Clinical Study Protocol
Johnson & Johnson Vision Care, Inc.

Clinical performance of senofilcon A investigational lens

Protocol CR-6481

Version: 3.0

Date: 17 March 2022

Investigational Products: senofilcon A prototype lens

Keywords: Sphere platform, Test lens: senofilcon A prototype, Control lens: delefilcon A (Dailies Total 1), daily wear, daily disposable, dispensing, Revitalens, subjective performance.

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

Confidentiality Statement:

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PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Clinical performance of senofilcon A investigational lens
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SPONSOR NAME AND ADDRESS

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

MEDICAL MONITOR

Name: [redacted]
Title: [redacted]
Address: [redacted]
24 Hour Contact Telephone #: [redacted]
Email: [redacted]

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

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

AUTHORIZED SIGNATURES

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

Author / Study Responsible Clinician	See Electronic Signature Report [redacted]	DATE
Clinical Operations Manager	See Electronic Signature Report [redacted]	DATE
Biostatistician	See Electronic Signature Report [redacted]	DATE
Biostatistical Review	See Electronic Signature Report [redacted]	DATE
Data Management	See Electronic Signature Report [redacted]	DATE
Medical Safety Officer	See Electronic Signature Report [redacted]	DATE
Approver	See Electronic Signature Report [redacted]	DATE

CHANGE HISTORY

Version	Originator	Description of Change(s) and Section Number(s) Affected	Justification for Change	Date
1.0	[redacted]	Original Protocol	N/A	04 Feb 2022
2.0	[redacted]	• Updated foil example • DT1 package insert added • Changed the order of the primary/secondary endpoints and hypotheses • Updated sample size • General formatting corrections • Updated [redacted]	• Edits add clarity and accuracy to protocol • Re-estimated sample size using recently collected data for the Control lens to properly power the study	11 Mar 2022
3.0	[redacted]	Section 4.3 updates: • Updated section 4.3 to correctly state up to 360 subjects will be enrolled with 330 to complete, not 360 / 306. Section 3.4, 4.3 updates: • Modified the number of sites to read 18-20, instead of up to 18.	• Accuracy	17 Mar 2022

SYNOPSIS

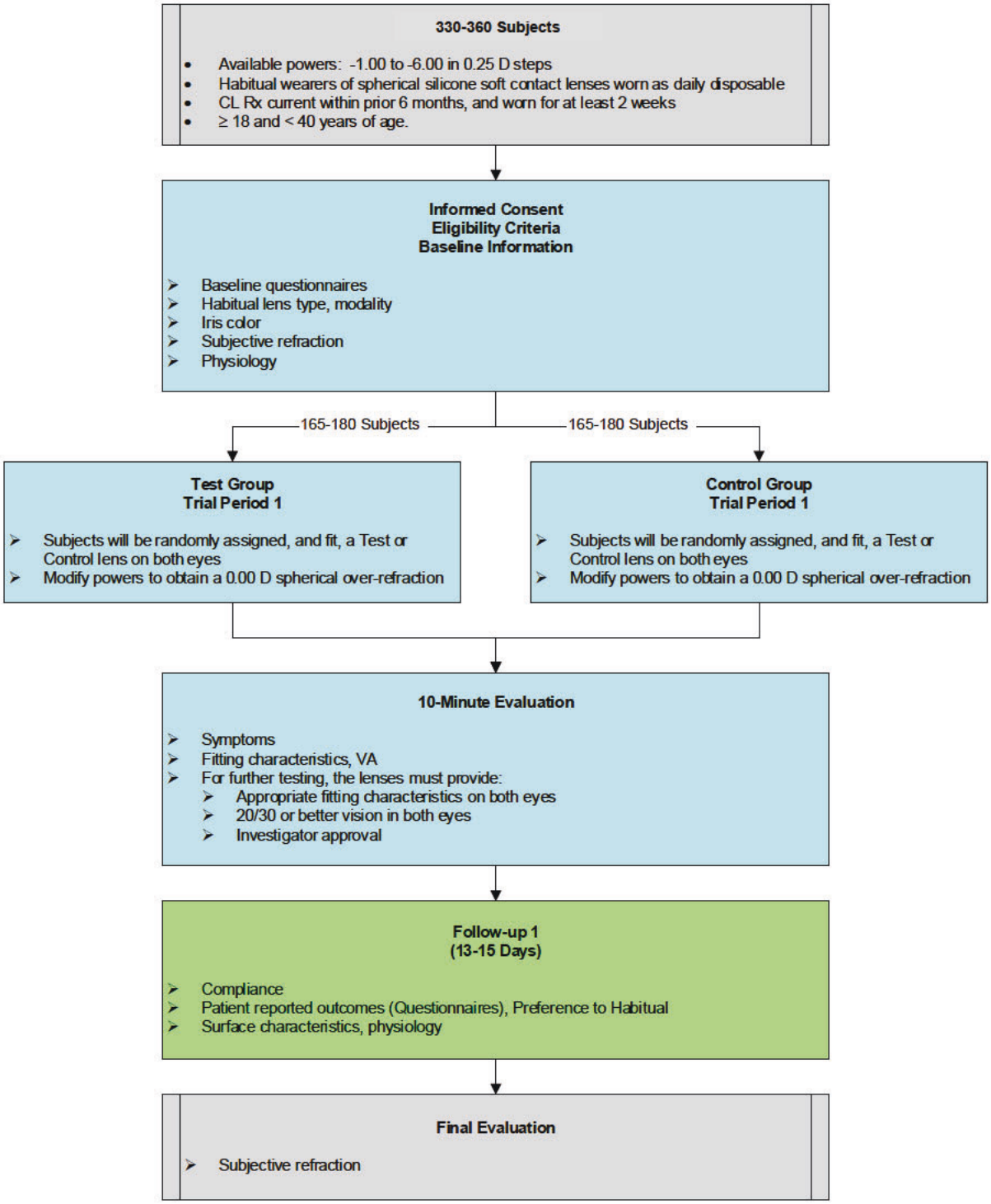
Protocol Title	Clinical performance of senofilcon A investigational lens
Sponsor	JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256
Clinical Phase	Clinical trial phase: Claims Design control phase: Phase 3
Trial Registration	This study will be registered on ClinicalTrials.gov by the Sponsor
Test Article(s)	Investigational Products: senofilcon A prototype as the Test lens Approved Products: Dailies Total 1 as the Control lens
Wear and Replacement Schedules	Wear Schedule: daily wear Replacement Schedule: daily disposable
Objectives	Primary Objectives: This study is being conducted to evaluate the clinical performance of an investigational soft contact lens against the clinical performance of a marketed product.
Study Endpoints	Primary endpoint(s): Subjective responses concentrated on comfort towards the end of the day. Secondary endpoint(s): Subjective responses concentrated on digital device use, night driving, and all day comfort. Other observations: Subjective responses concentrated on other aspects of vision, comfort, and/or handling.
Study Design	This study is a controlled, randomized, subject-masked, 2-arm parallel, 2-week dispensing, bilateral evaluation where the study lenses are worn for a minimum of 5 days per week and 6 hours per day. There will be a total of 2 visits: 1. Visit 1: Screening, baseline evaluation and lens fitting. 2. Visit 2: Follow-up evaluation, final evaluation. See the flow chart at the end of the synopsis table for the schematic of the study visits and procedures of main observations (Figure 1).
Sample Size	Up to 360 subjects will be enrolled to complete approximately 330 (approximately 165 in each arm).

Study Duration	Once enrolled, each subject will be in the study for 2 weeks. The enrollment period is 4 weeks per site, making the entire study duration approximately 6 weeks.
Anticipated Study Population	The study will enroll habitual wearers of spherical silicone hydrogel contact lenses, daily wear reusable and daily disposable. Subjects may be of any race or ethnicity that meet the eligibility criteria.
Eligibility Criteria - Inclusion	Potential subjects must satisfy all of the following criteria to be enrolled in the study: Inclusion Criteria after Screening The subject must: 1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form. 2. Appear able and willing to adhere to the instructions set forth in this clinical protocol. 3. Be between 18 and 39 (inclusive) years of age at the time of screening. 4. By self-report, habitually wear spherical soft silicone hydrogel contact lenses in both eyes in a daily wear or daily disposable wear modality (i.e. not extended wear modality). Habitual wear is defined as a minimum of 6 hours of wear per day, for a minimum of 5 days per week during the past 30 days. 5. Have a habitual contact lens prescription that is current within the prior 6 months, and they must have worn that prescription for at least 2 weeks prior to entering the study. 6. Possess a wearable pair of spectacles that provide correction for distance vision. Inclusion Criteria at Baseline Evaluation 7. The spherical equivalent of the subject's vertex-corrected distance refraction must be between -1.00 and -6.00 DS (inclusive) in each eye. 8. The magnitude of the cylindrical component of the subject's vertex-corrected distance refraction must be between 0.00 and 1.00 DC (inclusive) in each eye. 9. The best corrected, monocular, distance visual acuity must be 20/25or better in each eye.

Eligibility Criteria – Exclusion	Potential subjects who meet any of the following criteria will be excluded from participating in the study: Exclusion Criteria after Screening The subject must not: 1. Be currently pregnant or lactating. 2. Be currently using any ocular medications or have any ocular infection of any type. 3. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that the investigator believes might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g. rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1 for additional details regarding excluded systemic medications. 4. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g. SynergEyes, SoftPerm) within the past 6 months. 5. Be currently wearing monovision or multifocal contact lenses. 6. Be currently wearing lenses in an extended wear modality. 7. Have participated in a contact lens or lens care product clinical trial within 30 days prior to study enrollment. 8. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site. Exclusion Criteria at Baseline Evaluation The subject must not: 9. Have clinically significant (grade 3 or higher on the FDA grading scale) slit lamp findings (e.g., corneal edema, neovascularization or staining, tarsal abnormalities or bulbar injection) or other corneal or ocular disease or abnormalities that the investigator believes might contraindicate contact lens wear or may otherwise compromise study endpoints (including entropion, ectropion, chalazia, recurrent styes, glaucoma, history of recurrent corneal erosions, aphakia, moderate or above

	corneal distortion, herpetic keratitis). (Specify method of determination if needed). 10. Have a history of strabismus or amblyopia. 11. Have fluctuations in vision due to clinically significant dry eye or other ocular conditions. 12. Have had or have planned (within the study period) any ocular or intraocular surgery (e.g., radial keratotomy, PRK, LASIK, iridotomy, retinal laser photocoagulation, etc.).
Disallowed Medications/Interventions	No ocular medications. See section 9.1 for details regarding disallowed systemic medications.
Measurements and Procedures	Subjects will respond to a GSI/MRD questionnaire.
Microbiology or Other Laboratory Testing	None
Study Termination	The occurrence of an Unanticipated Adverse Device Effect (UADE) or Serious Adverse Event (SAE) for which a causal relationship to a test article cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled.
Ancillary Supplies/ Study-Specific Materials	RevitaLens, preservative-free 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, ACRONYMS AND DEFINITIONS OF TERMS

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

1. INTRODUCTION AND BACKGROUND

This study will investigate the clinical performance of an investigational Test lens against a marketed Control lens.

1.1. Name and Descriptions of Investigational Products

This study will evaluate a senofilcon A-based prototype against a commercially available marketed product Dailies Total 1 (DT1). 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. During the study, one of the study articles per subject will be worn bilaterally in a daily wear, daily disposable modality for at least 6 hours per day and 5 days per week for approximately 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 senofilcon A-based investigational lens, refer to the latest version of the Investigator's Brochure.

1.4. Summary of Known Risks and Benefits to Human Subjects

The risks of wearing soft contact lenses are well known and are described in the Investigator's Brochure and Informed Consent. The material safety testing/lens release criteria was determined based on the Risk Assessment. Benefits to the subjects include the correction of their refractive error.

For the most comprehensive risk and benefit information regarding senofilcon A-based investigational lens, refer to the latest version of the Investigator's Brochure.

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

The package insert for the DT1 Control lens can be found in the appendices. Prior clinical data of the investigational lens is summarized in the Investigator's Brochure.

The literature is absent of any articles pertaining to the investigational lens. Articles that pertain to the DT1 lenses do exist with a sampling shown here:

1. Wolffsohn, James, et al. "The influence of end of day silicone hydrogel daily disposable contact lens fit on ocular comfort, physiology and lens wettability." Contact Lens and Anterior Eye 38.5 (2015): 339-344.
2. Dumbleton, Kathryn A., et al. "A multi-country assessment of compliance with daily disposable contact lens wear." Contact Lens and Anterior Eye 36.6 (2013): 304-312.
3. Jayasree, Stephy VK, et al. "Quantification of water content in contact lenses combining terahertz imaging and optical coherence tomography." 2021 46th International Conference on Infrared, Millimeter and Terahertz Waves (IRMMW-THz). IEEE.

4. Montés-Micó, Robert, et al. "On-eye optical quality of daily disposable contact lenses for different wearing times." Ophthalmic and Physiological Optics 33.5 (2013): 581-591.

2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

2.1. Objectives

Primary Objective(s)
This study is being conducted to evaluate the clinical performance of an investigational soft contact lens against the clinical performance of a marketed product.

2.2. Endpoints

Primary Endpoint(s):

1. End of day comfort
   - Subjects will respond to the question, "Comfort at the End of the Day" [redacted].
     - Response set: Very Satisfied, Satisfied, Neither Satisfied nor Dissatisfied, Dissatisfied, and Very Dissatisfied.

Secondary Endpoint(s):

1. Digital device use
   - Subjects will respond to the question, "Reduction in the feeling of tired eyes from using a computer or other digital device" [redacted]
     - Response set: Not Applicable, Excellent, Very Good, Good, Fair, and Poor.

2. Comfort throughout the day
   - Subjects will respond to the question, "I could wear these contact lenses comfortably for as long as I wanted to" [redacted]
     - Response set: Strongly Disagree, Disagree, Neither Agree Nor Disagree, Agree, and Strongly Agree.

3. Comfortable vision while night driving
   - Subjects will respond to the question, "Ability to see comfortably while driving at night" [redacted]
     - Response set: Not Applicable, Excellent, Very Good, Good, Fair, and Poor.

Other Exploratory Endpoint(s):

Other exploratory endpoints including subjective questions regarding comfort, vision, handling, and preferences, such as:

1. Clarity of distance vision
   - Subjects will respond to the question, "Clarity of distance vision (i.e. looking at things that are more than 5 feet away, such as street signs)" [redacted].
     - Response set: Not Applicable, Excellent, Very Good, Good, Fair, and Poor.

