Tightness Grade (Push-up Test)
- Acceptable Fitting (yes/no)

Cosmetic Lens fit

Cosmetic lens fit assessment will be performed in each eye at post lens fitting by the investigator without the use of a slit-lamp at a distance of approximately 3 feet from the subject in:

- Primary Gaze
- Extreme Gaze (left and right)
- Extreme Up-gaze

Percentage of Eyes Reporting Moderate or Severe Ocular Symptoms (Subject-Reported)

Frequency (counts and percentages of eyes) of moderate or severe ocular symptoms with the study lens will be assessed at fitting. Severity of the symptoms can be:

0 = Not Applicable or Not Recorded
1 = Mild and results in little or no interference with lens wear
2 = Moderate AND / OR occasionally interferes with lens wear
3 = Severe AND / OR frequently interferes with lens wear

Ocular Physiology (Slit Lamp Findings)

Slit lamp findings will be assessed for each subject eye before and after each lens fitting using the FDA Grading scale (Grade 0=None, Grade 1=Trace, Grade 2=Mild, Grade 3=Moderate, Grade 4=Severe). Slit lamp finding assessments include the following metrics:

- Corneal Infiltrates (Yes/No)
- Corneal Edema
- Corneal Neovascularization
- Corneal Neovascularization Location
- Corneal Staining
- Corneal Staining Location
- Conjunctival Injection
- Tarsal Abnormalities
- Other

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

Clinical Evaluation of Two Cosmetic Contact Lenses

Protocol CR-6571

Version: 3.0

Date: 26 February 2025

Test Articles:

Control: 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey (Approved Product)

Test Product: Etafilcon A with PVP with cosmetic pattern (Investigational Product)

Commercially Available Product Lots: 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey

Keywords: etafilcon A, cosmetic contact lenses, beauty, daily wear, daily disposable non-dispensing, etafilcon A with cosmetic pattern, logMAR visual acuity, cosmetic acceptability

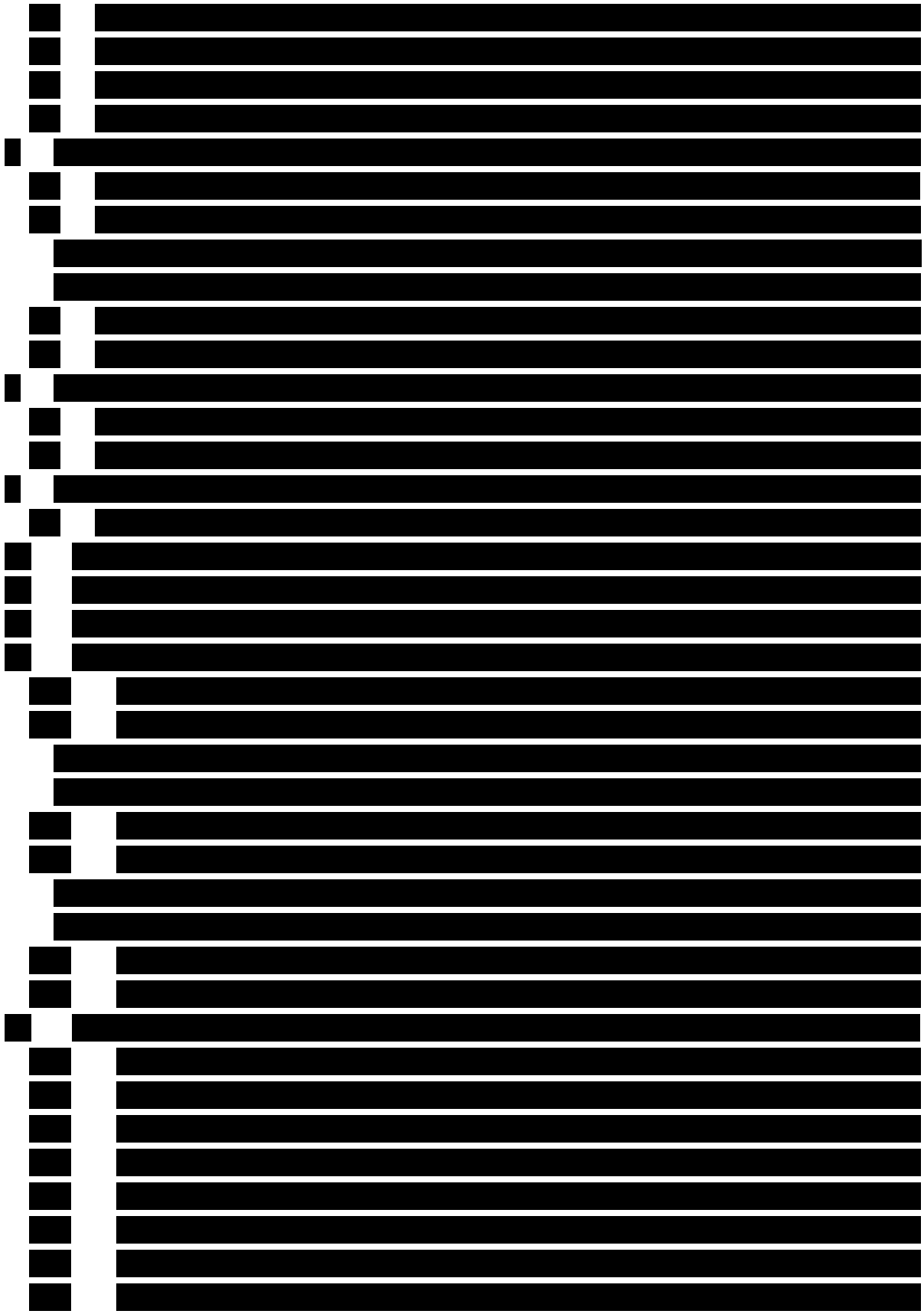
Statement of Compliance to protocol, GCP and applicable regulatory guidelines:

