Johnson & Johnson Vision Care, Inc.

Clinical Study Protocol

Title: Design Validation of senofilcon A with New UV-blocking Additive

Protocol: CR-6305

Version: 4.0, Amendment 3.0

Date: 14 November 2018

Investigational Products: ACUVUE OASYS® with Transitions™ Light Intelligent Technology™

Key Words: senofilcon A, ACUVUE OASYS®, ACUVUE OASYS with Transitions Light Intelligent Technology, daily wear reusable, dispensing

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

Confidentiality Statement:

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SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

Name: John R. Buch, O.D., M.S., F.A.A.O.
Title: Senior Principal Research Optometrist
Address: 7500 Centurion Parkway, Suite 100, Jacksonville, FL 32256
[redacted]
Email: jbuch@its.jnj.com
[redacted]

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

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

AUTHORIZED SIGNATURES

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

Author / Study Responsible Clinician	See Electronic Signature Report John R. Buch, O.D., M.S. Senior Principal Research Optometrist, JJVCI	DATE
Clinical Operations Manager	See Electronic Signature Report [redacted] Clinical Operations Manager, JJVCI	DATE
Biostatistician	See Electronic Signature Report [redacted] Biostatistician II, JJVCI	DATE
Biostatistician Reviewer	See Electronic Signature Report [redacted] Sr. Manager, Biostatistics JJVCI	DATE
Data Management	See Electronic Signature Report [redacted] Clinical Project Manager – Data & Systems, JJVCI	DATE
Reviewer	See Electronic Signature Report [redacted] Clinical Research Fellow, JJVCI	DATE
Approver	See Electronic Signature Report [redacted] Dir. Sphere - Light Management - Lens care, JJVCI	DATE

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Date
1.0	John R. Buch	Original Protocol	06 September 2018
2.0	John R. Buch	Amendments to make more compliant to ISO11980: 1. Added exclusion criteria of herpetic keratitis and pathological dry eye 2. Baseline ocular physiological findings must be Grade 0 or 1. Amendment recommended by IRB: 1. Include vitamin A analogs to Table 1. Clarified logMAR acuity room illumination, chart luminance, and which eye will read which chart.	19 September 2018
3.0	John R. Buch	Amendments to V2 include: • Clarified temporary use of suspect medications in Section 3.3.1. • Section 7.2: Visit 2 occurs 13-15 days following Visit 1. • Section 7.2: added applicable [redacted] for logMAR visual acuity [redacted] [redacted] Updated medication spelling errors • Table 1: Inserted study specific labels	08 October 2018
4.0	[redacted]	1. Updated verbiage in Hypotheses 3 and 4 to match the acceptance criteria in the Customer Requirement Document (VIS-Dval-000194/4) dated on August 29, 2018. 2. Added details to the sample size justification in section 14.3. 3. Updated the hypotheses 3 and 4 (null and alternative) in Section 14.	14 November 2018

SYNOPSIS

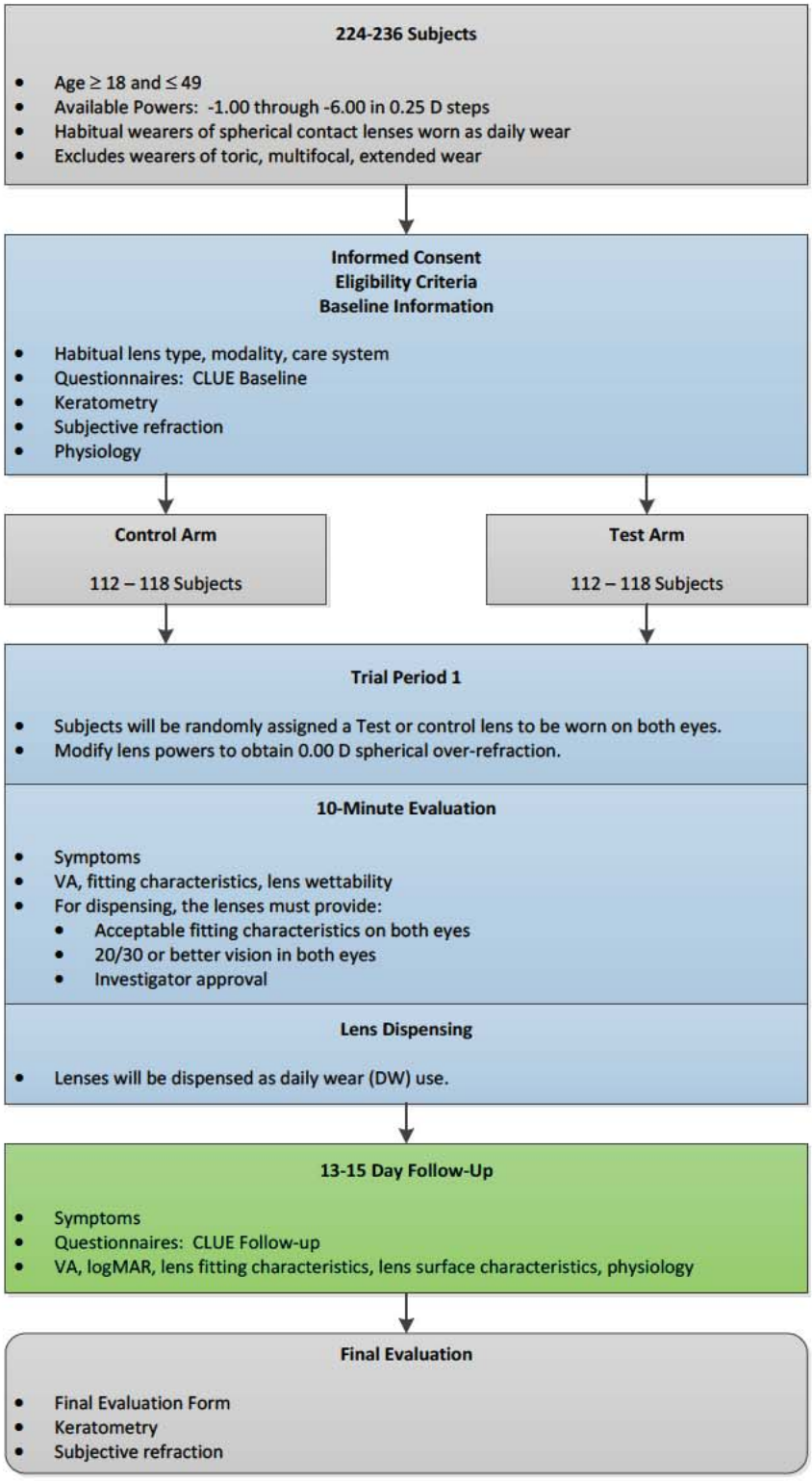
Protocol Title	Design Validation of senofilcon A with New UV-blocker Additive
Sponsor	JJVCI, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Design input validation
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor
Test Article(s)	Investigational Products: senofilcon A with new UV-blocking additive (i.e., ACUVUE OASYS with Transitions Light Intelligent Technology). Control Products: senofilcon A without new UV-blocking additive (i.e., ACUVUE OASYS®).
Wear and Replacement Schedules	Wear Schedule: daily wear Replacement Schedule: 2 weeks
Objectives	The primary purpose of this randomized study is to demonstrate that the 4GT Test lens senofilcon A with new UV-blocker, in its final lens design ECL600, meets the design validation requirements related to overall CLUE comfort, logMAR visual acuity, quality of vision in bright light, eye health, and fit acceptance.
Study Endpoints	Primary endpoints: logMAR visual performance, slit lamp findings (Graded 3 or higher), fit acceptance, overall CLUE comfort and satisfaction of vision in bright light. Secondary endpoints: CLUE handling and CLUE overall quality of vision.
Study Design	This is a 2-visit, multi-site, partially subject-masked, 2-arm parallel, controlled, randomized and dispensing trial. Subjects will be randomized to one of two study lenses for the entire duration of the study. The study lenses will be worn for a period of 2 weeks each in a bilateral fashion. Subjects will be advised to wear the study lens for a minimum of 5 days per week for at least 6 hours per day. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1Figure 1).
Sample Size	Multiple external investigational sites will enroll approximately 236 subjects with the intent of completing approximately 224.
Study Duration	The study is approximately two weeks per subject. The enrollment period is approximately two weeks, resulting in a

	total study duration of approximately four weeks from first subject first visit to last subject last visit.
Anticipated Study Population	Healthy adult males and females of any race and ethnicity will be recruited. All subjects will be habitual wearers of spherical soft contact lenses.
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. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Between 18 and 49 (inclusive) years of age at the time of informed consent. 4. Eligible presbyopes will be those that wear full distance contact lenses in both eyes, then wear reading glasses over them when needed for near vision. 5. The subject is a current spherical soft contact lens wearer in both eyes with a minimum of 6 hours/day and 5 days/week wear time over the last 30 days by self-report. 6. Subjects must be able and willing to wear the study lenses at least 6 hours a day, a minimum of 5 days per week 7. Subjects must own a wearable pair of distance spectacles. 8. The subject's vertex-corrected spherical equivalent distance refraction must be in the range of -1.00 to -6.00 D (inclusive) in each eye. 9. The subject's refractive cylinder must be 0.00 to -1.00 D (inclusive) in each eye. 10. The subject must have a spherocylindrical best corrected distance Snellen visual acuity of $20/25^{+3}$ 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 (subjects who become pregnant during the study will be discontinued). 2. Any active or ongoing systemic disease (e.g., Sjögren's Syndrome), infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis). 3. Subjects taking suspect oral medications for less than one year. (See Section 3.3.1 for suspect medications and more details). 4. Any prescribed or over the counter (OTC) ocular medication.

	5. Any known hypersensitivity or allergic reaction to Optifree® PureMoist® multi-purpose care solution or Eye-Cept® rewetting drop solution. 6. Toric, extended wear, monovision or multi-focal contact lens correction. 7. Any previous or planned (during the course of the study) ocular surgery (e.g., PRK, LASIK, etc.). 8. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment. 9. Participation in clinical trials involving the Test lens within 3 months prior to study enrollment. 10. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician). 11. Binocular vision abnormality or strabismus by self-report or prior medical history. 12. History of recurrent corneal erosions, herpetic keratitis, or pathological dry eye. 13. Any active ocular allergies, infections or other ocular abnormalities (entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma) that the investigator determines may interfere with the outcomes of this study or otherwise contraindicate participation in the study. 14. Any Grade 2 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA Slit Lamp Classification Scale. 15. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar) within the past 3 years of otherwise successful contact lens wear.
Disallowed Medications/Interventions	Suspect oral medications listed in Section 3.3.1 taken for less than one year on a continual (year-round, routine) basis. Any prescribed or over the counter (OTC) ocular medication.
Measurements and Procedures	Monocular distance visual acuity on logMAR scale using ETDRS charts, physiological responses, fitting characteristics, individual performance item (CLUE subjective question), CLUE overall comfort, vision and handling.
Microbiology or Other Laboratory Testing	The optical bench will be used to measure the light transmission characteristics for all worn Test lenses. The findings are for internal information only and will not be part of the final report.
Study Termination	The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen

	of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	Opti-Free® PureMoist® and preservative free rewetting drops/artificial tears
Principal Investigator(s) and Study Institution(s)/Site(s)	A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File.

Figure 1: Study Flowchart



COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

ADD	Plus Power Required for Near Use
ADE	Adverse Device Effect
AE	Adverse Event/Adverse Experience
BCVA	Best Corrected Visual Acuity
BSCVA	Best Spectacle Corrected Visual Acuity
CFR	Code of Federal Regulations
CLUE	Contact Lens User Experience
COAS	Complete Ophthalmic Analysis System
COM	Clinical Operations Manager
CRA	Clinical Research Associate
CRD	Customer Requirement Document
CRF	Case Report Form
CRO	Contract Research Organization
CT	Center Thickness
CTP	Clinical Technical Procedure
D	Diopter
DMC	Data Monitoring Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IEC	Independent Ethics Committee
IPP	Individual Patient Profiles
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent-to-Treat
JJVCI	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
OTC	Over the Counter
OU	Both Eyes
PD	Protocol Deviation

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

1. INTRODUCTION AND BACKGROUND

Medical devices include everything from simple tongue depressors to contact lenses to complex programmable pacemakers. Global regulations and standards require medical device manufacturers to have a quality system for the design, manufacture, packaging, labeling, and storage of finished medical devices. As a result, JJVCI must have a quality system that complies with several sets of regulations and standards from around the globe:

- US: FDA Quality System Regulation 21 CFR Part 820
- Europe: MDD 93/42/EEC ISO 13485:2003 Quality management systems
- Japan: Japan MHLW Ministerial Ordinance 169, 2004
- Canada: Canadian Medical Device Regulations

The investigational product used in this study was FDA-approved in April 2018. The intent of this study is to validate that the product meets all quality system/design control requirements in accordance with federal regulations.

The Test and Control contact lenses used in this study are both manufactured with senofilcon A material – the Test lens will contain the new UV-blocker. The new UV-blocker darkens in the presence of ultraviolet (UV) and high energy visible (HEV) light and lightens in its absence. That is, it has photochromic properties. Since no other photochromic contact lens is commercially available, the choice of predicate device was based on the similarity of base material.

In addition to correcting myopia and hyperopia, the Test lens will attenuate bright light. The lens has been evaluated on over 1,000 subjects with an excellent safety profile as described in the Investigator's Brochure (IB).[5] It is intended for daily wear only and replaced every two weeks.

1.1. Name and Descriptions of Investigational Products

Test lens: ACUVUE OASYS with Transitions Light Intelligent Technology. This product is made with a version of senofilcon A that has been modified with the addition of the new UV-blocker.

Control lens: ACUVUE OASYS®. This product is also made with senofilcon A making the comparison to the Test lens as valid as possible.

The Test and Control lenses are otherwise made with the same with respect to overall lens diameter (14.0 mm) and base curve radius (8.4 mm). The Test lens is approximately 15 microns thicker in the center than the Control lens (0.85 vs. 0.70 mm, respectively). Further details about the test articles are found in Section 6 of this protocol.

1.2. Intended Use of Investigational Products

The intended use of the investigative product is for correcting myopia and for the attenuation of bright light. During the study, each study article will be worn bilaterally in daily wear, reusable modality for at least 6 hours per day, and at least 5 days per week. The subject will wear only one of the study lenses for two weeks.

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 ACUVUE OASYS Transitions refer to the latest version of the Investigator's Brochure.

1.4. Summary of Known Risks and Benefits to Human Subjects

The benefits to the subject are the same for any contact lens, namely the correction of their refractive error, with the added benefit of the attenuation of bright light for those subjects randomized to wear the Test lens.

The risks to the subject are the same for any contact lens, namely those stated in the Informed Consent Form (ICF), with the added precaution that the Test lens should be worn on both eyes. Wearing only one photochromic lens may cause disturbances in motion perception when the lens is activated.

For the most comprehensive risk and benefit information regarding ACUVUE OASYS Transitions refer to the latest version of the Investigator's Brochure.

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

Prior clinical data is summarized in the Investigator's Brochure.

The literature is absent of any articles pertaining to soft contact lenses containing the new type of UV-blocker. A list of relevant literature references pertaining to glare, eyestrain, and light filtering is provided:

1. Agarwal, S., Goel, D., & Sharma, A. (2013). Evaluation of the factors which contribute to the ocular complaints in computer users. J Clin Diagn Res,7(2), 331-335.
2. Eperjesi, F., Fowler, C. W., & Evans, B. J. (2002). Do tinted lenses or filters improve visual performance in low vision? A review of the literature. Ophthalmic and Physiological Optics, 22(1), 68-77.
3. Hickcox, K. S., Narendran, N., Bullough, J. D., & Freyssinier, J. P. (2013). Effect of different coloured luminous surrounds on LED discomfort glare perception. Lighting Research and Technology, 1477153512474450.
4. Leguire, L. E., & Suh, S. (1993). Effect of light filters on contrast sensitivity function in normal and retinal degeneration subjects. Ophthalmic and Physiological Optics, 13(2), 124-128.
5. Morse, R. S. (1985, October). Glare filter preference: influence of subjective and objective indices of glare, sharpness, brightness, contrast and color. In Proceedings of the Human Factors and Ergonomics Society Annual Meeting(Vol. 29, No. 8, pp. 782-786). SAGE Publications.
6. Pérez-Carrasco, M. J., Puell, M. C., Sánchez-Ramos, C., López-Castro, A., & Langa, A. (2005). Effect of a yellow filter on contrast sensitivity and disability glare after laser in situ keratomileusis under mesopic and photopic conditions. Journal of Refractive Surgery, 21(2), 158-165.
7. Sheedy, J. E., Hayes, J., & ENGLE, J. (2003). Is all asthenopia the same?. Optometry & Vision Science, 80(11), 732-739.
8. Steen, R., Whitaker, D., Elliott, D. B., & Wild, J. M. (1994). Age-related effects of glare on luminance and color contrast sensitivity. Optometry & Vision Science, 71(12), 792-796.
9. Vincent, A. J., Spierings, E. L., & Messinger, H. B. (1989). A controlled study of visual symptoms and eye strain factors in chronic headache. Headache: The Journal of Head and Face Pain, 29(8), 523-527.
10. Wilkins, A. J., & Evans, B. J. (2010). Visual stress, its treatment with spectral filters, and its relationship to visually induced motion sickness. Applied Ergonomics, 41(4), 509-515.

