Clinical Study Protocol
Johnson & Johnson Vision Care, Inc.

Clinical Evaluation of Daily Disposable etafilcon A Cosmetic Contact Lenses

Protocol CR-6489

Version: 1.0

Date: 02 June 2022

Investigational Products: etafilcon A with PVP cosmetic lenses

Keywords: Beauty, etafilcon A with PVP cosmetic lenses, daily disposable, dispensing, logMAR visual acuity, subjective vision

Statement of Compliance to protocol, GCP and applicable regulatory guidelines:
This trial will be conducted in compliance with the protocol, ISO 14155:2020,[1] the International Council for Harmonization Good Clinical Practice E6(R2) (ICH GCP),[2] the Declaration of Helsinki,[3] and all applicable regulatory requirements.

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Clinical Evaluation of Daily Disposable etafilcon A Cosmetic Contact Lenses
Protocol Number: CR-6489
Version: 1.0
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SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

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 your assigned clinical research associate.

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

AUTHORIZED SIGNATURES

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

Author	See Electronic Signature Report [redacted]	DATE
Clinical Operations Manager	See Electronic Signature Report [redacted]	DATE
Biostatistician	See Electronic Signature Report [redacted]	DATE
Biostatistician Approver	See Electronic Signature Report [redacted]	[redacted]
Data Management	See Electronic Signature Report [redacted]	DATE
Medical Safety Officer	See Electronic Signature Report [redacted]	Date
Approver	See Electronic Signature Report [redacted]	DATE

CHANGE HISTORY

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

SYNOPSIS

Protocol Title	Clinical Evaluation of Daily Disposable etafilcon A Cosmetic Contact Lenses
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Confirmatory phase, Phase 3
Trial Registration	This study will be registered on ClinicalTrials.gov based on the following: confirmatory study meets the requirements for registration.
Test Article(s)	Investigational Products: etafilcon A with cosmetic pattern Control: Acuvue 1-Day Define Fresh Honey
Wear and Replacement Schedules	Wear Schedule: Daily Wear Replacement Schedule: Daily Disposable
Objectives	***Primary Objective:*** The primary objective of this study is to evaluate distance monocular high luminance, high contrast (HLHC) Visual Acuity (Logarithm of Minimal Angle of Resolution [logMAR]) of two investigational cosmetic lenses post lens fitting. ***Secondary Objective:*** The secondary objective of this study is to collect data for the control lens in the Asia-Pacific region to further support the portfolio of 1-Day Acuvue Define products.
Study Endpoints	Primary endpoint: • Distance monocular, high luminance, high contrast visual acuity (logMAR) Other Endpoints: • Subjective vision scores • Subjective comfort scores • Subjective handling scores • Monocular high luminance, low contrast (HLLC) visual acuity (logMAR) • Mechanical Lens fit • Cosmetic Lens fit • Hula Hoop • Ocular Physiology

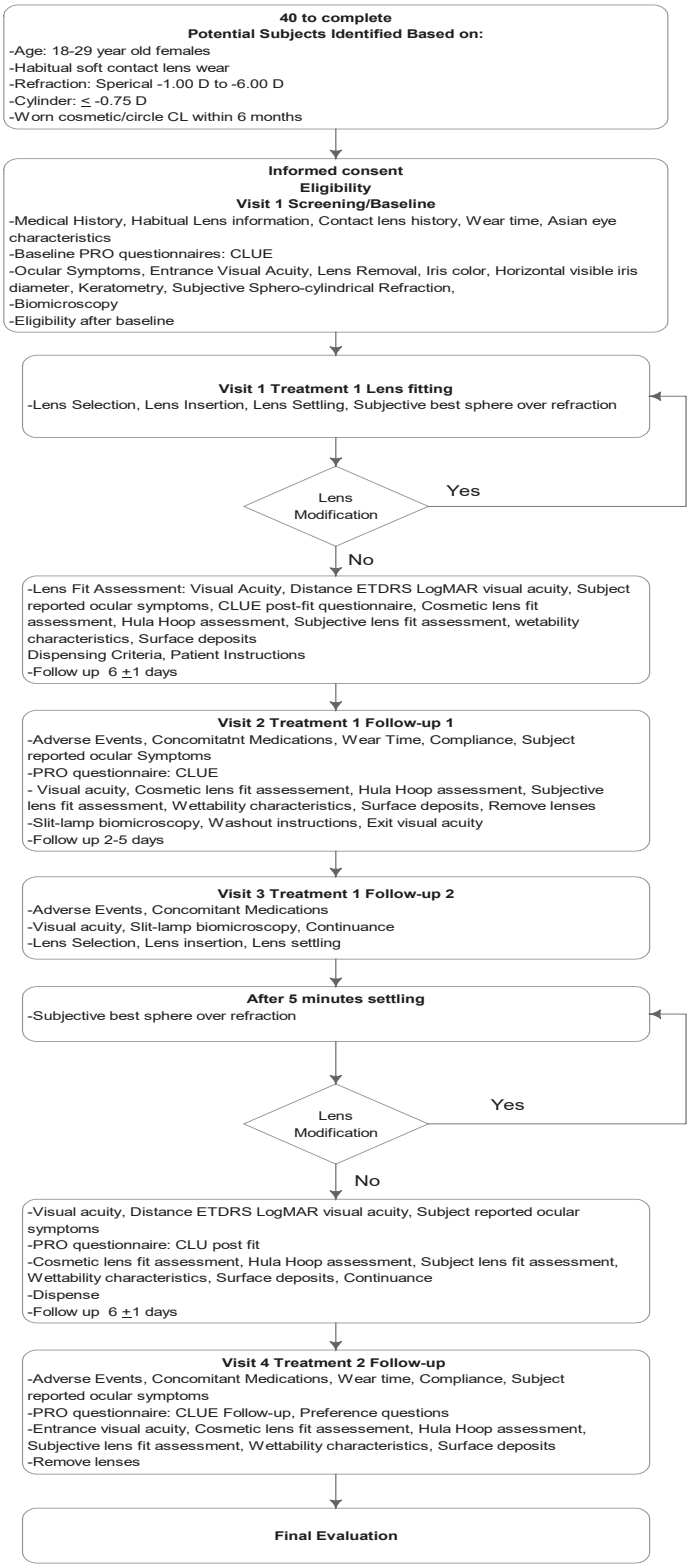
Study Design	This is a multi-site, 4-visit, brand-masked, bilateral, 2x2 cross-over dispensing study. Eligible subjects will be dispensed the study lenses in a random order for 6 (±1) days. A 2-to-5-day washout period between treatments will be utilized. Visit 1: Baseline and eligibility, insert treatment #1, logMAR vision, post-fit questionnaire, lens fit assessment. Dispense treatment #1 for 6 (±1) days Visit 2: Follow-up on treatment #1: Subjective questionnaire, lens fit, and physiology assessment. Washout for 2 to 5 days Visit 3: Insert treatment #2, logMAR vision, post-fit questionnaire, lens fit assessment. Dispense treatment #3 for 6 (±1) days Visit 4: Follow-up on treatment #2: Subjective questionnaire, lens fit. 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 60 subjects will be enrolled with the aim of approximately 46 subjects completing.
Study Duration	The study is expected to last up to 2 months. The enrollment period will also be up to 3 months.
Anticipated Study Population	We will aim to recruit up to 60 female subjects, ages 18 to 29 (inclusive). Subject must be habitual contact lens wearers who have purchased or worn cosmetic/circle contact lenses in the last 6 months. We will aim for a minimum of 60% of the subjects to be self-reported as Asian with Asian eye characteristics

Eligibility Criteria - Inclusion	Potential subjects must satisfy all of the following criteria to be enrolled in the study: 1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form 2. Females between 18 and 29 (inclusive) years of age at the time of screening 3. Appear able and willing to adhere to the instructions set forth in this clinical protocol (i.e. willing to wear only the study lenses and not use habitual lenses during the dispensing periods) 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 5. Be a current wearer of cosmetic/circle lenses in the last 6 months, by self-report. 6. The subject must be willing to be photographed and/or video-taped Inclusion Criteria After Baseline 7. 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 8. The subject's refractive cylinder must be less than or equal to 0.75 D (inclusive) in each eye 9. 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. Currently pregnant or lactating 2. 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 investigators discretion) 3. Use of systemic medications (eg, chronic steroid use) that are known to interfere with contact lens wear (at the investigators discretion) 4. Any previous, or planned (during the study) ocular surgery (eg, radial keratotomy, PRK, LASIK, etc.) 5. 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 investigators discretion) 6. Participation in any contact lens or lens care product clinical trial within seven (7) days prior to study enrollment. 7. Employee or family members of clinical site (eg, Investigator, Coordinator, Technician) Exclusion Criteria after Baseline Eligibility after Baseline: 8. 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 investigators discretion) 9. 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, PRO questionnaires (comfort, vision, and handling), lens fit assessment, cosmetic lens fit assessment/hula hoop assessment, 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	Tears Naturale re-wetting drops, FluStrips fluorescein strips, Bausch & Lomb Sensitive Eyes plus Saline, 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.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS, ACRONYMS AND DEFINITIONS OF TERMS

Add	Near addition; the additional power required for near vision correction
ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager
COVID-19	Coronavirus Disease 2019
CRA	Clinical Research Associate
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
[redacted]	[redacted]
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	The International Council for Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVC	Johnson & Johnson Vision Care, Inc.
LC	Limbus Center
LogMAR	Logarithm of Minimal Angle of Resolution
MedDRA©	Medical Dictionary for Regulatory Activities
MOP	Manual of Procedures
NIH	National Institutes of Health
OD	Right Eye
OHRP	Office for Human Research Protections
OHSR	Office for Human Subjects Research
OS	Left Eye
OU	Both Eyes

PD	Protocol Deviation
PHI	Protected Health Information
PI	Principal Investigator
PIG	Patient Instruction Guide
PRO	Patient Reported Outcome
PVP	Polyvinylpyrrolidone
QA	Quality Assurance
QC	Quality Control
SAE	Serious Adverse Event/Serious Adverse Experience
SAP	Statistical Analysis Plan
SAS	Statistical Analysis System
SD	Standard Deviation
SOP	Standard Operating Procedure
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Device Effect
VA	Visual Acuity

1. INTRODUCTION AND BACKGROUND

Cosmetic contact lenses can have patterns of varying size and opacities. When designing these cosmetic patterns, it is important to test the performance in a dispensing study on a cosmetic lens wearing population.

In the current study, objective and subjective performance measures of an investigational cosmetic soft contact lens will be collected and compared to a marketed cosmetic soft contact lens

1.1. Descriptions of Investigational Products

This study will include two types of cosmetic contact lenses. The Test lens is an investigational product and the Control lens is a marketed product. Further details about the test articles are found in Section 6 of this protocol.

1.2. Intended Use of Investigational Products

The intended use of the investigational product is to correct vision. The investigational product contains a cosmetic pattern, so it also affects the visual appearance of the eye. During this dispensing study, each lens type will be worn for approximately 1 week with a 2-5-day washout period between the treatments.

1.3. Summary of Findings from Nonclinical Studies

All previous pre-clinical findings were deemed satisfactory prior to proceeding with clinical trials on humans. For the most comprehensive nonclinical information regarding etafilcon A cosmetic contact lenses refer to the latest version of the Investigator Brochure (Etafilcon A Investigational Limbal Ring Contact Lenses with polyvinylpyrrolidone [PVP]).