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:

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[redacted]



[redacted]

PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Clinical Evaluation of Two Cosmetic Contact Lenses
Protocol Number: CR-6571
Version: 3.0
Date: 26 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
Clinician Reviewer	*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	*See Electronic Signature Report* [redacted]	DATE

[redacted]



SYNOPSIS

Protocol Title	Clinical Evaluation of Two Cosmetic Contact Lenses
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Confirmatory [redacted]
Trial Registration	This study will be registered on ClinicalTrials.gov based on the following: a confirmatory study meets the requirements for registration.
Test Article(s)	Investigational Product: etafilcon A with PVP with cosmetic pattern contact lens (Test) Approved Product: 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey (Control)
Wear and Replacement Schedules	Wear Schedule: Daily Wear Replacement Schedule: Daily Disposable
Objectives	**Primary Objective**: The primary objective of this study is to evaluate the Distance Monocular logMAR visual performance of the Investigational Lens: etafilcon A Daily Disposable Cosmetic Contact Lenses in comparison to 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey **Other Objectives:** Additional objectives include assessments of mechanical and cosmetic lens fit, subject reported ocular symptoms, and ocular physiology.
Study Endpoints	**Primary efficacy endpoint**: • Distance Monocular logMAR visual performance (high luminance high contrast) **Other safety endpoints**: • Mechanical Lens Fit • Cosmetic Lens Fit • Subject Reported Ocular symptoms • Ocular Physiology
Study Design	This is a single visit, single-masked, non-dispensing, randomized, controlled, 2×2 bilateral crossover study. Each subject will be bilaterally fitted with both study lenses in a random order over 1 visit. Each study lens will be worn bilaterally for approximately 90 minutes in a daily disposable mode. There will be an approximate 5-minute washout period between wear periods. Monocular VA for HLHC will be assessed at the evaluation using ETDRS charts. Visit 1: Screening, baseline evaluation and lens fit #1 and #2 and final evaluation 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	Up to 56 subjects will be enrolled with the aim of approximately 50 subjects completing.
Study Duration	The total study duration including the enrollment period is expected to be approximately 6 weeks.
Anticipated Study Population	Myopic contact lens wearing subjects in the age range of 18 to 39 (inclusive) years will be enrolled.
Eligibility Criteria - Inclusion	Potential subjects must satisfy all of the following criteria to be enrolled in the study:

	Inclusion Criteria following Screening The subject must: 1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Be between 18 and 39 (inclusive) years of age at the time of screening. 4. Be a current soft contact lens wearer in both eyes with a minimum of 6 hours/day and 5 days/week over the last 30 days by self-report. Inclusion Criteria at Baseline Evaluation: 5. The subject's vertex corrected spherical equivalent distance refraction must be in the range of -1.00 D to -6.00 D (inclusive) in each eye. 6. The subject's refractive cylinder must be less than or equal to 0.75 D (inclusive) in each eye. 7. Have spherical best corrected 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: 1. Be currently pregnant or lactating. 2. Have any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study (at the investigator's discretion). 3. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear (at the investigator's discretion). 4. Have any previous, or planned (during the study), ocular surgery (e.g., radial keratotomy, PRK, LASIK, etc.). 5. Have any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear (at the investigator's discretion). 6. Have participated in any contact lens or lens care product clinical trial within seven (7) days prior to study enrollment. 7. 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. Exclusion Criteria at Baseline Evaluation The subject must not: 8. Have any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion (at the investigator's discretion). 9. Have any clinically significant (Grade 3 or 4 on FDA scale) tarsal abnormalities, bulbar injection, corneal edema, corneal