2. Vision clarity throughout the day
   - Subjects will respond to the question, "I was very satisfied by the clarity of my vision throughout the day" [redacted]

3. Didn't have to think about the lenses
   - Subjects will respond to the question, "I didn't have to think about my lenses until I was ready to take them out" [redacted]
     - Response set: Agree Strongly, Agree Somewhat, Neither Agree Nor Disagree, Disagree Somewhat, and Disagree Strongly.

4. Ability to see comfortably using digital devices
   - Subjects will respond to the question, "Ability to see comfortably while using a computer or other digital device" [redacted]
     - Response set: Not Applicable, Excellent, Very Good, Good, Fair, and Poor.

5. Tired eyes
   - Subjects will respond to the question, "My eyes felt tired" [redacted]

6. Eye fatigue
   - Subjects will respond to the question, "Eye fatigue" [redacted]
     Response set: Always, Frequently, Occasionally, Rarely, Never, and Don't Know.

7. Vision at the end of the day
   - Subjects will respond to the question, "I had very good vision at the end of the day" [redacted]

8. Vision in dim lighting
   - Subjects will respond to the question, "I was satisfied with the quality of my vision in dim lighting" [redacted]

9. Dry eyes at the end of the day
   - Subjects will respond to the question, "I have experienced dry eyes at the end of the day" [redacted]

Response set for CLUE items: Strongly Disagree, Disagree, Neither Agree Nor Disagree, Agree, and Strongly Agree. [redacted] also has a "Not Applicable" response option.

2.3. Hypotheses

The primary hypothesis must be met for the objective of this study to be satisfied:

Primary Hypothesis

1. After approximately two weeks of wear, the Test lens will have superior performance to the Control lens with respect to end of day comfort.

The primary hypothesis must be met in order to begin testing any secondary hypotheses.

Secondary Hypotheses

1. After approximately two weeks of wear, the Test lens will have superior performance to the Control lens with respect to digital device use.

2. After approximately two weeks of wear, the Test lens will have superior performance to the Control lens with respect to comfort throughout the day.

3. After approximately two weeks of wear, the Test lens will have superior performance to the Control lens with respect to comfortable vision while night driving.

Exploratory Hypotheses
There will be no exploratory hypotheses. All exploratory endpoints will be descriptively summarized.

3. TARGETED STUDY POPULATION

3.1. General Characteristics

Approximately 180 subjects will be targeted to the Test Group and approximately 180 will be targeted to the Control Group. Within each lens group, the intent is to complete 165 (330 total subjects). Enrolled subjects will be habitual wearers of silicone hydrogel spherical contact lenses. All subjects will be the age of ≥18 and <40. Subjects will wear the study contact lenses approximately two weeks each on a daily wear (DW) daily disposable (DD) basis for a total study duration of approximately 14 days (2 weeks) per subject.

3.2. Inclusion Criteria

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

Inclusion Criteria after Screening

The subject must:

1. Read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Be between 18 and 39 (inclusive) years of age at the time of screening.
4. By self-report, habitually wear spherical soft silicone hydrogel contact lenses in both eyes in a daily wear or daily disposable wear modality (i.e. not extended wear

modality). Habitual wear is defined as a minimum of 6 hours of wear per day, for a minimum of 5 days per week during the past 30 days.
5. Have a habitual contact lens prescription that is current within the prior 6 months, and they must have worn that prescription for at least 2 weeks prior to entering the study.
6. Possess a wearable pair of spectacles that provide correction for distance vision.

Inclusion Criteria at Baseline Evaluation

7. The spherical equivalent of the subject's vertex-corrected distance refraction must be between -1.00 and -6.00 DS (inclusive) in each eye.
8. The magnitude of the cylindrical component of the subject's vertex-corrected distance refraction must be between 0.00 and 1.00 DC (inclusive) in each eye.
9. The best corrected, monocular, distance visual acuity must be 20/25 or better in each eye.

3.3. Exclusion Criteria

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

Exclusion Criteria after Screening:

The subject must not:

1. Be currently pregnant or lactating.
2. Be currently using any ocular medications or have any ocular infection of any type.
3. By self-report, have any ocular or systemic disease, allergies, infection, or use of medication that the investigator believes might contraindicate or interfere with contact lens wear, or otherwise compromise study endpoints, including infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive disease (e.g., Human Immunodeficiency Virus [HIV]), autoimmune disease (e.g. rheumatoid arthritis, Sjögren's syndrome), or history of serious mental illness or seizures. See section 9.1for additional details regarding excluded systemic medications.
4. Have habitually worn rigid gas permeable (RGP) lenses, orthokeratology lenses, or hybrid lenses (e.g. SynergEyes, SoftPerm) within the past 6 months.
5. Be currently wearing monovision or multifocal contact lenses.
6. Be currently wearing lenses in an extended wear modality.
7. Have participated in a contact lens or lens care product clinical trial within 14 days prior to study enrollment.
8. Be an employee (e.g., Investigator, Coordinator, Technician) or immediate family member of an employee (including partner, child, parent, grandparent, grandchild or sibling of the employee or their spouse) of the clinical site.

Exclusion Criteria at Baseline Evaluation

The subject must not:

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

3.4. Enrollment Strategy

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

The overall goal is to enroll approximately 360 subjects and complete 330 that are evenly distributed between the Test Group and the Control Group (Table 1).

Table 1: Enrollment Strategy Overall

Strata	Number of subjects per Enrollment		Number of Subjects per Completion	
	Test	Control	Test	Control
Habitual Daily Disposable	~126 (~7 per site)	~126 (~7 per site)	~116 (~6 per site)	~116 (~6 per site)
Habitual Daily Wear Reusable	~54 (~3 per site)	~54 (~3 per site)	~49 (~3 per site)	~49 (~3 per site)
Total	~180 (~10 per site)	~180 (~10 per site)	~165 (~9 per site)	~165 (~9 per site)

Subjects will be enrolled from 18-20 clinical sites and approximately 20 subjects are targeted to be enrolled within each site. Habitual wearers of daily disposable lenses will be targeted in a 7:3 ratio over daily wear reusable wearers within each site.

4. STUDY DESIGN AND RATIONALE

4.1. Description of Study Design

This study is a controlled, randomized, subject-masked, 2-arm parallel, 2-week dispensing, bilateral evaluation where the study lenses are worn for a minimum of 5 days per week and 6 hours per day. At study closure, participants will have no further access to the Test lenses.

The study begins with an initial visit (Visit 1). If a subject is found to meet all eligibility criteria, then they will be randomized and fit with either the Test or Control lenses in both eyes; otherwise, a subject will be deemed ineligible for this study. If the subject is dispensed study lenses at the initial visit, a follow-up visit will be conducted. The follow-up visit will occur approximately 2 weeks after the initial visit. Unscheduled visits may occur during the study.

4.2. Study Design Rationale

The purpose of this study is to evaluate the performance of a senofilcon A-based investigational lens in a 2-arm parallel design against a marketed product. In this parallel design, subjects are randomized to one of the two study arms and after randomization each participant will stay in their assigned treatment arm for the duration of the study. Randomization eliminates the selection bias and balances both the known and unknown confounding factors that may affect the study outcomes.

4.3. Enrollment Target and Study Duration

This study will have an enrollment target of 360 subjects, with a target of at least 330 to complete. The study will be conducted at 18-20 clinical sites, where the enrollment target for each site will be approximately 20 subjects. A subject will be considered enrolled upon signing of the informed consent form.

There will be 2 visits in total per subject; total study duration including the 4-week enrollment period is expected to be approximately 6 weeks. Subjects who are discontinued prior to the final evaluation may be replaced at the discretion of the study sponsor. The investigation will end at the time that the study data is hard locked.

Table 2: Duration of Study Visits

Visit	Description	≈ Duration
1	Informed consent, eligibility criteria, baseline data, trial fitting 1, dispense lenses. Study lenses to be worn 13-15 days to first follow-up visit.	2.0 hours
2	13-15 day follow-up for the study lens, subjective responses, VA, fitting characteristics, surface characteristics, physiology, Final Evaluation.	1.5 hours

5. TEST ARTICLE ALLOCATION AND MASKING

5.1. Test Article Allocation

Use of the test articles will be randomized using a lens fitting schedule supplied by the study biostatistician. The clinical site will follow the lens fitting schedule provided and will complete enrollment according to the randomization list and will not pre-select or pre-assign subjects.

Randomly-permuted block randomization will be used to avoid bias in the assignment of subjects to treatment and to enhance the validity of statistical comparisons across treatment groups. A computer-generated randomization scheme will be used to randomly assign subjects to one of the two lens groups (Test or Control). The randomization will be stratified by site and type of habitual lens wear (daily disposable and daily wear reusable). The ratio of habitual wearers of daily disposable lenses to habitual wearers of daily wear reusable lenses is 7:3 within each study site (7 habitual wearers of daily disposable lenses versus 3 habitual wearers of daily wear reusable lenses). See Table 1. 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).[5]

Randomization will be performed at Visit 1. The following must have occurred prior to randomization:

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

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

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

5.2. Masking

This is a single-masked trial. Subjects will be unaware of the identity of the investigational product. The investigators may be aware of the study lenses based on a slight difference in lens color (the Test lenses will be slightly more turquoise in color than the Control lens). Investigators and clinical site personnel involved in the data collection will not be masked as to the identity of the investigational product.

5.3. Procedures for Maintaining and Breaking the Masking

The identity of the study lenses will be masked to the subjects by over labeling the blister pack of the study lens. The label will contain the study number, lot number, sphere power, expiration date and the randomization codes.

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.

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

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

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
Manufacturer	Alcon	JJVC
Name	Dailies Total 1	TRP-200
Material	delefilcon A	senofilcon A
[redacted]	[redacted]	[redacted]
Packaging Form	Sterile blister pack	Sterile blister pack
Nominal Water Content (%)	33	38
Nominal Dk (edge corrected)	140	103
Inversion Indicator	No	123
Nominal Base Curve/Diameter @ 22°C (mm)	8.5 / 14.1	8.5 / 14.3
Nominal Center Thickness @ -3.00 D (mm)	0.090	0.085
Nominal Powers (D)	-1.00 through -6.00 in 0.25 steps	-1.00 through -6.00 in 0.25 steps

At least 1816 lenses per SKU per study lens will be made available based on the following factors: sample size, bilateral wear, daily replacement, 2-week duration, safety margin of 2X, and US distribution model for the range of lenses -1.00 through -6.00 DS.

6.2. Ancillary Supplies/Products

The following solutions will be used in this study. Note that RevitaLens will be used primarily to transport potential problematic lenses back to the Sponsor.

Table 4: Ancillary Supplies

	Solution			
Solution Name/Description	Acuvue® RevitaLens Multipurpose Solution	Single use Eye-Cept® Rewetting Drops	LacriPure Saline Solution	ScleralFil Preservative Free Saline Solution
Manufacturer	Johnson & Johnson Vision	Optics Laboratory	Menicon	Bausch & Lomb
Preservative	Alexidine dihydrochloride 0.00016% and polyquaternium-1 0.0003%	None	None	None

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

6.3. Administration of Test Articles

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

6.4. Packaging and Labeling

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

Primary Packaging

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

Contents: One contact lens in solution.

STERILE

LOT ABC123
SPH -1.00
EXP 2025/12/31
CR-1000 RC A

Secondary Packaging

Sponsored By/Parrainé par:

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

Contents/Contenu:

Contact Lenses in Solution
Lentilles cornéennes dans une solution

6.5. Storage Conditions

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

6.6. Collection and Storage of Samples

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

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

6.7. Accountability of Test Articles

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

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

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

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

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

Reference [redacted] Site Instructions for Test Article Receipt and Test Article Accountability for additional information.

7. STUDY EVALUATIONS

7.1. Time and Event Schedule

Table 5: Time and Events

Visit Information	Visit 1 Screening, Baseline, Treatment 1	Visit 2 2-week FU Treatment 1	Visit 2 Final Evaluation
Time Point		14 days after Visit 1 (+/- 1 day)	14 days after Visit 1 (+/- 1 day)
Estimated Visit Duration	2.0 hours	1.0 hours	0.5 hours
Statement of Informed Consent	x		
Demographics	x		
Medical History/Concomitant Medications	x	x	
Habitual Contact Lens Information	x		
Inclusion/Exclusion Criteria	x		
Study Questionnaires Baseline	x		
Entrance Visual Acuity	x	x	
Slit Lamp Biomicroscopy	x	x	x (if applicable)
Iris Color	x		
Subjective Spherocylindrical Refraction	x		x
Lens Selection	x		
Lens Insertion & Settling	x		
Visual Acuity and Over Refraction	x		
Lens Power Modification (if applicable)	x		
Subject Reported Ocular Symptoms	x	x	
Lens Fit Assessment	x	x	
Lens Wettability	x	x	
Surface characteristics		x	
Lens dispensing information and criteria	x		
Patient instructions	x		
Study Questionnaires FU		x	
Exit Acuity	x		x
Final Evaluation			x

7.2. Detailed Study Procedures

VISIT 1

The subjects must enter the visit wearing their habitual contact lenses.

Visit 1: Screening			
Step	Procedure	Details	[redacted] / Work aid
1.1	Statement of Informed Consent	Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form. **Note:** The subject must be provided a signed copy of this document.	
1.2	Demographics	Record the subject's year of birth, age, gender, race and ethnicity.	
1.3	Medical History and Concomitant Medications	Record the subject's medical history and concomitant medications.	
1.4	Habitual Lenses	Record the subject's habitual lens type, parameters, lens care solution, wear modality and approximate prescription date.	
1.5	Habitual Wear Time	Record the average wearing time and comfortable wearing time.	
1.6	SCL Rx Confirmation	The investigator confirms: 1. The subject is wearing a SCL Rx that has been confirmed current (up-to-date) within the prior 6 months. 2. The subject has worn the up-to-date SCL Rx for at least 2 weeks.	
1.7	Eligibility after Screening	All responses to Screening Inclusion Criteria questions must be answered "yes" and all responses to Exclusion Criteria must be answered "no" for the subject to be considered eligible. *If subject is deemed to be ineligible after screening, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms do not need to be completed as part of Final Evaluation.*	

Visit 1: Baseline			
Step	Procedure	Details	[redacted] / Work aid
1.8	Baseline Questionnaire	The subject will respond to the following Baseline Questionnaires based on their habitual lenses: 1. CLUE baseline 2. GSI Background 3. Activity history	[redacted]
1.9	Entrance Visual Acuity	Record the distance Snellen visual acuity (OD, OS, and OU) to the nearest letter with their habitual contact lens correction in place. Subjects must read the smallest line until at least 50% of the letters are read incorrectly.	[redacted]
1.10	Remove Habitual 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.	
1.11	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 3 or higher (FDA scale), the subject may not continue at this time, but may return up to one additional time to determine eligibility. If discontinued a final examination must be completed. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled.	[redacted]
1.12	Iris Color	The investigator will record the subject's iris color based on the scale provided.	**Appendix E**
1.13	Subjective Sphero-cylindrical Refraction	Complete subjective spherocylindrical refraction and record the resultant distance visual acuity (OD, OS, and OU) to the nearest letter.	[redacted]

Visit 1: Baseline			
Step	Procedure	Details	[redacted] / Work aid
1.14	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 baseline, proceed to Final Evaluation and complete Subject Disposition. Refraction and Biomicroscopy forms do not need to be completed as part of Final Evaluation.*	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted] / Work aid
1.15	Lens Selection	• Assign the study lens based on the randomization scheme provided by the biostatistician. • Select the contact lens power based on the spherical equivalent from the subjective sphero-cylindrical refraction. • Record the test condition.	**Appendix F**
1.16	Lens Insertion	Patient instruction: the investigator will demonstrate / explain that the visibility tint for Test and Control lenses are there by design. • 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. • Ensure the subject is given a Patient Instruction Guide.	
1.17	Lens Settling	Allow the study lenses to settle for a minimum of 5 minutes.	

