# Clinical Study Protocol
# Johnson & Johnson Vision Care, Inc.

Clinical performance of two daily disposable silicone hydrogel contact lenses ([redacted])

Protocol: CR-6495

Version: 2.0

Date: 19 August 2022

Investigational Products: Acuvue® Oasys MAX 1-Day contact lenses, Dailies Total 1 contact lenses.

Keywords: Contact lenses, daily wear, daily disposable, dispensing, senofilcon A, delefilcon A, subjective comfort, logMAR visual acuity, tear film stability.

**Statement of Compliance to protocol, GCP and applicable regulatory guidelines:**
This trial will be conducted in compliance with the protocol, ISO 14155:2020 Clinical investigation of medical devices for human subjects – Good clinical practice[1], and the Declaration of Helsinki[2], and all applicable regulatory requirements.

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## PROTOCOL TITLE, NUMBER, VERSION AND DATE

Title: Clinical performance of two daily disposable silicone hydrogel contact lenses ([redacted])
Protocol Number: CR-6495
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## SPONSOR NAME AND ADDRESS

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

## MEDICAL MONITOR

[redacted]

The Medical Monitor must be notified by the clinical institution/site by e-mail or telephone within 24 hours of learning of a Serious Adverse Event. The Medical Monitor may be contacted during business hours for adverse event questions. General study related questions should be directed towards 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[3], ISO 14155:2020[1], and the Declaration of Helsinki[2].

| | | |
|---|---|---|
| Author | [redacted] | 21st August 2022<br>DATE |
| Study Responsible Clinician | *See Electronic Signature Page*<br>[redacted] | DATE |
| Clinical Operations Manager | *See Electronic Signature Page*<br>[redacted] | DATE |
| Biostatistician | *See Electronic Signature Page*<br>[redacted] | DATE |
| Data Management | *See Electronic Signature Page*<br>[redacted] | DATE |
| Medical Safety Officer | *See Electronic Signature Report*<br>[redacted] | DATE |
| Approver | *See Electronic Signature Page*<br>[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 | 19 Jul 2022 |
| 2.0 | [redacted] | Dropped one of the Control lenses and reduced to a 2x2 crossover study | Business decision | 19 Aug 2022 |