	vascularization, corneal staining, or any other abnormalities of the cornea which would contraindicate contact lens wear.
Disallowed Medications/Interventions	See section 9.1 for details regarding disallowed systemic medications.
Measurements and Procedures	logMAR visual acuity, lens fit assessment, cosmetic lens fit assessment, ocular symptoms and safety parameters (slit lamp findings, entrance/exit visual acuity).
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of an Unanticipated Adverse Device Effect (UADE) or Serious Adverse Event (SAE) for which a causal relationship to a test article cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Single use Eye-Cept® Rewetting Drops, LacriPure Saline Solution, ScleralFil Preservative Free Saline Solution, or alternative products approved by the Sponsor.
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
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
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
LogMAR	Logarithm of Minimal Angle of Resolution
MPMVA	Maximum Plus to Maximum Visual Acuity
OD	Right Eye
OS	Left Eye
OU	Both Eyes
PIG	Patient Instruction Guide
PQC	Product Quality Complaint
PRK	Photorefractive Keratectomy
PRO	Patient Reported Outcome
PVP	Polyvinylpyrrolidone
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

Cosmetic contact lenses can have patterns of varying size and opacities. When designing these cosmetic patterns, it is important to allow a sufficient clear area in the center of the lens optical zone so that the wearer's vision is not negatively impacted by the pattern.

In the current study, we will assess the objective visual performance of an investigational cosmetic soft contact lens compared to an approved cosmetic soft contact lens.

1.1. Name and Descriptions of Investigational Products

This study will include two soft contact lenses with cosmetic patterns. The Control lens, 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey is an approved, commercially available, marketed product. The Test lens, Etafilcon A with PVP with cosmetic pattern, is an investigational product. Further details about the test articles are found in Section 6 of this protocol.

[redacted]

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective
The primary objective of this study is to evaluate the Distance Monocular high luminance high contrast (HLHC) logMAR visual performance of the test lens: Etafilcon A with PVP with a cosmetic pattern in comparison to 1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey.

Other Objectives
Additional objectives include assessments of mechanical and cosmetic lens fit, subject reported ocular symptoms, and ocular physiology.

2.2. Endpoints

Efficacy Endpoints

Primary Efficacy Endpoint

Visual Acuity (logMAR)
Monocular distance (4m) monocular VA under high-luminance high contrast (HLHC) will be measured post-lens fitting using ETDRS Charts.

Secondary Efficacy Endpoint
Not Applicable.

Safety Endpoints

Primary Safety Endpoint
Not Applicable.

Other Safety Endpoint
Not applicable.

Other Safety Endpoints

Mechanical Lens fit
Lens fitting will be assessed in each eye using a slit-lamp post lens fitting. Lens fitting characteristics to be reported are:

- Lens Centration Grade
- Decentered Direction
- Limbal Exposure Grade
- Edge Lift (Present or Absent)
- Primary Gaze Movement Grade
- Upgaze Movement Grade

- Lens Tightness Grade (Push-up Test)
- Acceptable Fitting (yes/no)

Cosmetic Lens fit

Cosmetic lens fit assessment will be performed in each eye at post lens fitting by the investigator without the use of a slit-lamp at a distance of approximately 3 feet from the subject in:

- Primary Gaze
- Extreme Gaze (left and right)
- Extreme Up-gaze

Percentage of Eyes Reporting Moderate or Severe Ocular Symptoms (Subject-Reported)

Frequency (counts and percentages of eyes) of moderate or severe ocular symptoms with the study lens will be assessed at fitting. Severity of the symptoms can be:

0 = Not Applicable or Not Recorded
1 = Mild and results in little or no interference with lens wear
2 = Moderate AND / OR occasionally interferes with lens wear
3 = Severe AND / OR frequently interferes with lens wear

Ocular Physiology (Slit Lamp Findings)

Slit lamp findings will be assessed for each subject eye before and after each lens fitting using the FDA Grading scale (Grade 0=None, Grade 1=Trace, Grade 2=Mild, Grade 3=Moderate, Grade 4=Severe). Slit lamp finding assessments include the following metrics:

- Corneal Infiltrates (Yes/No)
- Corneal Edema
- Corneal Neovascularization
- Corneal Neovascularization Location
- Corneal Staining
- Corneal Staining Location
- Conjunctival Injection
- Tarsal Abnormalities
- Other

2.3. Hypotheses

Primary Efficacy Hypothesis

The Test lens will be statistically non-inferior to the Control lens with respect to high luminance high contrast distance monocular visual acuity (logMAR) post lens fitting. A non-inferiority margin of 0.05 logMAR will be used.