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objectives

The primary purpose of this randomized study is to demonstrate that the 4GT Test lens senofilcon A with new UV-blocker, in its final lens design ECL600, meets the design validation requirements related to overall CLUE comfort, logMAR visual acuity, quality of vision in bright light, eye health, and fit acceptance.

Secondary Objectives

The secondary objective of this study is to demonstrate that the Test lens is equal or better than marketed product senofilcon A (ACUVUE OASYS®, Johnson & Johnson Vision Care, Inc.) with regards to overall CLUE vision and handling.

Other observations of interest include adverse events, keratometry, surface characteristics (deposits and wettability), daily wear time, reasons for discontinuation, and lens damage.

2.2. Endpoints

2.2.1 Primary Efficacy Endpoints:

CLUE Overall Comfort

Overall comfort scores will be assessed using the Contact Lens User Experience (CLUE™)[7] questionnaire at the two-week follow-up. 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.[7] The handling scores will be generated using the flexMIRT software Version 3 or higher (Chapel Hill, NC).

Distance Monocular Contact Lens Visual Acuity

Distance monocular contact lens visual performance (logMAR) is assessed for each subject eye at the two-week follow-up evaluation using EDTRS charts using high illumination and high contrast charts.

Vision Satisfaction in Bright Lighting

Vision satisfaction in bright lighting will be assessed using the individual item (Item ID: V015_1) "I was satisfied with the quality of my vision in bright lighting" from the CLUE™ questionnaire. This item uses the response scale, 1: Strongly Disagree, 2: Disagree, 3: Neither Agree nor Disagree, 4: Agree and 5: Strongly Agree.

2.2.1. Primary Safety Endpoints:

Slit Lamp Findings (Grade 3 or Higher)

Slit Lamp Findings will be assessed for each subject eye at all study visits (schedule and unscheduled). The percentage of eyes with Grade 3 or higher slit lamp findings will be analyzed and will include corneal infiltrates.

Fit Acceptance Rate

Acceptable lens fit will be assessed at all study visits (scheduled and unscheduled) for each subject eye. Fit acceptance rate will be based on the lens fit acceptance of eyes wearing the Test lens only. Fit rates of the Control lens will also be collected but are not a primary endpoint.

2.2.2. Secondary Endpoints:

CLUE Overall Vision and Handling

Overall vision and handling scores will be assessed using the Contact Lens User Experience (CLUE)[7] questionnaire at the two-week follow-up.

2.2.3. Other Endpoints:

Average daily wear time (in Hours):
Average daily wear time will be calculated as the number of hours between subjects reported time of insertion and time of removal of the study lenses, on an average day, at 2-Week Follow-up evaluation.

Subject's Reported Ocular Symptoms:
Frequency and severity by eye of subject's reported ocular symptoms and problems with the study lens at fitting and post-fitting evaluation visits including unscheduled visits.

Severity of the symptoms can be:

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

The related procedure is explained in [redacted] of the study protocol.

Lens fitting characteristics:
Frequency by eye of mechanical lens fitting characteristics at fitting and 2-Week Follow-up evaluations. Lens fitting characteristics to be reported are:

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

Additional Endpoints

- Adverse events
- Discontinuation
- Reasons for discontinuation
- Unscheduled lens replacement
- Reasons for unscheduled lens replacement including lens damage.

2.3. Hypotheses

2.3.1. Primary Hypotheses

All the following primary hypotheses must be met for the objectives of this study to be satisfied:

1. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will have patient reported comfort at the 2-Week Follow Up visit that is non-inferior to that of

subjects wearing predicate device on a daily wear basis. A non-inferiority margin of -5 CLUE points will be used.

2. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will report distance monocular visual acuity (logMAR: bright room luminance/high contrast charts) at the 2-Week Follow Up visit that is non-inferior to that of subjects wearing predicate device on a daily wear basis. A non-inferiority margin of 0.05 logMAR will be used.

3. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will have patient reported outcome (Agree and Strongly Agree) on the Quality of Vision in Bright Light at the 2-Week Follow Up visit that is non-inferior to that of subjects wearing predicate device on a daily wear basis. A non-inferiority margin of 10% will be used.

4. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will have a percentage of any Grade 3 or higher slit lamp findings at all visits (scheduled and unscheduled) that is non-inferior to that of subjects wearing predicate device on a daily wear basis. A non-inferiority margin of 5% will be used.

5. At least 90% of eyes wearing the JJVCI Investigational contact lenses on a daily wear basis will have acceptable fits across the fitting and follow-up visits.

2.3.2. Secondary Hypotheses

1. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will have patient reported handling at the 2-Week Follow Up visit that is non-inferior to that of subjects wearing predicate device on a daily wear basis. A non-inferiority margin of -5 CLUE points will be used.

2. Subjects wearing the JJVCI Investigational contact lenses on a daily wear basis will have patient reported vision at the 2-Week Follow Up visit that is non-inferior to that of subjects wearing predicate device on a daily wear basis. A non-inferiority margin of -5 CLUE points will be used.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Healthy adults of any race or ethnicity will be invited to participate. The eligible participants will be habitual wearers of spherical soft contact lenses as described below in Sections 3.2 and 3.3.

3.2. Inclusion Criteria

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

Inclusion Criteria after Screening

1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Between 18 and 49 (inclusive) years of age at the time of informed consent.
4. Eligible presbyopes will be those that wear full distance contact lenses in both eyes, then wear reading glasses over them when needed for near vision.
5. The subject is a current spherical soft contact lens wearer in both eyes with a minimum of 6 hours/day and 5 days/week wear time over the last 30 days by self-report.
6. Subjects must be able and willing to wear the study lenses at least 6 hours a day, a minimum of 5 days per week
7. Subjects must own a wearable pair of distance spectacles.

Inclusion Criteria after Baseline

8. The subject's vertex-corrected spherical equivalent distance refraction must be in the range of -1.00 to -6.00 D (inclusive) in each eye.
9. The subject's refractive cylinder must be 0.00 to -1.00 D (inclusive) in each eye.
10. The subject must have a spherocylindrical best corrected distance Snellen visual acuity of $20/25^{+3}$ 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 after Screening:

1. Currently pregnant or lactating (subjects who become pregnant during the study will be discontinued).
2. Any active or ongoing systemic disease (e.g., Sjögren's Syndrome), infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis).
3. Subjects taking suspect oral medications for less than one year. (See Section 3.3.1 for suspect medications and more details).
4. Any prescribed or over the counter (OTC) ocular medication.
5. Any known hypersensitivity or allergic reaction to Optifree® PureMoist® multi-purpose care solution or Eye-Cept® rewetting drop solution.
6. Toric, extended wear, monovision or multi-focal contact lens correction.
7. Any previous or planned (during the course of the study) ocular surgery (e.g., PRK, LASIK, etc.).
8. Participation in any contact lens or lens care product clinical trial within 30 days prior to study enrollment.

9. Participation in clinical trials involving the Test lens within 3 months prior to study enrollment.
10. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).
11. Binocular vision abnormality or strabismus by self-report or prior medical history.
12. History of recurrent corneal erosions, herpetic keratitis, or pathological dry eye.

Exclusion Criteria after Baseline

13. Any active ocular allergies, infections or other ocular abnormalities (entropion, ectropion, extrusions, chalazia, recurrent styes, glaucoma) that the investigator determines may interfere with the outcomes of this study or otherwise contraindicate participation in the study.
14. Any Grade 2 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection) on the FDA Slit Lamp Classification Scale.
15. Any previous history or signs of a contact lens-related corneal inflammatory event (e.g., past peripheral ulcer or round peripheral scar) within the past 3 years of otherwise successful contact lens wear.

3.3.1. Systemic Medications

Certain systemic medications are known to have a higher likelihood to interfere with contact lens wear, chiefly by disrupting the tear film. Several articles[1,2,3], websites[4,5], and text book chapters[6,7] discuss this topic with the general consensus shown in Table 1. Subjects taking these medications on a continual (year-round, routine) basis that have demonstrated successful contact lens wear for at least one year will generally be allowed to participate in this study. Subjects taking these medications on a routine basis but less than one year will not be allowed to participate in the study.

Note that subjects taking these medications on a temporary basis (e.g., antihistamines for seasonal allergy) will be allowed to participate if the medication has sufficient time to leave the body prior to the study. This is dependent on the half-life of the drug, body weight / fat, age, genetics, liver / kidney function, and metabolism of the subject. Given these unknowns, subjects taking the medications on a temporary basis must have ceased that medication at least one month prior to signing the informed consent.

[1] Gomes, José Alvaro P., et al. "TFOS DEWS II iatrogenic report." The ocular surface 15.3 (2017): 511-538.
[2] Silbert, Joel A. "A review of therapeutic agents and contact lens wear." Journal of the American Optometric Association 67.3 (1996): 165-172.
[3] Muntingh, G. L. "Drug and contact lens interactions." South African Family Practice 47.8 (2005): 24-28.
[4] https://www.clspectrum.com/issues/2003/september-2003/medication-effects-on-the-anterior-segment-and-con
[5] http://www.richmondeye.com/ocular-side-effects-of-medications/
[6] Lima, Claudia Assis, Newton Kara-Jose, and Jason J. Nichols. "Indications, Contraindications, and Selection of Contact Lenses." Contact Lenses in Ophthalmic Practice. Springer, New York, NY, 2004. 7-16.
[7] Bartlett, Jimmy D., and Siret D. Jaanus. "Clinical ocular pharmacology." (2008): 575-578.

Table 1: Disallowed systemic medications (less than one year of continual use).

Class of Drug	Common Indication(s)	Common Examples
Estrogens	Menopause, osteoporosis, vaginitis	Vagifem, Estrace, Climara, Vivelle-Dot, Premarin, Minivelle, etc., …
Antihistamines	Allergic rhinitis, sedation, hives, allergic conjunctivitis, skin allergy, itching, motion sickness	Hydroxyzine, Promethegan, Phenadoz, Vistaril, Claritin, Zyrtec, Astepro, Astelin, Optivar, Pataday, Allegra, Benadryl, 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

3.4. Enrollment Strategy

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

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This study is a randomized, 2-visit, partially subject-masked, 2-arm parallel, dispensing trial. Approximately 236 subjects (118 subjects /arm) will be screened and enrolled to ensure that at least 224 subjects (112 subjects/arm) to complete.

The study begins with an initial visit (Visit 1). If a subject is found to meet all eligibility criteria, they will be randomized to one of two study lenses (Test or Control) in a bilateral fashion.

If the subject is dispensed study lenses at the initial visit, one follow-up visit will be conducted. The follow-up visit will occur approximately two weeks after the initial visit. Unscheduled follow-up visits may occur during the study. Subjects will be advised to wear the study lenses at least

five (5) days per week for at least six (6) hours per day for a period of two weeks. There is no planned lens replacement scheduled for during this study.

4.2. Study Design Rationale

The purpose of this study is to provide evidence that the investigational contact lens, senofilcon A with new-UV blocker meets all criteria specified by the Customer Requirements Document (CRD). Since this contact lens was approved for daily wear at a replacement rate of 2-weeks, a parallel study design with a 2-week follow-up evaluation was chosen as the most optimal design to evaluate the criteria specified in the CRD.

4.3. Enrollment Target and Study Duration

- Approximately 112 subjects are targeted to complete the Test arm of the study, and an additional 112 subjects are targeted to complete the Control arm of the study.
- 10 clinical sites will be recruited to participate, and each site will enroll approximately 20-24 subjects.
- Enrollment is defined at the point when the Informed Consent is signed. Termination is defined at the completion of the Final Evaluation.
- Each site will have approximately 2 weeks to enroll all their subjects unless otherwise approved by the Sponsor. Each subject will be in the study approximately 2 weeks, making the entire study approximately 4 weeks in duration.

Table 2: Target number of subjects by arm and site

	Test	Control	Total
Randomization	116	116	232
Completion	112	112	224
Number of sites	10	10	10
Subjects/site (Min-Max)	10-12	10-12	20-24

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

A computer-generated randomization scheme will be used to randomly assign subjects, in blocks of 4, to one of the two possible study lenses (TEST or CONTROL). 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).

The study site must follow the randomization scheme provided and complete enrollment according to the randomization list and not pre-select or assign subjects. The randomized assignment of subjects will be performed at the first visit prior to the first fitting. The following must have occurred prior to randomization:

- Informed consent has been obtained
- Subject meets all the inclusion / not meets exclusion criteria
- Subject history and baseline information has been collected.

5.2. Masking

The dynamic nature of the Test lens makes it impossible to completely mask the study lens assignment. The subjects will be aware if they are wearing a photochromic lens or non-photochromic lens due to the function nature of the photochromic dye. Additionally, there is a slight difference in physical appearance between the Test and Control lenses when the Test lens is activated by outdoor light that makes it difficult to mask investigative personnel. However, the Control lens will be masked in the event that OASYS is the subject's habitual lens by chance, making this a partial-subject masked study.

Every attempt will be made to keep the other clinical trial personnel involved in the study (e.g. Data management, Biostatistician and Clinical Operations) unaware of the lens assignment. The identity of the study lenses will be masked by over labeling the blister packs with a label containing the study number, lot number, sphere power, expiration date and the randomization codes. Only the personnel involved in the over labeling and the Statistician generating the randomization scheme will have access to the decode information translating the randomization codes into Test and Control arms. The medical monitor will also have access to the decode information in case breaking the mask is necessary for the urgent medical treatment of a subject.

5.3. Procedures for Maintaining and Breaking the Masking

The test articles mask shall not be broken unless information concerning the lens type is necessary for the urgent medical treatment of a subject. The Sponsor must be notified before the mask is broken.

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/randomization scheme 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 randomization scheme
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

6. STUDY INTERVENTION

6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 3: Test Articles

	Control	Test
Name	OASYS	ECL600
Manufacturer	JJVCI	JJVCI
[redacted]	[redacted]	[redacted]
Lens Material	senofilcon A	senofilcon A
Nominal Base Curve @ 22ºC	8.4	8.4
Nominal Diameter @ 22ºC	14.0	14.0
Nominal Distance Powers (D)	-1.00 to -6.00 in 0.25 steps	-1.00 to -6.00 in 0.25 steps
Water Content (%)	38	38
Center Thickness (-3.00 D)	0.070	0.085
Oxygen Permeability (Dk)	103	103
Modality in Current Study	Daily wear	Daily wear
Replacement Frequency	Single use	Single use
Packaging Form (vial, blister, etc.)	Sterile blister pack	Sterile blister pack

There are 21 powers (sku's) from -1.00 through -6.00 D. Approximately 90 lenses per sku will be made available based on the following factors: sample size, bilateral wear, biweekly replacement, safety margin of 2x, and US distribution model.

6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 4: Ancillary Supplies

	Solution 1	Solution 2
Solution Name / Description	Opti-Free® PureMoist®	Eye-Cept® Rewetting Drops
Lot Number or Other Identifier	Varies	Varies
Manufacturer	Alcon Laboratories, Fort Worth, TX	Optics Laboratories
Maximum Preservative	0.001% polyquaternium-1, 0.0006% myristamidopropyl dimethylamine	NA

6.3. Administration of Test Articles

Test articles will be dispensed to subject 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 Control articles will be packaged in their commercial blister packs with investigational over-label to mask their identity. The Test articles will be packaged in blisters as the primary packaging and labeled with investigational foil. The test articles will be in plastic bags as the secondary packaging form. The sample study label is shown below:

6.5. Storage Conditions

Test articles will be maintained at ambient temperatures at the clinical site. Test articles must be kept under secure conditions and out of direct sunlight.

6.6. Collection and Storage of Samples

All worn study lenses will be collected from the subject, placed in labeled glass vials with Opti-Free® PureMoist®, and stored refrigerated or frozen until they are shipped back to the Sponsor. The lenses will be shipped in special containers to keep the lenses refrigerated.