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted] / Work aid
1.18	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 record the best corrected distance visual acuity to the nearest letter (OD and OS).	[redacted]
1.19	Lens Power Modification (if applicable)	Adjust the lens power if the subject's best sphere over-refraction is not plano. For each power modification, select the adjusted fitting lens power as appropriate and repeat steps 1.16 through 1.18. One power modification is allowed.	
1.20	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
1.21	Post-Fit Questionnaire	Subjects will respond to the MRD/GSI Post-Fit Questionnaire.	[redacted]
1.22	General Lens Fit Assessment	Evaluate lens centration, movement on blink, and push-up test for each eye. An unacceptable fit is deemed by one of the following criteria: • limbal exposure at primary gaze or with extreme eye movement. • edge lift. • excessive movement in primary and up gaze. • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push-up test. **Note:** if lens fit is unacceptable for either eye, the subject will be discontinued from the study.	[redacted]
1.23	White Light Lens Surface Wettability	Record the white light lens wettability of both lenses.	[redacted]
1.24	Visual Acuity	Record the distance 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]

Visit 1: Treatment 1 Lens Fitting			
Step	Procedure	Details	[redacted] / Work aid
1.25	Continuance	For the subject to continue in the study, they must meet all three of the following criteria: • Visual acuity is 20/30 or better OD and OS. • The lens fit is acceptable OD and OS. • Investigator approval. If the Investigator does not approve the dispensing of the first study lens, then the study is terminated for that subject.	
1.26	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 daily disposable only. 3. All subjects will be provided a bottle of ACUVUE RevitaLens to return any problematic lenses to the investigational site. 4. Rewetting drops are permitted if needed. 5. A patient instruction booklet will be provided. 6. Has the subject been informed that the lenses contain a visibility tint by design? **Note 1**: Ensure that the subject has enough lenses to last them to their next scheduled visit with no extras. In the event a lens is lost or damaged, and the subject has run out of lenses, the subject will return to the investigator site for replacement. **Note 2**: The subject's habitual contact lenses cannot be worn at any time during the study. **Note 3**: Remind the subjects to bring back any unworn lenses to the next visit. **Note 4**: Remind the subject to bring a habitual form of correction to next visit.	
1.27	Schedule next visit	Schedule the follow-up visit to occur in 14 ± 1 days (counting the day of this visit as day 0, the subject may return on day 13 through 15).	

VISIT 2

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

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted] / Work aid
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	Return unworn lenses	Collect any unworn study lenses from the subject.	
2.5	Subject Reported Ocular Symptoms	Subjects will respond to a verbal open-ended symptoms questionnaire.	[redacted]
2.6	Follow-Up Questionnaire	Subjects will respond to the following questionnaires: 1. CLUE Follow-up 2. GSI Product Performance 3. Lens preference to habitual	[redacted]
2.7	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]

Visit 2: Treatment 1 Follow-Up 1			
Step	Procedure	Details	[redacted] / Work aid
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. • excessive movement in primary and up gaze. • insufficient movement in all three of the following conditions: primary gaze, up gaze, and push-up test. **Note:** if lens fit is unacceptable subject will be discontinued from the study.	[redacted]
2.9	Wettability Characteristics	Record the white light lens wettability of both lenses.	[redacted]
2.10	Surface Deposits	Record any front and back surface lens deposits.	[redacted]
2.11	Lens Removal	Both lenses will be removed and discarded.	
2.12	Slit Lamp Biomicroscopy	FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" grade for all observations listed. Note: If the subject has Grade 3 or 4 slit lamp findings on the FDA scale, then they must be followed as an adverse event. Adverse events must be reported to the JJVC monitors immediately. After the slit lamp examination, at the discretion of the Investigator, rinse the subject's eyes thoroughly with rewetting drops or saline.	[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	Exit Refraction	Perform bare-eye subjective spherocylindrical refraction with a phoropter and record the best-corrected distance visual acuity (OD, OS and OU) to the nearest letter. **Note**: This step is not necessary if the subject was exited due to screen failure.	[redacted]
F.3	Exit Slit Lamp Biomicroscopy (for subjects that are discontinued early)	FDA Slit Lamp Classification Scale will be used to grade the findings. If no slit lamp finding is noted on the EDC form it is considered as a zero "0" grade for all observations listed. Note: If the subject has Grade 3 or 4 slit lamp findings on the FDA scale, then they must be followed as an adverse event. Adverse events must be reported to the JJVC monitors immediately. If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. This step is not necessary if the subject was exited due to screen failure. **Note**: This step is not necessary if the subject was exited due to screen failure, or if biomicroscopy was performed as part of the final follow-up visit procedures (i.e., immediately prior to the final evaluation).	[redacted]

7.3. Unscheduled Visits

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

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

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

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

The following information will be collected during an unscheduled visit.

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.1	Reason for unscheduled visit	Indicate if the only reason for the visit is that the subject requires additional test articles. If the reason is other than resupply of previously dispensed lenses, specify the reason for the visit.	
U.2	Chief Complaints (if applicable)	Record the subject's chief complaints for reasons for the unscheduled visit.	
U.3	Adverse Events and Concomitant Medications Review (if applicable)	Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes, and any adverse events.	
U.4	Entrance VA (if applicable)	Record the entrance distance visual acuity (OD, OS, OU) to the nearest letter.	[redacted]

Unscheduled Visit			
Step	Procedure	Details	[redacted]
U.5	Subjective Sphero-cylindrical Refraction (if applicable)	Perform bare-eye subjective spherocylindrical refraction with a phoropter (adopt the maximum plus to maximum visual acuity (MPMVA) approach and use the duo-chrome test for binocular balancing) and record the best corrected distance visual acuity to the nearest letter (OD, OS, OU).	[redacted]
U.6	Slit Lamp Biomicroscopy (if applicable)	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. After the slit lamp examination, at the discretion of the Investigator, rinse the subject's eyes thoroughly with rewetting drops or saline.	[redacted]
U.7	Dispensing (if applicable)	If the subject requires additional lenses to complete the wear period and is eligible to do so, provide additional lenses per the dispensing instructions given in the detailed study procedures.	
U.8	Exit Visual Acuity (if applicable)	Record the subject's exit distance visual acuity (OD, OS, OU) to the nearest letter.	[redacted]

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

7.4. Laboratory Procedures

Not Applicable.

8. SUBJECTS COMPLETION/WITHDRAWAL

8.1. Completion Criteria

Subjects are considered to have completed the study if they:

- provided informed consent.
- they are eligible.
- have not withdrawn/discontinued from the study for any reason described in section 8.2.
- completed all visits through the final visit2.
- If all visits were completed but an additional visit is considered necessary for subject care, follow the requirements for unscheduled visits in section 7.3.

8.2. Withdrawal/Discontinuation from the Study

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

- Subject withdrawal of consent.
- Subject not compliant to protocol such as study lens wear time or habitual lens wear while enrolled in the study.
- Subject lost to follow-up.
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant).
- Subject develops significant or serious adverse events necessitating discontinuation of study lens wear.
- Subjects who have experienced a Corneal Infiltrative Event (CIE).
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment).
- Subject missed a study visit.
- Subject not compliant with study lens wear schedule (i.e. wears study lenses less than at least 6 hours per day for at least 5 days a week over the 2 week wear period)
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort or unacceptable fit.

For discontinued subjects, the Investigator will:

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

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

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

9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study.

- Disallowed medications for this study include: medications that may interfere with contact lens wear (see section 9.1). Habitual medications used by successful soft contact lens wearers are considered acceptable.
- Concomitant therapies that are disallowed include: NA

9.1. Systemic Medications

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

A summary of disallowed systemic medications is shown in Table 6. Subjects with a history of taking these medications will be allowed to enroll only if:

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

Or:

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

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

Table 6: Disallowed systemic medications

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

Examples of disallowed systemic antihistamines are given in Table 7. Subjects with a history of taking systemic antihistamines will be allowed to enroll only if:

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

Or:

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

Table 7: Disallowed systemic antihistamines

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

10. DEVIATIONS FROM THE PROTOCOL

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

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

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

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

Protocol waivers are prohibited.

Table 8 lists examples of deviations that will constitute major and minor protocol deviations for this study.

Table 8: Examples of major and minor protocol deviations

Deviation category	Major deviation	Minor deviation
Out-of-window visit	Visit attended 2 days or more than out of visit window defined in study procedures	Visit attended 1 day or fewer out of visit window defined in study procedures
Unanswered PRO questions	For questionnaires where data is related to a primary or secondary endpoint, 2 or more PRO questions are unanswered (i.e., left blank).	For questionnaires where data is related to a primary or secondary endpoint, 1 or fewer PRO questions are unanswered (i.e., left blank). For questionnaires where data where data is not related to a primary or secondary endpoint, any PRO questions are unanswered (i.e., left blank).
Insufficient wear of study lenses	Subject does not wear study lenses for at least 6 hours on at least 5 days of a study lens wear period.	NA

In the case of a major protocol deviation, the decision of whether or not the subject will be excluded from the Per-Protocol analysis population will be made at the time of cohort review.

11. STUDY TERMINATION

If more than 2 subjects in the investigational soft contact lens group develop serious expected (e.g., definite or probable MK) or unexpected device related adverse events, the study will be suspended. Upon review and consultation with IRB, and JJVC Safety Management Team , the study may be terminated.

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

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

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

JJVC (and the IEC/IRB, 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 (Refer to Form Control No. [redacted] for test article return instructions).

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

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

13. ADVERSE EVENTS

13.1. Definitions and Classifications

Adverse Event (AE) – An AE is "any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or other persons, whether or not related to the investigational medical device."

Note: This definition includes events related to the investigational medical device or the comparator, and to the procedures involved. For users or other persons, this definition is restricted to events related to investigational medical devices.[1]

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

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

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

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

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

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

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

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

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

- Contact Lens Induced Peripheral Ulcer (CLPU)
- Significant Infiltrative Events (SIE)
- Superior Epithelial Arcuate Lesions (SEALs)
- Any Temporary Loss of > 2 Lines of BSCVA
- Other grade 3 or higher corneal findings, such as abrasions or edema

- Non-contact lens related corneal events - e.g. Epidemic Keratoconjunctivitis (EKC)
- Asymptomatic Corneal Scar
- Any corneal event which necessitates temporary lens discontinuation > 2 weeks

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

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

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

Adverse Device Effect (ADE) – An ADE is an "adverse event related to the use of an investigational medical device."

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.[1]

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

13.2. Assessing Adverse Events

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

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

13.2.1. Causality Assessment

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

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

13.2.2. Severity Assessment

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

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

13.3. Documentation and Follow-Up of Adverse Events

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

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

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

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

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

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

In addition, if an infiltrate(s) is present, he/she will complete the Corneal Infiltrate Assessment eCRF. Where necessary, a culture of the corneal lesion will be collected to determine if the

infection is microbial in nature. If cultures are collected, the date of culture collection and laboratory utilized will be recorded.

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

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

13.4. Reporting Adverse Events

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

13.4.1. Reporting Adverse Events to Sponsor

Serious/Significant Adverse Events

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

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

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

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

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

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

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

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

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

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

13.5. Event of Special Interest

None.

13.6. Reporting of Pregnancy

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

14. STATISTICAL METHODS

14.1. General Considerations

Statistical Analysis will be undertaken by the sponsor or under the authority of the sponsor. A general description of the statistical methods to be implemented in this clinical trial is outlined below. 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).[5] 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 efficacy 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 is designed and powered to demonstrate superiority of the Test lens compared to the Control lens with respect to the primary and secondary endpoints. Sample size was calculated to achieve a statistical power of 90% for each primary and secondary endpoint.