2.4. Criteria of Study Success

The Test lens must demonstrate statistically significant non-inferiority relative to the Control lens, with respect to HLHC distance logMAR VA post lens fitting to satisfy the primary objective of the study.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Subjects aged 18 to 39 years (inclusive) who are habitual soft contact lens wearers will be recruited for this clinical study. Subjects must meet all the inclusion and none of the exclusion criteria listed in Section 3.2 and 3.3.

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. Be a current soft contact lens wearer in both eyes with a minimum of 6 hours/day and 5 days/week over the last 30 days by self-report.

Inclusion Criteria at Baseline Evaluation

5. The subject's vertex corrected spherical equivalent distance refraction must be in the range of -1.00 D to -6.00 D (inclusive) in each eye.
6. The subject's refractive cylinder must be less than or equal to 0.75 D (inclusive) in each eye.
7. Have spherical best corrected visual acuity of 20/25 or better in each eye.

3.3. Exclusion Criteria

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

Exclusion Criteria following Screening
The subject must not:

1. Be currently pregnant or lactating.
2. Have any systemic disease (eg, Sjögren's Syndrome), allergies, infectious disease (eg, hepatitis, tuberculosis), contagious immunosuppressive diseases (eg, HIV), autoimmune disease (eg rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study (at the investigator's discretion).
3. Use of systemic medications (eg, chronic steroid use) that are known to interfere with contact lens wear (at the investigator's discretion).
4. Have any previous, or planned (during the study), ocular surgery (eg, radial keratotomy, PRK, LASIK, etc.).
5. Have any previous history or signs of a contact lens-related corneal inflammatory event (eg, past peripheral ulcer or round peripheral scar), or any other ocular abnormality that would contraindicate contact lens wear (at the investigator's discretion).
6. Have participated in any contact lens or lens care product clinical trial within seven (7) days prior to study enrollment.
7. 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.

Exclusion Criteria at Baseline Evaluation
The subject must not:

8. Have any ocular allergies, infections or other ocular abnormalities that are known to interfere with contact lens wear and/or participation in the study. This may include, but not be limited to entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, or corneal distortion (at the investigator's discretion).
9. Have any clinically significant (Grade 3 or 4 on FDA scale) tarsal abnormalities, bulbar injection, corneal edema, corneal vascularization, corneal staining, or any other abnormalities of the cornea which would contraindicate contact lens wear.

[redacted]

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is a single-visit, bila tera l, single-ma sked, non-dispensing, randomized, controlled, 2 (lens) × 2 (period) crossover study. Up to 56 subjects will be enrolled with the target of approximately 50 to complete the study.

If a subject meets all eligibility criteria, they will be randomized to one of two lens wear sequences (Test/Control or Control/Test) in a bilateral fashion. Subjects will not be masked to the variant/pattern of the lenses due to visible differences in the study lenses; however, subjects will be masked to the lens brands. There will be a 5-minute washout period between wear periods.

[redacted]

4.3. Enrollment Target and Study Duration

This study will have an enrollment target of 56 subjects, with a target of at least 50 to complete. The study will be conducted at 1 clinical site. A subject will be considered enrolled upon signing of the informed consent form.

There will be 1 visit per subject. The study is expected to last approximately 6 weeks. Subjects who are discontinued prior to the final evaluation may be replaced at the discretion of the study sponsor. The investigation will end at the time that the study data is hard locked.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn bilaterally in a randomized fashion using a 2×2 crossover design with two study Lens types and two periods.

A computer-generated randomization scheme will be used to randomly assign subjects to one of two unique sequences of lens wear (Test lens/Control lens and Control lens/Test lens). [redacted]

The randomization of subjects will be performed at the study visit prior to the first fitting. The clinica1 site must follow the randomization scheme provided. The following must have occurred prior to randomization:

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

[redacted]

5.2. Masking

This will be a single-ma sked study. Due to potentially visible differences between the study lens, subjects and clinica l site personnel (investigators, etc.) may be aware of the different study lenses. However, the contact lens manufacturer (brand) will be masked to both subjects and clinical site personnel.