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

6.7. Accountability of Test Articles

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

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

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

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

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 5: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Follow-up, Final Evaluation
Time Point	Day 1	Day 14 ± 1
Estimated Visit Duration	2.5 hours	1.5 hours
Statement of Informed Consent	x	
Demographics	x	
Medical History/Concomitant Medications	x	x
Habitual Contact Lens Information	x	
Inclusion/Exclusion Criteria	x	
Baseline Questionnaires	x	
Entrance Visual Acuity	x	
Iris Color	x	
Keratometry	x	x
Subjective Sphero-Cylindrical Refraction	x	x
Slit Lamp Biomicroscopy	x	x
Lens Selection	x	
Lens Insertion & Settling	x	
Visual Acuity and Over Refraction	x	
Lens Power Modification	x	
Subject Reported Ocular Symptoms	x	x
Visual acuity (distance Snellen)	x	x
Lens Fit Assessment	x	x
Lens Wettability	x	x
Dispense Patient Instruction Guide	x	
Dispense Test Article	x	

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 Follow-up, Final Evaluation
Time Point	Day 1	Day 14 ± 1
Estimated Visit Duration	2.5 hours	1.5 hours
Lens wear Compliance		x
Wearing Time and Compliance		x
Follow-up Questionnaire		x
Distance ETDRS logMAR Visual Acuity		x
Surface Deposits		x
Study Completion		x
Lens Removal and Storage		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 date of birth, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Questions regarding the subjects' medical history and concomitant medications.	
1.4	Habitual Lenses	Questions regarding the subject's habitual lens type and parameters.	
1.5	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible.	

Visit 1: Screening			
Step	Procedure	Details	[redacted]
		If the subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms are not required.	

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
1.6	Baseline Questionnaire	The subject will respond to the CLUE Baseline Questionnaire.	[redacted]
1.7	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]
1.8	Remove Habitual Lens	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.	
1.9	Iris Color	The investigator will record the subject's iris color based on the scale provided.	[redacted]
1.10	Keratometry	Record the keratometry readings OD and OS in diopters. This can come from any appropriate instrument so long as the same instrument is used at the Final Evaluation.	[redacted]
1.11	Subjective Sphero-cylindrical Refraction	Complete subjective spherocylindrical refraction and record the resultant distance visual acuity (OD, OS, and OU) to the nearest letter. Best corrected distance visual acuity (BVA) must be 20/25+3 or better in each eye.	[redacted]
1.12	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings and determine eligibility. If any of these slit lamp findings are grade 2 or higher, the subject may not continue at this time, but may return up to one additional time to determine eligibility. If after a total of 2 attempts the subject is deemed	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted]
		ineligible, then complete the Final Evaluation. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	
1.13	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. If subject is deemed to be ineligible after the first or second baseline, proceed to Final Evaluation and complete all forms.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.14	Lens Selection	Assign the study lens based on the randomization scheme. Select the contact lens power based on subjective refraction. Record the test condition.	
1.15	Lens Insertion	The Investigator or the subject inserts the study lenses. Record the time of lens insertion. Check for lens damage under the slit lamp before proceeding with lens settling. Replace damaged lenses if applicable.	
1.16	Lens Settling	Allow the study lenses to settle for a minimum of 5 minutes.	
1.17	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, binocular blur, or other suitable test for binocular balancing) and record the best corrected distance Snellen visual acuity to the nearest letter (OD, OS, and OU).	[redacted]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
1.18	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 (1.15-1.17). One power modification is allowed per eye.	
1.19	Time Interval	Please wait for at least 10 minutes from final lens insertion to continue.	
1.20	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.21	Visual Acuity	Record the distance Snellen visual acuity with the contact lenses (OD, OS, and OU) to the nearest letter. Smaller lines must be shown until the subject incorrectly identifies at least 50% of the letters.	[redacted]
1.22	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 Josephson push up **Note**: if lens fit is unacceptable subject will be discontinued from the study.	[redacted]
1.23	Lens Wettability	Perform the white light lens wettability procedure and record the results.	[redacted]
1.24	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.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted]
		If the Investigator does not approve the dispensing of the first study lens based on subject feedback (e.g., unsatisfactory comfort), then the study is terminated for that subject.	
1.25	Dispense	The lenses will be dispensed for 13-15 days 1. The subjects should wear their lenses similar to the inclusion criteria: ≥ 6 hours per day, ≥ 5 days per week. 2. The lenses will be worn as daily wear only. 3. All subjects will be provided Opti-Free PureMoist to be used in a rub regime. 4. Preservative-free rewetting drops are permitted if needed. 5. A patient instruction booklet will be provided. 6. The lenses must be stored in the supplied case out of direct sunlight. • Note 1: In the event a lens is lost or damaged, the subject will return to the investigator site for replacement (extra lenses cannot be given at the dispensing visit). • Note 2: The subject's habitual contact lenses cannot be worn at any time during the study. • Note 3: Instruct subjects to bring their spectacles to the next visit.	

VISIT 2

The follow-up will occur 13-15 days following Visit 1. The subjects must enter the visit wearing their study contact lenses.

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.	Follow-Up Questionnaires	The subject will respond to the Follow-Up Questionnaires.	[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.	Distance ETDRS LogMAR Visual Acuity	Perform 4 m distance ETDRS LogMAR visual acuity test OD and OS under the following conditions: Bright room illumination / high contrast charts a. Room illumination > 400 lux b. Chart luminance 120-200 cd/m^2 c. One high contrast chart per eye. 1) OD: chart HC-1 2) OS: chart HC-2	[redacted]
2.8.	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	[redacted]

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted]
		• insufficient or excessive movement in all three of the following conditions: primary gaze, up gaze, and Josephson push up	
2.9.	Lens Wettability	Perform the white light lens wettability procedure and record the results.	[redacted]
2.10.	Surface Deposits	Record any front and back surface lens deposits.	[redacted]
2.11.	Lens Removal & Storage	Both lenses will be removed and stored wet in a labeled container with Opti-Free PureMoist. The lenses can be stored refrigerated or frozen prior to shipment back to the Sponsor. Lenses will be stored at JJVCI for 45 days after LSLV for laboratory testing (Section 7.4).	
2.12.	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the subject has a Grade 3 or higher slit lamp finding, it will be recorded as an Adverse Event and the subject will be followed to resolution. Adverse events must be reported to the JJVCI monitors immediately. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]

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.	
F.2	Keratometry	Record the keratometry readings OD and OS in diopters. This can come from any appropriate instrument so long as the same instrument was used at the Baseline Evaluation.	[redacted]

Final Evaluation			
Step	Procedure	Details	[redacted]
F.3	Subjective spherocylindrical Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best corrected distance visual acuity to the nearest letter (OD, OS, and OU).	[redacted]

7.3. Unscheduled Visits

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

- 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. The investigational sites only need to complete steps U.1, U.2, and U.6 for asymptomatic subjects that simply require a replacement lens.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Chief Complaints	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.2	Adverse Events and Concomitant Medications Review	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.3	Entrance VA	Record the entrance distance visual acuity (OD, OS and OU) to the nearest letter.	[redacted]

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.4	Subjective Sphero-cylindrical Refraction	The investigator will complete a subjective refraction (sphere and cylinder) and record the resultant distance visual acuity OD, OS, and OU to the nearest letter.	[redacted]
U.5	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops may be instilled.	[redacted]
U.6	Dispensing (if applicable)	Additional lenses may be dispensed if one is lost or torn during the wearing period.	
U.7	Exit Visual Acuity	Record the subject's exit distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]

7.4. Laboratory Procedures

The optical bench will be used to measure the light transmission characteristics for all worn Test lenses. The findings are for internal information only and will not be part of the final report.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent
- they are eligible
- Completed all required study visits

8.2. Withdrawal/Discontinuation from the Study

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

- Subject death during the study period
- Subject withdrawal of consent
- Subject not compliant to protocol
- Subject lost to follow-up
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant)
- Subject develops significant or serious adverse events causing discontinuation of study lens wear
- 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 a scheduled study visit

- 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
- Subject out of visit window visit with two or more days

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
- Collect all unused test article(s) from the subject

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

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Suspect disallowed oral medications taken for less than one year on a continual (year-round, routine) basis are listed in Section 3.3.1. Document any prescribed or over the counter (OTC) ocular medication currently being taken.

10. DEVIATIONS FROM THE PROTOCOL

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

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

11. STUDY TERMINATION

The occurrence of one or more Unanticipated Serious Adverse Device Effect (USADE), or any SAE where the relationship to study agent cannot be ruled out, may result in stopping further dispensing of test article. In the event of a USADE or SAE, the Sponsor may unmask the treatment

regimen for the subject(s) and will discuss this with the Investigator before any further subjects are enrolled.

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

JJVCI 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 JJVCI, it is determined that it would be unwise to continue at the clinical site.

JJVCI (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 1 to entry: This definition includes events related to the investigational medical device or the comparator.
Note 2 to entry: This definition includes events related to the procedures involved.
Note 3 to entry: 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
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event

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

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

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

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

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

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

- Contact Lens Induced Peripheral Ulcer (CLPU)
- Significant Infiltrative Events (SIE)

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

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

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

- Non-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 to entry: 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 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device."[1]

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

13.2. Assessing Adverse Events

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

- Seriousness/Classifications (see definition in Section 13.1)
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; unlikely related; possibly related; 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; severe for all events - see definition in Section 13.2.2)
- Outcome – not recovered or not resolved; recovering or resolving; recovered or resolved with sequelae; recovered or resolved; death related to adverse event; unknown
- Actions Taken – none; temporarily discontinued; permanently discontinued; other

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

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

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

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

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

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

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

Subjects who present with an adverse event shall be followed by the Investigator, within licensure, until all signs and symptoms have returned to pre-treatment status, stabilized, or been satisfactorily resolved. If further treatment beyond licensure is required, the patient will be referred to the appropriate health care provider. The Investigator will use his/her clinical judgment as to whether 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, fax, or telephone, but no later than 24 hours following discovery of the event. The Investigator is obligated to pursue and obtain information requested by the Sponsor in addition to that information reported on the eCRF. All subjects experiencing a serious/significant adverse event must be followed up and all outcomes must be reported.

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

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

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

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

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

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

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

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

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

13.4.3. Event of Special Interest

None.

13.5. 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. At the Investigator's discretion, the study participant may be followed by the Investigator through delivery. However, this data will not be collected as part of the clinical study database. Pregnant participants are not discontinued from contact lens or solution related studies for safety concerns, but due to general concerns relating to pregnancy and contact lens use. Specifically, pregnant women are discontinued due to fluctuations in refractive error and/or visual acuity that occur secondary to systemic hormonal changes, and not due to unforeseen health risks to the mother or fetus.

14. STATISTICAL METHODS

14.1. General Considerations

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

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

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

14.2. Sample Size Justification

This study was designed and powered to show non-inferiority of the Test lens compared to the Control lens with respect to logMAR Visual Acuity, Slit Lamp Findings (Grade 3 or higher) and CLUE comfort. It was assumed there was no difference between the Test and Control lens with respect to slit lamp findings and a 1 letter difference (0.02) between the Test and Control lenses with respect to visual acuity logMAR. Based on data from 3 historical studies, it was assumed there was a 2-point difference between the Test and Control lenses with respect to CLUE comfort based on the summary statistics from the first period of the historical studies.

In addition to the endpoints mentioned above, this study was also powered to demonstrate non-inferiority of the Test lens relative to the Control lens with respect to vision satisfaction in bright lighting and the proportion of eyes with acceptable fitting while the Test lens is significantly superior to 90%.

Unless otherwise specified, the sample size was calculated to achieve a statistical power of at least 80% and a type I error of 5%.

A total of 5 historical studies were utilized in the sample size calculation. Table 6 displays the studies, their corresponding study design and the number of subjects enrolled and completed per-protocol.

Table 6: Historical Studies Included in Sample Size Calculation

Study	Study Design	Endpoints Collected	No. Enrolled	No. Completed Per-Protocol
[redacted]	2X3 Crossover	CLUE, SLF Lens Fit	135	132
[redacted]	2X3 Crossover	CLUE, Visual Acuity (logMAR), SLF, Lens Fit	133	121
[redacted]	2X3 Crossover	CLUE, SLF Lens Fit	92	78
[redacted]	Single-Arm	SLF, Lens Fit	54	48
[redacted]	Single-Arm	SLF, Lens Fit	56	41

Table 7: Descriptive Summary of CLUE Scores by Domain Pooled Across Historical Studies [redacted] – 2-Week Follow-up Evaluation Period 1 only

CLUE Domain [Mean(SD)[1]]	Test	Control
Comfort	66.66 (21.066)	63.90 (24.197)
Handling	69.32 (18.454)	71.11 (20.429)

Overall Quality of Vision	64.49 (17.221)	64.44 (23.351)

[1]SD = Standard Deviation

Table 8: Descriptive Summary of Visual Acuity (logMAR) - [redacted] – 2-Week Follow-up Evaluation- Period 1 only

Visual Acuity High Illumination High Contrast	**Test**	**Control**
[Mean(SD)[1]]	-0.088 (0.0.0862)	-0.0622 (0.0740)

[1]SD = Standard Deviation

Table 9: Descriptive Summary of Mechanical Lens Fitting Pooled Across all Historical Studies

Any Unacceptable Lens Fit[1] [n(%)]	**Test n (%)**	**Control n (%)**
Fitting Evaluation	0(0.0)	0 (0.0)
2-Week Follow-up	0 (0.0)	0 (0.0)

[1]The percent of any unacceptable fit is calculated using Total Unique eyes as a denominator

Table 10: Descriptive Summary of Slit Lamp Findings Pooled Across all Historical Studies

SLF Grade 2	**Test n (%)**	**Control n (%)**
Corneal Edema	0 (0.0)	0 (0.0)
Conjunctival Injection	59 (6.86)	59 (21.85)
Tarsal Abnormalities	51 (5.93)	24 (8.89)
Corneal Neovascularization	3 (0.35)	0 (0.0)
Corneal Staining	3 (0.35)	0 (0.0)
Other Findings	0 (0.0)	0 (0.0)
Total Eyes (N)	860	270
Any SLF Grade 2[2]	116 (13.48)	83 (33.74)
Any SLF Grade 3+	0 (0.0)	0 (0.0)
Total Unique Eyes	860	270
Total Unique Subjects	430	135

%= nx100/N; SD=Standard Deviation
[1]All SLF reported for this study are combined for the purposes of summarizing
[2] The percent (%) of Any Grade 2 is calculated using the Total Unique Eyes as the denominator

Table 11: Descriptive Summary of Individual Item from [redacted] – 2-Week Follow-up

Questionnaire Item/ Response	Test	Control
Vision Satisfaction in Bright Light [n(%)]		
Strongly Agree	72 (29.75)	51 (21.07)
Agree	129 (53.31)	130 (53.72)
Neither Agree Nor Disagree	24 (9.92)	21 (8.68)
Disagree	17 (7.02)	33 (13.64)
Strongly Disagree	0 (0.0)	7 (2.89)

CLUE Comfort Scores

With respect to CLUE comfort, based on historical data from Period 1, a mean difference of 2 points was assumed and a standard deviation of 21, an additive equivalence test in PROC Power for two sample means was used to Test for non-inferiority. A non-inferiority margin of -5 points was used since this is considered to be no more than a 10% shift in the distribution of CLUE scores.

Mechanical Lens Fit (Test Lens)

The estimated sample size to test the primary hypothesis (H0 PT ≤ P0, H1: PT > P0) is 100. The sample size was calculated using PROC POWER for one sample proportion using an exact Test of a Binomial Proportion.

Visual Performance (logMAR)

Sample size calculation for visual performance (logMAR) was carried out using an approximation of the power of an F-test derived from the non-centrality parameter calculated form the observed F statistic of a linear model.[8]

Model details:
visual performance was analyzed using a linear mixed model. Lens type was included as the only fixed effect. A compound symmetric (CS) covariance matrix was used to model the correlation between measurements on the same subject across study periods. Below is the variance-covariance matrix used in the visual performance model.

$$\sum_{Visual\ Acuity} \begin{pmatrix} 0.004047 & 0.002894 \\ 0.002894 & 0.004737 \end{pmatrix}$$

Slit Lamp Findings

There were no Grade 3 or higher SLFs observed in any of the historical studies. Assuming no difference between study lenses and a correlation 0.70 between left and right eyes within the same subject (intra-subject correlation), a reference rate of no more than 5% was assumed (worse-case scenario) with a non-inferiority odds ratio margin of 2. A total of 2000 replicating trials were simulated, each replicated sample was analyzed using a generalized estimating equation (GEE)

model with a binary distribution and the logit as the link function. Each model included lens type as the only fixed, eye was included as a random effect. The Odds ratio and corresponding 95% confidence interval was used estimate differences between the Test and Control lenses. The upper limit of each 95% confidence interval was compared to 2; if the upper limit was below 2 then NI=1; otherwise NI=0. Statistical power was calculated as the average NI. A sample size of 224 (112 per arm) was chosen to achieve a minimum statistical power of 80%.