1.4. Summary of Known Risks and Benefits to Human Subjects

The following risks/adverse events can be associated with wearing soft contact lenses in general:

- The eyes may burn, sting and/or itch.
- There may be a feeling of something in the eye (foreign body, scratched area).
- There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral corneal ulcers and corneal erosion.
- There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis and conjunctivitis, some of which are clinically acceptable in low amounts.
- There may be excessive watering, unusual eye secretions, or redness of the eye.
- Poor visual acuity, blurred vision, rainbows or halos around objects, photophobia, or dry eyes may also occur if the lenses are worn continuously or for too long a time.
- Due to the reduction in light transmittance with cosmetically tinted lenses, some patients may experience visual symptoms while wearing the Study Contact Lenses. In addition, some patients may experience reduced peripheral awareness due to the opaque iris pattern.

There is no direct benefit to the subjects for participating in the study, although they will be able to try out investigational cosmetic contact lenses. The information from this study will aid if the further development and assessment of new potential cosmetic contact lenses.

For the most comprehensive clinical information regarding etafilcon A cosmetic contact lenses with PVP refer to the latest version of the Investigator's Brochure (Etafilcon A Investigational Limbal Ring Contact Lenses with PVP).

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

There have been no serious or unanticipated adverse events and no loss of best correct VA reported in previous etafilcon A with PVP cosmetic contact lens clinical studies. There was one significant adverse event in [redacted], which was a small non-staining white corneal lesion. The site deemed this as not related to the study lenses as it was present prior to enrollment and stable at the final evaluation. See [redacted] Clinical Study report[4] for more information on this finding.

For the most comprehensive clinical information regarding etafilcon A cosmetic contact lenses with PVP refer to the latest version of the Investigator's Brochure (Etafilcon A Investigational Limbal Ring Contact Lenses with PVP).

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective
The primary objective of this study is to evaluate the objective vision Logarithm of Minimal Angle of Resolution (logMAR) under high illuminance/high contrast lighting conditions of the investigational cosmetic study lenses post lens fitting.

Secondary Objective:
The secondary objective of this study is to collect data for the control lens in the Asia-Pacific region to further support the portfolio of 1-Day Acuvue Define products.

2.2. Endpoints

Primary Endpoint:
Visual Acuity (logMAR)
Monocular visual acuity (OD and OS) measured post-lens fitting using ETDRS Charts under high contrast letters in bright illuminance conditions at distance (4 meters) will be the primary endpoint. Additional measurements of visual acuity will be collected using high and low contrast charts in bright illuminance conditions. Visual acuity will also be measured using normal illumination and normal contrast charts, while wearing goggles. See [redacted] and [redacted] in Appendix E for details regarding the collection of visual acuity (logMAR).

Other Exploratory Endpoints:

- Subjective vision scores
- Subjective comfort scores
- Subjective handling scores
- Distance monocular HLLC visual acuity (logMAR)
- Mechanical Lens fit
- Cosmetic Lens fit
- Hula Hoop
- Ocular Physiology

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

2.3. Hypotheses

Primary Hypothesis

1. While wearing the Test lenses, the proportion of eyes with high luminance high contrast distance (4 meters) logMAR visual acuity less than 0.176 logMAR (i.e., 20/30 Snellen VA) will be superior to 0.90.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Females aged 18 to 29 years (inclusive) who are habitual soft contact lens wearers and current wearers of circle/cosmetic contact lenses in the last 6 months will be recruited for this clinical study. While patients within the age range will be eligible to enroll, preference should be given to patients aged 18-24 years. Subjects must meet all the inclusion and none of the exclusion criteria listed in Section 3.2 and Section 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

1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form
2. Females between 18 and 29 (inclusive) years of age at the time of screening
3. Appear able and willing to adhere to the instructions set forth in this clinical protocol (i.e. willing to wear only the study lenses and not use habitual lenses during the dispensing periods)
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
5. Be a current wearer of cosmetic/circle lenses in the last 6 months, by self-report
6. The subject must be willing to be photographed and/or video-taped

Inclusion Criteria at Baseline

7. 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
8. The subject's refractive cylinder must be less than or equal to 0.75 D (inclusive) in each eye
9. 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

1. Currently pregnant or lactating
2. 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 investigators discretion)
3. Use of systemic medications (eg, chronic steroid use) that are known to interfere with contact lens wear (at the investigators discretion)
4. Any previous, or planned (during the study) ocular surgery (eg, radial keratotomy, PRK, LASIK, etc.)
5. 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 investigators discretion).
6. Participation in any contact lens or lens care product clinical trial within seven (7) days prior to study enrollment
7. Employee or family members of clinical site (eg, Investigator, Coordinator, Technician)

Exclusion Criteria at Baseline

8. 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 investigators discretion)
9. 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.

3.4. Enrollment Strategy

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

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This is a 4-visit, bilateral, dispensing, brand-masked, randomized, 2×2 crossover trial. Up to 60 subjects will be enrolled with a target of 46 subjects to complete the study.

At Visit 1 (Day 0), eligible subjects will be randomized to one of two lens wear sequences (Test/Control or Control/Test) in a bilateral fashion. Subjects will be fit into their first study lenses per the randomization scheme. Subjects will be scheduled to return after 6 ± 1 days for their follow-up evaluation (Visit 2). After Visit 2, a washout period of 2 to 5 days will occur in between Visit 2 and Visit 3. During the washout period subjects will be instructed to wear their habitual contact lenses. At Visit 3, subjects will be fit into their second study lenses per the randomization scheme and will be dispensed for 6 ± 1 days. Subjects will return for their follow-up evaluation and then will be exited from study (Visit 4). Unscheduled visits may occur during the course of this study. Subjects will be advised to wear the study lenses at least six (6) hours per day during each dispensing period (5 to 7 days).

4.2. Study Design Rationale

While the primary objective of this study is to assess logMAR visual acuity post-lens fitting for the investigational study lens, a controlled, bilateral, 2x2 crossover with a dispensing period of 6 ± 1 days was chosen as the design for this study. This was considered as the optimal design as it will address both the primary objective as well as provide clinical data for the control lens in the Asia-Pacific region. The intent for collecting data on a marketed product is to further support the portfolio of 1-Day Acuvue Define products. Though the primary hypothesis is to test only the investigational study lens, the study design is not anticipated to have an impact on subjects' visual acuity since this endpoint is objective in nature, there will be 2 to 5 days washout period between study lenses, and different EDTRS charts will be utilized for each eye (left vs. right) to help reduce potential for any memorization of the eye chart during collection of visual acuity.

4.3. Enrollment Target and Study Duration

Approximately 60 female ages 18 to 29 years (inclusive) who are habitual soft contact lens wearers and who have purchased or worn circle/cosmetic contact lenses in the last 6 months, will be enrolled in this 4-visit, multi-site clinical study. A minimum of 60% of the enrolled subjects will be of Asian descent and with Asian eye characteristics (Appendix C). Additionally, subjects who are more frequent beauty contact lens wearers (at least once a month for the last 6 months) will also be enrolled.

Subjects may be screened over the telephone and invited to the site for screening and enrollment procedures. Enrollment is defined as execution of the informed consent and/or assent form.

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

The study lenses will be worn in a bilateral and random fashion using a 2×2 crossover design. A computer-generated randomization scheme will be used to randomly assign subjects to one of the two possible lens wear sequences: Test/Control or Control/Test. The random scheme

will be generated using the PROC PLAN procedure from Statistical Analysis System (SAS) Software Version 9.4 or higher (SAS Institute, Cary, NC).[6]

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

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

When dispensing test articles, the following steps should be followed to maintain randomization codes:

1. Investigator or designee (documented on the Delegation Log) will consult the lens fitting schedule to obtain the test article assignment for that subject prior to dispensing.
2. Investigator or designee will record the subject's number on the appropriate line of the lens fitting schedule.
3. Investigator or designee will pull the appropriate test articles from the study supply. All test articles that are opened, whether dispensed (placed/fit on eye or dispensed outside the clinical site) or not, must be recorded on the Test Article Accountability Log in the "Dispensed" section.

5.2. Masking

Due to differences in cosmetic pattern between the Test and Control lenses, subjects in this study cannot be double-masked. However, subjects, investigators, and clinical site personnel will be unaware of the identity (brand) of both study lenses.

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

5.3. Procedures for Maintaining and Breaking the Masking

The identity of the test article shall not be broken unless information concerning the identity of the study lenses is necessary for the urgent medical treatment of a subject. The Sponsor must be notified as soon as possible if mask is broken.

If the masked need to be broken, the site investigatory or clinical site personnel designee will pull the appropriate test articles from the study supply. All test articles opened, whether dispensed (placed/fit on eye or dispensed outside the clinical site) or not, must be record on the Test Article Accountability Log in the "Dispensed" section.

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Article

		Control	Test
Name		1-Day ACUVUE Define – Fresh Honey	Investigational etafilcon A daily disposable cosmetic lens
Manufacturer		Johnson & Johnson	Johnson & Johnson
[redacted]		[redacted]	[redacted]
Lens Material		etafilcon A	etafilcon A
Nominal Base Curve @ 22°C		8.5 mm	8.5 mm
Nominal Diameter @ 22°C		14.2 mm	14.2 mm
Nominal Distance Powers (D)		-1.00 to -6.00 D	-1.00 to -6.00 D
Modality in Current Study		Daily	Daily
Replacement Frequency		Daily	Daily
Packaging Form (vial, blister, etc.)		Blister	Blister

Each subject will wear approximately 12 of each lens type.

6.2. Ancillary Supplies/Products

The following solutions will be used in this study:
Sensitive Eyes Plus (Bausch & Lomb) or country-specific alternative approved by the sponsor, FluStrips (Contacare) or country-specific alternative approved by the sponsor, and Tears Naturale Free (Alcon) or country-specific alternative approved by the sponsor.

Table 2: Ancillary Supplies

	Solution		
Solution Name/Description	Sensitive Eyes plus Saline (or other sponsor-approved product)	Tears Naturale Free (or other sponsor-approved product)	FluStrips Fluorescein (or other sponsor-approved product)
Manufacturer	Bausch & Lomb	Alcon	Contacare Ophthalmics Diagnostics (EOU)
Preservative	None	None	None
Other distinguishing items (dye, packaging, approval status, etc.	NA	NA	D&C Yellow No. 8, 0.6 mg

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.

6.4. Packaging and Labeling

The test articles will be packaged in blisters as the primary packaging. The test articles will be over-labeled to mask the subject and investigators to the identity of the lens. The test articles will be in plastic bags as the secondary packaging form. The sample study label is shown below:

Primary Packaging

CAUTION: INVESTIGATIONAL DEVICE
LIMITED BY U.S. LAW
TO INVESTIGATIONAL USE
EXCLUSIVELY FOR
CLINICAL INVESTIGATIONS

Contents: One contact lens in solution.

STERILE

LOT ABC123
SPH -1.00
EXP 2025/12/31
CR- 6489 RC A

Secondary Packaging

Sponsored By/Parrainé par:

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

Contents/Contenu:

_____
Contact Lenses in Solution
Lentilles cornéennes dans une solution

6.5. Storage Conditions

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

6.6. Collection and Storage of Samples

No samples will be collected as part of the study procedures.

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

6.7. Accountability of Test Articles

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

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

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

The Investigator will collect all unused test articles from the subjects at the end of the subject's participation. Subject returned unused test articles must be separated from the clinical study inventory of un-dispensed test articles and must be labeled with the subject number and date of return. Following final reconciliation of test articles by the monitor, the Investigator or monitor will destroy all unused test articles per sponsor approved method.