Sample size calculation was based on historical data from 4 hard locked studies (, , , and) and the interim read data from a single-arm study . , , and used a 2×2 crossover design and is a two-arm parallel study. The Test lens in these studies are the same as the Test lens in the current study. The 2-week follow-up evaluation data for the Test lens in the first study period from the three crossover studies and , and the interim data from for the Control lens (DT1) were used in the sample size estimation. Table 9 below presents the descriptive statistics for the primary and secondary endpoints from these studies.[6-9]

Table 9: Descriptive Summary for the Primary and Secondary Endpoints at 2-week Follow-up from Historical and Interim Data

Study	Endpoint	Response	Test Lens (TRP-200)	Control Lens (DT1)
Test lens:	End of day comfort (Primary): "Comfort at the End of the Day"	Very Satisfied	108 (47.6%)	16 (22.2%)
		Satisfied	80 (35.2%)	19 (26.4%)
		Neither Satisfied nor Dissatisfied	19 (8.4%)	9 (12.5%)

Study	Endpoint	Response	Test Lens (TRP-200)	Control Lens (DT1)
Control Lens: [redacted]		Dissatisfied	13 (5.7%)	20 (27.8%)
		Very Dissatisfied	7 (3.1%)	8 (11.1%)
Test lens: [redacted] Control Lens: [redacted]	Digital Device Use (Secondary 1): "Reduction in the feeling of tired eyes from using a computer or other digital device"	Not Applicable	11 (4.8%)	2 (2.8%)
		Excellent	86 (37.9%)	14 (19.4%)
		Very Good	66 (29.1%)	15 (20.8%)
		Good	43 (18.9%)	28 (38.9%)
		Fair	10 (4.4%)	9 (12.5%)
		Poor	11 (4.8%)	4 (5.6%)
Test lens: [redacted] Control Lens: [redacted]	Comfort throughout the day (Secondary 2): "I could wear these contact lenses comfortably for as long as I wanted to"	Strongly Disagree	10 (2.7%)	11 (15.3%)
		Disagree	44 (11.9%)	22 (30.6%)
		Neither Agree Nor Disagree	33 (8.9%)	8 (11.1%)
		Agree	155 (41.8%)	15 (20.8%)
		Strongly Agree	129 (34.8%)	16 (22.2%)
Test lens: [redacted] Control Lens: [redacted]	Comfortable vision while night driving (Secondary 3): "Ability to see comfortably while driving at night"	Not Applicable	8 (2.2%)	2 (2.8%)
		Excellent	184 (49.6%)	19 (26.4%)
		Very Good	99 (26.7%)	18 (25%)
		Good	60 (16.2%)	19 (26.4%)
		Fair	13 (3.5%)	9 (12.5%)
		Poor	7 (1.9%)	5 (6.9%)

For sample size estimation, a 20% difference in subjects endorsing the best two response options (Top 2 box, T2B) was assumed between the Test and Control lens groups, to obtain a relatively conservative sample size for a statistical power of 90% for the primary endpoint and for each secondary endpoint. The type I error rate used in the sample size calculation was based on the significance level specified in Section 14.4 (i.e., 2-sided alpha of 0.05 for the primary endpoint test, 0.025 for each of the first two secondary endpoints tests, and 0.0125 for the last secondary endpoint test). Sample size was estimated using the PROC POWER procedure in the SAS software Version 9.4 based on the Pearson chi-square test for two proportions.

<u>End of day comfort</u>

End of Day Comfort will be measured using a single item "Comfort at the End of the Day" at 2-week follow-up with a 5-point Likert scale (1: Very Satisfied, 2: Satisfied, 3: Neither Satisfied nor Dissatisfied, 4: Dissatisfied and 5: Very Dissatisfied). Responses will be

converted into a binary variable for the purpose of analysis (Very Satisfied or Satisfied = 1 and others = 0). Assuming a 20% difference in T2B between the study lenses (Test = 68% and Control = 48%), sample size was calculated to achieve 90% power for demonstrating statistical superiority at a 2-sided type I error of 0.05.

Digital device use

Digital device use will be measured using a single item "Reduction in the feeling of tired eyes from using a computer or other digital device" at 2-week follow-up with a 5-point Likert scale (1: Excellent, 2: Very Good, 3: Good, 4: Fair and 5: Poor) with a "Not Applicable" response option. Responses will be converted into a binary variable for the purpose of analysis (Excellent or Very Good = 1 and others = 0) and "Not Applicable" will not be included in the analysis. Assuming a 20% difference in T2B between the study lenses (Test = 61% and Control = 41%), sample size was calculated to achieve 90% power for demonstrating statistical superiority at a 2-sided type I error of 0.025.

Comfort throughout the day

Comfort throughout the day will be measured using a single item "I could wear these contact lenses comfortably for as long as I wanted to" at 2-week follow-up with a 5-point Likert scale (1: Strongly Disagree, 2: Disagree, 3: Neither Agree Nor Disagree, 4: Agree and 5: Strongly Agree). Responses will be converted into a binary variable for the purpose of analysis (Strongly Agree or Agree = 1 and others = 0). Assuming a 20% difference in T2B between the study lenses (Test = 63% and Control = 43%), sample size was calculated to achieve 90% power for demonstrating statistical superiority at a 2-sided type I error of 0.025.

Comfortable vision while night driving

Comfortable vision while night driving will be measured using a single item "Ability to see comfortably while driving at night" at 2-week follow-up with a 5-point Likert scale (1: Excellent, 2: Very Good, 3: Good, 4: Fair and 5: Poor) with a "Not Applicable" response option. Responses will be converted into a binary variable for the purpose of analysis (Excellent or Very Good = 1 and others = 0) and "Not Applicable" will not be included in the analysis. Assuming a 20% difference in T2B between the study lenses (Test = 73% and Control = 53%), sample size was calculated to achieve 90% power for demonstrating statistical superiority at a 2-sided type I error of 0.0125.

Table 10 below summarizes the required number of completed subjects to achieve 90% statistical power for the primary and secondary endpoints.

Table 10: Sample Size Estimation for the Primary and Secondary Endpoints

Endpoint Type	Endpoint	Two-sided Type I Error	Sample Size (N/arm)	Power
Primary	End of day comfort	0.05	126	90%
			95	80.2%
Secondary	Digital device use	0.025	153	90%

Endpoint Type	Endpoint	Two-sided Type I Error	Sample Size (N/arm)	Power
			118	80.2%
	Comfort throughout the day	0.025	153	90.1%
			118	80.3%
	Comfortable vision while night driving	0.0125	165	90.2%
			129	80.2%

As shown in Table 10, about 165 subjects per arm will be required to achieve a statistical power of 90% for all primary and secondary endpoints, assuming a 20% difference in the proportion of subjects endorsing T2B between the Test group and the Control group. Therefore, the plan is to enroll approximately 360 subjects with a target of 330 to complete the study (165 per arm).

14.3. Analysis Populations

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

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

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

14.4. Level of Statistical Significance

The study-wise type I error rate will be controlled at two-sided 0.05 level using a multi-branched gatekeeping testing approach combined with the truncated Hochberg procedure. The primary endpoint (end of day comfort) will be tested at the two-sided type I error rate of 0.05. The primary endpoint will serve as a gatekeeper for the first two secondary endpoints (digital device use and comfort throughout the day), and t two secondary endpoints will gatekeep the last secondary endpoint.

If the primary hypothesis is met, the first two secondary endpoints will be tested using the truncated Hochberg procedure (Dmitrienko et al., 2008; Dmitrienko et al., 2011).[10,11] A truncated version of the Hochberg procedure with a prespecified truncation fraction ($0 \leq f < 1$), which is separable, needs to be used within the family of the first two secondary endpoints for a positive alpha to be carried over to the last secondary endpoint if at least one null

hypothesis is rejected. According to the truncated Hochberg procedure with a truncation fraction of $f = \frac{1}{2}$, the larger p-value obtained from these two secondary tests will be compared to the endpoint-specific alpha level 0.0375, and the smaller p-value will be compared to the endpoint-specific alpha level 0.025.

- If the secondary test with the larger p-value is successful and the one with the smaller p-value is not successful, then alpha of 0.025 passes to the last secondary endpoint (comfortable vision while night driving).
- If the secondary test with the smaller p-value is successful and the one with the larger p-value is not successful, then alpha of 0.0125 passes to the last secondary endpoint.
- If both secondary tests are successful, the unused alpha available for testing the last secondary endpoint will be 0.05.
- If both secondary endpoints fail to show superiority, the last secondary endpoint cannot be tested.

14.5. Primary Analyses

The primary analysis will be conducted on the Intent-to-Treat (ITT) population with observed cases (use only available datapoints and no imputation for missing data).

End of Day Comfort

End of Day Comfort will be measured using the individual item "Comfort at the End of the Day" at 2-week follow-up. Item responses will be converted into a binary variable for the purpose of analysis (Very Satisfied or Satisfied = 1 and others = 0). The dichotomized item responses will be analyzed using a generalized linear mixed model with a binomial distribution and the logit as the link function. The model will include lens type as a fixed effect and site as a (G-side) random effect. Other subject characteristics such as age, gender, race, iris category, habitual lens type will be included as fixed effects when appropriate.

Hypothesis Testing

The null and alternative hypotheses for testing superiority of the Test lens relative to the Control lens with respect to end of day comfort are as follows:

$$H_0: OR \leq 1$$
$$H_A: OR > 1$$

Where OR represents the odds ratio of having "Very Satisfied" or "Satisfied" rating for the Test lens compared to the Control at the 2-week follow-up. Comparisons between Test and Control will be carried out using the 95% confidence interval (CI) constructed for the odds ratio (Test over Control). Superiority will be declared if the lower bound of the 2-sided 95% confidence interval is above 1.

14.6. Secondary Analyses

Secondary analyses will be conducted on the Intent-to-Treat (ITT) population with observed cases (use only available datapoints and no imputation for missing data).

All secondary endpoints will be analyzed separately using the same model as described for the primary endpoint. Item responses will be converted into binary variables as follows: Excellent or Very Good = 1 and others = 0 for digital device use ("Reduction in the feeling of tired eyes from using a computer or other digital device") and comfortable vision while night driving ("Ability to see comfortably while driving at night"), and Strongly Agree or Agree = 1 and others = 0 for comfort throughout the day ("I could wear these contact lenses comfortably for as long as I wanted to").

According to the testing strategy presented in section 14, if the primary hypothesis is met, the secondary endpoints will be tested as follows:

- for the first two secondary endpoints (digital device use and comfort throughout the day), comparisons between Test and Control will be carried out using the corresponding adjusted two-sided CI (96.25% CI for alpha = 0.0375 or 97.5% CI for alpha = 0.025), depending on the relative magnitude of the obtained nominal p-values, constructed for the odds ratio (Test over Control) separately for each endpoint;
- for the last secondary endpoint (comfortable vision while night driving), a two-sided 95% CI (alpha = 0.05), 97.5% CI (alpha = 0.025), or 98.75% CI (alpha = 0.0125) will be estimated for odds ratio and the confidence level will be determined based on the success of the previously tested secondary endpoints.

Superiority will be declared if the lower bound of the corresponding CI is above 1.

14.7. Other Exploratory Analysis

All other exploratory endpoints will be descriptively summarized. A future planned post-hoc meta-analysis may be conducted using these endpoints.

14.8. Interim Analysis

Not applicable

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 on the primary and secondary analyses, sensitivity analysis may be conducted on the ITT population using multiple imputation methods if the proportion of subject dropout is greater than 15%. The SAS/STAT procedures PROC MI and PROC MIANALYZE will be utilized with a parametric regression method used to make at least 20 imputations.

14.10. Procedure for Reporting Deviations from Statistical Plan

The analysis will be conducted according to that specified in above sections. There are no known reasons for which it is planned to deviate from these analysis methods. If for any reason

a change is made, the change will be documented in the study report along with a justification for the change.

15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

15.1. Electronic Case Report Form/Data Collection

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

External data sources for this study include: Not Applicable.

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

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

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

15.2. Subject Record

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

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

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

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

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

15.3. Trial Registration on ClinicalTrials.gov

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

16. DATA MANAGEMENT

16.1. Access to Source Data/Document

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

16.2. Confidentiality of Information

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

16.3. Data Quality Assurance

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

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

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

16.4. Data Monitoring Committee (DMC)

Not applicable

17. CLINICAL MONITORING

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

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

18. ETHICAL AND REGULATORY ASPECTS

18.1. Study-Specific Design Considerations

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

18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, section 4 of the ICH E6(R2) guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording,

and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64th WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with section 8 of the ICH E6(R2) guidelines on Good Clinical Practice (GCP),[2] and applicable regulatory requirements.

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

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

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

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

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

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

- New information that may adversely affect the safety of the subjects or the conduct of the study
- Major protocol deviations as required by the IEC/IRB
- Report of deaths of subjects under the Investigator's care
- Notification if a new Investigator is responsible for the study at the clinical site
- Any other requirements of the IEC/IRB

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

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

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

18.4. Informed Consent

Each subject or their representative, must give written consent according to local requirements after the nature of the study has been fully explained. The consent form must be signed before performance of any study-related activity. The consent form that is used must be approved by both the Sponsor and by the reviewing IEC/IRB. The informed consent is in accordance with principles that originated in the Declaration of Helsinki,[3] current ICH GCP[2] and ISO 14155:2020[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) and other applicable personal data protection and security laws and regulations.[12,13] Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person’s related health and medical information, to properly inform the concerned persons

about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

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

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

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

19. STUDY RECORD RETENTION

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

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

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

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

20. FINANCIAL CONSIDERATIONS

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

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

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

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

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

21. PUBLICATION

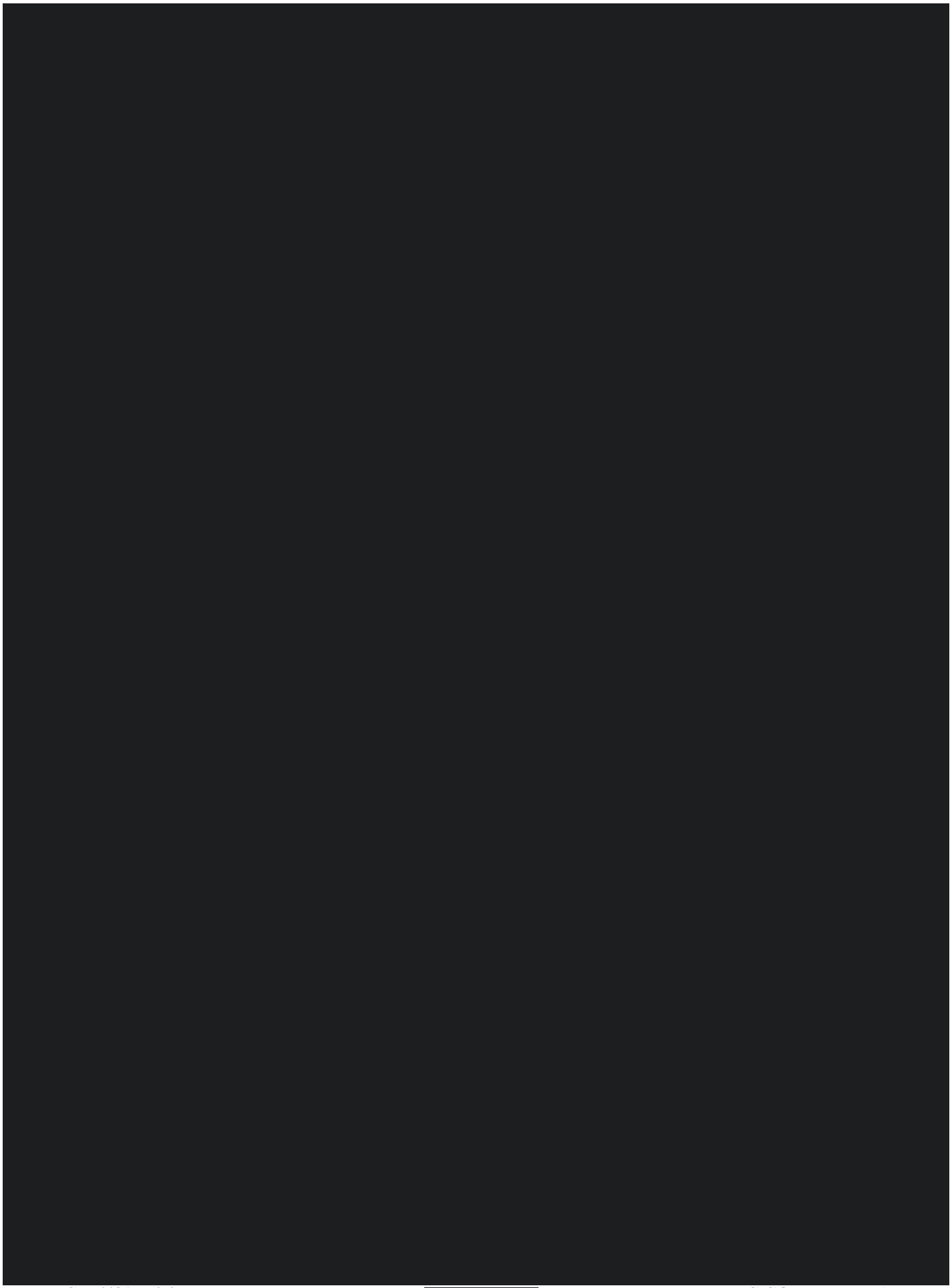
This is a multicenter study. The participating institution and Principal Investigations for this study agree that, should this study results be published, the first publication of the results of this study shall be made in conjunction with the presentation of a joint, multicenter publication of the study results with the investigators and the institutions from all appropriate sites contributing data, analyses and comments.