Using a reference rate for the control of 5% and no more than a 5% difference between the Test and Control lenses translate to an odds ratio margin of 2. A reference rate of 5% was used as the worst-case scenario.

Individual Questionnaire Items

Vision satisfaction in bright lighting sample size estimates were calculated using historical data from CR-5960.[7] One-thousand boot strap samples were simulated based on the historical data. For each replicated sample a generalized linear mixed model was used with a multinomial distribution and the cumulative logit as the link function. Lens type was included in the model as the only fixed effect.

Using a reference rate of 50% for the Control lens and assuming no difference between the Test and Control a 10% difference translate to a cumulative odds ratio margin of 0.67. the reference rate of 0.50 was used as the worst-case scenario.

Table 12: Sample Size Estimates and Power Calculations for Primary Endpoints

Endpoint	Number per Subjects to Complete	Power
Distance Monocular Visual Acuity (logMAR)	30	86%
SLFs (Grade 3 or Higher)	224	80%
Acceptable lens Fit (Test Lens Only)	100	82%
CLUE Comfort	224	87%
Vision Satisfaction in Bright Lighting	40	87%

Table 13: Sample Size Estimates and Power Calculations for Secondary Endpoints

Endpoint	Number per Subjects to Complete	Power
CLUE Handling	224	63%
CLUE Overall Quality of Vision	224	71%

As indicated in Table 12 and 13 above, the sample size chosen for this study was primary driven by slit lamp findings (Grade 3 or higher) and overall comfort. The plan is to enroll 236 eligible subjects (118 subject per arm) with a target of 112 subjects to complete each arm in the study. During the enrollment period, the subject drop-out rate with be closely monitored, if an unexpectedly high dropout rate is observed, then the targeted total enrollment number maybe be increased accordingly to ensure that a minimum of 224 subjects complete the study.

14.3. Analysis Populations

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

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

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

Safety variables will be summarized on both safety and PP populations whereas efficacy variables will be summarized on the per-protocol and Intent-to-Treat population.

14.4. Level of Statistical Significance

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

14.5. Primary Analysis

Primary efficacy analysis:
All the efficacy analyses will be conducted on PP population. As sensitivity analysis, the efficacy analysis will be repeated on the ITT population
regardless of missing data.

Visual Acuity
Distance monocular visual acuity (logMAR) will be tested under bright illumination low contrast conditions at the 2-week follow-up evaluation and will be analyzed using a Bayesian normal random-effects model to compare the Test and Control lenses. The regression model will include lens type as the only fixed effect. Clinical site and subject will be included as random effects. Other subject characteristics such as gender and age will be included as fixed effects when appropriate.

The Model:
Let y_{ijkl} the visual acuity (logMAR) for the l^{th} subject at the k^{th} site, assigned to the i^{th} lens for the j^{th} eye. The likelihood for y_{ijkl} is constructed as follows:

$$y_{ijkl} \sim \mathrm{N}(\mu_{ijkl}, {\sigma_{ijkl}}^2)$$

Where,

$$\mu_{ijkl} = \mu_0 + \beta_1 Lens + \gamma_{l(k)} + \alpha_k$$

In this model, lens we define $Lens_l$=0 for the Control lens and $Lens_i$=1 for the Test lens. So β_1 stands for the difference between the Test and Control lens with respect to logMAR visual performance. A negative β_1 indicates the Test performed better than the Control lens.

We assume random subject effects are independent and identically distributed (i.i.d) as $\gamma_j \sim$ N(0, $\sigma^2_{subject}$) as random subject and, the random site effect is i.i.d as $\alpha_k \sim$ N(0, σ^2_{site}) for i=1,2 (lens), j=1, 2 (eye), k=1, 2, 3, 4, 5, 6 (site).

For the β coefficients, independent non-informative priors N(0, 1000) will be used. For the variance of random effects σ^2_{eye} and σ^2_{site} independent non-informative conjugate priors inverse-gamma(0.001, 0.001) will be used. For σ^2_{ijkl}, non-informative conjugate priors inverse-gamma(0.001, 0.001) will be used where σ^2_{ijkl}, is the variance of y_{ijkl}. The metropolis sampler algorithm as implemented in the SAS/STAT MCMC 14.2 procedure will be used to estimate the posterior distribution of the unknown parameters. Inferences will be made based on the 95% posterior credible intervals for relevant parameters.

Hypothesis Testing

The null and alternative hypothesis for visual acuity (logMAR) to test for non-inferiority of the Test lens relative to the Control lens is as follows:

$$H_o: \beta_1 \geq 0.05$$
$$H_A: \beta_1 < 0.05$$

Non-inferiority will be declared if the upper limit of the 95% credible interval of the difference between the Test and Control is below 0.05, i.e. P($\beta_1 < 0.05$) ≥ 0.975.

CLUE Overall Comfort

CLUE Comfort scores will be analyzed using a Bayesian normal random-effects model to compare the Test and Control lenses at the 2-week follow-up evaluation. The regression model will include baseline CLUE comfort scores and lens type as fixed effects. Clinical site will be included as random effects. Other subject characteristics such as age, gender, race and iris category will be included as fixed covariates when appropriate.

The Model:

Let y_{ijkl} denote the CLUE Comfort score for the k^{th} subject at the j^{th} site, assigned to the i^{th} lens. The likelihood for y_{ijkl} is constructed as follows:

$$y_{ijkl} \sim \text{N}(\mu_{ijkl}, {\sigma_{ijkl}}^2)$$

Where

$$\mu_{ijkl} = \mu_0 + \beta_1 Lens + \beta_2 \text{baseline} + \gamma_k$$

In this model, we define Lens=0 for the Control lens and $\text{Lens} = 1$ for the Test lens. So β_1 stands for the difference between the Test and Control lens with respect to CLUE comfort; A positive β_1 indicates the Test performed better than the Control.

We assume random site effects are independent and identically distributed (i.i.d) as $\gamma_j \sim$ N(0, σ^2_{site}) for site for i=1, 2 (lens), j=1, 2, 3, 4, 5, 6 (site), k=1…..n (subject/site) .

For the β coefficients, independent non-informative priors N(0, 1000) will be used. For the variance of random effect of σ^2_{site} an independent non-informative conjugate prior, inverse-gamma

(0.001, 0.001) will be used. Starting values for the mean and variance of CLUE scores will be 60 and 400 (since standard deviation of CLUE is normalized to be 20), respectively. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC 14.2[14] procedure will be used to estimate the posterior distribution of the unknown parameters. Inferences will be made based on the 95% posterior credible intervals for relevant parameters.

Hypothesis Testing
The null and alternative hypotheses for CLUE comfort non-inferiority of the Test lens relative to the Control lens are as follows:

$$H_o: \beta_1 \leq -5$$

$$H_A: \beta_1 > -5$$

Non-inferiority will be declared if the lower bound of the 2-sided 95% credible interval of the difference between the Test lens and the Control lens is greater than -5, i.e., $P(\beta_1 > -5) \geq 0.975$.

Vision Satisfaction in Bright Lighting

Vision satisfaction in bright lighting at the 2-week follow-up evaluation will be analyzed using a Bayesian multinomial model for ordinal data. The regression model will include lens type as the only fixed effect. Clinical site will be included as a random effect. Other subject characteristics such as age, gender, race and iris category will be included when appropriate.

The Model:

Let y_{ijk}= (y_{ijk1} , y_{ijk2} , y_{ijk3}, y_{ijk4}, y_{ijk5}) denote the rating for the k^{th} subject, from the j^{th} site, assigned to the i^{th} study lens. Possible values of y_{ijk} are 1if the subject rating of vision satisfaction in bright lighting are X and 0 otherwise (x=1 for Strongly Agree and X=5 for Strongly Disagree, respectively). The likelihood is constructed as follows:

$$y_{ijk} \sim \text{Multinomial } (P_{ijk1},\ P_{ijk2}\ , P_{ijk3}, P_{ijk4}, P_{ijk5})$$

$$P_{ijk1} = \gamma_{ijk1}$$

$$P_{ijkX} = \gamma_{ijkX} - \gamma_{ijk(X-1)}\ 2 \leq n \leq 4$$

$$P_{ijk5} = 1 - \sum_{x=1,..4} P_{ijkX}$$

$$\text{Logit}(\gamma_{ijklmX}) = \theta_n + \beta_1 Lens + \ \gamma_j$$

Where $\theta_n$is the intercept for levels n=1,2,3,4, $P_{ijk1} = \Pr(\gamma_{ijk1} = 1)$ with respect to the vision satisfaction in bright lighting item. We assume the random clinical site effects are i.i.d as $\gamma_j \sim N(0, \sigma^2_{site})$ for i=1,2 (lens), j=1, 2, 3, 4, 5, 6(site) and k=1,…..n (subject/site)

In this model, the lens I will be determined by the period j and sequence k, therefore i is denoted as a function of j and k. We define $Lens_i$=0 for the Control lens and $Lens_i$=1 for the Test lens.

Independent vague N(0, 1000) priors for the regression coefficients β_i i=1,…5. For θ_n, we are considering the following priors

$$\pi0(\theta1) \sim N(0,100)$$
$$\pi0(\theta2|\ \theta1) \sim N(0,100)I(\theta>\theta1)$$
$$\pi0(\theta3|\ \theta2) \sim N(0,100)I(\theta>\theta2)$$
$$\pi0(\theta4|\ \theta3) \sim N(0,100)I(\theta>\theta3)$$

For the variance of random effects independent vague normal priors will also be used; σ_s^2 ~inverse-gamma(0.001, 0.001). The Metropolis sample algorithim as implemented in the SAS/Stat MCMC Procedure will be used to estimate the posterior distributions of the unknown parameters. Inferences will be made based on the posterior credible interval for the relevant parameters.

Hypothesis Testing

The null and alternative hypotheses for non-inferiority are as follows:

$$H_o:\ p_t - p_c \leq -0.1$$
$$H_A:\ p_t - p_c > -0.1$$

where p_T and p_C are the proportions of patients with positive response (agree or strongly agree) in Test group and Control group, respectively. Non-inferiority will be established if the lower limit of the 2-sided 95% credible interval of the difference ($p_T - p_C$) is above -0.1 (i.e. P($p_t - p_c > -0.1$|data) ≥ 0.975.

Primary Safety Analysis:

Safety analysis will be conducted on safety population by treatment actually received by subjects.

Acceptable Lens Fit:

Acceptable lens fit will be analyzed using a Bayesian beta-binomial models for correlated binary data. The regression model will include lens type as the only fixed effects

The Model:

Let Y1 and Y2 denote the binary outcomes of acceptable lens fit for the left and right eyes, respectively, when wearing the test lens. Considering the correlation, ρ, between Y1 and Y2, the distribution of the sum Y = Y1 + Y2 is obtained by the mixture of two variables. One of them follow a binomial distribution Bin(2, p) with mixing probability (1-p) 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 p:

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

Where $I_{A1} = \{0, 1, 2\}$ and $I_{A2} = \{0, 2\}$

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

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

The posterior distribution of (p, ρ) given (y, z) is

$$P(p, \rho \mid \mathbf{z}, \mathbf{y}) = P(\mathbf{y}, \mathbf{z} | p, \rho)\, \pi_0(p, \rho),$$

Where, π_0 is joint prior distribution of (p, ρ). Here we assume p and ρ to be independent with a prior beta(α,β) for p and uniform(0,1) for ρ. Hence the joint distribution of (p, ρ) is given by π_0 (p, ρ| α, β)$\propto p^{\alpha-1}(1-p)^{\beta-1}$. The Metropolis sampler algorithm as implemented in the SAS/STAT MCMC Procedure will be used to estimate the posterior distributions of the parameters (p, ρ). Inferences will be made based on a posterior credible interval for the relevant parameters.

Hypothesis Testing

With respect to Acceptable lens fit the null and alternative hypothesis for superiority is as follows:

$$H_0 = p_T \leq 0.90$$
$$H_1 = p_T > 0.90$$

Where, p_T represents the proportion of subject eyes that achieve acceptable fit for the Test lens. Success for acceptable fit will be declared if the lower bound of the 2-sided 95% credible interval of the proportion is greater than 0.90; i.e. $P(p_T > 0.90) \geq .975$.

If the full planned model fails to converge, reduced versions may be considered.

Slit Lamp Findings

Grade 3 or higher slit lamp findings will be analyzed using a Bayesian Logistic regression random-effects model to compare the Test and Control lenses. The regression model will include baseline slit lamp findings and lens type. Site and subject will be included in the model as random effects.

Let y_{ijkl}=1 if a Grade 3 or higher SLF is observed and y_{ijk} =0 otherwise for the l^{th} subject, from the k^{th} site, assigned to the i^{th} study lens for the j^{th} eye.

$$y_{ijkl} \sim \text{Binary}\ (p_{ijkl})$$

$$p_{ijkl} = \frac{\exp(\beta_0 + \beta_1 Lens + \beta_2 \text{Baseline SLF}_l + \gamma_k + \delta_l)}{1 + \exp(\beta_0 + \beta_1 Lens + \beta_2 \text{Baseline SLF}_l + \gamma_k + \delta_l)}$$

We assume the random effect for subject are i.i.d as $\delta_l \sim N(0, \sigma^2_{subject/site})$ for the random for clinical site are i.i.d as $\gamma_k \sim N(0, \sigma^2_{site})$ for i=1,2 (lens), j=1, 2 (eye), k=1, 2, 3, 4, 5, 6 (site) and l=1,…n (subject/site).

In this model, we define $Lens_i$=0 for the Control lens and $Lens_i$=1 for the Test lens. For the β coefficients, independent non-informative priors $N(0, 10000)$ will be used. For the variance of random effects of $\sigma^2_{subject}$ and σ^2_{site}, independent non-informative conjugate priors inverse-gamma (0.001, 0.001) will be used. The Metropolis-Hastings algorithm as implemented in the SAS/STAT 14.2 PROC MCMC procedure will be used to estimate posterior distributions of the unknown parameters. Inferences will be made based on the posterior credible interval for the relevant parameters.

Hypothesis Testing

The null and alternative hypothesis for Non-inferiority is as follows:

$$H_0 = p_T - p_C \geq 0.05$$
$$H_1 = p_T - p_C < 0.05\,,$$

where p_T and p_C are the proportions of Grade 3 or higher SLFs in Test group and Control group, respectively.

Non-inferiority will be established if the upper limit of the 2-sided 95% credible interval of the difference $(p_T - p_C)$ is below 0.05(i.e. $p(p_T - p_C < 0.05|\text{data}) \geq .975$).

If the full planned model fails to converge, reduced versions may be considered. In the event that the number of Grade 3 or higher SLFs is too small Grade 2 or higher SLFs will be analyzed and tested as described above.

14.6. Secondary Analysis

Secondary efficacy analysis:

CLUE Overall Quality of Vision and Handling

CLUE Overall Quality of Vision and Handling will be analyzed using the same statistical method described for CLUE Overall Comfort

Secondary safety analysis:

Not Applicable

14.7. Other Exploratory Analyses

Not applicable.

14.8. Interim Analysis

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

14.9. Procedure for Handling Missing Data and Drop-Outs

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

Subject dropout is expected to be one of the main reasons of missing data in this clinical trial. Past clinical trials don't provide the evidence that subject dropout is systematic or not-at-random. To evaluate the impact of missing data, sensitivity analysis may be considered by automatically sampling all missing values and incorporating them in the Markov chain for the parameters using the PROC MCMC procedure.

14.10. Procedure for Reporting Deviations from Statistical Plan

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

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

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

External Date 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. Once completed, the eCRFs will be reviewed for accuracy and completeness and signed by the Investigator. The sponsor or sponsor's representatives will be authorized to gain access to the subject recordation for the purposes of monitoring and auditing the study.

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

The content and structure of the eCRFs are compliant with ISO14155:2011.[1]

15.2. Subject Record

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

- subject identification

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

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

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

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, JJVCI 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 JJVCI. The Investigator may use this information for the purposes of the study only. It is understood by the Investigator that JJVCI 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 JJVCI 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 JJVCI and for inspection by local and regulatory authorities.

17. MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

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

18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements. GCP is an international

ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements.

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

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

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

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

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

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

- Report of deaths of subjects under the Investigator's care
- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

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

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

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

18.4. Informed Consent

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

Before entry into the study, the Investigator or an authorized member of the clinical site personnel must explain to potential 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 States[11] 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 JJVCI.

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 JJVCI management representative prior to study initiation.

JJVCI 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

JJVCI 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

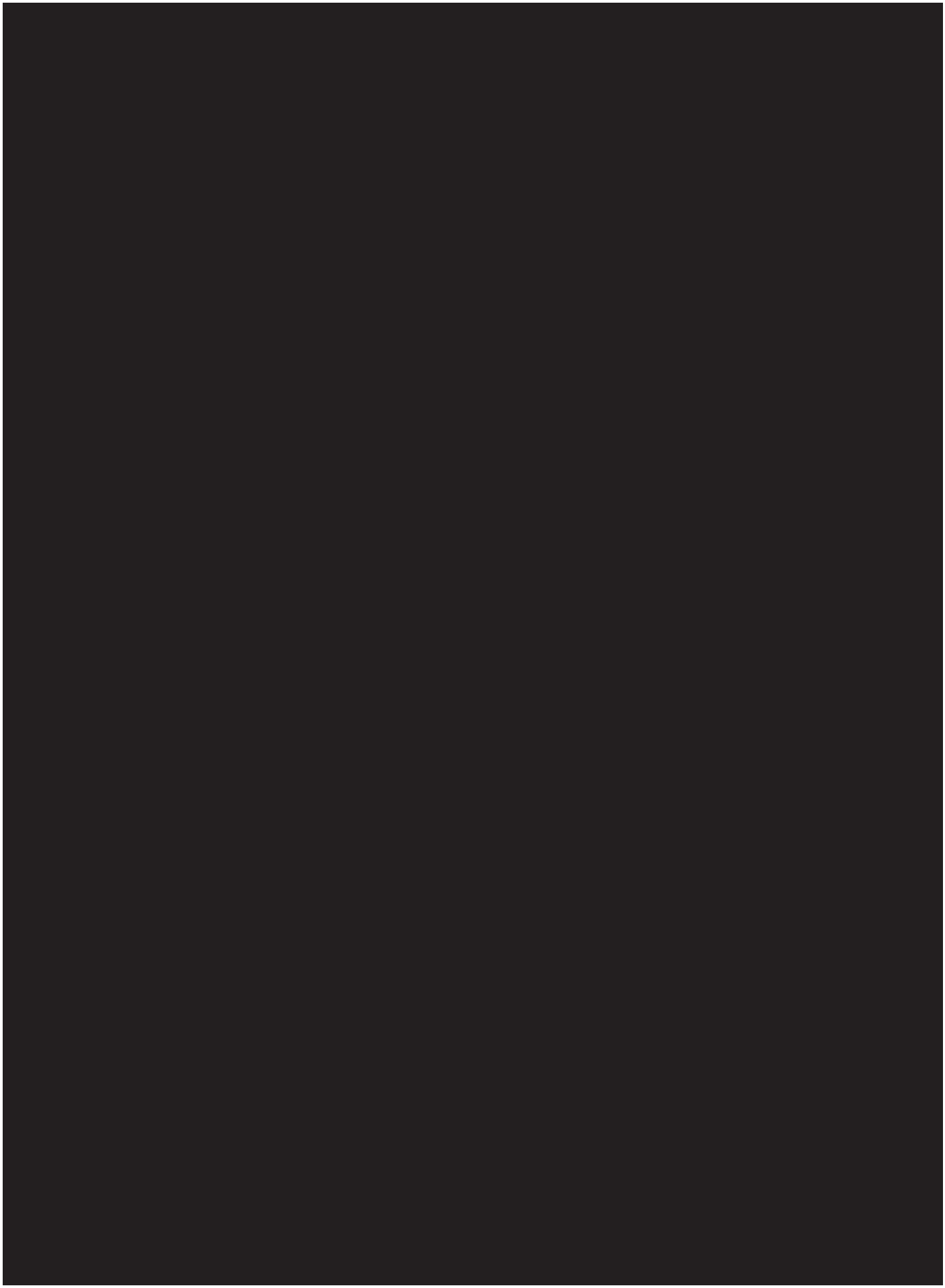
This study will be registered on ClinicalTrials.gov by the Sponsor.

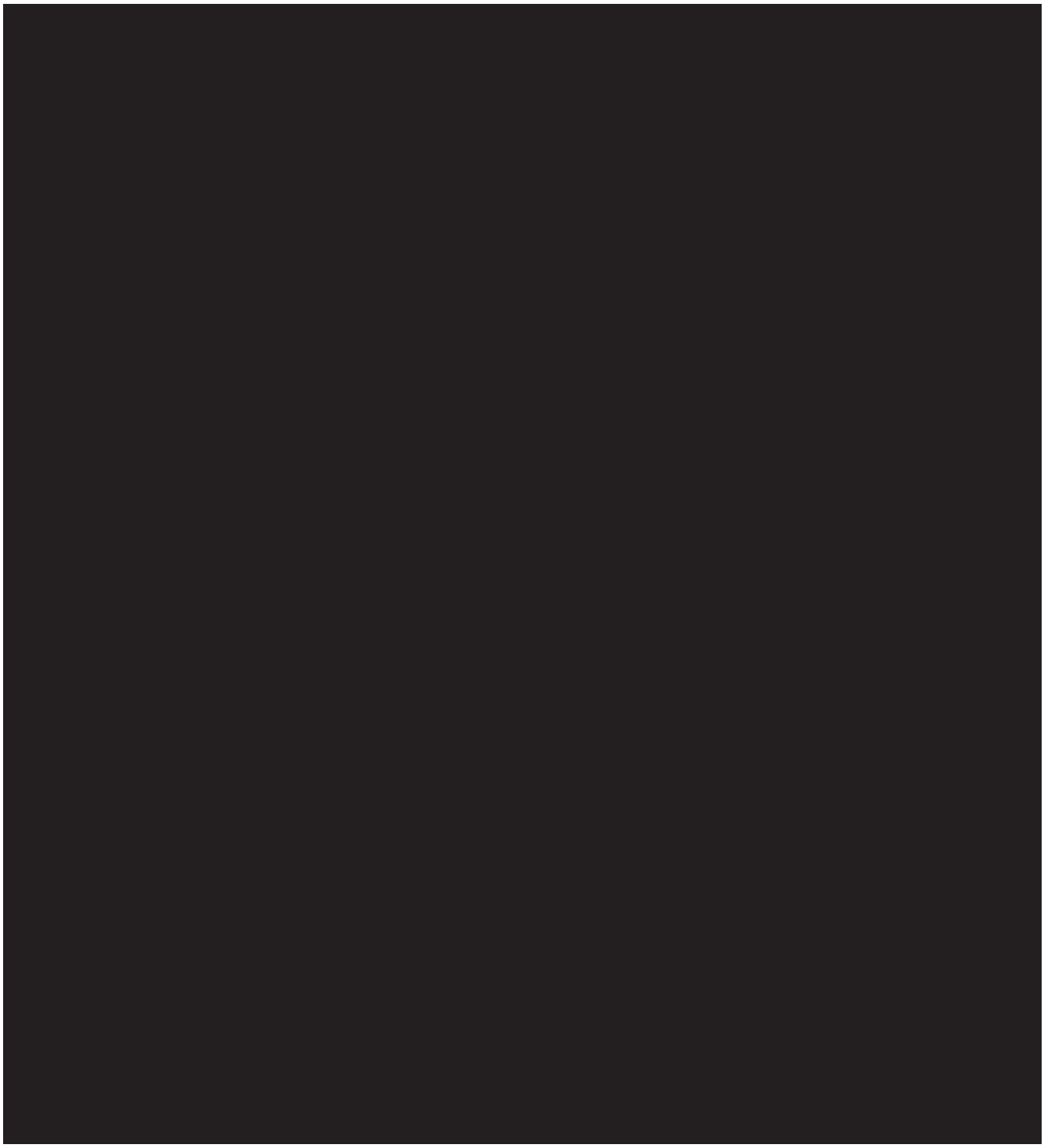
22. REFERENCES

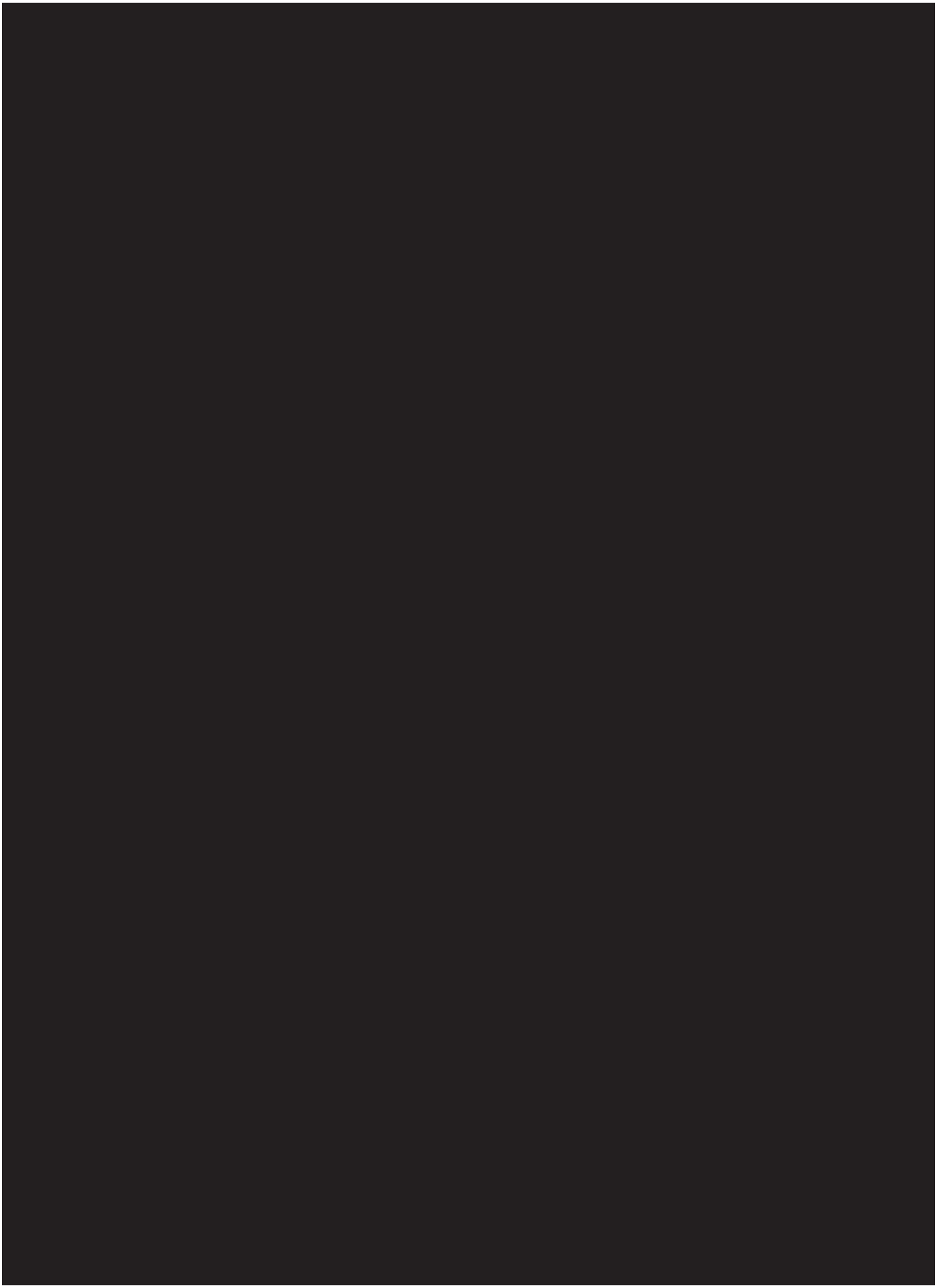
1. ISO 14155:2011: Clinical investigation of medical devices for human subjects – Good clinical practice.
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP): http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki – Ethical principles for Medical Research Involving Human Subjects. http://www.wma.net/en/30publications/10policies/b3/index.html.
4. United States (US) Code of Federal Regulations (CFR). In https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR (Ed.).

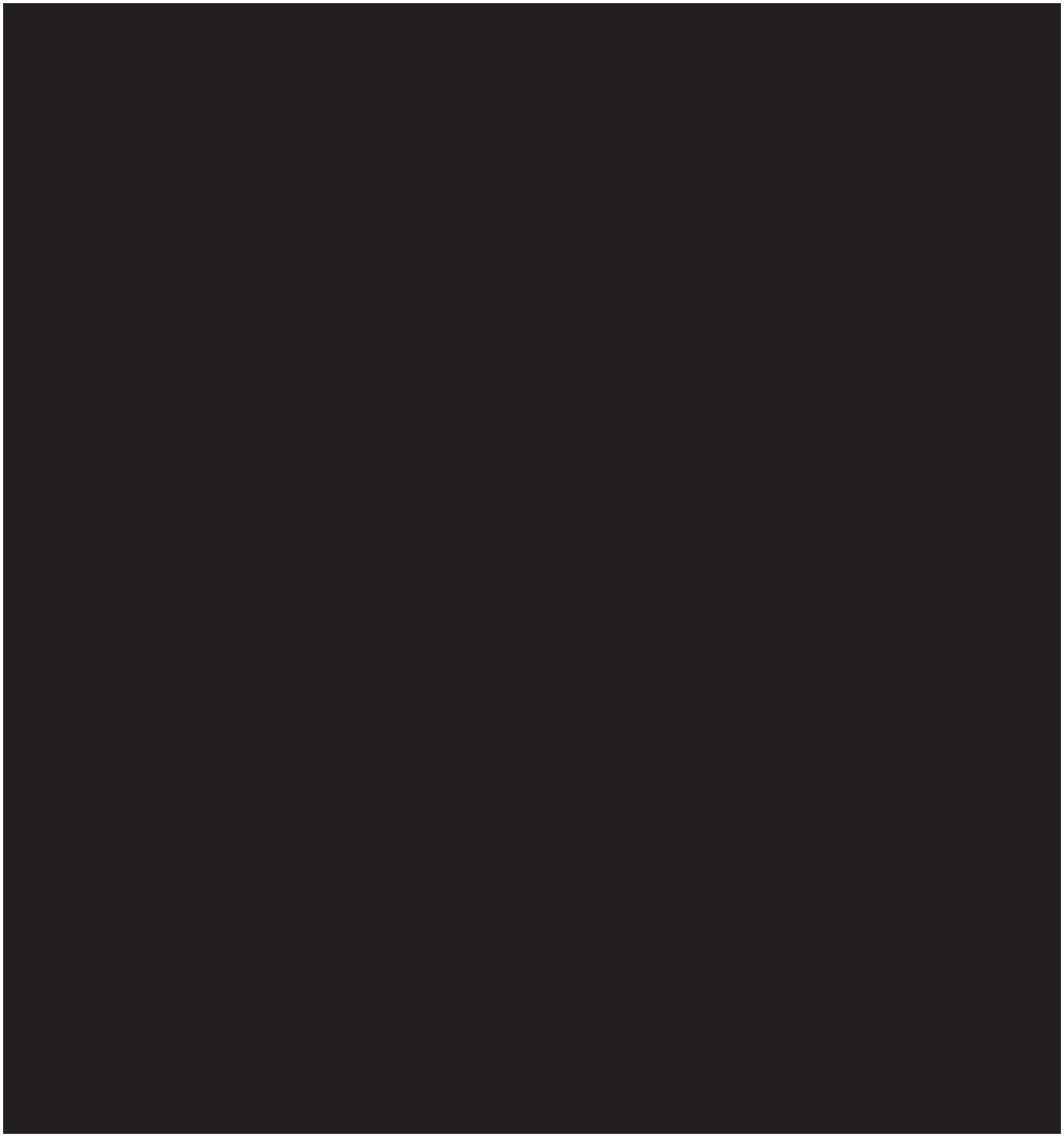
5. Buch, J. [redacted] *Design Validation of senofilcon A with New UV-blocking Additive.* 2018
6. Buch, J. [redacted] *).Clinical Evaluation of Test Lenses Manufactured with Different Curing Methods.*2017
7. Buch, J. [redacted] *Evaluation of Approved and Investigational Contact Lenses.* 2018
8. Buch, J. [redacted] *Contact Lenses with New UV-blocker Manufactured with Different Techniques.* August 01, 2018
9. Buch, J. [redacted] *Diagnostic Contact Lens Fitting with new UV-blocker Prototype: Study 1.*April 24 2018
10. Buch, J. [redacted] *).Diagnostic Contact Lens Fitting with new UV-blocker Prototype: Study 2.*May 08 2018
11. Health Information Portability and Accountability Act (HIPAA). In https://www.hhs.gov/hipaa/for-professionals/privacy/index.html (Ed.).