5.3. Procedures for Maintaining and Breaking the Masking

While this study is a single-ma sked study, there is no foreseeable situation in which the clinica l site personnel (investigators, etc.) would need to know the identity of the manufacturer of the study contact lenses (Bra nd).

However, if specific treatment/course of action would be dictated by knowing the contact lens manufacturer of the study lens, 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.

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	Daily Disposable Soft contact lens	
Design / Description	Etafilcon A with PVP with cosmetic pattern	1-DAY ACUVUE® DEFINE® with LACREON®, FRESH Honey
Manufacturer	Johnson & Johnson Vision Care, Inc.	
Packaging Form	Blister packaging in sterile packing solution	
Packaging Solution	Moist Packing Solution with PVP	
Lens Material	etafilcon A	
Sphere Powers (DS)	-1.00 to -6.00 in 0.25 steps	
Nominal Base Curve (mm)	8.5	
Nominal Lens Diameter (mm)	14.2	
Wear Modality in Current Study	Da ily wear	
Replacement Frequency	Da ily disposable	
[redacted]	[redacted]	[redacted]

For each lens type, Test and Control, the total number of lenses that will be used (not including lenses that are replaced due to droppage, loss, or damage) is expected to be approximately 224 lenses (target enrollment of 56 subjects and bilateral fitting per subject).

6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies

	Non-Preserved Rewetting Drops / Multipurpose Lens Care Solution		
Solution Name/Description	Single use Eye-Cept® Rewetting Drops	LacriPure Saline Solution	SclералFil Preservative Free Saline Solution
Manufacturer	Optics Laboratory	Menicon	Bausch & Lomb
Preservative	None	None	None
Other distinguishing items (dye, packaging, approval status, etc.	N/A	N/A	N/A

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

6.3. Administration of Test Articles

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent.
- they are eligible.

- have not withdrawn/discontinued from the study for any reason described in section 8.2.
- completed all visits through the final visit.
- 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 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 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

If subjects are prematurely discontinued, subject enrollment will continue to meet the intended sample size. Subjects who are discontinued will be replaced.

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include: None
Concomitant therapies that are disallowed include: None

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 takingmedications 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, artrial fibrillation, andrenal 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
Analgesics	Urinary tract infection	Phenazopyridine HCL

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

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

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

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

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

Protocol waivers are prohibited.

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.

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 tra ined 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 clinica l 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. Wa s 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:

- Dea th
- Serious deterioration in the health of the subject that resulted in any of the following:
  - Life-threa tening 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
- Feta l distress, fetal 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 1: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.

Unanticipated Adverse Device Effect (UADE) – A UADE is any serious adverse effect on health or safety or any life-threa tening 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 investiga tiona l pla n, 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 Rela ted – 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-cha llenge.

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 da ily 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.

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 (SAS Institute, Cary, NC)[7]. Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. Unscheduled visits will be summarized separately and will be excluded from the statistical analysis.

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

LogMAR (assumes the Test lens is approximately half a letter worse than the Control lens). A non-inferiority [redacted]

[redacted]

[redacted]

[redacted]

14.3. Analysis Populations

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

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

Per-Protocol Population:
All subjects who successfully complete all visits and do not substantially deviate from the protocol 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 to file.

14.4. Level of Statistical Significance

The primary efficacy hypothesis will be evaluated using a one-sided Type I error rate of 0.025.

14.5. Missing Data Handling Rules

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

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

14.7. Safety Endpoints Analyses

Primary Safety Endpoint
Not applicable.

Secondary Safety Endpoint
Not applicable.

Other Safety Endpoints
All secondary safety analyses will be conducted on the safety population with observed case data.

The secondary safety endpoints, including Mechanical Lens Fit evaluated with a slit-la mp after lens fitting, Cosmetic Lens Fit a ssessed without a slit-la mp from a distance of about 3 feet, and Ocular Physiology (SLFs) measured at baseline and the exit evaluation using the FDA Grading Scale, will be summarized by lens type and timepoint. Lens fitting characteristics and ocular findings will be summarized as counts and percentages.

[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.

External data sources for this study include: Not Applicable

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

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

The content and structure of the eCRFs are compliant with ISO14155.[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)[11] in the United States and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person's related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

- 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.

Essentia l 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]

[redacted]

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

1-DAY ACUVUE® DEFINE® with LACREON®

B. Pre-fitting Examination

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

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

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

C. Initial Power Determination

A spectacle refraction should be performed to establish the patient's baseline refractive status and to guide in the selection of the appropriate lens power. Vertex distance compensation is generally only necessary for refractions ± 4.00D, but may sometimes also be required for lower refractions in the case of large vertex distances.