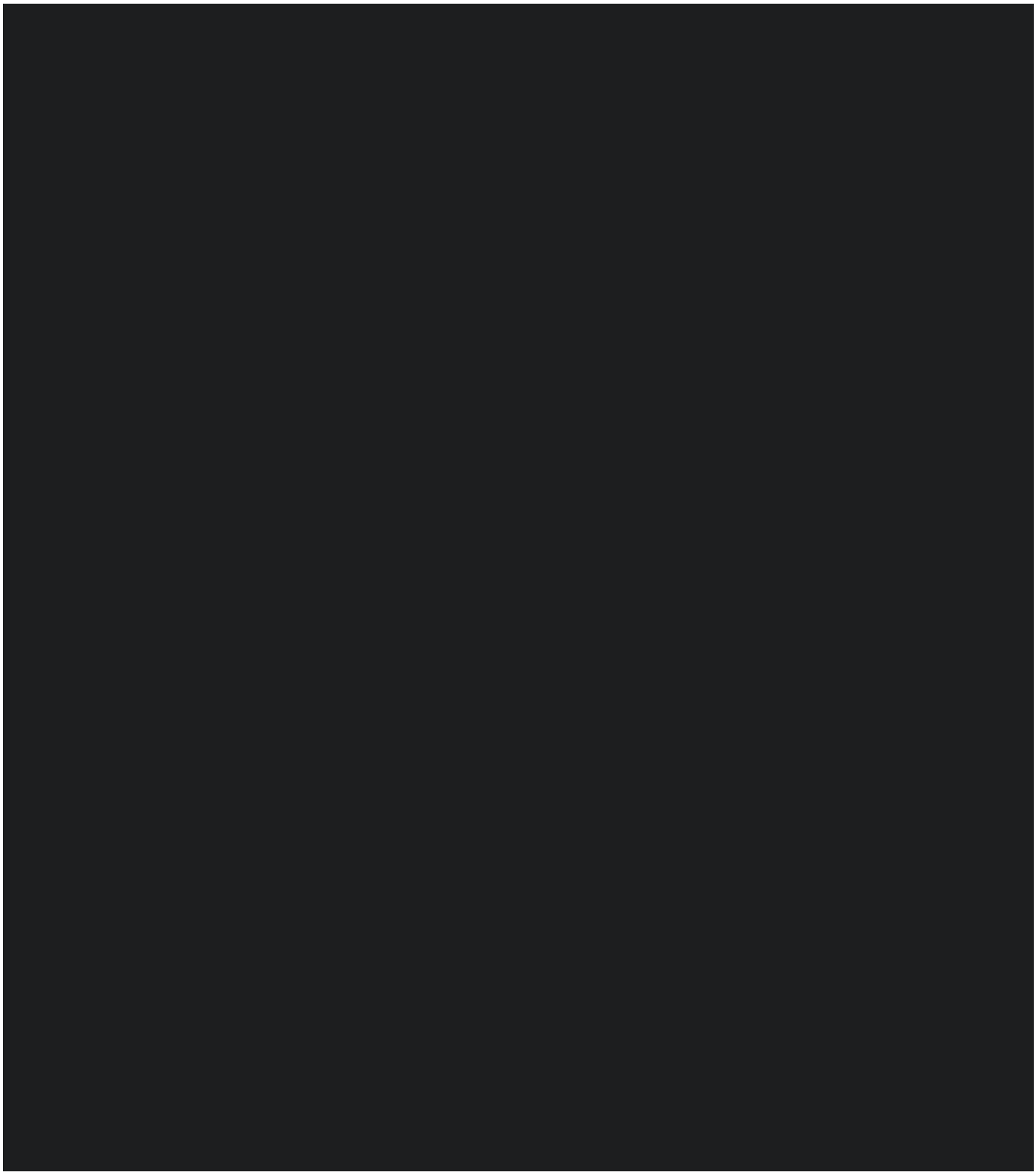
22. REFERENCES

1. ISO 14155:2020: Clinical Investigation of Medical Devices for Human Subjects — Good Clinical Practice. Available at https://www.iso.org/standard/45557.html
2. International Conference on Harmonization Good Clinical Practice E6 (ICH-GCP). Available at http://www.ich.org/products/guidelines/efficacy/article/efficacy-guidelines.html
3. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
4. United States (US) Code of Federal Regulations (CFR). . Available at https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
5. *SAS Institute Inc. 2016 SAS/STAT® 14.3 User's Guide. Cary, NC: SAS Institute Inc.*
6. Buch J. *Clinical Study Report* [redacted] *Evaluation of Prototype Lenses with Experimental UV/HEV Blocker*
7. Buch J. *Clinical Study Report* [redacted] *Vision Evaluation of Contact Lenses with new UV/HEV Filter* December 08, 2021.
8. Buch J. *Clinical Study Reports* [redacted] *Evaluation of Prototype Lenses with Experimental UV/HEV* November 11, 2021.
9. Buch J. *Clinical Study Report* [redacted] *Validation of senofilcon A with new UV/HEV Filter* January 12, 2022.
10. Dmitrienko A, Tamhane AC, Wiens BL. General Multistage Gatekeeping Procedures. *Biometrical Journal.* 2008;50(5):667-677.
11. Dmitrienko A, Kordzakhia G, Tamhane AC. Multistage and Mixture Parallel Gatekeeping Procedures in Clinical Trials. *Journal of Biopharmaceutical Statistics.* 2011;21(4):726-747.
12. Health Information Portability and Accountability Act (HIPAA). Available at https://www.hhs.gov/hipaa/for-professionals/privacy/index.html
13. Regulation (EU) 2017/745 of the European Parliament and of the Council of 5 April 2017 on medical devices. Available at http://data.europa.eu/eli/reg/2017/745/2017-05-05

APPENDIX A: PATIENT REPORTED OUTCOMES (STUDY QUESTIONNAIRES)

[redacted]





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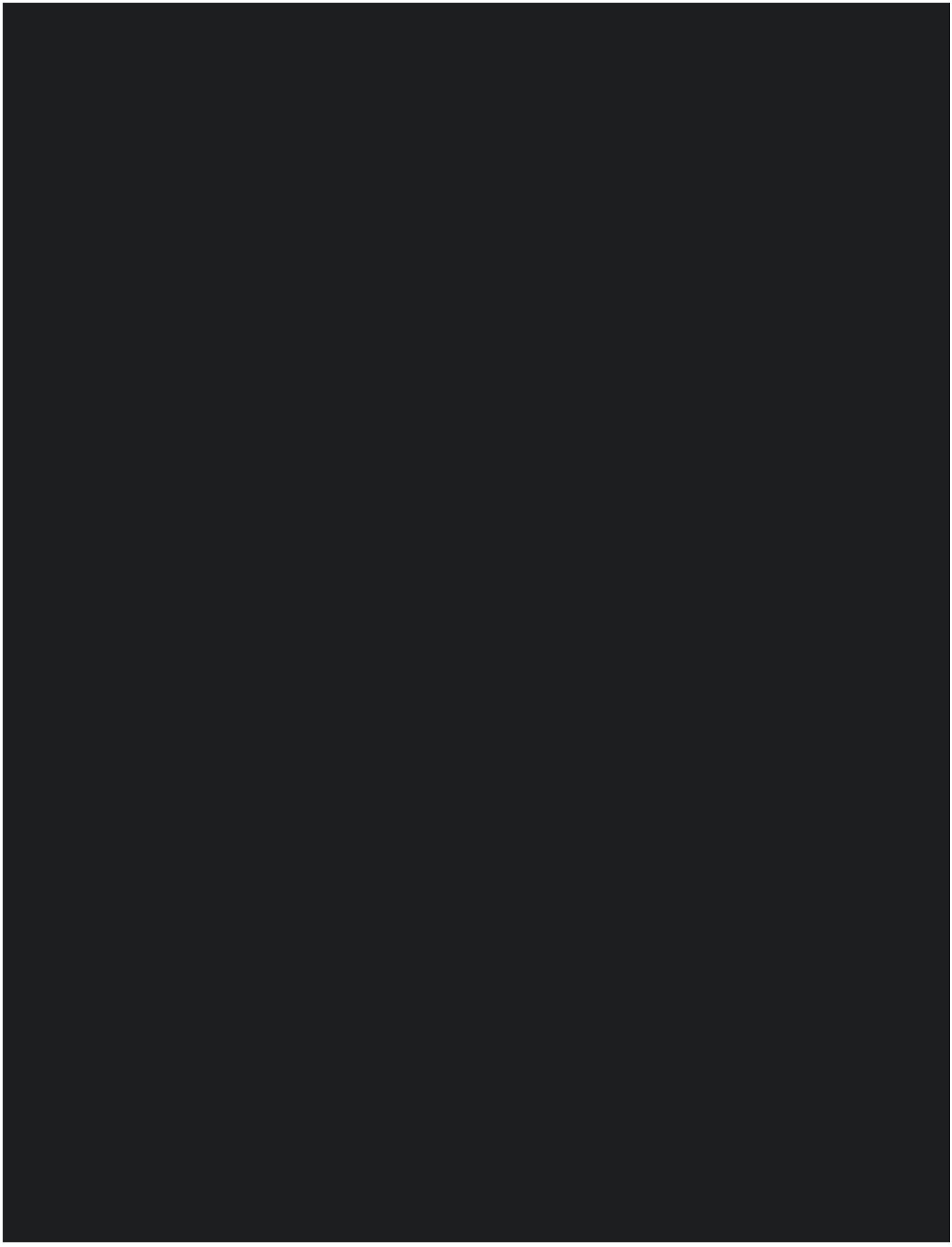

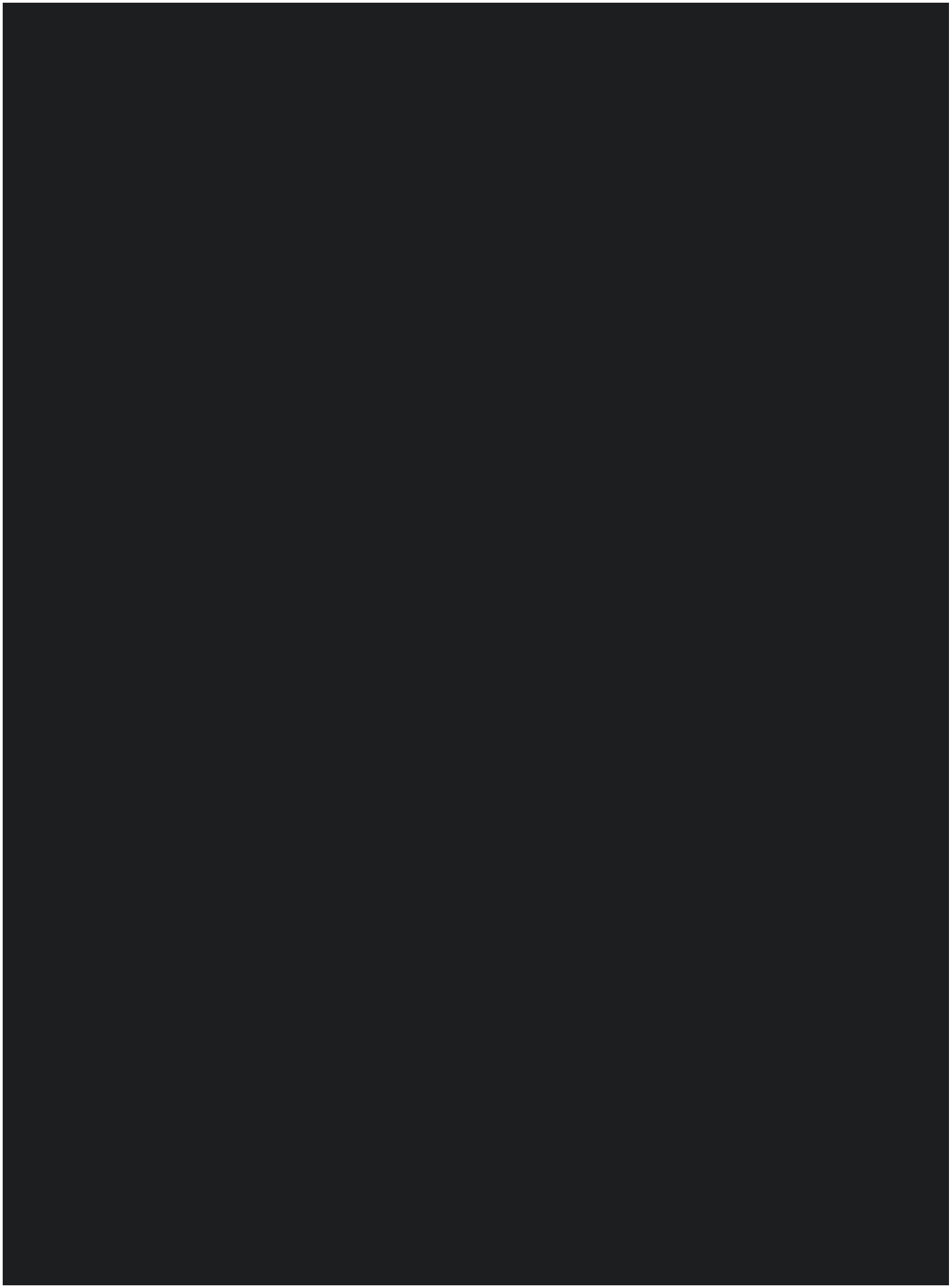

[redacted]