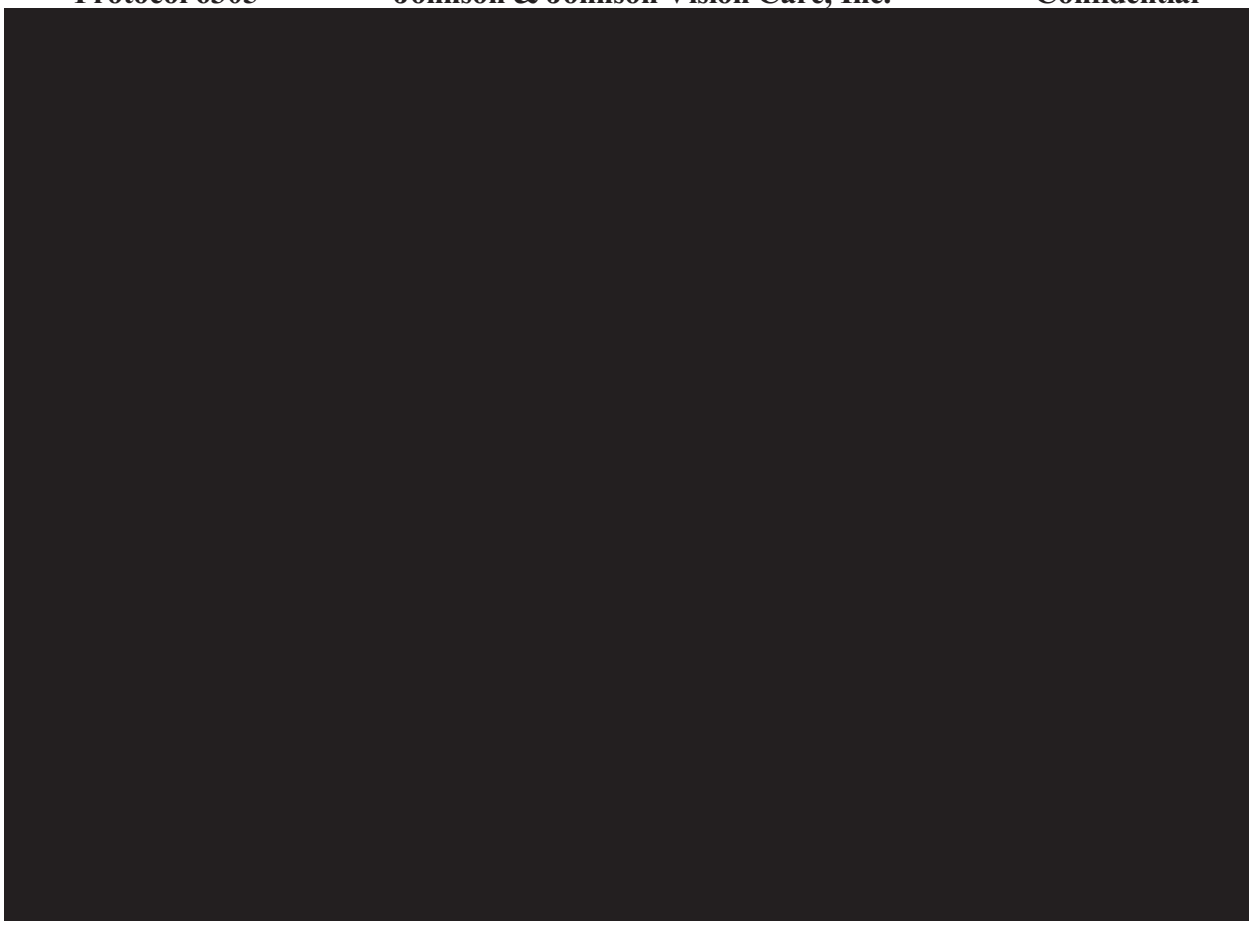
APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)











APPENDIX B: PATIENT INSTRUCTION GUIDE

A Patient Instruction Guide will be provided separately.

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

ACUVUE OASYS®

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

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

TORIC FITTING GUIDELINES

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

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

A. How to Determine Lens Cylinder and Axis Orientation

1. Locate the Orientation Marks

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

Figure 1

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

2. Observe Lens Rotation and Stability

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

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

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

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

4. Adaptation

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

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

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

D. Other Suggestions

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

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

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

Assessing Rotation

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

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

B. How to Determine the Final Lens Power

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

For the Sphere:

If sphere alone or combined sphere and cylinder Rx ≈+4.00D, compensate for vertex distance. If sphere alone or combined sphere and cylinder Rx ≥+ 4.00D, vertex compensation is not necessary.

For the Cylinder:

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

Case Examples:

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

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

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

Monovision fitting success can be improved by the following suggestions:

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

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

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

PATIENT MANAGEMENT

Dispensing Visit

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

Follow-up Examinations

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

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

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

Here is the Rx Prescribed:

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

Example 2

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

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

The fitting indicates the following:

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

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

Here is the Rx Prescribed:

O.S. –4.50 –1.75 x 90

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

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

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

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

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

WEARING SCHEDULE

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

For Daily Wear:

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

MULTIFOCAL FITTING GUIDELINES

A. Presbyopic Needs Assessment & Patient Education

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

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

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

These lenses are available in the following ADD powers:

- Lens "LOW" = "low" near ADD lens (Max +1.25 ADD)
- Lens "MID" = "medium" near ADD lens (Max +1.75 ADD)
- Lens "HIGH" = "high" near ADD lens (Max +2.50 ADD)

B. Fitting Instructions

1. Determine the following:

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

2. Select the initial trial lens as follows:

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

The maximum suggested wearing time for these lenses is:

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

For Extended Wear:

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

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

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

REPLACEMENT SCHEDULE

For Lenses Prescribed for Frequent Replacement:

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

For Lenses Prescribed for Disposable Wear:

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

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

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

  ADD: +0.75 to +1.25 use a "LOW" near ADD lens on each eye
  ADD: +1.50 to +1.75 use a "MID" near ADD lens on each eye
  ADD: +2.00 to +2.50 use a "HIGH" near ADD lens on each eye

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

4. Assess distance and near vision binocularly and monocularly.

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

C. Multifocal Troubleshooting

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

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

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

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

LENS CARE DIRECTIONS

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

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

For Lenses Prescribed for Frequent Replacement Wear:

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

For Lenses Prescribed for Disposable Wear:

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

Care for a Dried Out (Dehydrated) Lens

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

Care for Sticking (Non-Moving) Lenses

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

EMERGENCIES

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

MONOVISION FITTING GUIDELINES

A. Patient Selection

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

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

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

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

B. Eye Selection

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

1. Ocular Preference Determination Methods

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

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

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

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

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

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

C. Special Fitting Characteristics

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

Example: A presbyopic emmetropic patient who requires a +1.75D ADD would have a +1.75D lens on the near eye and the other eye left without a lens. A presbyopic patient requiring a +1.50D ADD who is –2.00D myopic in the right eye and –1.50D myopic in the left eye may have the right eye corrected for distance and the left uncorrected for near.

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

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

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

HOW SUPPLIED

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

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

REPORTING OF ADVERSE REACTIONS

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

Johnson & Johnson Vision Care, Inc.
7500 Centurion Parkway
Jacksonville, FL 32256
USA
Tel: 1-800-949-2020
www.acuvue.com

20400606

Printed in USA
Revision date: 06/15
Revision number: AO-06-15-01

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

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

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

ACUVUE®
OASYS
BRAND CONTACT LENSES

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

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

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

SYMBOLS KEY

The following symbols may appear on the label or carton:

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

DESCRIPTION

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

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

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

Lens Properties:

• Specific Gravity (calculated):	0.98 – 1.12
• Refractive Index:	1.42
• Light Transmittance:	95% minimum
• Surface Character:	Hydrophilic
• Water Content:	38%
• Oxygen Permeability:	
VALUE	**METHOD**
103 x 10^{-11} (cm²/sec) (ml O_2/ml x mm Hg) @ 35°C	Fatt (boundary corrected, edge corrected)
122 x 10^{-11} (cm²/sec) (ml O_2/ml x mm Hg) @ 35°C	Fatt (boundary corrected, non-edge corrected)

Lens Parameters:

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

AVAILABLE LENS PARAMETERS

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

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

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

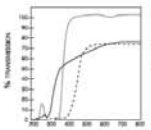
Diameter:	14.5 mm
Center Thickness:	Minus Lens - varies with power (e.g. -4.00D: 0.080 mm) Plus Lens - varies with power (e.g. +4.00D: 0.172 mm)
Base Curve:	8.6 mm
Powers:	plano to -6.00D (in 0.25D increments) -6.50D to -9.00D (in 0.50D increments) +0.25D to +6.00D (in 0.25D increments) Cylinder: -0.75D,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

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

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

TRANSMITTANCE CURVE

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



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

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

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

ACTIONS

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

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

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

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

INDICATIONS (USES)

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

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

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

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

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

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

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

- For corneal protection in lid and corneal abnormalities such as entropion, trichiasis, tarsal scars, and recurrent corneal erosion. In addition, they are indicated for protection where sutures or ocular structure malformation, degeneration or paralysis may result in the need to protect the cornea from exposure or repeated irritation.
- For corneal pain relief in conditions such as bullous keratopathy, epithelial erosion and abrasion, filamentary keratitis, and post-keratoplasty.
- For use as a barrier during the healing process of epithelial defects such as chronic epithelial defects, corneal ulcer, neurotrophic and neuroparalytic keratitis, and chemical burns.
- For post surgical conditions where bandage lens use is indicated such as post refractive surgery, lamellar grafts, corneal flaps, and additional ocular surgical conditions.
- For structural stability and protection in piggy back lens fitting where the cornea and associated surfaces are too irregular to allow for corneal rigid gas permeable (RGP) lenses to be fit. In addition, the use of the lens can prevent irritation and abrasions in conditions where there are elevation differences in the host/graph junction or scar tissue.

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

CONTRAINDICATIONS (REASONS NOT TO USE)

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

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

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

WARNINGS

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

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

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

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

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

†New England Journal of Medicine, September 21, 1989; 321 (12), pp. 779-783

Specific Instructions for Use and Warnings:

- **Water Activity**

  Instructions for Use

  Do not expose contact lenses to water while wearing them.

  WARNING:

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

- **Soaking and Storing Your Lenses**

  Instructions for Use

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

  WARNING:

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

ADVERSE REACTIONS

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

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

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

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

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

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

GENERAL FITTING GUIDELINES

A. Patient Selection:

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

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

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

B. Pre-fitting Examination:

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

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

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

C. Initial Power Determination

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

D. Base Curve Selection (Trial Lens Fitting)

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

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

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

E. Final Lens Power (Spherical)

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

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

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

PRECAUTIONS

Special Precautions for Eye Care Professionals:

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

  The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing Eye Care Professional.
- Patients who wear these lenses to correct presbyopia using monovision may not achieve the best corrected visual acuity for either far or near vision. Visual requirements vary with the individual and should be considered when selecting the most appropriate type of lens for each patient.
- Fluorescein, a yellow dye, should not be used while the lenses are on the eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used in eyes, the eyes should be flushed with a sterile saline solution that is recommended for in-eye use.
- Eye Care Professionals should instruct the patient to remove lenses immediately if the eyes become red or irritated.

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

Handling Precautions:

- Before leaving the Eye Care Professional's office, the patient should be able to promptly remove the lenses or should have someone else available who can remove the lenses for him or her.
- DO NOT use if the sterile blister package is opened or damaged.
- Always wash and rinse hands before handling lenses. Do not get cosmetics, lotions, soaps, creams, deodorants, or sprays in the eyes or on the lenses. It is best to put on lenses before putting on makeup. Water-based cosmetics are less likely to damage lenses than oil-based products.
- DO NOT touch contact lenses with the fingers or hands if the hands are not free of foreign materials, as microscopic scratches of the lenses may occur, causing distorted vision and/or injury to the eye.
- Carefully follow the handling, insertion, removal, and wearing instructions in the Patient Instruction Guide for these lenses and those prescribed by the Eye Care Professional.
- Always handle lenses carefully and avoid dropping them.
- Never use tweezers or other tools to remove lenses from the lens container unless specifically indicated for that use. Slide the lens up the side of the bowl until it is free of the container.
- Do not touch the lens with fingernails.
- Close supervision is necessary for the Therapeutic use of these lenses. Ocular medications used during treatment with a bandage lens should be closely monitored by the Eye Care Professional. In certain ocular conditions, only the Eye Care Professional will insert and remove the lenses. In these cases, patients should be instructed not to handle the lenses themselves.

Lens Wearing Precautions:

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

Lens Care Precautions:

- Different solutions cannot always be used together and not all solutions are safe for use with all lenses. Use only recommended solutions.
- Never use solutions recommended for conventional hard contact lenses only.
- Chemical disinfection solutions should not be used with heat unless specifically indicated on product labeling for use in both heat and chemical disinfection.
- Always use fresh, unexpired lens care solutions and lenses.
- Do not change solution without consulting with your Eye Care Professional.
- Always follow directions in the package inserts for the use of contact lens solutions.
- Use only a chemical (not heat) lens care system. Use of a heat (thermal) care system can damage these lenses.
- Sterile unpreserved solutions, when used, should be discarded after the time specified in the directions.
- Do not use saliva or anything other than the recommended solutions for lubricating or wetting lenses.
- Always keep the lenses completely immersed in the recommended storage solution when the lenses are not being worn (stored). Prolonged periods of drying will reduce the ability of the lens surface to return to a wettable state. Follow the lens care directions in "Care For A Dried Out (Dehydrated) Lens" if lens surface does become dried out.

Other Topics to Discuss with Patients:

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

Who Should Know That the Patient is Wearing Contact Lenses?

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

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

WARNING:

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

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

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

  Instructions for Use

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

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

  WARNING:

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

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

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

- **Rub and Rinse Time**

  Instructions for Use

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

  WARNING:

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

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

- **Lens Case Care**

  Instructions for Use

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

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

APPENDIX D: [redacted]

- [redacted] Lens Fitting Characteristics
- [redacted] Subject Reported Ocular Symptoms/Problems
- [redacted] Front and Back Surface Lens Deposit Grading Procedure
- [redacted] Determination of Distance Spherocylindrical Refractions
- [redacted] Biomicroscopy Scale
- [redacted] Keratometry Procedure
- [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] **Lens Fitting Characteristics**

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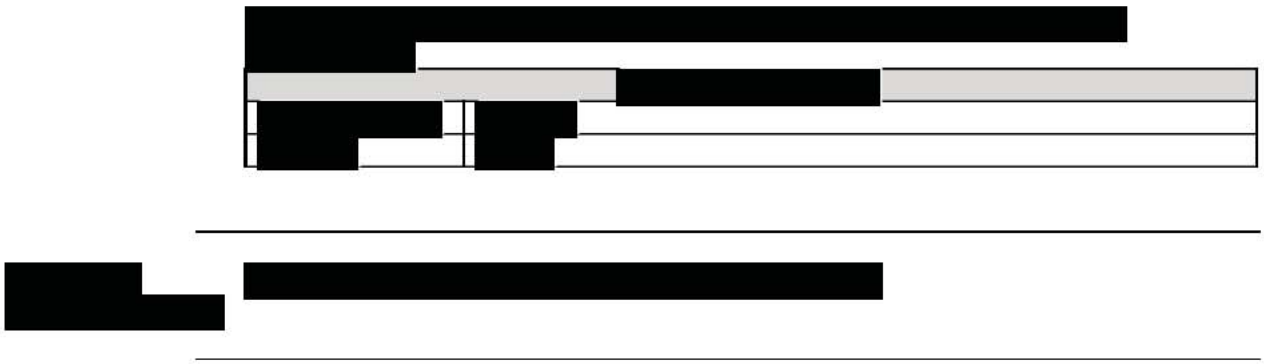