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

[redacted]

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 3: Time and Events

Visit Information	Visit 1 Screening, Baseline, Dispense Treatment 1	Visit 2 Treatment 1 Follow-up, Washout	Washout	Visit 3 Dispense Treatment 2	Visit 4 Treatment 2 Follow-up, Final Evaluation
Time Point	Day 0	6 ± 1 days from V1	2 - 5 days	2-5 days from V2	Day 6 ± 1 days from V3
Estimated Visit Duration	2 hours	1 hour		1 hour	1 hour
Study Informed Consent	X				
Inclusion/Exclusion Screening Criteria	X				
Demographics	X				
Medical History & medication review	X	X		X	X
Habitual Lens Info	X				
CLUE Baseline	X				
HVID	X				
Keratometry	X				
Entrance/Exit VA	X	X		X	X
Subjective Refraction	X				
Biomicroscopy	X	X		X	X
Subject Reported Ocular Symptoms	X	X		X	X
Eligibility after baseline exam	X				
Randomization	X				
Lens Fitting #1	X				
Lens Fitting #2				X	
Over-refraction/optimization	X			X	
CLUE Post-Fit	X			X	
CLUE Follow-Up		X			X
logMAR VA	X			X	
Cosmetic Lens Fit Assessment	X	X		X	X
Hula Hoop Assessment	X	X		X	X
Lens Fit Assessment	X	X		X	X
Wettability Characteristics	X	X		X	X

Visit Information	Visit 1 Screening, Baseline, Dispense Treatment 1	Visit 2 Treatment 1 Follow-up, Washout	Washout	Visit 3 Dispense Treatment 2	Visit 4 Treatment 2 Follow-up, Final Evaluation
Time Point	Day 0	6 ± 1 days from V1	2 - 5 days	2-5 days from V2	Day 6 ± 1 days from V3
Estimated Visit Duration	2 hours	1 hour	[redacted]	1 hour	1 hour
Lens Surface/Deposits Assessment	X	X		X	X
Lens Dispensing & Instruction	X			X	
Washout instructions		X			
Adverse Event Review		X		X	X
Final Evaluation					X

7.2. Detailed Study Procedures

VISIT 1

The subjects must present to Visit 1 wearing their habitual contact lenses.

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note**: The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's year of birth, gender, race and ethnicity.	
1.3	Asian Eye Characteristics	Confirm if the subject meets the criteria listed in Appendix C.	Appendix D
1.4	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.5	Habitual Lenses	Questions regarding the subject's habitual lens type, parameters, wear schedule and duration.	

Visit 1: Screening			
Step	Procedure	Details	[redacted]
1.6	Wear time and Comfortable Wear Time with Habitual Lenses	Record the subject's wear time and comfortable wear time with their habitual contact lenses.	
1.7	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible. If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Visual Acuity, Refraction and Biomicroscopy forms are not required.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.8	CLUE Baseline Questionnaire	The subject will respond to the PRO Baseline CLUE Questionnaire	Appendix A
1.9	Entrance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual contact lens correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.10	Remove Habitual Contact Lenses	The subject's habitual lenses will be removed and stored in their own lens case. If they forgot to bring their lens case, one will be provided to them.	
1.11	Iris Color	Record iris color in both eyes (self-reported)	
1.12	Horizontal visible iris diameter (HVID)	Measure the horizontal visible iris diameter for each eye separately using a pd stick in normal room illumination. Measure from the edge of the iris nasally to the edge of the iris temporally. Record in mm to one decimal place.	
1.13	Keratometry	Record the keratometry readings OD and OS.	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.14	Subjective Sphero-cylindrical Refraction	Complete subjective spherocylindrical refraction and record the resultant distance visual acuity (OD, OS and OU) to the nearest letter. Note: The subjects contact lens powers based on the vertexed (12 mm), spherical equivalent must be between -1.00 and -6.00 D.	
1.15	Slit Lamp Findings	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any slit lamp findings are Grade 3 or higher, the subject is ineligible to continue. Continue to the Final Evaluation Form and dismiss the subject. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	
1.16	Eligibility after Baseline	All responses to Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria questions must be answered "no" for the subject to be considered eligible.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.17	Lens Selection	Assign the study lens based on the randomization scheme. Select the contact lens power based on the vertexed (12 mm), spherical equivalent subjective refraction.	
1.18	Lens Insertion	The Subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable. **Note:** Designated site staff should observe the insertion process. If it appears that the subject attempts to insert a lens that is "inside-out", they should interfere to avoid incorrect insertion.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		Note 2: If the lens moves excessively on the eye after insertion, ask the subject to remove the lens, confirm lens is not inverted (correct if it is) and reinsert.	
1.19	Lens Settling	Allow the study lenses to settle for a minimum of 5 minutes.	
1.20	Subjective Best Sphere Over Refraction	Perform subjective best sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU).	[redacted]
1.21	Lens Power Modification (if applicable)	Adjust the lens power if the subject's best sphere over-refraction is not plano. For each power modification, repeat steps (1.16 to 1.19). Two power modifications are allowed.	
1.22	Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with the study contact lens correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.23	Distance ETDRS logMAR Visual Acuity	Per [redacted], please confirm room illuminance and chart luminance acceptable ranges for both high/low contrast visual acuity testing. 1. Under high illumination and high chart luminance, record the distance (4 meter) ETDRS high contrast visual acuity twice OD (HC1-HC2) and twice OS (HC3-HC4). 2. Under high illumination and high chart luminance, record the distance (4 meter) ETDRS low contrast visual acuity twice OD (LC1-LC2) and twice OS (LC3-LC4). 3. With the goggles on, under normal illumination and chart luminance, record the distance (4 meter) ETDRS high contrast visual acuity twice OD	[redacted]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		(HC5-HC6 and twice OS (HC7-HC8). Allow subject to adjust to dim condition for 3 minutes. Letter-by-letter results will be recorded into the electronic data capture form, which will calculate the visual performance score for each chart read.	
1.24	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.25	CLUE Post-Fit Questionnaire	The subject will respond to the CLUE Post-Fit Questionnaire	[redacted], Appendix A
1.26	Cosmetic Lens Fit Assessment (without slit-lamp)	The Cosmetic Lens Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
1.27	Hula Hoop Assessment (without slit-lamp) *If unacceptable cosmetic fit in any gaze.*	If there is an unacceptable cosmetic fit in any gaze, the Hula Hoop Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
1.28	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • Presence of limbal exposure (appearance of clear cornea) in any gaze; • Presence of edge lift; • Presence of unacceptable movement (excessive or insufficient) in <u>all three</u> of the following conditions: primary gaze, up gaze, and tightness on push up.	[redacted]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		Note: if lens fit is unacceptable subject will be discontinued from the study.	
1.29	Wettability Characteristics	Record the white light lens wettability of both lenses.	[redacted]
1.30	Surface Deposits	Record any front and back surface lens deposits.	[redacted]
1.31	Continuance	For the subject to continue in the study, they must meet all three of the following criteria: • Visual acuity is 20/30 or better OD and OS • The lens fit is acceptable OD and OS • Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject.	
1.32	Dispense	The lenses will be dispensed for a 5 to 7 day wearing period. During this time, they are required to wear the lenses at least 6 hours per day. • Dispense enough lenses to last the subject to their scheduled follow-up visit. Do not dispense extras*. • The lenses will be worn as daily wear/daily disposable only. • Rewetting drops are permitted if needed. • A patient instruction booklet will be provided. • Subjects will be scheduled for their 5-7-day follow-up visit, ensuring that they wear the study lens at least 6 hours on the day of the follow-up visit. * Note: In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality Complaint Form. The	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.	

VISIT 2

The subjects must present to Visit 2 wearing the study lenses and having worn them continuously for at least six (6) hours on the day of the visit immediately prior to attending the visit.

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
2.1	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
2.2	Wearing Time	Record the average wearing time and comfortable wearing time.	
2.3	Compliance	Confirm compliance with the prescribed wear schedule.	
2.4	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.5	CLUE Follow-Up Questionnaire	The subject will respond to the CLUE Follow-Up Questionnaire	[redacted]
2.6	Visual Acuity	Record the distance Snellen visual acuity with the contact lenses (OD, OS and OU) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
2.7	Cosmetic Lens Fit Assessment (without slit-lamp)	The Cosmetic Lens Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
2.8	Hula Hoop Assessment (without slit-lamp) *If unacceptable cosmetic fit in any gaze.*	If there is an unacceptable cosmetic fit in any gaze, the Hula Hoop Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
2.9	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement. • edge lift. • excessive movement in primary and up gaze. • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push-up test. **Note:** if lens fit is unacceptable subject will be discontinued from the study.	
2.10	Wettability Characteristics	Record the white light lens wettability of both lenses.	
2.11	Surface Deposits	Record any front and back surface lens deposits.	
2.12	Remove lenses	The lenses will be removed and discarded.	
2.13	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the subject has a Grade 3 slit lamp finding, it will be recorded as an Adverse Event and the subject will be monitored as per the guidelines given in section 13. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	
2.14	Washout instructions	Subjects are instructed to wear their spectacles or habitual contact lenses for 2-5 days.	
2.15	Exit VA	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual spectacles (where applicable). Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	

VISIT 3

The subjects must present to Visit 3 not wearing their habitual contact lenses.

Visit 3: Treatment 2 Treatment			
Step	Procedure	Details	[redacted]
3.1	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
3.2	Visual Acuity	Record the distance Snellen visual acuity with the contact lenses (OD, OS and OU) to the nearest letter. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
3.3	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the subject has a Grade 3 slit lamp finding, it will be recorded as an Adverse Event and the subject will be monitored as per the guidelines given in section 13. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
3.4	Continuance	Confirm the subject is able to continue in the study.	
3.5	Lens Selection	Assign the study lens based on the lens fitting schedule. Select the contact lens power based on subjective best sphere refraction.	
3.6	Lens Insertion	The Subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable.	
3.7	Lens Settling	Allow the study lenses to settle for a minimum of 5 minutes.	
3.8	Subjective Best Sphere Over Refraction	Perform subjective best sphere refraction over the study lenses with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome	[redacted]

Visit 3: Treatment 2 Treatment			
Step	Procedure	Details	[redacted]
		test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU). **Note:** The endpoint criterion for the duo-chrome test is the lens power at which the red and green sides of the chart appear to be equally distinct. However, if the subject's response changes from "red" to "green" with only a 0.25D change in power and no report that the two sides appear to be equally sharp, the refraction endpoint should be the lens power that leaves the red chart sharper.	
3.9	Lens Power Modification (if applicable)	Adjust the lens power if the subject's best sphere over-refraction is not plano. For each power modification, repeat steps (3.7-3.9). Two power modifications are allowed.	
3.10	Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with the study contact lens correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
3.11	Distance ETDRS logMAR Visual Acuity	Per [redacted], please confirm room illuminance and chart luminance acceptable ranges for both high/low contrast visual acuity testing. 1. Under high illumination and high chart luminance, record the distance (4 meter) ETDRS high contrast visual acuity twice OD (HC1-HC2) and twice OS (HC3-HC4). 2. Under high illumination and high chart luminance, record the distance (4 meter) ETDRS low contrast visual acuity twice OD (LC1-LC2) and twice OS (LC3-LC4). 3. With the goggles on, under normal illumination and chart luminance, record the distance (4 meter) ETDRS high contrast visual acuity twice OD (HC5-HC6 and twice OS (HC7-HC8). Allow	[redacted]

Visit 3: Treatment 2 Treatment			
Step	Procedure	Details	[redacted]
		subject to adjust to dim condition for 3 minutes. Letter-by-letter results will be recorded into the electronic data capture form, which will calculate the visual performance score for each chart read.	
3.12	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
3.13	CLUE Post-Fit Questionnaire	The subject will respond to the CLUE Post-Fit Questionnaire	[redacted] Appendix A
3.14	Cosmetic Lens Fit Assessment (without slit-lamp)	The Cosmetic Lens Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
3.15	Hula Hoop Assessment (without slit-lamp) *If unacceptable cosmetic fit in any gaze.*	If there is an unacceptable cosmetic fit in any gaze, the Hula Hoop Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
3.16	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement. • edge lift. • excessive movement in primary and up gaze. • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push-up test.	[redacted]

Visit 3: Treatment 2 Treatment			
Step	Procedure	Details	[redacted]
		Note: if lens fit is unacceptable subject will be discontinued from the study.	
3.17	Wettability Characteristics	Record the white light lens wettability of both lenses.	
3.18	Surface Deposits	Record any front and back surface lens deposits.	
3.19	Continuance	For the subject to continue in the study, they must meet all three of the following criteria: • Visual acuity is 20/30 or better OD and OS • The lens fit is acceptable OD and OS • Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject. • Subject is willing to wear the lenses for the dispensing period for 6 hours per day and will not wear their habitual lenses during the dispensing period.	
3.20	Dispense	The lenses will be dispensed for a 5 to 7 day wearing period. During this time, they are required to wear the lenses at least 6 hours per day. • Dispense enough lenses to last the subject to their scheduled follow-up visit. Do not dispense extras*. • The lenses will be worn as daily wear/daily disposable only. • Rewetting drops are permitted if needed. • A patient instruction booklet will be provided. • Subjects will be scheduled for their 5-7-day follow-up visit, ensuring that they wear the study lens at least 6 hours on the day of the follow-up visit. * Note: In the event a lens is lost or damaged, the subject will return to the clinical site for replacement. As much as reasonably possible, a damaged lens and packaging should be returned to the clinical site (wet, if possible) and then returned to the Sponsor. If lens damage is present, complete the Product Quality	

Visit 3: Treatment 2 Treatment			
Step	Procedure	Details	[redacted]
		Complaint Form. The lens will be stored in labeled vial with saline, and clearly differentiated from the other worn lenses that will be shipped back to the Sponsor.	