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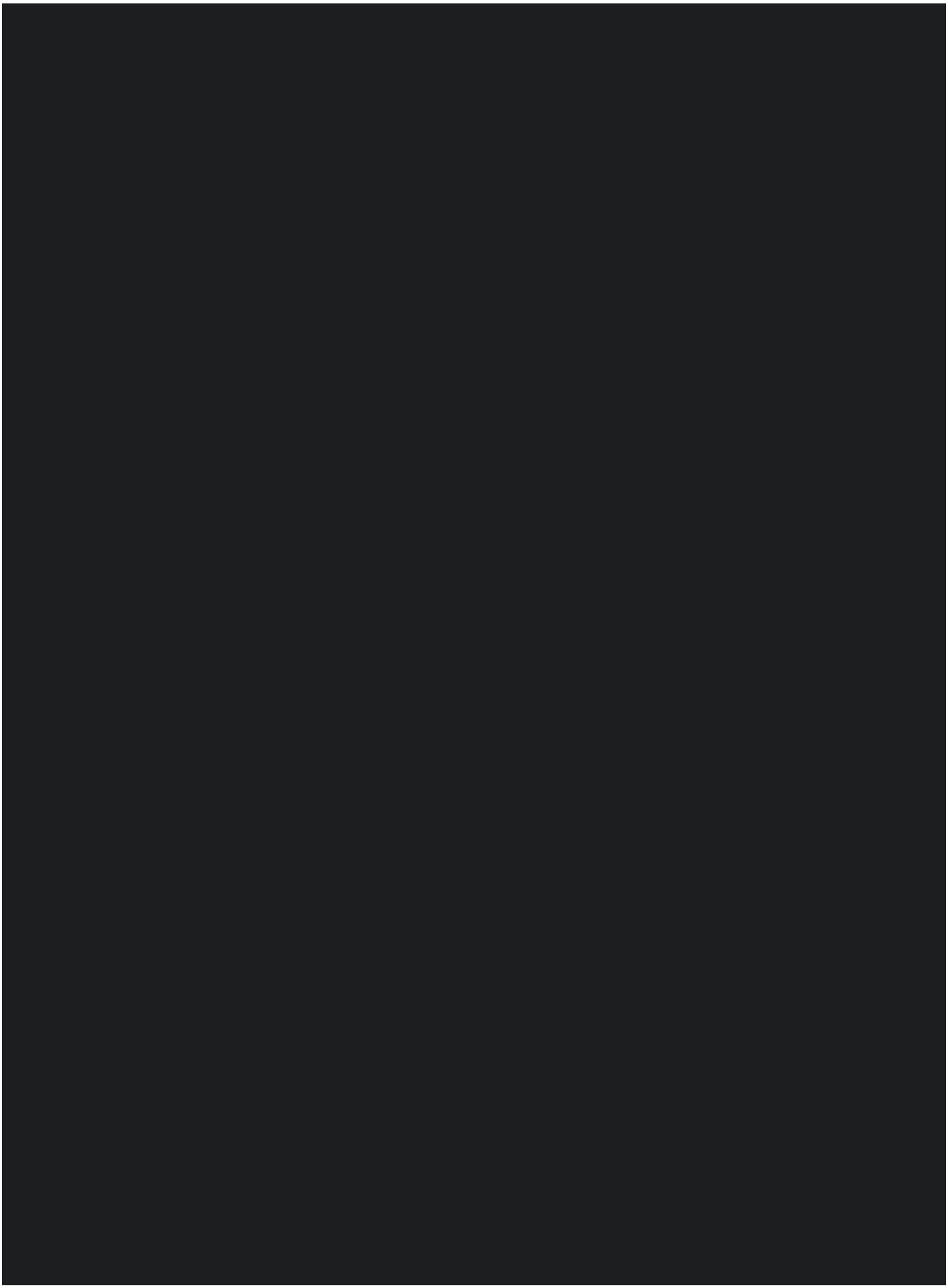

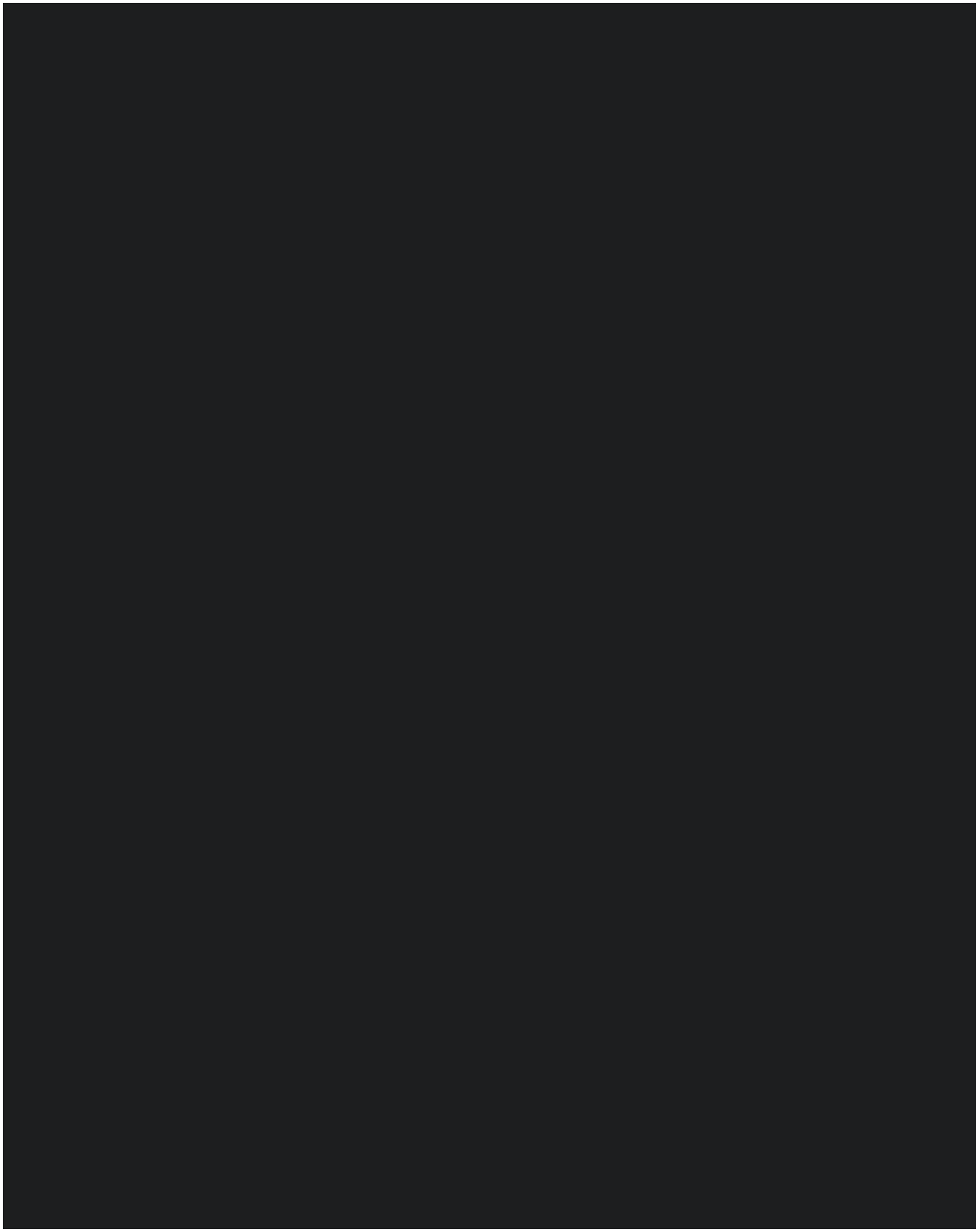

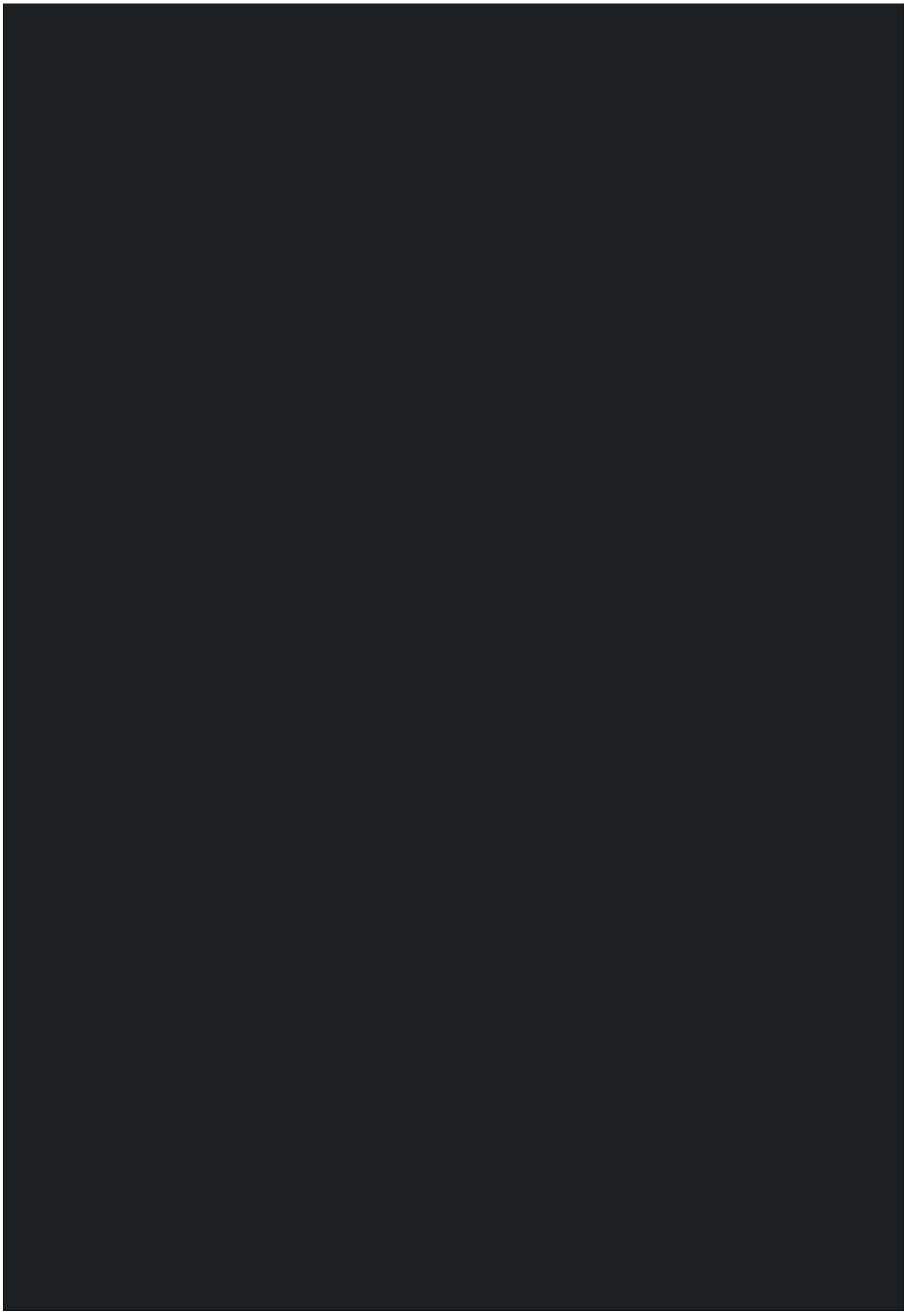

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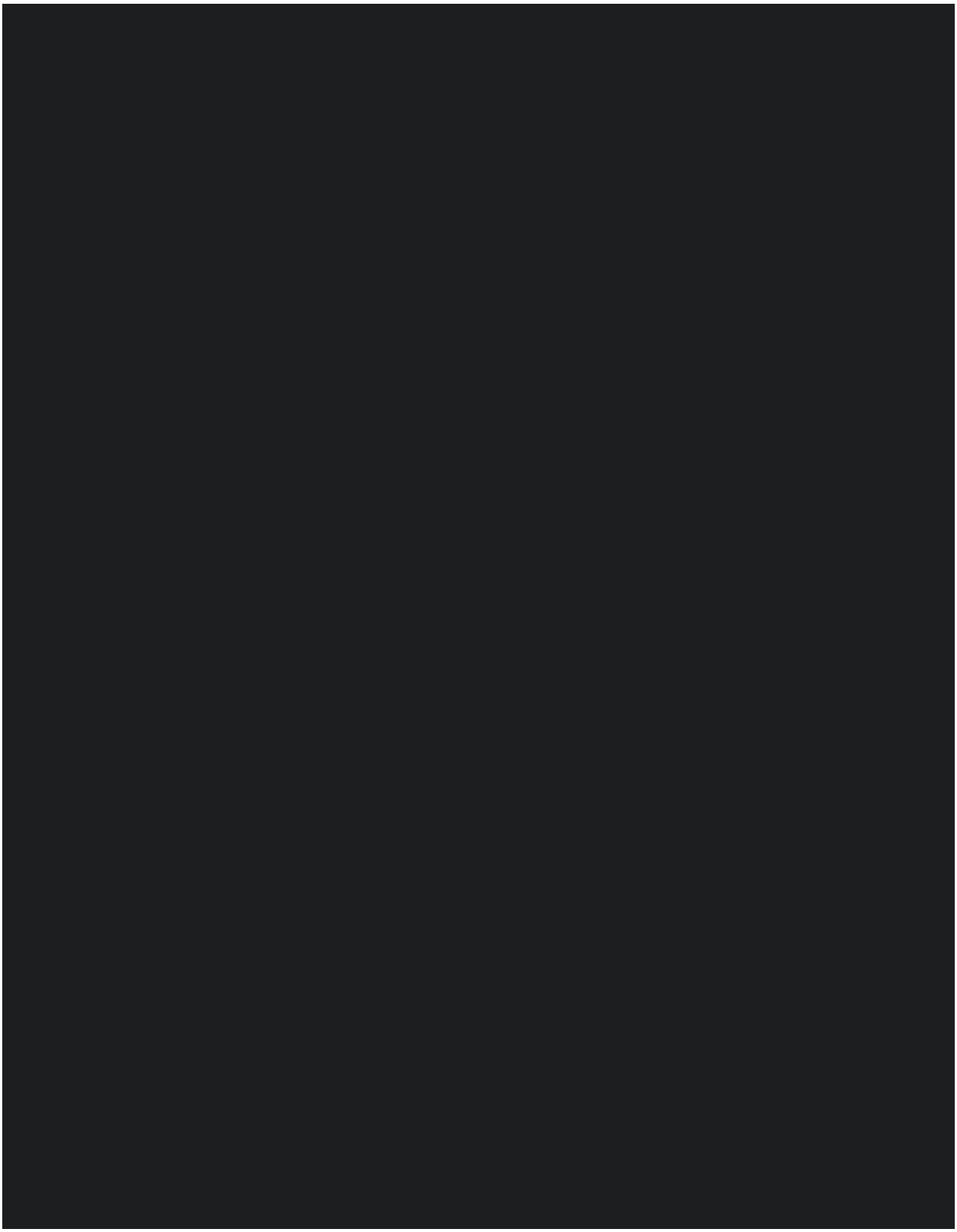


APPENDIX B: PATIENT INSTRUCTION GUIDE

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

APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

DAILIES TOTAL1®

Alcon	**DAILIES TOTAL1® and DAILIES TOTAL1® Multifocal** (delefilcon A) soft contact lenses for Daily Disposable Wear	W900236420

Important: This package insert is effective as of December 2019 and applicable to the delefilcon A contact lenses described below. Please read carefully and keep this information for future use. This package insert is intended for the eye care professional, but should be made available to patients upon request. The eye care professional should provide the patient with appropriate instructions that pertain to the patient's prescribed lenses. Copies of this package insert are available without charge from Alcon by calling Customer Service at 1-800-241-5999 or download from our website at www.alcon.com. In addition, a *Patient Instruction Booklet* is available which is recommended to be given to patients.