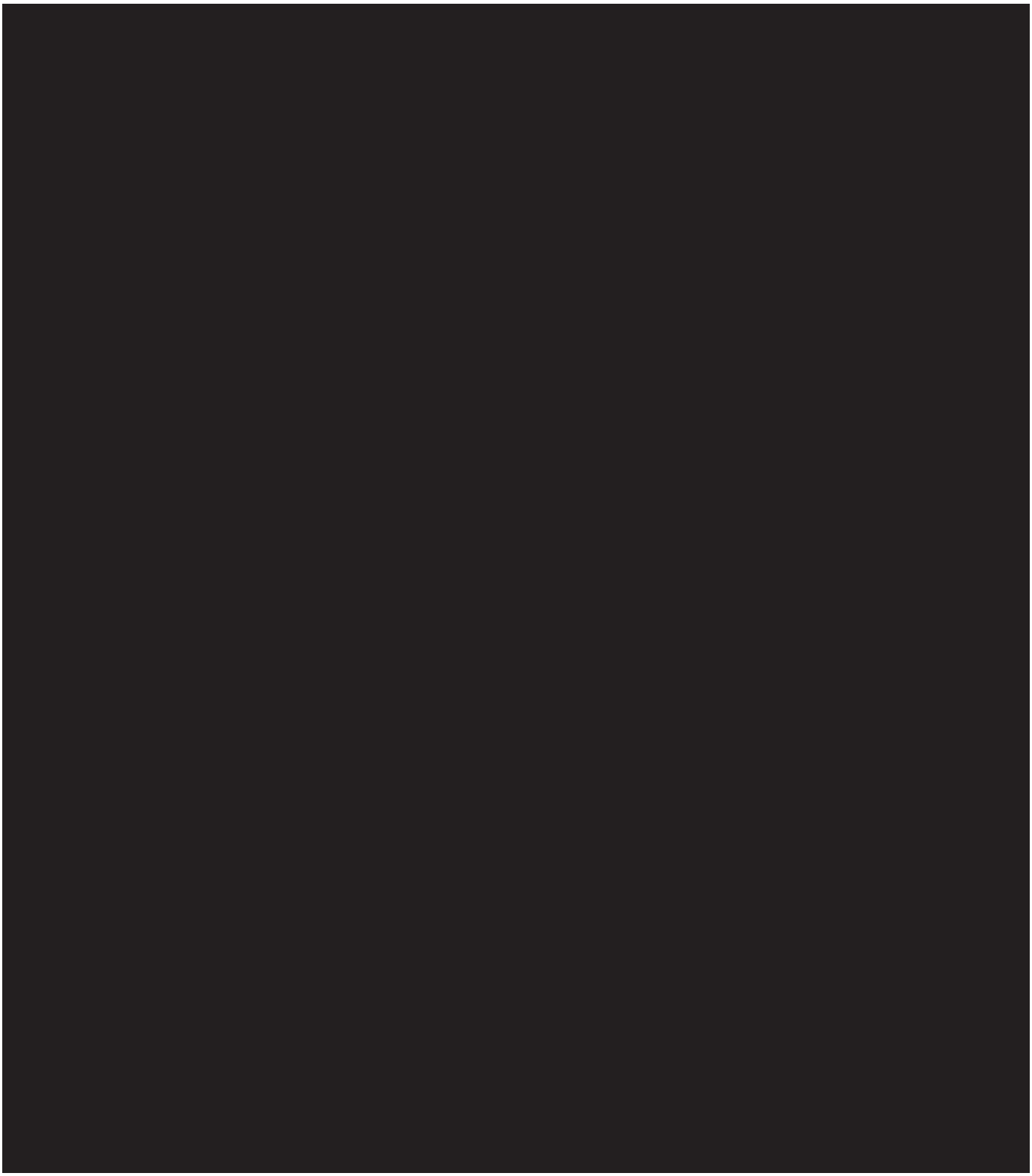

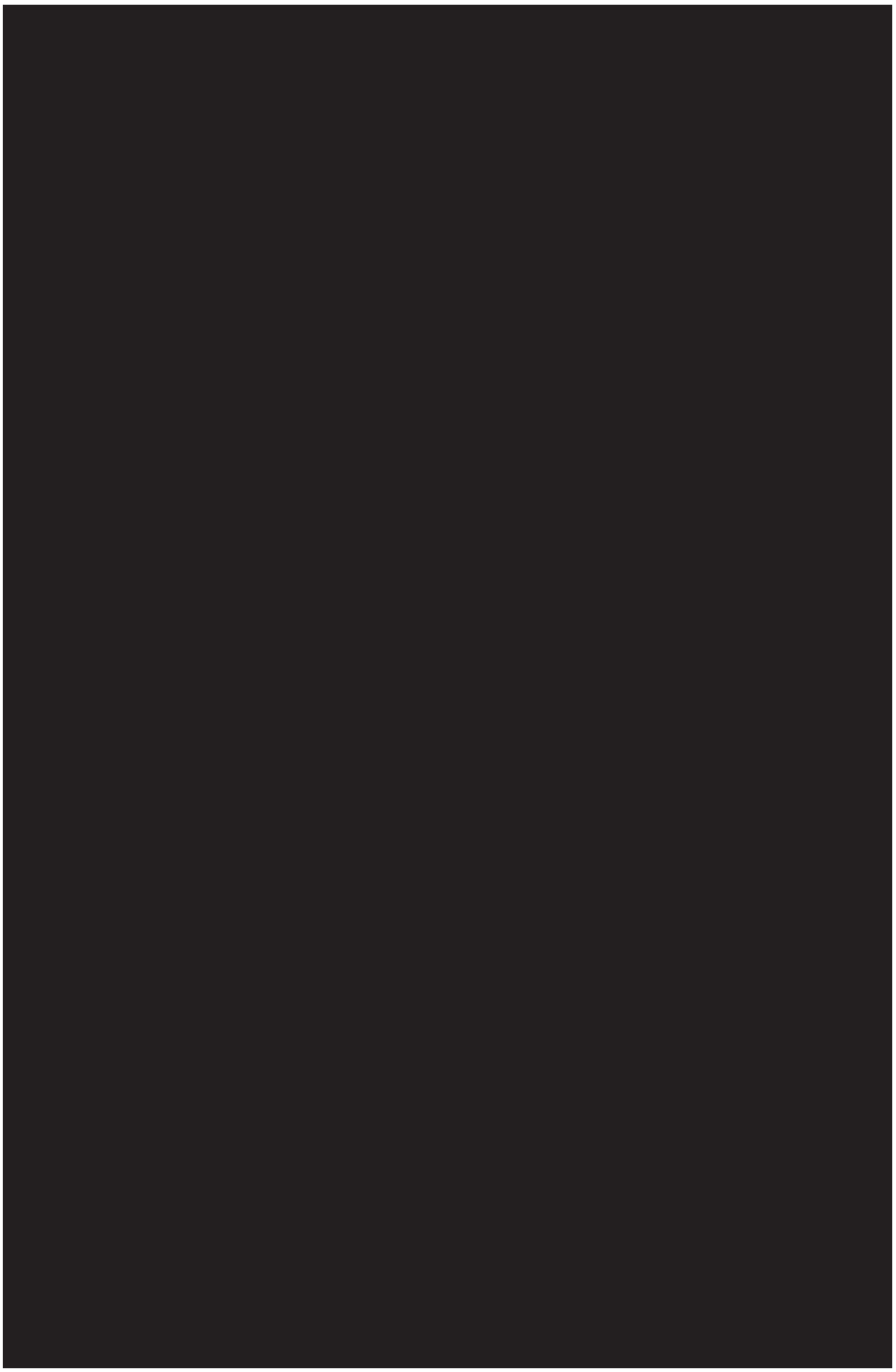

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[redacted] FRONT AND BACK SURFACE LENS DEPOSIT GRADING PROCEDURE

[redacted] **Front and Back Surface Lens Deposit Grading Procedure**

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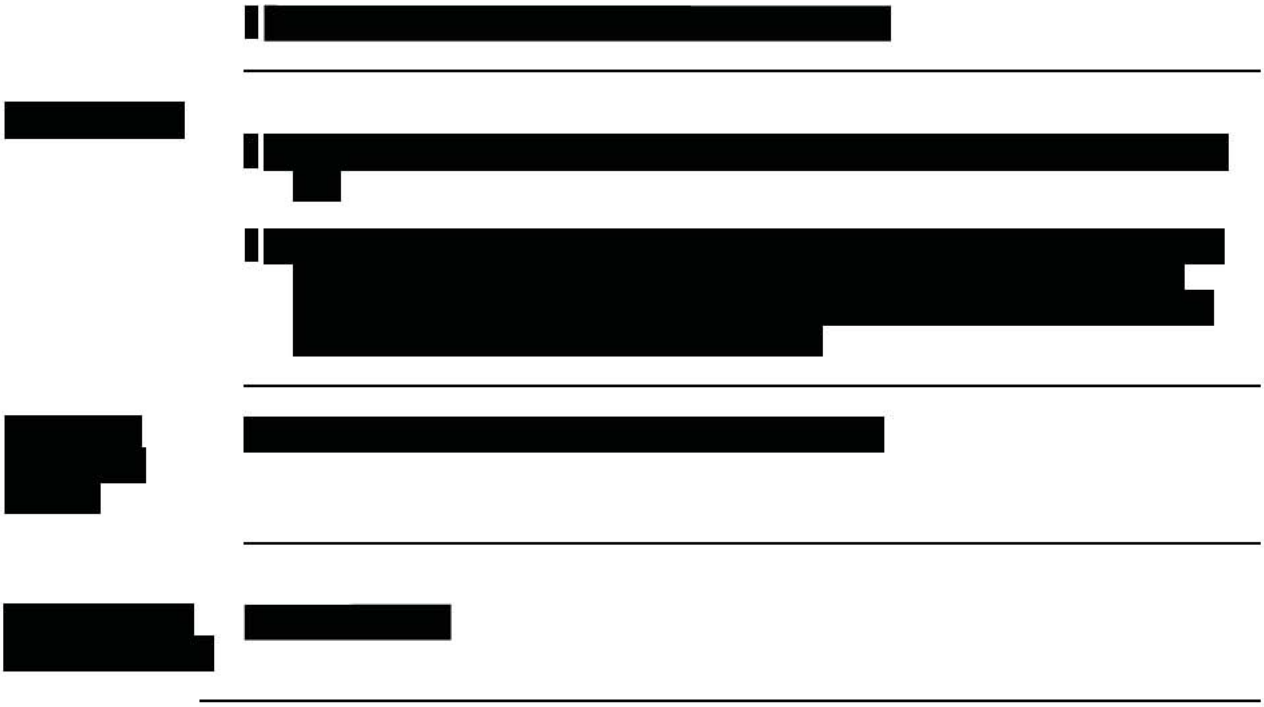

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[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted] **Determination of Distance Spherocylindrical Refractions**

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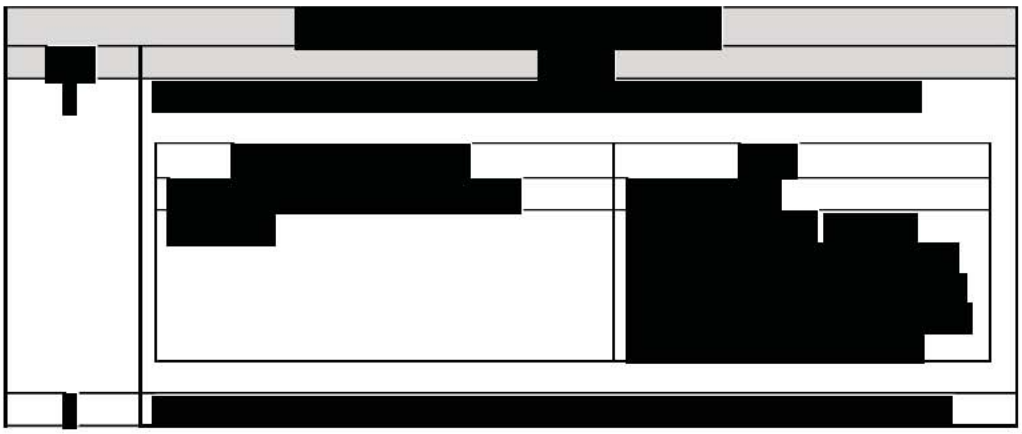

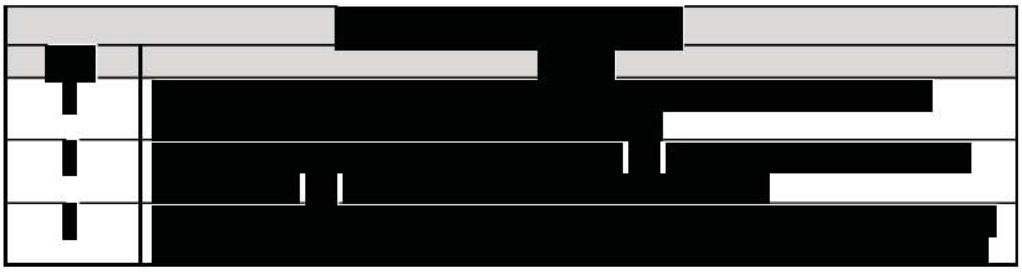

[redacted] BIOMICROSCOPY SCALE

[redacted] **Biomicroscopy Scale**

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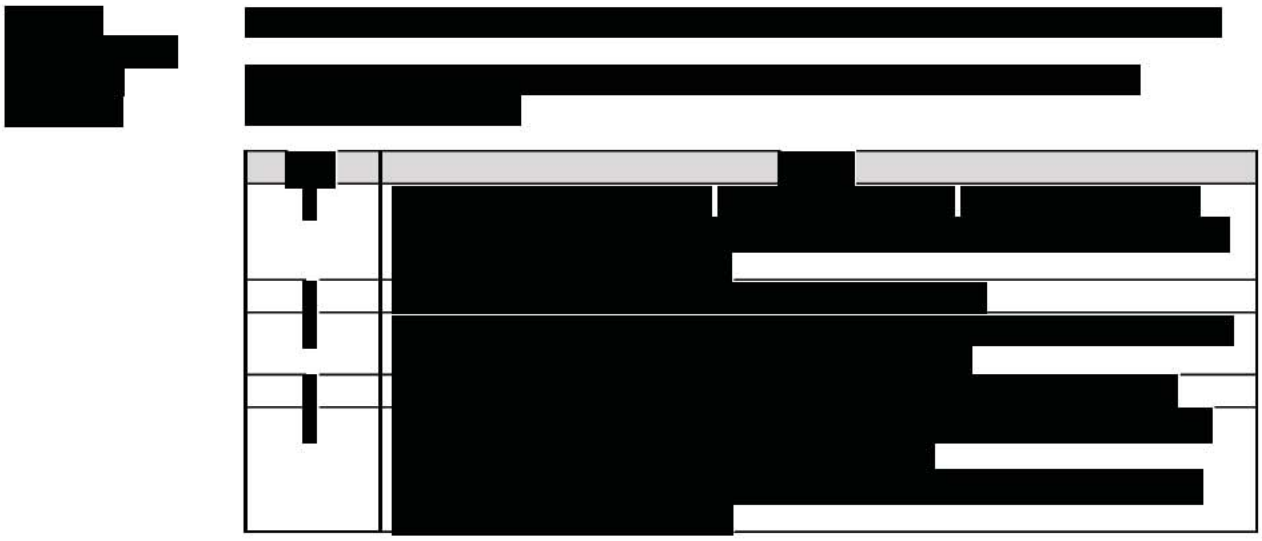