D. Base Curve Selection (Trial Lens Fitting)

For the 1-DAY ACUVUE® DEFINE® Contact Lenses, an 8.5 mm/14.2 mm trial lens should be selected for patients regardless of keratometry readings. However, corneal curvature measurements should be performed to establish the patient's baseline ocular status.

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

1. Criteria of a Properly Fit Lens

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

2. Criteria of a Flat Fitting Lens

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

3. Criteria of a Steep Fitting Lens

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

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

E. Final Lens Power

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

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

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

Monovision fitting success can be improved with the following suggestions:

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

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

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

PATIENT MANAGEMENT

Dispensing Visit

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

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

REVIEW THESE INSTRUCTIONS WITH THE PATIENT SO THAT HE OR SHE CLEARLY UNDERSTANDS THE PRESCRIBED WEARING AND REPLACEMENT SCHEDULE (DAILY DISPOSABLE).

Follow-up Examinations

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

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

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

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

B. Recommended Procedures for Follow-Up Visits:

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

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

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

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

MONOVISION FITTING GUIDELINES

A. Patient Selection

Monovision Needs Assessment

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

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

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

Patient Education

All patients do not function equally well with monovision correction. Patients may not perform as well for certain tasks with this correction as they have with spectacles (multifocal, bifocal, trifocal, readers, progressives). Each patient should understand that monovision, as well as other presbyopic alternatives, can create a vision compromise that may reduce visual acuity and depth perception for distance and near tasks. Therefore, caution should be exercised. During the fitting process, it is necessary for the patient to realize the disadvantages as well as the advantages of clear near vision, and straight ahead and upward gaze that monovision contact lenses provide.

B. Eye Selection

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

1. **Ocular Preference Determination Methods**

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

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

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

1. **Refractive Error Method**

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

2. **Visual Demands Method**

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

   Example:

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

C. Special Fitting Characteristics

1. Unilateral Vision Correction Requirement

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

   Example:

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

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

2. **Near ADD Determination**

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

3. **Trial Lens Fitting**

   A trial fitting is performed in the office to allow the patient to experience monovision correction. Lenses are fit according to the "General Fitting Guidelines" for base curve selection described in this guide.

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

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

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

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

4. **Adaptation**

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

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

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

5. **Other Suggestions**

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

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

WEARING SCHEDULE

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

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

The maximum suggested wearing time for these lenses is:

Day	Hours
1	6-8
2	8-10
3	10-12
4	12-14
5 and after	all waking hours

REPLACEMENT SCHEDULE

1-DAY ACUVUE® DEFINE® Contact Lenses when prescribed for daily disposable wear should be discarded upon removal.

When disposed of after a single daily use, these lenses may reduce the risk of developing giant papillary conjunctivitis.[4]

When worn as a daily disposable lens, the lenses may provide improved comfort for many patients who experience mild discomfort and itching associated with allergies during contact lens wear, compared to lenses replaced at intervals of greater than 2 weeks.

Clinical Research has shown that when worn on a daily disposable basis, these lenses may provide improved comfort for 2 out of 3 patients who reported suffering from discomfort associated with allergies during contact lens wear.

[4] The CLAO Journal, July 1999, Volume 25, Number 3

LENS CARE DIRECTIONS

When lenses are dispensed, the Eye Care Professional should provide the patient with appropriate and adequate warnings and instructions for daily disposable lens wear.

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

Basic Instructions:

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

Care for a Sticking (Non-Moving) Lens

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

EMERGENCIES

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

HOW SUPPLIED

Each multi-pack contains individually packaged lenses. Each lens comes in its own foil-sealed plastic package containing borate buffered saline solution with povidone. This package is designed specifically to keep the lens sterile while the package is sealed. In the European Union, Borates (boric acid & sodium borate) are defined as CMR 1B substances in a concentration above 0.1% weight by weight and are safe when product is used according to label instructions.