## SYNOPSIS

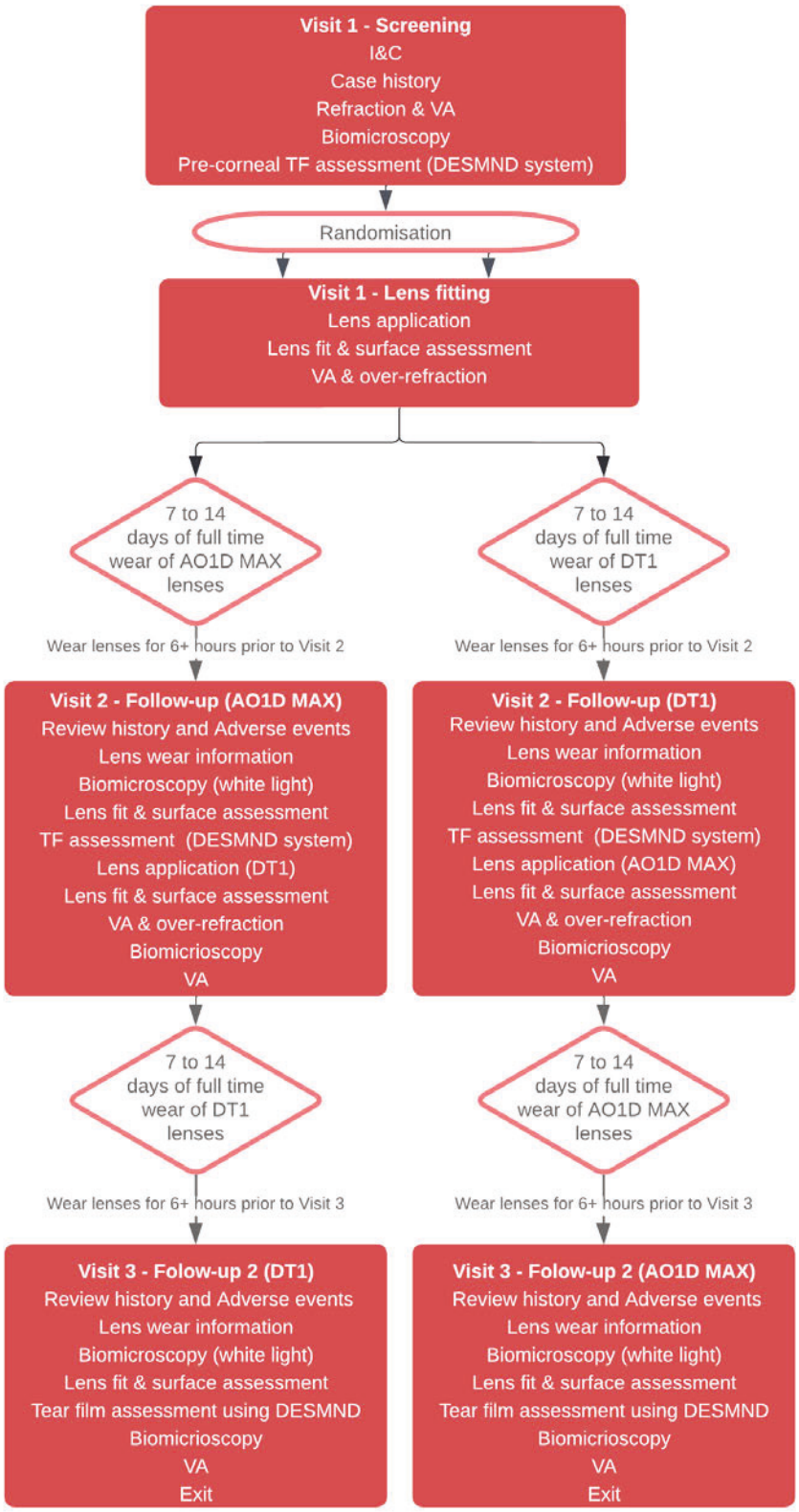
| | |
|---|---|
| Protocol Title | Clinical performance of two daily disposable silicone hydrogel contact lenses ([redacted]) |
| Sponsor | JJVC, 7500 Centurion Parkway, Jacksonville, FL 32256 |
| Clinical Phase | Clinical trial phase: Post Market<br>Development phase: Phase 4 |
| Trial Registration | This study will be registered on ClinicalTrials.gov based on the following: although the study is a pilot study of a new type of clinical measurement, it involves the use of marketed contact lenses and it is being conducted in the United Kingdom. |
| Test Article(s) | Investigational Products:<br>Acuvue® Oasys MAX 1-Day daily disposable contact lenses<br>Dailies Total 1 daily disposable contact lenses |
| Wear and Replacement Schedules | Wear Schedule: daily wear<br>Replacement Schedule: daily disposable |
| Objectives | Assess lens fit acceptance of the Acuvue® Oasys MAX 1-day contact lens and the Dailies Total 1 daily disposable contact lens. |
| Study Endpoints | Primary Endpoint(s):<br>Lens fit acceptance.<br><br>Other Exploratory Endpoint(s):<br>Slit lamp findings, tear film stability, patient reported outcomes. |
| Study Design | This is a subject-masked, randomized, bilateral, 2x2 crossover dispensing clinical investigation. Each subject will be fitted bilaterally with one test article in each of the two periods. Subjects will wear a pair of Acuvue® Oasys MAX 1-day contact lenses for 7 to 14 days and a pair of Dailies Total 1 contact lenses for 7 to 14 days in a randomized order.<br><br>There will be a total of 3 visits:<br>Visit 1: Screening, baseline evaluation, and lens fit #1.<br>Visit 2: Clinical evaluation, and lens fit #2.<br>Visit 3: Clinical evaluation, and final evaluation.<br><br>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 16 subjects will be enrolled, with recruitment ceasing once 10 subjects have successfully completed the study. |
| Study Duration | September 2022 to November 2022 |
| Anticipated Study Population | Current daily disposable contact lens wearers aged 18 to 40 with normal, healthy eyes. |