VISIT 4

The subjects must present to Visit 4 wearing test article for at least six (6) hours on the day of the visit.

Visit 4: Treatment 2 Follow-Up			
Step	Procedure	Details	[redacted]
4.1	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
4.1	Wearing Time	Record the average wearing time and comfortable wearing time.	
4.2	Compliance	Confirm compliance with the prescribed wear schedule.	
4.3	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
4.4	CLUE Follow-Up Questionnaire	The subject will respond to the CLUE Follow-Up Questionnaire	[redacted]
4.5	Preference questions	The subject will respond to the preference Follow-Up Questionnaire	[redacted]
4.6	Entrance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with study contact lens in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
4.7	Cosmetic Lens Fit Assessment (without slit-lamp)	The Cosmetic Lens Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E
4.8	Hula Hoop Assessment (without slit-lamp) *If unacceptable cosmetic fit in any gaze.*	If there is an unacceptable cosmetic fit in any gaze, the Hula Hoop Assessment will be assessed by the investigator (without slit-lamp) in primary gaze and extreme gaze (right, left, and upgaze) at a normal conversation distance (approximately three (3) feet away from the subject).	Appendix E

Visit 4: Treatment 2 Follow-Up			
Step	Procedure	Details	[redacted]
4.9	Subjective Lens Fit Assessment	Evaluate overall lens fit acceptance (acceptable or unacceptable) based on centration, movement and other fitting characteristics. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement. • edge lift. • excessive movement in primary and up gaze. • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push-up test. **Note**: if lens fit is unacceptable subject will be discontinued from the study.	[redacted]
4.10	Wettability Characteristics	Record the white light lens wettability of both lenses.	[redacted]
4.11	Surface Deposits	Record any front and back surface lens deposits.	[redacted]
4.12	Remove lenses	The lenses will be removed and discarded	

FINAL EVALUATION

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

Final Evaluation			
Step	Procedure	Details	[redacted]
F.1	Final Exam Form	Indicate if the subject completed the study successfully. If subject discontinued from the study, indicate the reason.	

Final Evaluation			
Step	Procedure	Details	[redacted]
F.2	Exit Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" Grade for all observations listed. After the slit lamp examination, at the discretion of the Investigator, rinse the subject's eyes thoroughly with preservative-free saline.	[redacted]
F.3	Exit Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual spectacles (where applicable). Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]

7.3. Unscheduled Visits

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

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

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

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

The following information will be collected during an unscheduled visit.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Reason for unscheduled visit	Indicate if the only reason for the visit is that the subject requires additional test articles. If the reason is other than resupply of previously dispensed lenses, specify the reason for the visit.	
U.2	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.3	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.4	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]
U.5	Subjective Sphero-cylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS and OU).	[redacted]
U.6	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
U.7	Dispensing (if applicable)	If the subject requires additional lenses to complete the wear period and is eligible to do so, provide additional lenses per the dispensing instructions given in the detailed study procedures.	
U.8	Exit Visual Acuity (if applicable)	Record the subject's exit distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

NOTE: If the only reason for the unscheduled visit is that the subject requires additional test articles, only the dispensing information needs to be recorded.

7.4. Laboratory Procedures

Not applicable.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent.
- they are eligible.
- have not withdrawn/discontinued from the study for any reason described in section 8.2.
- completed all visits through the final visit four (4).

8.2. Withdrawal/Discontinuation from the Study

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

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

For discontinued subjects, the Investigator will:

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

Additional subjects will be enrolled if a subject discontinues from the study prematurely.

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study.
Disallowed medications for this study include See section 9.1.
Concomitant therapies that are disallowed include: See section 9.1.

9.1. Systemic Medications

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

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

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

Or:

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

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

Table 4: Disallowed systemic medications

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

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

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

Or:

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

Table 5: Disallowed systemic antihistamines

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

10. DEVIATIONS FROM THE PROTOCOL

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

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

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

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

Protocol waivers are prohibited.

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

Table 6: Examples of major and minor protocol deviations

Deviation category	Major deviation	Minor deviation
Out-of-window visit	Visit attended 2 or more days out of visit window defined in study procedures	Visit attended 1 day out of visit window defined in study procedures
Wear time following dispensing period (Visit 1 and Visit 3)	Subject wears the lenses for 3 or less or 9 or more days.	Subject only wears the study lenses for 4 or 8 days.
Washout period (between Visit 2 and Visit 3)	If the duration is 1 or less or 10 or more days	Not Applicable
Unanswered PRO questions	For questionnaires where data is related to a primary or secondary endpoint, 3 or more PRO questions are unanswered (i.e., left blank).	For questionnaires where data is related to a primary or secondary endpoint, 2 or fewer PRO questions are unanswered (i.e., left blank). For questionnaires where data where data is not related to a primary or secondary endpoint, any PRO questions are unanswered (i.e., left blank).
Insufficient wear of study lenses (on the day of Visit 2 and Visit 4)	Subject presents having worn the study lenses 1 hour or less.	Subject presents having worn the study lenses 2-5 hours.

11. STUDY TERMINATION

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

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

JJVC reserves the right to terminate the study at any time for any reason. Additionally, the IEC/IRB reserves the right to terminate the study if an unreasonable risk is determined. The study can be terminated by the Principal Investigator at the individual clinical site due to

specific clinical observations, if in their opinion, after a discussion with JJVC, it is determined that it would be unwise to continue at the clinical site.

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

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

12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

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

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

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness).
- Who received the complaint.
- Study number.
- Clinical site information (contact name, site ID, telephone number).
- Lot number(s).
- Unique Subject Identifier(s).
- Indication of who first observed complaint (site personnel or subject).
- OD/OS indication, along with whether the lens was inserted.

- Any related AE number if applicable.
- Detailed complaint description (scheduled/unscheduled visit, wear time, symptoms, resolution of symptoms, etc.).
- Eye Care Provider objective (slit lamp) findings if applicable.
- Confirmation of product availability for return (and tracking information, if available), or rationale if product is not available for return [redacted]

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

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

13. ADVERSE EVENTS

13.1. Definitions and Classifications

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

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

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

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

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

- Death
- Serious deterioration in the health of the subject that resulted in any of the following:
- Life-threatening illness or injury
- Permanent or persistent impairment of a body structure or a body function
- Hospitalization or prolongation of patient hospitalization

- Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
- Chronic disease
- Foetal distress, foetal death or a congenital physical or mental impairment of birth defect.

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

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

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

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

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

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

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

- Non-significant Infiltrative Event (NSIE)

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

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device."
NOTE 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
NOTE 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.[7]

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

13.2. Assessing Adverse Events

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

- Seriousness/Classifications (see definition in section 13.1).
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related, unlikely related, possibly related, or related - see definition in section 13.2.1).
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild, moderate, or severe - see definition in section 0).
- Outcome – not recovered or not resolved, recovering or resolving, recovered or resolved with sequelae, recovered or resolved, death related to adverse event, or unknown.
- Actions Taken – none, temporarily discontinued, permanently discontinued, or other.

13.2.1. Causality Assessment

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

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

13.2.2. Severity Assessment

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

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

13.3. Documentation and Follow-Up of Adverse Events

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

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

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

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

- Adverse event (diagnosis not symptom).
- Drawings or photographs (where appropriate) that detail the finding (e.g., size, location, and depth, etc.).
- Date the clinical site was notified.
- Date and time of onset.
- Date and time of resolution.
- Adverse event classification, severity, and relationship to test articles, as applicable.
- Treatment regimen instituted (where appropriate), including concomitant medications prescribed, in accordance with applicable licensing requirements.
- Any referral to another health care provider if needed.
- Outcome, ocular damage (if any).
- Likely etiology.
- Best corrected visual acuity at the discovery of the event and upon conclusion of the event, if the AE is related to the visual system.

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

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

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

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether a subject reporting with an adverse event will continue in the study. If a subject is discontinued from the study, it will be the responsibility of the Investigator to record the reason for discontinuation. The Investigator will also document the adverse event appropriately and complete the Adverse Event eCRF. Any subjects with ongoing adverse events related to the test article, study treatment or study procedures, as of the final study visit date, should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator. Non-ocular adverse events that are

not related to the test article, study treatment, or study procedures may be recorded as "ongoing" without further follow-up.

13.4. Reporting Adverse Events

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

13.4.1. Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events

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

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

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

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

Unanticipated (Serious) Adverse Device Effect (UADE)

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

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

Non-Serious Adverse Events

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

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

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

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

13.5. Event of Special Interest

Not applicable

13.6. Reporting of Pregnancy

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

14. STATISTICAL METHODS

14.1. General Considerations

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

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 or higher (SAS Institute, Cary, NC).[6] 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 by lens type (Test and Control (1-Day Acuvue Define Fresh Honey), timepoint (Baseline, Fitting Evaluation, Lens Dispensing, 1-Week Follow-up), and analysis population (ITT, PP or safety), as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, standard deviation (SD), median, minimum and maximum). Frequency count and percentage of subjects or eyes within each category will be provided for categorical data.

14.2. Sample Size Justification

This study was designed and powered to test that the proportion of eyes with distance high luminance high contrast logMAR visual acuity less than 0.176 logMAR VA is superior to 0.90. Clinical study [redacted] was used in the sample size calculation since this historical study also collected distance monocular HLHC logMAR VA post-lens fitting and utilized the same study design. Moreover, the 1-Day Acuvue Define FRESH GREEN lenses evaluated in [redacted] are a part of the portfolio for 1-DAY Acuvue Define with Lacreon (Product Health & Safety Clinical Risk Assessment[9]). Furthermore, all 1-Day Acuvue Define with Lacreon products utilize the same contact lens design ([redacted]), lens material (etafilcon A), and manufacturing processes, and specifications for lens mechanical and optical parameters ([redacted]). Table 7 below displays full details regarding visual acuity data for [redacted].