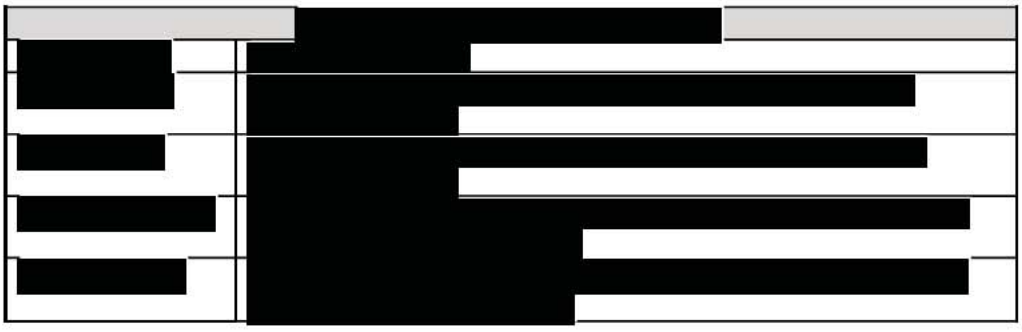

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Keratometry Procedure

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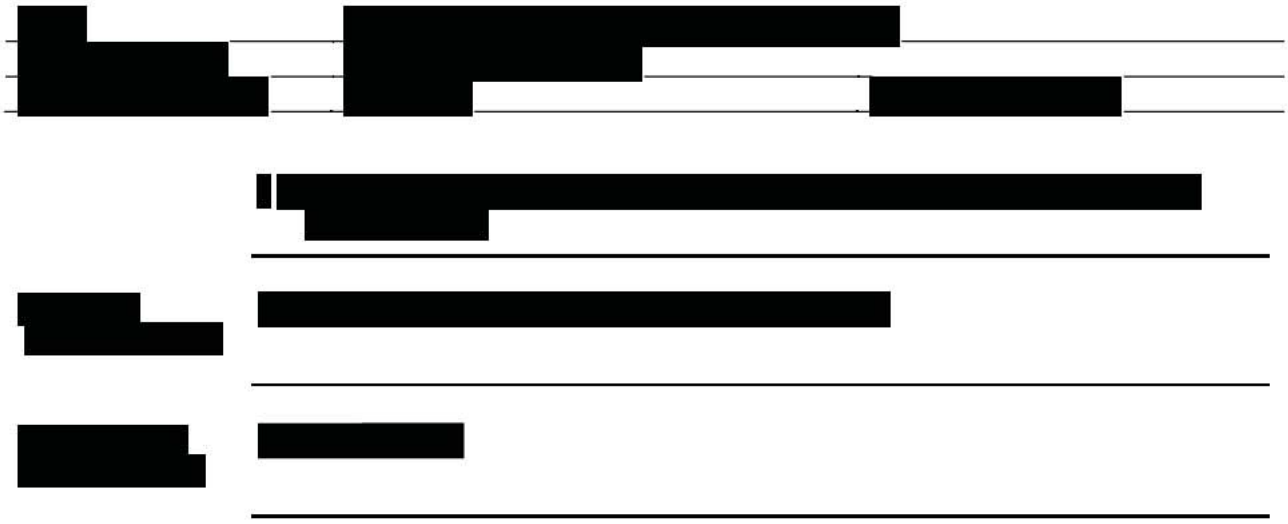

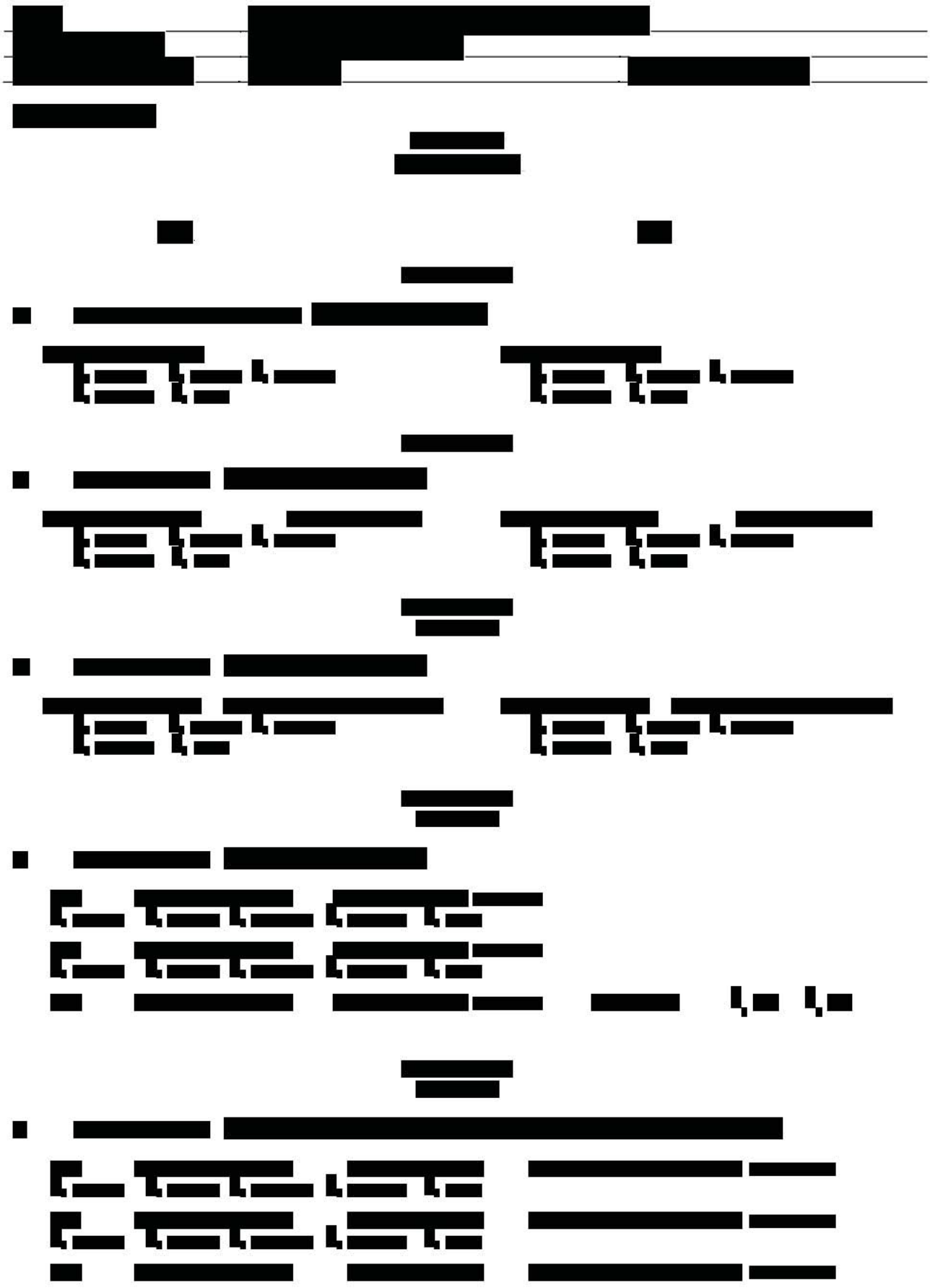

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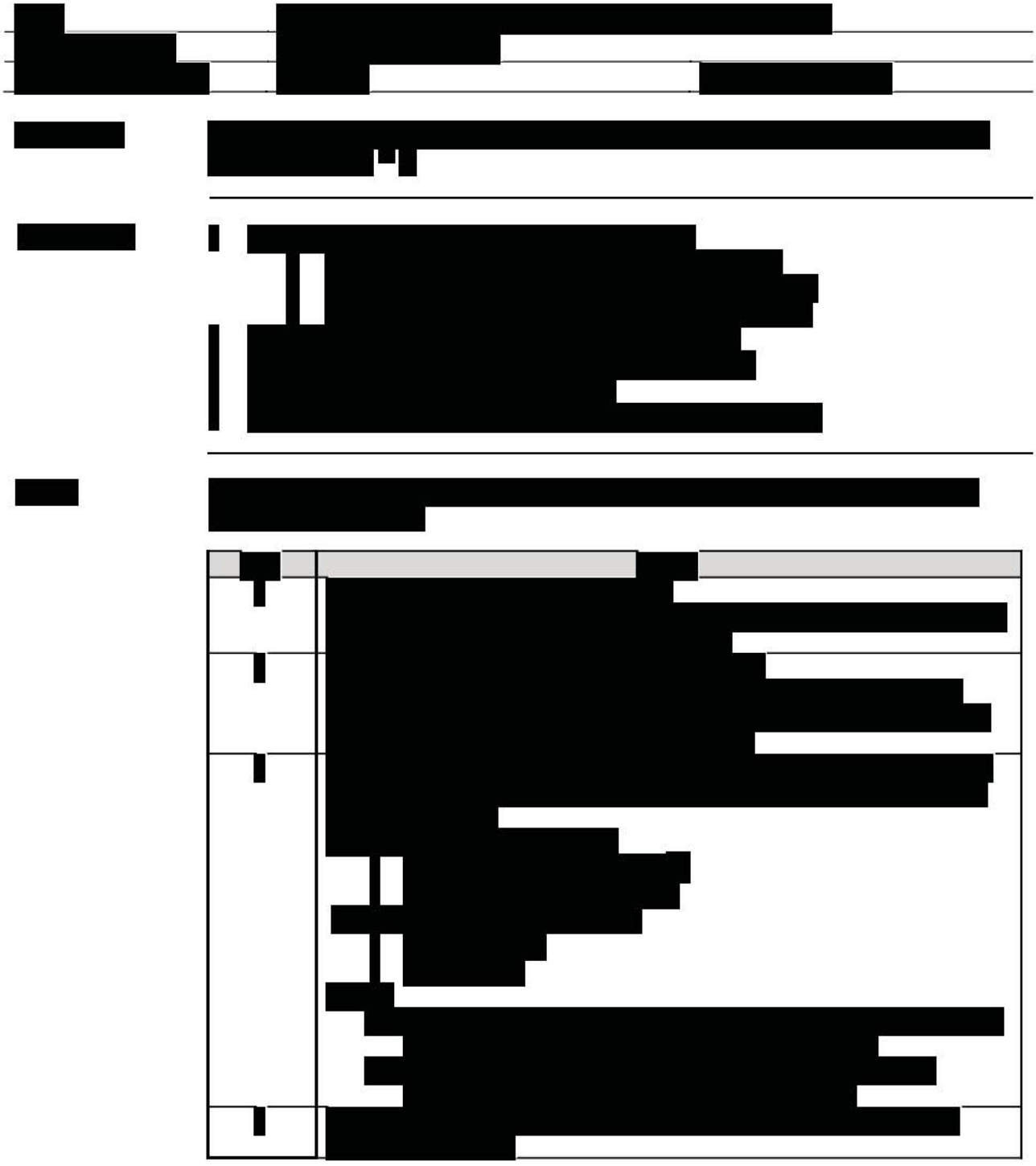

[redacted] PATIENT REPORTED OUTCOMES

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Patient Reported Outcomes

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[redacted] WHITE LIGHT LENS SURFACE WETTABILITY

[redacted] **White Light Lens Surface Wettability**

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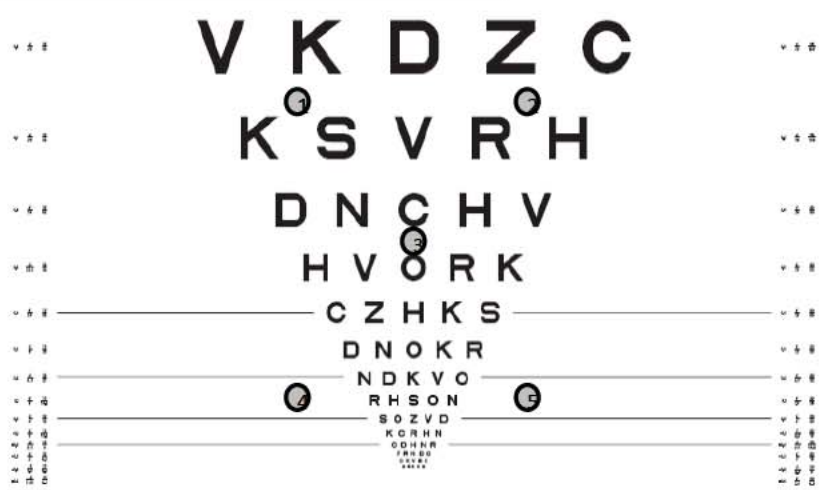
[redacted]	[redacted] 
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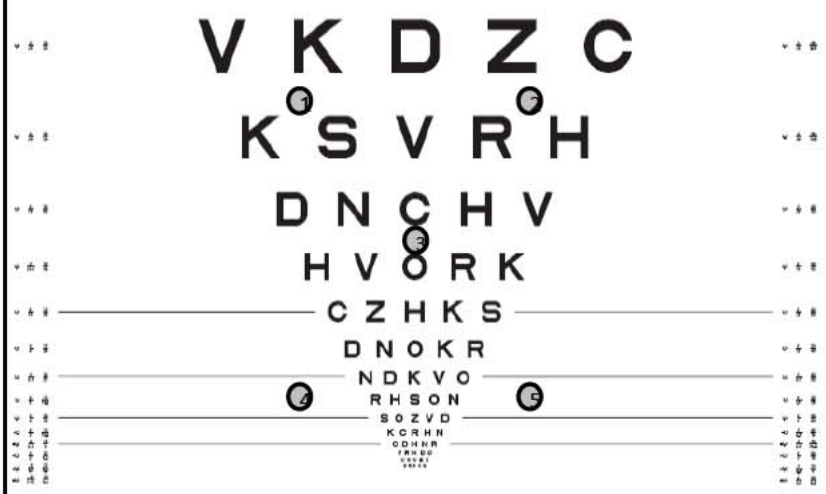
[redacted]	[redacted] 
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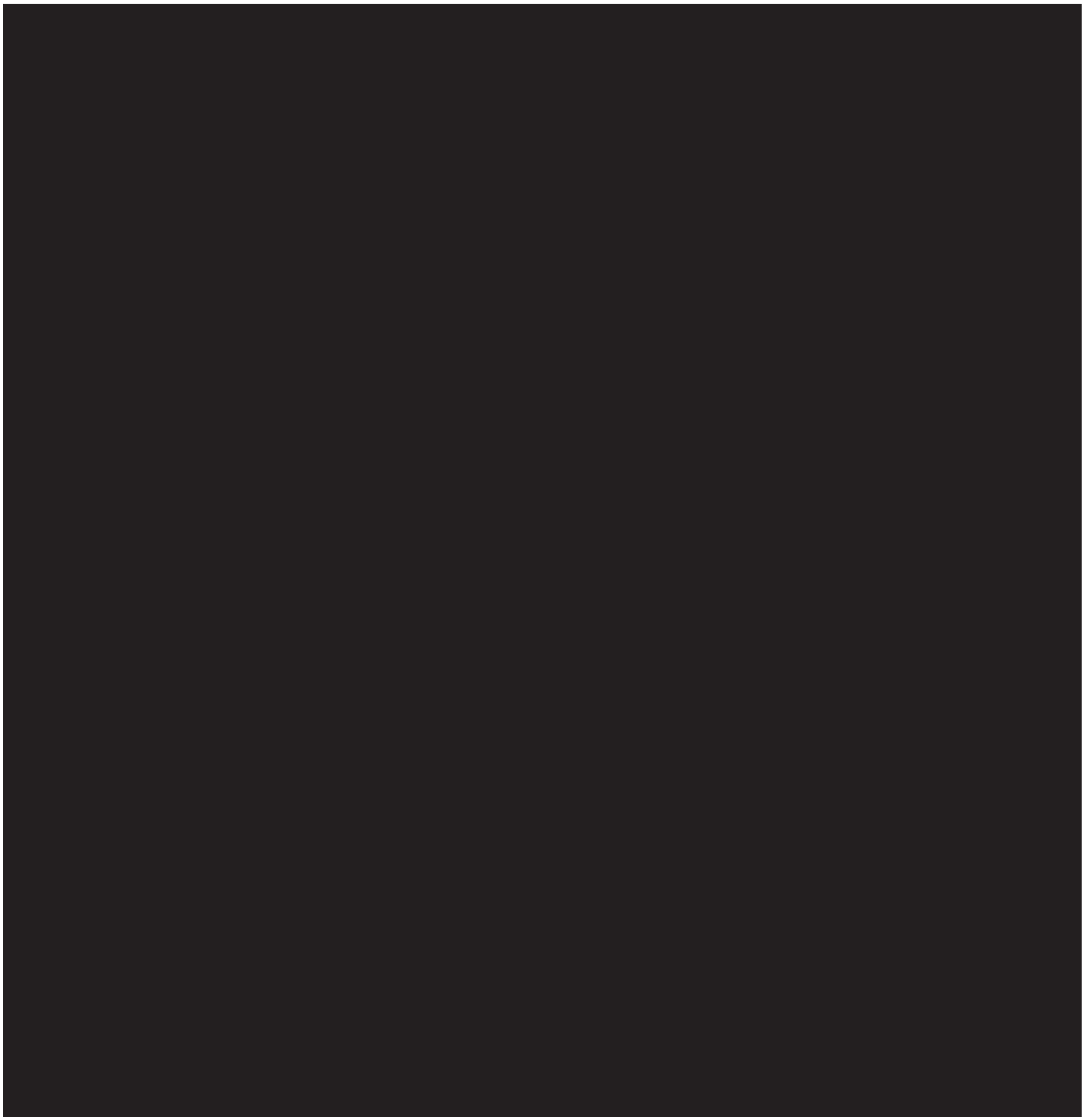

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PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6305: Design Validation of senofilcon A with New UV-blocking Additive

Version and Date: 4.0, Amendment 3.0 14 November 2018

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

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

Principal Investigator:

_____ _____

Signature Date

_____

Name and Professional Position (Printed)

Institution/Site:

_____

Institution/Site Name

_____

Institution/Site Address