REPORTING OF ADVERSE REACTIONS

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

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

20602165

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PACKAGE INSERT & FITTING INSTRUCTION GUIDE

1-DAY ACUVUE® DEFINE® BRAND CONTACT LENSES with LACREON®

(etafilcon A) Soft (hydrophilic) Contact Lenses
Cosmetically Tinted with UV Blocker
for Daily Disposable Wear

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

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

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

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

SYMBOLS KEY

The following symbols may appear on the label or carton:

SYMBOL	DESCRIPTION
	Caution, Consult Instructions for Use
	Date of Manufacture
	Manufacturer
	Use-By Date (expiration date)
LOT	Batch Code
STERILE	Sterilized Using Steam Heat
	Indicates a Single Sterile Barrier System
DIA	Diameter
BC	Base Curve
D	Diopter (lens power)
CE 2797	CE Mark and Identification number of Notified Body
UK CA 0086	UK Conformity Assessment Marking and Identification Number of Notified Body
UV BLOCKING	UV Blocking
	Lens Orientation Correct
	Lens Orientation Incorrect (Lens Inside Out)

SYMBOL	DESCRIPTION
EC REP	Authorized Representative in the European Community
	Contains Hazardous Substances
	Do Not Re-Use (Single Use)
	Do Not Use if Package is Damaged
MD	Medical Device Symbol
A. B.	Package Opening Icon (Blister)
	Package Opening Icon (Carton)
UV BLOCKING UV BLOCKING	UV Blocking
	Fee Paid for Waste Management
Rx only	CAUTION: US Federal law restricts this device to sale by or on the order of a licensed practitioner
A	**ACCENT STYLE**
N	**NATURAL SHINE®**
V	**VIVID STYLE**

Visit www.acuvue.com/guides for additional information about symbols.

DESCRIPTION

The 1-DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® Technology are soft (hydrophilic) contact lenses available as spherical lenses. The lens material (etafilcon A) is a copolymer of 2-hydroxyethyl methacrylate and methacrylic acid cross-linked with 1, 1, 1-trimethylol propane trimethacrylate and ethylene glycol dimethacrylate.

The 1-DAY ACUVUE® DEFINE® Brand Contact Lenses are tinted blue using Reactive Blue Dye #4 to make the lenses more visible for handling. The lenses contain a pigmented area that will alter or enhance the appearance of the natural iris. The lens is colored with one or more of the following color additives: iron oxides, titanium dioxide, phthalocyaninato (2-) copper, phythalocyanine green, and Reactive Blue Dye #4.

The 1-DAY ACUVUE® DEFINE® Contact Lenses are available in the following variants (i.e., patterns):

- **ACCENT STYLE**
- **NATURAL SHINE**
- **VIVID STYLE**

A benzotriazole UV absorbing monomer is used to block UV radiation. The UV Blocking averages 97% in the UVB range of 280 nm to 315 nm and 81% in the UVA range of 316 nm to 380 nm.

Lens Properties:

The physical/optical properties of the lens are:

- Specific Gravity (calculated): 0.98 -1.13
- Refractive Index: 1.40
- Light Transmittance: 85% minimum
- Surface Character: Hydrophilic
- Water Content: 58%
- **Oxygen Permeability (Dk):**

VALUE	METHOD
21.4 x 10^{-11} (cm^2/sec) (ml O_2/mL x mm Hg) @ 35°C	Fatt (boundary corrected, edge corrected)
28.0 x 10^{-11} (cm^2/sec) (ml O_2/mL x mm Hg) @ 35°C	Fatt (boundary corrected, non-edge corrected)

AVAILABLE LENS PARAMETERS

The 1-DAY ACUVUE® DEFINE® Contact Lenses are hemispherical shells of the following dimensions:

Diameter (DIA): 14.20 mm

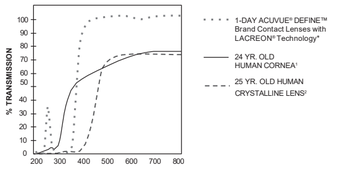
Center Thickness: Low minus lens-varies with power (e.g., -3.00D, 0.084 mm) Plus lens-varies with power (e.g., +1.00D, 0.130 mm)

Base Curve (BC): 8.5 mm

Powers (D): -9.00D to -6.50D (in 0.50D increments) -6.00D to -0.25D (in 0.25D increments) 0.00 to +1.00D (in 0.50D increments)

TRANSMITTANCE CURVE

1-DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® Technology vs. 24 yr. old human cornea and 25 yr. old human crystalline lens.



* The data are representative measurements taken through the central 3-5 mm portion for the thinnest marketed lens (-3.00D lens, 0.084 mm center thickness).

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

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

ACTIONS

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

The UV Blocking for 1-DAY ACUVUE® DEFINE® Contact Lenses averages 97% in the UVB range of 280 nm to 315 nm and 81% in the UVA range of 316 nm to 380nm for the entire power range.

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. You 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. The Eye Care Professional should be consulted for more information.