℞ only

CAUTION: Federal law (United States) restricts this device to sale by or on the order of a licensed eye care professional.

PRODUCT DESCRIPTION

DAILIES TOTAL1® Multifocal (delefilcon A) soft contact lenses are made from a lens material that is 33% water and 67% (delefilcon A) polymer, a silicone containing hydrogel with added phosphatidylcholine. The core lens material containing 33% water transitions through a water gradient to a hydrogel surface layer that exceeds 80% water. Lenses contain the color additive copper phthalocyanine, a light blue tint, which makes them easier to see when handling.

Lens Properties

- Refractive Index hydrated: 1.42
- Light Transmittance: 93% (@ 610 nm, -1.00 D)
- Oxygen Permeability (Dk): 140 x 10^{-11} (cm^2/sec)(ml O_2 /ml x mm Hg), measured at 35° C (intrinsic Dk-Coulometric method)
- Water Content: 33% by weight in normal saline
- Surface Water Content: ≥ 80%

Lens Parameters

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

Lens Parameters Available[1]

DAILIES TOTAL1® (delefilcon A) spherical contact lenses

- Chord Diameter: 14.1 mm
- Center Thickness: 0.09 mm @ -3.00 D (varies with power)
- Base Curve: 8.5 mm
- Powers: -0.50 to -6.00 D (0.25 D steps)
  -6.50 to -12.00 D (0.50 D steps)
  +0.50 to +6.00 D (0.25 D steps)

DAILIES TOTAL1® Multifocal (delefilcon A) contact lenses

- Chord Diameter: 14.1 mm
- Center Thickness: 0.09 mm @ -3.00 D (varies with power)
- Base Curve: 8.5 mm
- Powers: +6.00 D to -10.00 D (0.25 D steps)
  ADD: LO, MED, HI

NOTE: Hereafter, **DAILIES TOTAL1® spherical contact lenses** and **DAILIES TOTAL1® Multifocal contact lenses** will simply be referred to as delefilcon A contact lenses unless product distinction is necessary.

ACTIONS

When hydrated and placed on the cornea, **delefilcon A** contact lenses act as a refracting medium to focus light rays on the retina.

INDICATIONS (Uses)

DAILIES TOTAL1® (delefilcon A) spherical soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes with up to approximately 1.50 diopters (D) of astigmatism that does not interfere with visual acuity.

DAILIES TOTAL1® Multifocal (delefilcon A) soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) and/or presbyopia in phakic or aphakic persons with non-diseased eyes who may require a reading addition of +3.00 (D) or less and who may have up to approximately 1.50 diopters (D) of astigmatism that does not interfere with visual acuity.

The lenses are to be prescribed for single use, daily disposable wear. The lenses are not intended to be cleaned or disinfected and should be discarded after a single use.

CONTRAINDICATIONS (Reasons Not To Use)

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

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

WARNINGS

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

- Problems with contact lenses and lens care products could result in serious injury to the eye. It is essential that patients follow their eye care professional's directions and all labeling instructions for proper use of lenses and lens care products. **Serious eye problems, including corneal ulcers, can develop rapidly and lead to loss of vision.**
- Daily wear lenses are not indicated for overnight wear, and patients should be instructed not to wear lenses while sleeping. Clinical study results have shown that the risk of serious adverse reactions is increased when contact lenses are worn overnight[2].
- Studies[2] have shown that contact lens wearers who are smokers have a higher incidence of adverse reactions than nonsmokers.
- If a patient experiences eye discomfort, foreign body sensation, excessive tearing, vision changes, or redness of the eye, the patient should be instructed to immediately remove lenses and promptly contact his or her eye care professional. It is recommended that contact lens wearers see their eye care professional regularly as directed.

PRECAUTIONS

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

Special Precautions for the Eye Care Professional

Due to the small number of patients enrolled in the 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, central and peripheral thickness and optic zone diameter.

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

- Fluorescein, a yellow dye, should not be used while the lenses are on the patient's eyes. The lenses absorb this dye and become discolored. Whenever fluorescein is used, the eyes should be flushed thoroughly with sterile saline solution that is recommended for in eye use prior to inserting lenses. Avoid dispensing saline from an aerosol can directly into the eye.
- Patients who wear contact lenses to correct presbyopia may not achieve the best possible 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.
- Before leaving the eye care professional's office, the patient should be able to promptly remove their lenses or should have someone else available who can remove their lenses for them.
- Eye care professionals should instruct the patient to remove the lenses immediately if the eye becomes red or irritated.
- Routine eye examinations are necessary to help assure the continued health of the patient's eyes. Eye care professionals should make arrangements with the patient for appropriate follow-up visits. Alcon recommends that patients see their eye care professional once each year, or more often, as recommended by the eye care professional.
- Diabetics may have reduced corneal sensitivity and thus are more prone to corneal injury and do not heal as quickly or completely as non-diabetics.
- Visual changes or changes in lens tolerance may occur during pregnancy or use of oral contraceptives. Caution patients accordingly.

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

Handling Precautions

- Be sure that before leaving the eye care professional's office the patient is able to promptly remove lenses or have someone else available to remove them.
- Good hygiene habits help promote safe and comfortable lens wear. **Always wash, rinse and thoroughly dry hands with a lint-free towel before handling lenses.**
- **REMOVE A LENS IMMEDIATELY** if an eye becomes red or irritated.
- Always handle lenses carefully. Never use tweezers or other sharp objects such as fingernails to remove lenses from the lens container unless specifically indicated for that use.
- Do not use if blister package is damaged or not sealed completely. This may result in product contamination which can lead to a serious eye infection.
- Ensure that the correct lens for each eye is available. Shake the blister pack gently prior to opening. Remove the lens from the blister pack by carefully pouring the lens onto the palm of your clean hand. Ensure the lens is right side out. Inspect lenses prior to insertion. Do not insert damaged lenses.
- To insert lenses:
  - Wash and rinse hands thoroughly and dry completely with a clean, lint free towel before handling lenses.
  - Place a lens on the tip of your clean and dry right or left index finger, place the middle finger of the same hand close to lower eyelashes and pull down the lower eyelid.
  - Use the fingers of the other hand to lift the upper eyelid.
  - Place the lens directly on the eye (cornea) and gently roll finger away from the lens.
  - Look down and slowly remove the hand, releasing the lower lid.
  - Look straight ahead and slowly remove the other hand, releasing the upper lid.
  - Blink gently.
- To remove lenses:
  - Wash and rinse hands thoroughly and dry completely with a clean, lint free towel before handling lenses. **Make sure hands are clean and completely dry.**
  - Blink fully several times.
  - While looking up, slide the lens down onto the white part of the eye.
  - Remove the lens by pinching gently between the thumb and forefinger. Do not pinch the eye tissue.
  - If the lens is difficult to grasp, dry fingers once more and try again. Do not use rewetting drops in this instance.
- If a lens decenters on the eye, it may be possible to recenter it by:
  - Closing the eye and massaging the lens into place, or
  - Looking in the direction of the lens and blinking gently, or
  - Gently pushing the off-centered lens onto the cornea with light finger pressure on the edge of the upper or lower eyelid.
- If a lens tears in the eye it will feel uncomfortable. Advise wearers it is impossible to lose a contact lens or part of a contact lens behind the eye and to remain calm. Lens pieces may be removed by pinching them as for normal lens removal, carefully avoiding pinching the eye tissue. If the lens pieces do not seem to remove easily, rinsing with saline is recommended. If this does not help, the wearer should contact an eye care professional for assistance.

Lens Wearing Precautions:

- Patients should never exceed the prescribed wearing schedule regardless of how comfortable the lenses feel. Doing so may increase the risk of adverse effects.
- The lens should move freely on the eye at all times. If the lens sticks (stops moving) on the eye, follow the recommended directions in the *Care for a Sticking Lens* section. If non-movement of the lens continues, the patient should be instructed to consult their eye care professional immediately.
- The eye care professional should be consulted about wearing lenses during water sports and water related activities. Exposure to water or other non-sterile liquids while wearing

contact lenses in activities such as swimming, water skiing, and hot tubs may increase the risk of ocular infection, including but not limited to *Acanthamoeba keratitis*.
- Never allow contact lenses to come into contact with non-sterile liquids (including tap water and saliva) as microbial contamination can occur, which may lead to permanent eye damage.
- Eye irritation, infection, or lens damage may result if cosmetics, lotion, soap, cream, hair spray, deodorant, aerosol products or foreign particles come in contact with lenses.
- Environmental fumes, smoke, and vapors should be avoided in order to reduce the chance of lens contamination or physical trauma to the cornea.
- Lenses should be disposed of each day upon removal from the eye.
- Discard any lens which has become dehydrated or damaged. Replace with a sterile, fresh, new lens.
- Note the correct lens power for each eye to prevent getting them mixed up.
- Always carry spare lenses with you or have back-up spectacles available.
- Do not share lenses with anyone as this may spread micro-organisms which could result in serious eye health problems.
- Do not use lenses beyond their expiration date.

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

Who Should Know that the Patient is Wearing Contact Lenses:
- Patients should inform their health care practitioners that they are wearing contact lenses.
- Patients should inform their employers that they are wearing contact lenses. Some jobs may require the use of eye protection equipment or may require that contact lenses not be worn.

It is strongly recommended that patients be provided with a copy of the **DAILIES TOTAL1® and DAILIES TOTAL1® Multifocal** (delefilcon A) Contact Lenses *Patient Instruction Booklet* available from Alcon and understand its contents prior to dispensing the lenses.

WATER ACTIVITIES
Do not expose contact lenses to water while wearing them.
Warning:
Water can harbor microorganisms that can lead to severe infection, vision loss or blindness. If lenses have been submersed in water when showering or swimming, discard them and replace with a new pair. Ask the Eye Care Professional for recommendations about wearing lenses during any activity involving water.

ADVERSE EFFECTS
Patients should be instructed to check eyes regularly to make sure they look well, feel comfortable and vision is clear. Potentially serious complications are usually accompanied by one or more of the following signs or symptoms:
- Moderate to severe eye pain not relieved by removing the lens
- Foreign body sensation
- Excessive watering or other eye secretions including mucopurulent discharge
- Redness of the eyes
- Photophobia (light sensitivity)
- Burning, stinging or itching or other pain associated with the eyes
- Comfort is less compared to when the lens was first placed on eye
- Poor visual acuity (reduced sharpness of vision)
- Blurred vision, rainbows or halos around objects
- Feeling of dryness

WHAT TO DO IF A PROBLEM OCCURS
Patients should be instructed that if any of the above signs or symptoms are noticed, he or she should:
- **IMMEDIATELY REMOVE THE LENSES.**
- **If the discomfort or problem stops,** discard the lens and replace it with a new one.
- **If the discomfort or problem continues after removing lens(es) or upon insertion of a new lens, IMMEDIATELY remove the lens(es) and contact the eye care professional for identification of the problem and prompt treatment to avoid serious eye damage.**
- **The patient should be informed that a serious condition such as corneal ulcer, infection, corneal vascularization, or iritis may be present, and may progress rapidly. Less serious reactions such as abrasions, infiltrates, and bacterial conjunctivitis must be managed and treated carefully to avoid more serious complications.**
- Additionally, contact lens wear may be associated with ocular changes that require consideration of discontinuation or restriction of wear. These include but are not limited to local or generalized corneal edema, epithelial microcysts, epithelial staining, infiltrates, neovascularization, endothelial polymegathism, tarsal papillary changes, conjunctival injection or iritis.

ADVERSE EFFECT REPORTING
If a patient experiences any serious adverse effects associated with the use of **DAILIES TOTAL1®** brand (delefilcon A) contact lenses, please notify: Alcon Medical Safety in the USA at 1-800-757-9780.

FITTING GUIDE AND PATIENT BOOKLET
Conventional methods of fitting contact lenses apply to delefilcon A contact lenses. For a detailed description of the fitting techniques, refer to the **DAILIES TOTAL1®** and **DAILIES TOTAL1® Multifocal** (delefilcon A) Contact Lenses *Professional Fitting and Information Guide*. Both the professional fitting guide and a patient instruction booklet are available free of charge from:
Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX, USA 76134-2099
1-800-241-5999

LENS WEAR & REPLACEMENT SCHEDULES
DAILY WEAR (less than 24 hours, while awake):
- To avoid tendency of the daily wear patient to over-wear the lenses initially, stress the importance of adhering to a proper, initial wearing schedule. Normal daily wear of lenses assumes a minimum of 6 hours of non lens wear per 24 hour period.
- It may be advisable for patients who have never worn contact lenses previously to be given a wearing schedule that gradually increases wearing time over a few days. This allows more gradual adaptation of the ocular tissues to contact lens wear.
- The maximum daily wearing time should be determined by the eye care professional based upon the patient's physiological eye condition because individual responses to contact lenses vary. There may be a tendency for patients to over-wear the lenses initially. The eye care professional should stress the importance of adhering to the initial maximum wearing schedule. Studies have not been conducted to show that delefilcon A contact lenses are safe to wear during sleep, therefore patients should be advised to remove their lenses while sleeping. Normal daily wear of lenses assumes a minimum of 6 hours of non-lens wear per 24 hour period. Optimum individual wearing schedule will vary.
- Delefilcon A contact lenses are intended to be worn once (daily disposable wear) and then discarded at the end of each wearing period. The patient should be instructed to start the next wearing period with a fresh new lens.