Table 7: [redacted] Distance Monocular High Luminance High Contrast logMAR Visual Acuity – Fitting Evaluation – ITT Population

	Fresh Green – Pilot Line (Test) N= 112	**Fresh Green – Line 26 (Control) N=110**
logMAR VA		
Mean (SD)	-0.0471(0.08531)	-0.0495(0.08283)
Median	-0.0400	-0.0600
Min - Max	-0.3000 – 0.2400	-0.2600 – 0.1600
logMAR VA < 0.176 n(%)		
Yes	111 (99.1)	110 (100.0)
No	1 (0.9)	0 (0.0)
Total	112	110

N=Total number of eyes.
SD: Standard Deviation, Min: Minimum, Max: Maximum

The sample size was calculated using a 2-sided type I error rate of 5% with at least 80% statistical power. logMAR visual acuity scores were converted to a binary response as $Y = 1$ if a subject eye had logMAR VA < 0.176 and $Y = 0$ (i.e., logMAR VA => 0.176). Based on the historical data, this binary outcome has a 99% success rate for the proportion of eyes with logMAR VA less than 0.176. To generate the correct data structure for this study (2x2 crossover), a reference rate of 97% was used as a worst-case scenario for the probability of event Y. A correlation of 0.80 was used to model the covariance between the left and right eyes within the same treatment, and 0.50 was used to model both the covariance between treatments within the same eye as well as between eyes and treatments. While subjects will wear the study lenses in a random order, logMAR visual acuity post-fitting data collected from subjects wearing the Test lens in period 2 is not expected to be impacted by the Control lens they wore in period 1 since a wash-out period of 2-5 days will be utilized between study lenses and, subjects' visual acuity is an objective outcome which depends what they have on eye at

that moment of data collection. Therefore, this method treated the Test and Control lenses independently.

Given the rare event binary outcome, Y=0 a Bayesian beta-binomial model with correlated binary data (Diniza et al; 2010)[9] was chosen for the sample size estimation. A total of 2000 trial were simulated using the reference rate and correlations specified above. For each simulated trial, the lower bound of the 95% central posterior credible interval constructed for the proportion of eye with logMAR VA less than 0.176 was compared to a margin of 0.90. Based on the historical information and success criteria described above, a total of 46 subjects are required to complete the study in order to test the primary hypothesis with at least 80% statistical power (Table 8). To account for subject drop and/or screen failures up to 60 subjects will be enrolled with the target of 46 subjects to complete the study.

Table 8: Sample Size Estimate and Statistical Power

Endpoint	Number of Subjects to Complete	Statistical Power (%)
Proportion of eyes with logMAR VA < 0.176	46 (33 per arm)	82.0

14.3. Analysis Populations

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

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

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

14.4. Level of Statistical Significance

The planned primary analysis for this study will be conducted with an overall type I error rate of 5%.

14.5. Primary Analysis

The primary analysis will be conducted on the ITT population.

Visual Acuity (logMAR)

Distance monocular high luminance high contrast logMAR VA scores post-fitting will be converted into a binary response for the purposes of analysis. ***YY=1*** if an eye has logMAR VA less than 0.176 and ***YY=0*** otherwise. The dichotomized variable ***YY*** will be analyzed using a Bayesian beta-binomial model for correlated binary data[9].

The Model:
Let Y_1 and Y_2 denote the binary outcomes of logMAR VA less than 0.176 (Yes/No) in left and right eyes, respectively, post-fitting for the Test lens. Considering the correlation, ρ, between Y_1 and Y_2, the distribution of the sum $Y = Y_1 + Y_2$ is obtained by the mixture of two variables. One of them follow a binomial distribution $Bin(2,p)$ with mixing probability $(1-\rho)$ and the other one follows a modified Bernoulli distribution, $MBern(p)$, taking value 0 and 2 rather than conventional 0 and 1, with mixing probability ρ:

$$P(Y = y|\, p,\rho) = (1-\rho)Bin(2,p)I_{A1} + \rho MBern(p)I_{A2}\,,$$

where $I_{A1} = \{0,1,2\}$, $I_{A2} = \{0,2\}$ and p is the probability of success (i.e., acceptable lens fitting).

To overcome the complexity of the mixture likelihood a latent variable Z_i, i = 1, 2 is introduced in the model to indicate in which component of the model the observation y_i, i=1, 2, belongs to, that is,

$$Z_i = \begin{cases} 1, \text{if the observation belong to the MBern(p)}, \\ 0, \text{if the observation belong to the Bin(2,p)} \end{cases}$$

The joint distribution of the augmented data $(Y_i, Z_i), i = 1,2$, is given by

$$\mathrm{P}(\mathrm{Y}=\mathrm{y_i}, \mathrm{Z}=\mathrm{z_i}|\, \mathrm{p}, \rho) = \rho^{\mathrm{z_i}} \mathrm{p}^{\mathrm{y_i z_i}/2} (1-\mathrm{p})^{(2-\mathrm{y_i})\mathrm{z_i}/2} (1-\rho)^{1-\mathrm{z_i}} \binom{2}{\mathrm{y_i}} \mathrm{p}^{\mathrm{y_i}(1-\mathrm{z_i})} (1-\mathrm{p})^{(2-\mathrm{y_i})(1-\mathrm{z_i})}$$

The probability p links to the regression variables through a logit transformation as follow:

$$\text{logit}\,(\mathrm{p}) = \beta_0 + \beta_1 \text{lens}$$

It is assumed that β_0, β_1 and ρ to be independent with a non-informative prior N(0, 1000) for β_0 and β_1, and beta(0.5, 0.5) for ρ. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC procedure will be used to estimate the posterior distributions of the parameters (β_0, β_1, ρ). Inferences will be made based on a posterior credible interval for the relevant parameters.

Bayesian Estimation and Statistical Evaluation of Hypothesis:
Superiority of the Test lens relative to the pre-defined threshold with respect to the proportion of eyes with logMAR VA less than 0.176 will be evaluated using Bayesian statistics.

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

$$H_o: P_T \leq 0.90$$

$$H_A: P_T > 0.90$$

Where P_T is the probability of the event (i.e., the probability of having logMAR VA < 0.176 in on eye while wearing the Test lens). Based on the central posterior probability distribution of the proportion p_T, superiority is interpreted as 95% probability of the Test lens being statistically higher than the pre-specified threshold of 0.90 (i.e., $P_T > 0.90$). If the lower bound of the 95% central posterior credible interval is above 0.90, it can be concluded that there is a 95% probability that the P_T is superior to 0.90 (statistically higher) based on the observed sample (i.e., P(p_{Test}> 0.90) ≥ 0.975).

In the case of all eyes have a logMAR VA less than 0.176 (i.e., zero events of logMAR VA 0.176 or higher), a Bayesian hierarchical model accounting for zero event problem will be considered[10].

14.6. Secondary Analysis

Not applicable.

14.7. Other Exploratory Analysis

Not applicable.

14.8. Interim Analysis

No interim read will be conducted.

14.9. Procedure for Handling Missing Data and Drop-Outs

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

14.10. Procedure for Reporting Deviations from Statistical Plan

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

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

The data for this study will be captured on electronic case report forms (eCRFs) using the BioClinica 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 ISO14155:2020.[7]

15.2. Subject Record

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

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

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

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

15.3. Trial Registration on ClinicalTrials.gov

This study will be registered on ClinicalTrials.gov based on the following: confirmatory study meets the requirements for registration.

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

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

16.2. Confidentiality of Information

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

16.3. Data Quality Assurance

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

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

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

16.4. Data Monitoring Committee (DMC)

Not required.

17. CLINICAL MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

Potential subjects will be fully informed of the risks and requirements of the study and, during the study, subjects will be given any new information that may affect their decision to continue participation. Subjects will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. 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, section 4 of the ICH E6(R2) guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with section 8 of the ICH E6(R2) guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements.

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

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

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

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

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

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

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

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

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

18.4. Informed Consent

Each subject or their representative, must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH GCP[2] and ISO 14155:2020[7] guidelines, applicable regulatory requirements, and Sponsor Policy.

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

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

18.5. Privacy of Personal Data

The collection, processing and disclosure of personal data and medical information related to the Study Subject, and personal data related to Principal Investigator and any clinical site personnel (e.g., name, clinic address and phone number, curriculum vitae) is subject to compliance with the Health Information Portability and Accountability Act (HIPAA) in the United State[12] and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person’s related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

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

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

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

19. STUDY RECORD RETENTION

In compliance with the ICH GCP guidelines,[2] the Investigator/Institution will maintain all CRFs and all subject records that support the data collected from each subject, as well as all study documents as specified in ICH GCP[2] and all study documents as specified by the applicable regulatory requirement(s). The Investigator/Institution will take measures to prevent accidental or premature destruction of these documents.

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

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

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

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

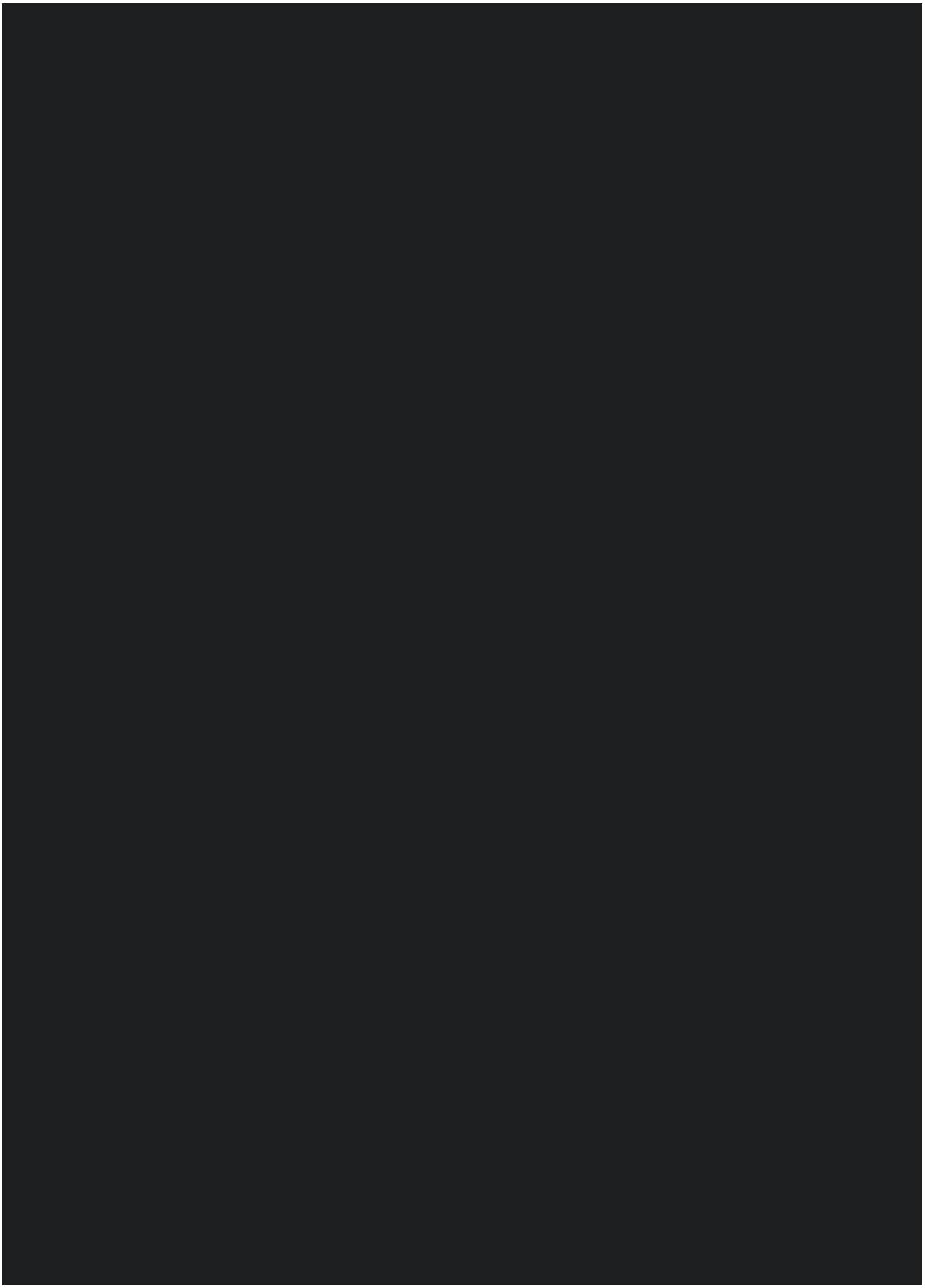
This study will be registered on ClinicalTrials.gov by the Sponsor.