INDICATIONS (USES)

The 1-DAY ACUVUE® DEFINE® Contact Lenses are indicated for daily disposable wear to enhance or alter the appearance of the eye. These lenses are also indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have 1.00D or less of astigmatism.

The 1-DAY ACUVUE® DEFINE® Contact Lenses contain a UV Blocker to help protect against transmission of harmful UV radiation to the cornea and into the eye.

These lenses should be prescribed for daily disposable use only. No cleaning or disinfection is required. Lenses should be discarded upon removal.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE these lenses when any of the following conditions exist:

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

WARNINGS

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

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

- Eye Discomfort
- Excessive Tearing
- Vision Changes
- Loss of Vision
- Eye Redness
- Other Eye Problems

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

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

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

Specific Instructions for Use and Warnings:

- **Water Activity**

Instruction for Use

Do not expose contact lenses to water while wearing them.

WARNING:

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

PRECAUTIONS

Special Precautions for Eye Care Professionals:

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.
- The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing Eye Care Professional.
- Patients who wear these lenses to correct presbyopia using monovision or multifocal correction may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes unless otherwise indicated. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.
- Eye Care Professionals should instruct the patient to remove lenses immediately if the eyes become red or irritated.
- Eye Care Professionals should instruct the patient to always have a functional pair of spectacles with a current prescription available to use if the patient becomes unable to wear contact lenses, or in circumstances where contact lens wear is not advised.

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

Handling Precautions:

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove lenses or should have someone else available who can remove the lenses for him or her.
- **DO NOT** use if the sterile blister package is opened or damaged.
- Always wash, rinse, and dry hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup.
- **DO NOT** touch contact lenses with fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, and wearing instructions in the "Patient Instruction Guide" for 1-DAY ACUVUE® DEFINE® Contact Lenses contact lens and those prescribed by the Eye Care Professional.
- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.

Lens Wearing Precautions:

- Due to the reduction in light transmittance with cosmetically tinted lenses, some patients may experience visual symptoms while wearing the 1-DAY ACUVUE® DEFINE® Contact Lenses. In addition, some patients may experience peripheral awareness due to the opaque iris pattern.
- If the lens sticks (stops moving) on the eye, follow the recommended directions in *"Care for a Sticking (Non-Moving) Lens"*. The lens should move freely on the eye for the continued health of the eye. If non-movement of the lens continues, the patient should be instructed to immediately consult his or her Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. Sharing lenses greatly increases the chance of eye infections.
- If aerosol products, such as hair spray, are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.
- Ask the Eye Care Professional about wearing lenses during sporting activities.
- The patient should be advised to never rinse the lenses in water from the tap. Tap water contains many impurities that can contaminate or damage the lenses and may lead to eye infection or injury.

Lens Care Precautions:

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

Other Topics to Discuss with Patients:

- Always contact the Eye Care Professional before using any medicine in the eyes.
- Certain medications, such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness may cause dryness of the eye, increased lens awareness, or blurred vision. Should such conditions exist, proper remedial measures should be prescribed. Depending on the severity, this could include the use of lubricating drops that are indicated for use with soft contact lenses or the temporary discontinuance of contact lens wear while such medication is being used.
- Oral contraceptive users could develop visual changes or changes in lens tolerance when using contact lenses. Patients should be cautioned accordingly.
- Do not change lens type (e.g. brand name, etc.) or parameters (e.g. diameter, base curve, lens power, etc.) without consulting the Eye Care Professional.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of the patient's eyes. The patient should be instructed as to a recommended follow-up schedule.

Who Should Know That the Patient is Wearing Contact Lenses?

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

ADVERSE REACTIONS

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

- The eye may burn, sting and/or itch.
- There may be less comfort than when the lens was first placed on the eye.
- There may be a feeling of something in the eye (foreign body, scratched area).
- There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral corneal ulcers, or corneal erosion. There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis, and conjunctivitis; some of which are clinically acceptable in low amounts.
- There may be excessive watering, unusual eye secretions or redness of the eye.
- Poor visual acuity, blurred vision, rainbows or halos around objects, photophobia, or dry eyes may also occur if the lenses are worn continuously or for too long a time.

The patient should be instructed to conduct a simple 3-part self-examination at least once a day. They should ask themselves:

- How do the lenses feel on my eyes?
- How do my eyes look?
- Have I noticed a change in my vision?

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

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

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

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

GENERAL FITTING GUIDELINES

A. Patient Selection

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

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

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

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6571 Clinical Evaluation of Two Cosmetic Contact Lenses

Version and Date: 3.0 26 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], and 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