EMERGENCY LENS CARE
Cleaning and disinfection of daily disposable lenses is not recommended. The patient should be reminded to have replacement lenses or back-up spectacles available at all times.

CARE FOR A STICKING LENS
If the lens sticks (stops moving) or begins to dry on the eye, instruct the patient to apply several drops of a recommended lubricating solution (used in accordance with package labeling). The patient should wait until the lens begins to move freely on the eye before attempting to remove it. It is important that the patient wash and dry their hands thoroughly before removing the lens. If the lens continues to stick, the patient should IMMEDIATELY consult the eye care professional.

IN OFFICE USE OF TRIAL LENSES
Eye care professionals should educate contact lens technicians concerning proper use of trial lenses.
Each contact lens is shipped sterile in a blister pack containing phosphate buffered saline solution. Hands should be thoroughly washed and rinsed and dried with a lint-free towel prior to handling a lens. In or [redacted] he blister pack should not be opened until immediately prior to use. For fitting and diagnostic purposes lenses should be disposed of after a single use and not be re-used from patient to patient.

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 or fresh saline solution and immediately contact the eye care professional or visit a hospital emergency room without delay.

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

HOW SUPPLIED
Each lens is packaged in a foil-sealed plastic container containing phosphate buffered saline solution with approximately 0.3% of polymeric wetting agents consisting of copolymers of polyamidoamine and poly(acrylamide-acrylic) acid and is steam sterilized. The package is marked with the base curve, diameter, dioptric power (and ADD power for multifocal lenses), manufacturing lot number, date of manufacture, and expiration date.

The following may appear on the labels or cartons:

Symbol/Abbreviation	Description
Rx only	CAUTION: Federal law (United States) restricts this device to sale by or on the order of a licensed eye care professional.
	Single sterile barrier system
STERILE	Sterilized using steam
EXP	Use-by date (Expiry date)
LOT	Batch code
en	Two letter code for the language (Example shown: English)
	Do not re-use
	Do not use if blister package is damaged
DIA	Diameter
BC	Base curve
PWR	Power
L	Left
R	Right
D	Diopter (lens power)
ADD	Addition power
MAX ADD	Maximum effective addition power
LO	Low
MED	Medium
HI	High
CE	European conformity mark
	Caution
	Consult instructions for use
EC REP	Authorized representative in the European Community
	Manufacturer
	Date of manufacture
MD	Medical device
	Packaging waste license sign

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

1-800-241-5999

www.alcon.com

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

Alcon

[1] Check for actual product availability as additional parameters may be introduced over time.
[2] Schein, OD, Glynn RJ, Poggio EC, Seddon JM, Kenyon KR. The Relative Risk of Ulcerative Keratitis Among Users of Daily Wear and Extended Wear Soft Contact lenses. *N Eng J Med*. 1989; 321 (12):773-783.

APPENDIX D: [redacted]

[redacted]
Lens Fitting Characteristics
Subject Reported Ocular Symptoms/Problems
Front and Back Surface Lens Deposit Grading Procedure
Determination of Distance Spherocylindrical Refractive Error
Biomicroscopy Scale
Distance and Near Snellen Visual Acuity Evaluation
Patient Reported Outcomes
White Light Lens Surface Wettability

[redacted] LENS FITTING CHARACTERISTICS

[redacted]

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS

[redacted]

[redacted] FRONT AND BACK SURFACE LENS DEPOSIT GRADING PROCEDURE

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIVE ERROR

[redacted]

[redacted]

[redacted]

[redacted]

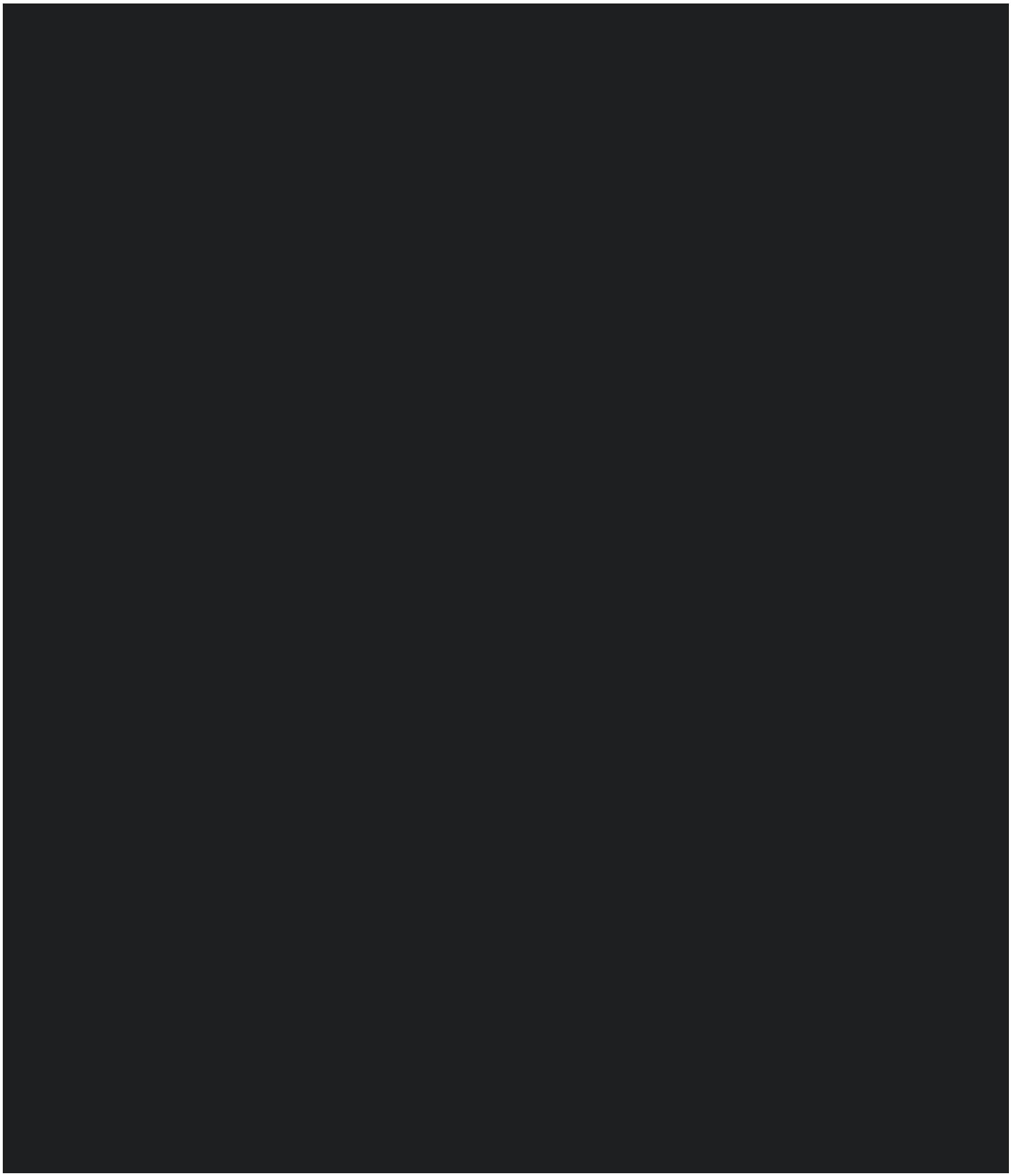
[redacted]

[redacted] **BIOMICROSCOPY SCALE**

[redacted]

[redacted]

[redacted]



[redacted]

[redacted] DISTANCE AND NEAR SNELLEN VISUAL ACUITY EVALUATION

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] PATIENT REPORTED OUTCOMES

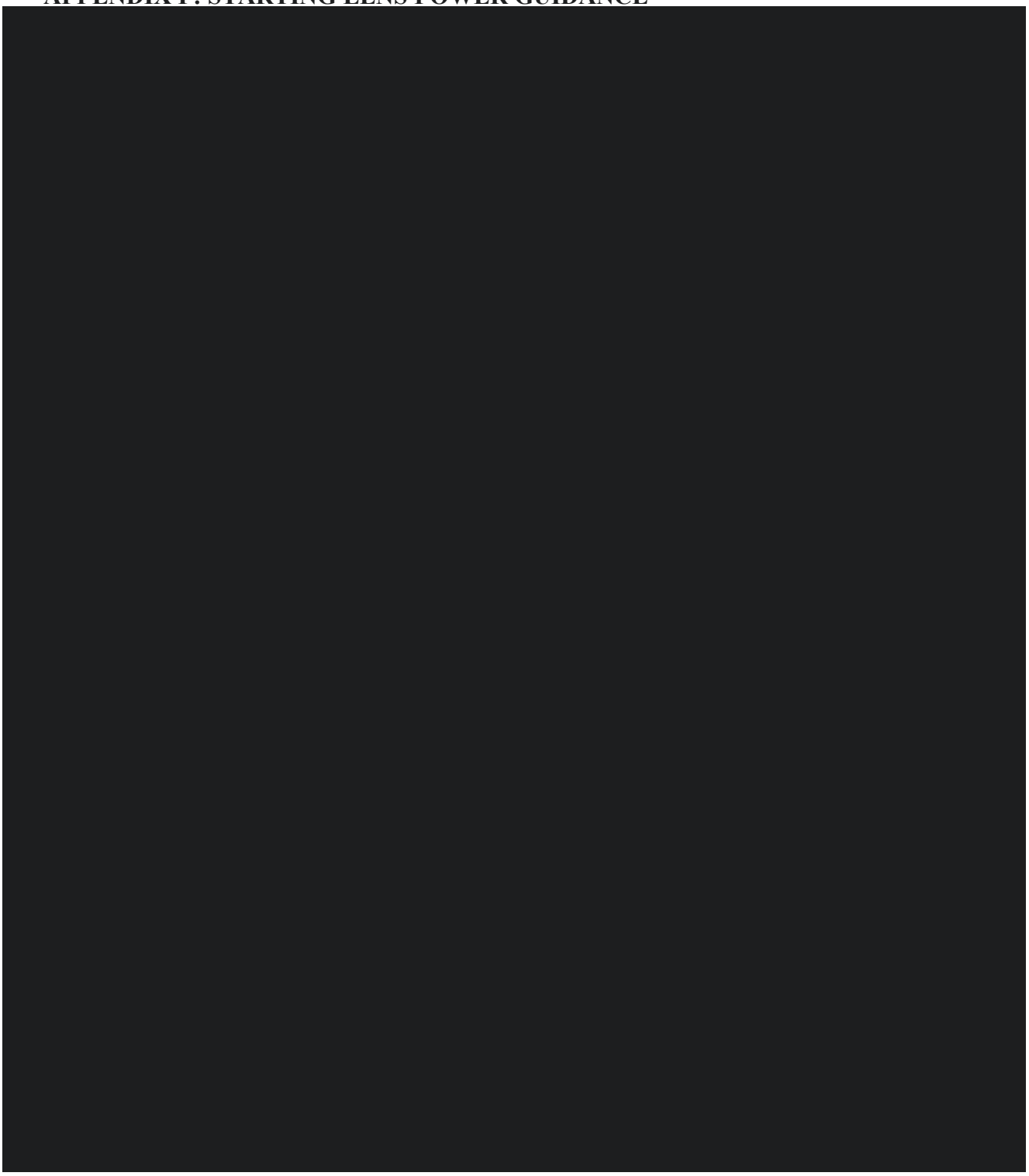
[redacted]

[redacted] WHITE LIGHT LENS SURFACE WETTABILITY

[redacted]

APPENDIX E: IRIS COLOR SCALE

APPENDIX F: STARTING LENS POWER GUIDANCE



APPENDIX G: GUIDELINES FOR COVID-19 RISK MITIGATION

1.0 PURPOSE

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

2.0 SCOPE

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

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

3.0 DEFINITIONS

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

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

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

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

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

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

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

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

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

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

4.0 GUIDANCE FOR STUDY DOCUMENTS

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

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

4.1 Additional Risks Related to the COVID-19 Pandemic:

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

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

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

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

4.1.1 Informed Consent:

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

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

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

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

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

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

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

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

4.1.3 Protocol Compliance Investigator(s) Signature Page:

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

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

4.1.4 Study Site Initiation Training Slides:

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

5.0 GUIDANCE FOR REMOTE SUBJECT VISITS

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

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

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

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

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

6.0 STUDY CONDUCT DURING PANDEMIC

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

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

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

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

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

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

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

6.1 Monitoring Visits

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

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

6.1.1 Study Site Initiation:

During the period that this Work Instruction is in effect, Site Initiation Meetings and training of study site staff will be conducted remotely. The JJVCI study team will conduct training via Skype, Zoom, Microsoft Teams or similar software as well as utilize online training materials, as applicable. Study site training will be documented utilizing Site Initiation Report (Form Control No. [redacted]) per Study Site Initiation (Form Control No. [redacted]).

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

6.1.2 Interim Monitoring Visits (if applicable):

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

To ensure data integrity during the conduct of all JJVC studies, clinical study teams will follow the study specific Clinical Monitoring Plan (Form Control No. [redacted]).

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

6.1.3 Study Site Closure:

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

Attachment A: Study Site Correspondence

XXXX XX, 2020

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

Dear <<Principal Investigator>> and Study Team,

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

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

Protocol:

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

Protocol Signature Page:

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

Informed Consent:

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

COVID-19 Risk Control Checklist for Clinical Studies:

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

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

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

Please file this letter in your site file study correspondence.

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

Study Number
Site Number
Principal Investigator (PI) Name

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

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

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

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

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

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

Principal Investigator Signature and Date

RESOURCE LINKS

US Resource Links

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

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

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

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

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

OUS Resource Links

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

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

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

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

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

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

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

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

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

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

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

PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6481 Clinical performance of senofilcon A investigational lens

Version and Date: 3.0 17 March 2022

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

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

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

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

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

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

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

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

Principal Investigator: _____ _____
Signature Date

_____
Name and Professional Position (Printed)

Institution/Site: _____
Institution/Site Name

_____
Institution/Site Address