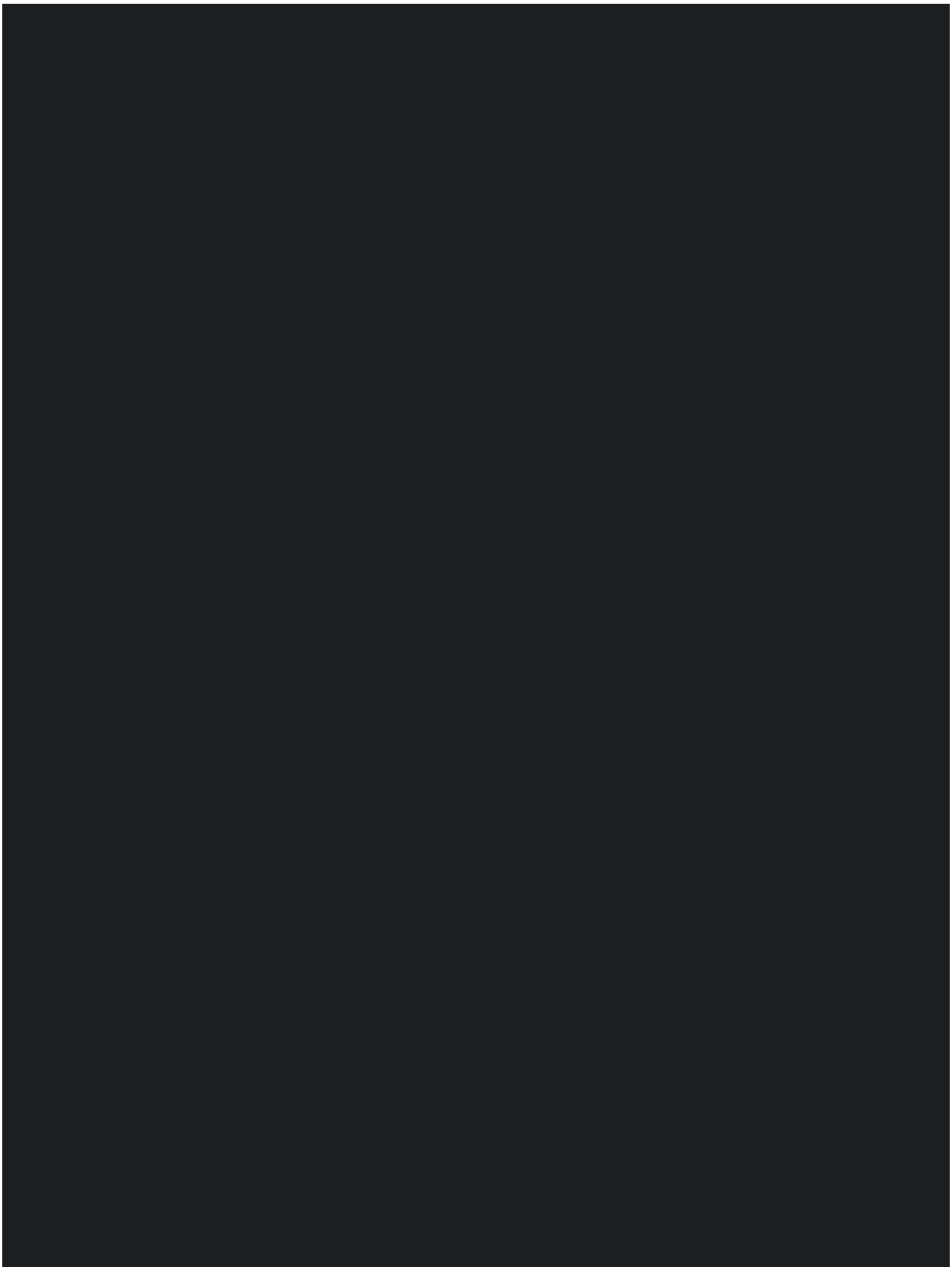
22. REFERENCES

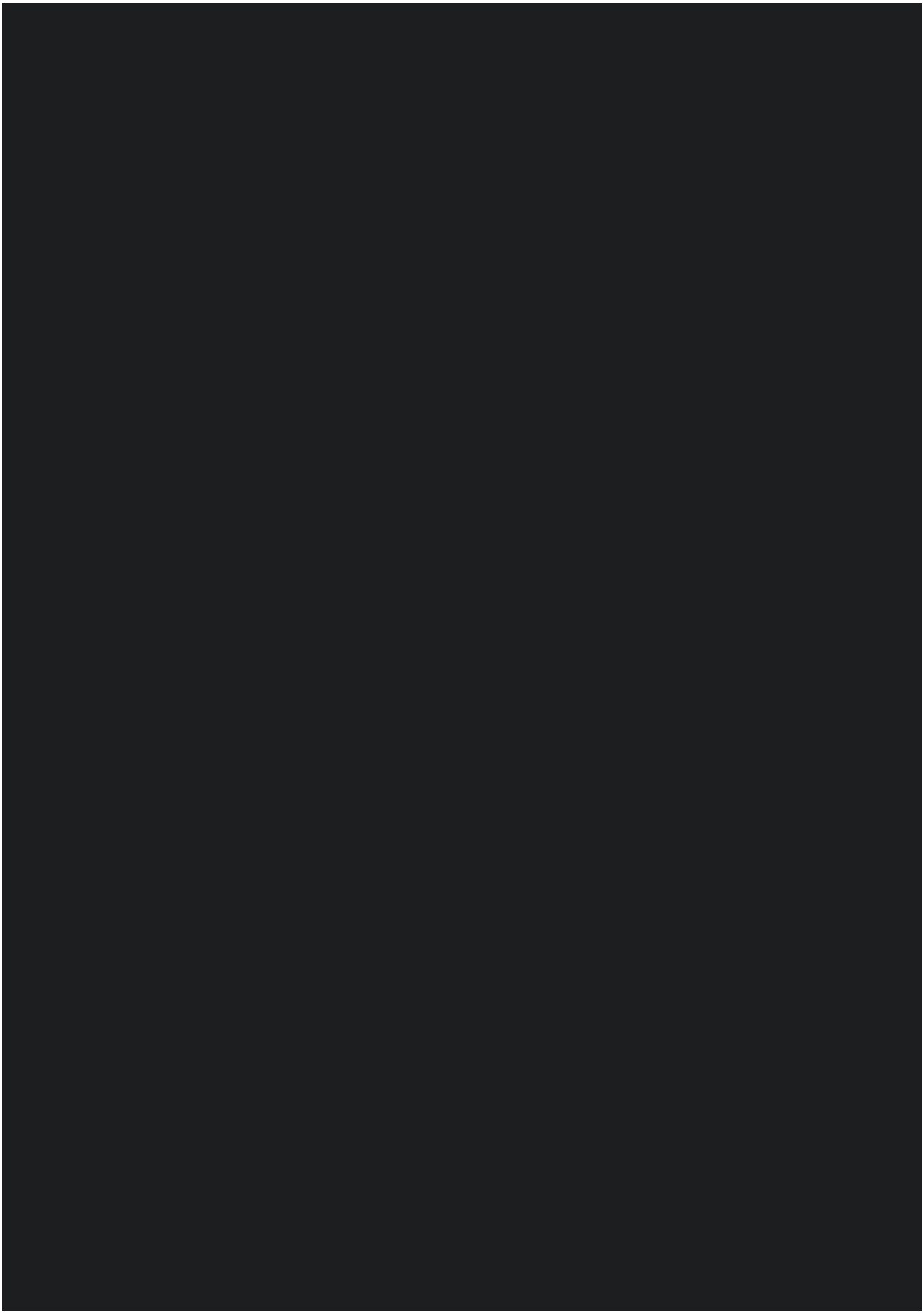
1. ISO 14155:2020: Clinical investigation of medical devices for human subjects — Good clinical practice, Available at: https://www.iso.org/standard/71690.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP), Available at: https://www.ich.org/page/efficacy-guidelines
3. Declaration of Helsinki – Ethical principles for Medical Research Involving Human Subjects, Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
4. Bishop M. [redacted] *Clinical Study Report* [redacted] *Clinical Report*: "*"Clinical Evaluation of Daily Disposable Etafilcon A Cosmetic Contact Lenses"" published on* October 19, 2018.
5. Wirth R, al e. Development of the Contact Lens User Experience: CLUE Scales. *Optom Vis Sci.* 2016;93(8):801-808.
6. *SAS Institute Inc: SAS® 9.4 Statements: Reference, Third Edition.* Cary, NC SAS Institute Inc; 2014.
7. ISO 14155:2011: Clinical investigation of medical devices for human subjects – Good clinical practice., Available at: https://www.iso.org/standard/71690.html
8. Bishop M. [redacted] *Protocol.* [redacted] *Clinical Report*: "*Clinical Evaluation of Daily Disposable Etafilcon A Cosmetic Contact Lenses" published on*.
9. Product Health & Safety Clinical Risk Assessment [redacted] *Product Health & Safety Clinical Risk Assessment*. June 1, 2020.
10. Record [redacted] Rev 10 *1•DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® (etafilcon A) Device Master Record*.
11. Procedure [redacted] *1-DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® (etafilcon A)*.
12. Health Information Portability and Accountability Act (HIPAA), Available at: https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
13. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR

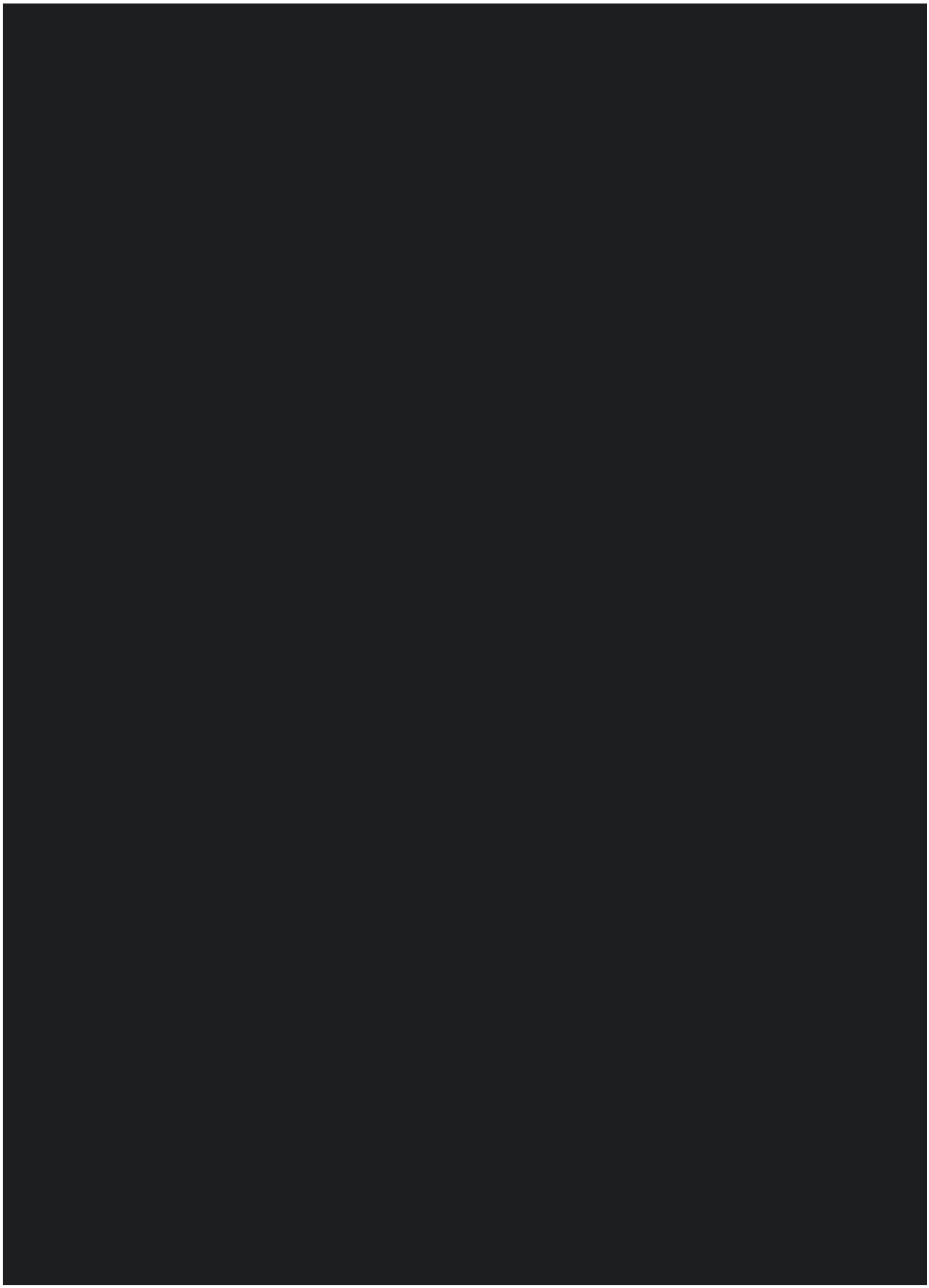
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

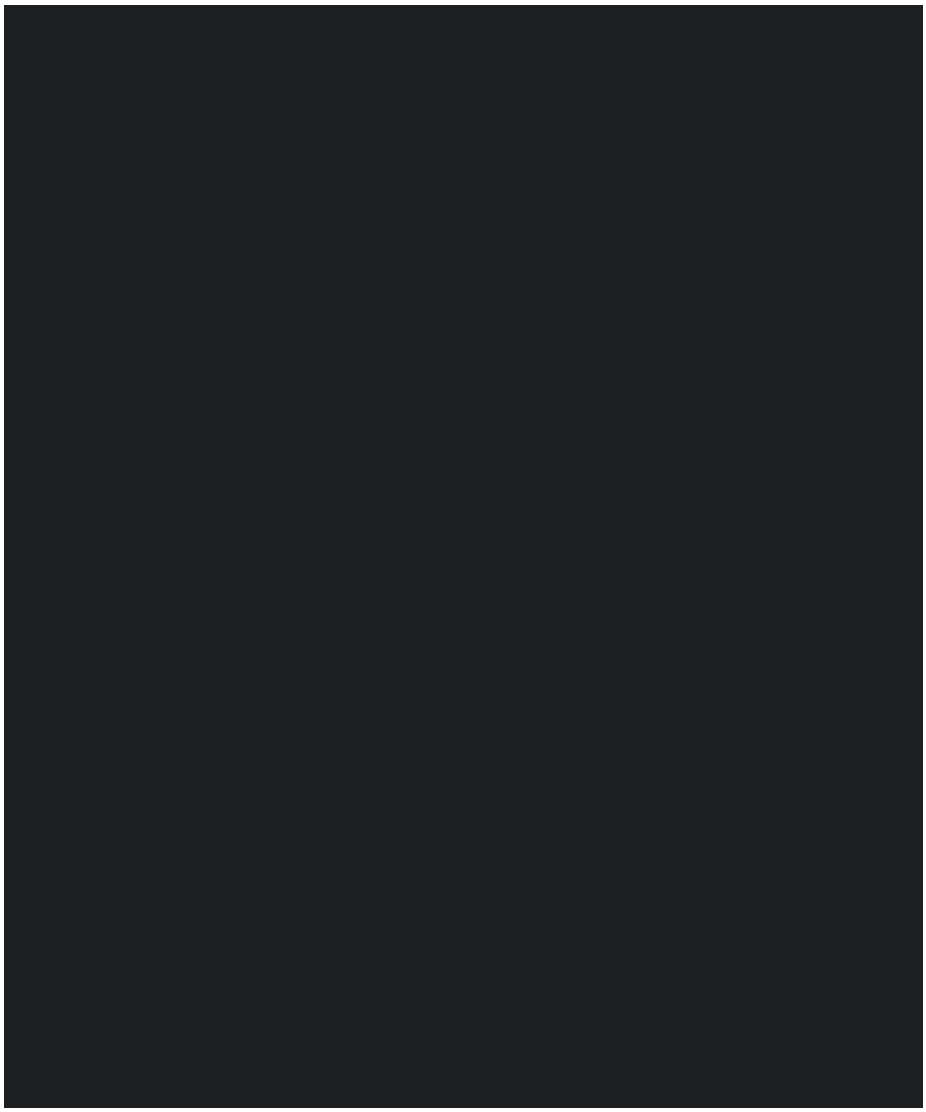
[redacted]











APPENDIX B: PATIENT INSTRUCTION GUIDE

The Patient Instruction Guide (PIG) will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

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

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

If vision is acceptable, perform a slit lamp examination to confirm adequate fit (centration and movement). If the fit is acceptable, dispense the lenses and instruct 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 "1-DAY ACUVUE® DEFINE™ Brand Contact Lenses Patient Instruction Guide." Copies are available for download at www.acuvue.com.

MONOVISION FITTING GUIDELINES

A. Patient Selection

Monovision Needs Assessment

For a good prognosis, the patient should have adequately corrected distance and near visual acuity in each eye. The amblyopic patient with significant astigmatism (greater than 1.00D) in one eye may not be a good candidate for monovision correction with the 1-DAY ACUVUE® DEFINE™ Contact 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 such activities 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 or 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."

2. **Refractive Error Method**

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

3. **Visual Demands Method**

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

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

C. Special Fitting Characteristics

1. Unilateral Vision Correction Requirement

There are circumstances where only one contact lens is required for vision correction purposes (e.g., presbyopic emmetripoc patient would only require a near lens, whereas a bilateral myope would require corrective lenses on both eyes).

Due to the indication of altering and/or enhancing the natural appearance of the eye, the non-corrected eye may be fit with a 0.00D lens to ensure consistent appearance.

Example: A presbyopic emmetropic patient who requires a +1.75D ADD would have a +1.75D lens on the near eye and a 0.00D lens (uncorrected) may be fit on the other eye.

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 eye may be fit with a 0.00D lens (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 this patients who cannot their meet state driver's licensing requirements with a monovision correction.
- Make use of proper illumination when carrying out visual tasks.

Monovision fitting success can be improved by the following suggestions:

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

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

All patients should be supplied with a copy of the "1-DAY ACUVUE® DEFINE™ Brand Contact Lenses with LACREON® Technology (etafilcon A) Patient Instruction Guide." Copies are available for download at 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 "1-DAY ACUVUE® DEFINE™ Brand
- Contact Lenses with LACREON® Technology PATIENT INSTRUCTION GUIDE." Copies are available for download at www.acuvue.com.

REVIEW THESE INSTRUCTIONS WITH THE PATIENT SO THAT HE OR SHE CLEARLY UNDERSTANDS THE PRESCRIBED WEARING AND REPLACEMENT SCHEDULES.

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.

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.

CR-6489, V 1.0

The maximum suggested wearing time for these lenses is:

DAYS	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 prescribed for daily disposable wear, the Eye Care Professional should provide the patient with appropriate and adequate warnings and instructions for daily disposable lens wear at the time they are dispensed.

The Eye Care Professional should review with patients that no cleaning or disinfection is needed with daily 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

If the lens sticks (stops moving), the patient should be instructed to apply a few drops of the recommended lubricating or rewetting solution directly to the eye and wait until the lens begins to move freely on the eye before removing it. If non-movement of the lens continues after a few minutes, the patient should **immediately** 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 sterile lens is supplied in a foil-sealed plastic package containing buffered saline solution with povidone. The plastic package is marked with base curve, diameter, diopter power, variant, lot number, and expiration date.

[redacted]

REPORTING OF ADVERSE REACTIONS

All serious adverse experiences and adverse reactions observed in patients wearing these lenses or experienced with these 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

20400760

Printed in U.S.A.
Revision date: 08/14
Revision number: D-08-14-04

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.

define™ 1-DAY ACUVUE®
BRAND
CONTACT LENSES
with LACREON®

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

JJVC CONFIDENTIAL

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

SYMBOLS KEY

The following symbols may appear on the label or carton:

SYMBOL	DEFINITION
	Consult Instructions for Use
	Date of Manufacture
	Manufactured by or in
	Use By Date (expiration date)
LOT	Batch Code
STERILE	Sterile Using Steam or Dry Heat
DIA	Diameter
BC	Base Curve
D	Diopter (lens power)
	Quality System Certification Symbol
	UV-Blocking
	Fee Paid for Waste Management
Rx Only	CAUTION: Federal law restricts this device to sale by or on the order of a licensed practitioner
A	ACCENT STYLE
S_H	NATURAL SHIMMER™
N	NATURAL SHINE™
S_P	NATURAL SPARKLE™
V	VIVID STYLE

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 SHIMMER™
- NATURAL SHINE™
- NATURAL SPARKLE™
- 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:	70% minimum
• Surface Character:	Hydrophilic
• Water Content:	58%

Oxygen Permeability:

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

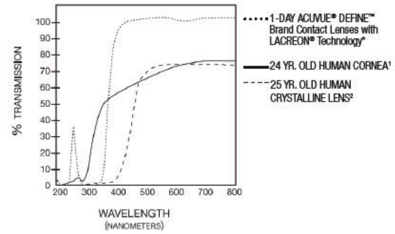
AVAILABLE LENS PARAMETERS

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

Diameter:	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:	8.5 mm
Power Range:	-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 CURVES

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).

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

[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 Heath, 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 onto 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 380 nm for the entire power range.

Note: Long-term exposure to UV radiation is one of the risk factors associated with cataracts. Exposure is based on a number of factors such as environmental conditions (altitude, geography, cloud cover) and personal factors (extent and nature of outdoor activities). UV–blocking contact lenses help provide protection against harmful UV radiation. However, clinical studies have not been done to demonstrate that wearing UV–blocking contact lenses reduces the risk of developing cataracts or other eye disorders. The Eye Care Professional should be consulted for more information.

INDICATIONS (USES)

The 1-DAY ACUVUE® DEFINE™ Contact Lenses are indicated for daily disposble 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 proect against transmission of harmful UV radiation to the cornea and into the eye.

CONTRAINDICATIONS (REASONS NOT TO USE)

DO NOT USE the 1-DAY ACUVUE® DEFINE™ Contact 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 solution (i.e., rewetting eye 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,**
- **Or Other Eye Problems,**

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

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

Instructions for Use

Do not expose contact lenses to water while wearing them.

WARNING:

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

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 the 1-DAY ACUVUE® DEFINE™ Contact Lenses to correct presbyopia using monovision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.
- Eye Care Professionals should instruct the patient to remove the lenses immediately if the eyes become red or irritated.

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

Handling Precautions:

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

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 the Eye Care Professional.
- Never wear lenses beyond the period recommended by the Eye Care Professional.
- The patient should be advised to never allow anyone else to wear their lenses. They have been prescribed to fit their eyes and to correct their vision to the degree necessary. Sharing lenses greatly increases the chance of eye infections.
- If aerosol products, such as hair spray, are used while wearing lenses, exercise caution and keep eyes closed until the spray has settled.
- Avoid all harmful or irritating vapors and fumes while wearing lenses.

Lens Care Precautions:

- 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.
- 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 vi[redacted]

If the patient reports any probl[redacted]e 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 THE 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. The patient 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 1-DAY ACUVUE® DEFINE™ Contact Lenses should be chosen based on:

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

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

B. Pre-fitting Examination

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

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

Based on this evaluation, if it is determined that the patient is eligible to wear the 1-DAY ACUVUE® DEFINE™ Contact Lenses, the Eye Care Professional should proceed to the lens fitting instructions as outlined below.

C. Initial Power Determination

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

D. Base Curve Selection (Trial Lens Fitting)

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.

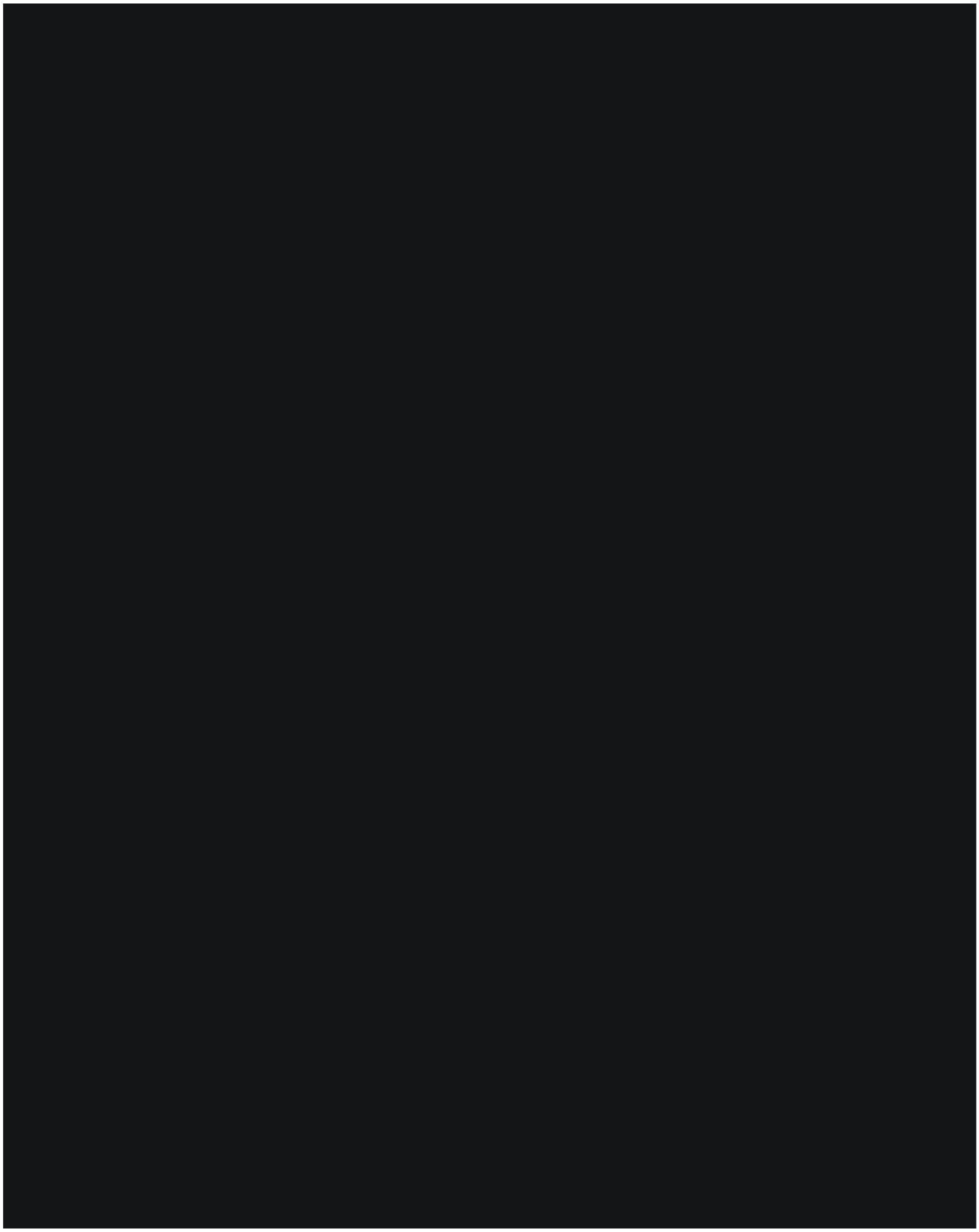
3. Criteria of a Steep Fitting Lens

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.

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.

APPENDIX D: ASIAN EYE CRITERIA ASSESSMENT PROCEDURE



APPENDIX E: HULA HOOP AND COSMETIC LENS FIT ASSESSMENT

The Cosmetic Lens Acceptance will be assessed by the investigator (without slit-lamp) in [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

APPENDIX F: [redacted]

- [redacted] LENS FITTING CHARACTERISTICS
- [redacted] SUBJECT REPORTED OCULAR SYMPTOMS
- [redacted] FRONT AND BACK SURFACE LENS DEPOSIT GRADING PROCEDURE
- [redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS
- [redacted] BIOMICROSCOPY
- [redacted] KERATOMETRY
- [redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION
- [redacted] DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE
- [redacted] PATIENT REPORTED OUTCOMES
- [redacted] WHITE LIGHT LENS SURFACE WETTABILITY
- [redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

[redacted] LENS FITTING CHARACTERISTICS

[redacted]

[redacted] [redacted]

[redacted]

[redacted]

[redacted] [redacted]

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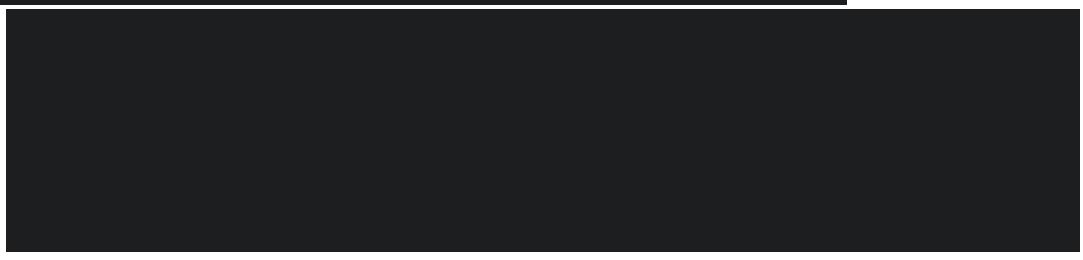
[redacted] SUBJECT REPORTED OCULAR SYMPTOMS

[redacted]

[redacted] FRONT AND BACK SURFACE LENS DEPOSIT GRADING PROCEDURE

[redacted]

[redacted]



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- [redacted]

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[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] **BIOMICROSCOPY SCALE**

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] KERATOMETRY

[redacted]

[redacted] DISTANCE AND NEAR VISUAL ACUITY EVALUATION

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] DISTANCE LOGMAR VISUAL ACUITY MEASUREMENT PROCEDURE

[redacted]

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[redacted]

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[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] PATIENT REPORTED OUTCOMES

Title: Patient Reported Outcomes
Document Type: [redacted]
Document Number: [redacted] **Revision Number:** 3

[redacted] [redacted]

[redacted]

[redacted] [redacted]

[redacted]

[redacted] [redacted]

[redacted]

[redacted] [redacted]

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[redacted] [redacted]

[redacted]

[redacted] WHITE LIGHT LENS SURFACE WETTABILITY

[redacted]

[redacted] VISUAL ACUITY CHART LUMINANCE AND ROOM ILLUMINATION TESTING

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APPENDIX G: COVID-19 RISK MITIGATION GUIDELINES [redacted]

1.0 PURPOSE

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

2.0 SCOPE

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

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

3.0 DEFINITIONS

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

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

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

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

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

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

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

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

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

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

4.0 GUIDANCE FOR STUDY DOCUMENTS

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

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

4.1 Additional Risks Related to the COVID-19 Pandemic:

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

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

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

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

4.1.1 Informed Consent:

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

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

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

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

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

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

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

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

4.1.3 Protocol Compliance Investigator(s) Signature Page:

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

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

4.1.4 Study Site Initiation Training Slides:

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

5.0 GUIDANCE FOR REMOTE SUBJECT VISITS

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

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

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

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

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

6.0 STUDY CONDUCT DURING PANDEMIC

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

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

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

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

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

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

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

6.1 Monitoring Visits

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

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

6.1.1 Study Site Initiation:

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

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

6.1.2 Interim Monitoring Visits (if applicable):

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

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

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

6.1.3 Study Site Closure:

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

Attachment A: Study Site Correspondence

XXXX XX, 2020

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

Dear <<Principal Investigator>> and Study Team,

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

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

Protocol:

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

Protocol Signature Page:

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

Informed Consent:

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

COVID-19 Risk Control Checklist for Clinical Studies:

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

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

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

Please file this letter in your site file study correspondence.

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

Study Number
Site Number
Principal Investigator (PI) Name

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

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

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

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

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

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

Principal Investigator Signature and Date

RESOURCE LINKS

US Resource Links

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

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

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

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

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

OUS Resource Links

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

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

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

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

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

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

- Infection prevention and control for COVID-19: Interim guidance for outpatient and ambulatory care settings. (2020, May 23 May). Retrieved from Government of Canada: https://www.canada.ca/en/public-health/services/diseases/2019-novel-coronavirus-infection/guidance-documents/interim-guidance-outpatient-ambulatory-care-settings html

- Information for Members On Coronavirus (COVID-19). (n.d.). Retrieved from Canadian Association Of Optometrists: https://opto.ca/sites/default/files/resources/documents/information_for_members_on_coronavirus.pdf

- Coronavirus (COVID-19) resources for health professionals, including aged care providers, pathology providers and health care managers. (2020, September 24). Retrieved from Australian Government Department of Health: https://www health.gov.au/resources/collections/coronavirus-covid-19-resources-for-health-professionals-including-aged-care-providers-pathology-providers-and-health-care-managers

- Environmental Cleaning and Disinfection Principles for COVID-19. (n.d.). Retrieved from Australian Government Department of Health: https://www.health.gov.au/sites/default/files/documents/2020/03/environmental-cleaning-and-disinfection-principles-for-covid-19.pdf

- Infection control guidelines and advice. (n.d.). Retrieved from Optometry Australia : https://www.optometry.org.au/practice-professional-support/coronavirus-covid-19-what-optometrists-need-to-know/covid-19-clinical-advice/infection-control-guidelines-and-advice/

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6489 Clinical Evaluation of Daily Disposable etafilcon A Cosmetic Contact Lenses

Version and Date: 1.0 02 June 2022

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

I agree to conduct this study according to ISO 14155:2020,[7] GCP and ICH guidelines,[2] the Declaration of Helsinki,[3] United States (US) Code of Federal Regulations (CFR),[13] and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. The Principal Investigator is responsible for ensuring that all clinical site personnel, including Sub-Investigators adhere to all ICH[2] regulations and GCP guidelines regarding clinical trials during and after study completion.

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

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

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

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

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

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

Principal Investigator:

_____ _____
Signature Date

_____
Name and Professional Position (Printed)

Institution/Site:

_____
Institution/Site Name

_____
Institution/Site Address