| | |
|---|---|
| Eligibility Criteria - Inclusion | Potential subjects must satisfy all of the following criteria to be enrolled in the study:<br><br>Inclusion Criteria following Screening:<br><br>1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.<br>2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.<br>3. Between 18 and 40 (inclusive) years of age at the time of screening.<br>4. They agree not to participate in other clinical research while enrolled on this study.<br>5. They have worn the same brand of soft daily disposable silicone hydrogel contact lenses at least eight hours per day for at least four days per week over the past 4 weeks.<br>6. They own a wearable pair of spectacles if needed for distance vision correction (by self-report).<br><br>Inclusion Criteria at Baseline Evaluation:<br><br>7. They can attain a best-corrected logMAR distance visual acuity of at least 0.20 in each eye.<br>8. They have spherical contact lens prescription in the range -1.00 to -6.00 DS (based on the calculated ocular refraction).<br>9. They have up to maximum of 1.00 DC of refractive astigmatism (based on the calculated ocular refraction). |
| Eligibility Criteria – Exclusion | Potential subjects who meet any of the following criteria will be excluded from participating in the study:<br><br>Exclusion Criteria following Screening:<br><br>1. Currently pregnant or lactating.<br>2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g. rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study or may pose a risk to study personnel.<br>3. They have an ocular disorder, which would normally contraindicate contact lens wear.<br>4. They have had cataract surgery.<br>5. They have had corneal refractive surgery.<br>6. They are using any topical medications such as eye drops or ointments. |

| | |
|---|---|
| | 7. Any known hypersensitivity or allergic reaction to sodium fluorescein.<br>8. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear. See section 9.1 for additional details regarding excluded systemic medications.<br>9. Participation in any contact lens or lens care product clinical trial within 2 weeks prior to study enrollment.<br>10. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).<br><br>Exclusion Criteria at Baseline Evaluation:<br><br>11. They have any corneal distortion resulting from previous hard or rigid lens wear or have keratoconus.<br>12. Any Efron Grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection).<br>13. They have a pre-corneal tear film break-up time less than five seconds when evaluated on the Digital Eye Strain Manchester Device (DESMD) tear film imaging system. |
| Disallowed Medications / Interventions | No ocular topical medications (including comfort drops) from 24 hours prior to study visits or during the wear of any study lenses.<br>No systemic medications that in the view of the investigator may affect the ocular surface or contact lens wear from 24 hours prior to study visits.<br><br>See section 9.1 for details regarding disallowed systemic medications. |
| Measurements and Procedures | Assessment of acceptable fit rate. Assessment of tear film stability using the DESMD tear film analysis system, slit lamp biomicroscopy, logMAR visual acuity assessment. |
| Microbiology or Other Laboratory Testing | None. |
| Study Termination | The occurrence of one or more Unanticipated Adverse Device Effect (UADE), or any SAE where relationship to study agent cannot be ruled out, will result in stopping further dispensing investigational product. In the event of a UADE or SAE, the Sponsor Medical Monitor may unmask the treatment regimen of subject(s) and may discuss this with the Principal Investigator before any further subjects are enrolled. |
| Ancillary Supplies/ Study-Specific Materials | Any Sponsor-approved saline pods and fluorescein strips |

| | |
|---|---|
| Principal Investigator(s) and Study Institution(s)/Site(s) | A full list of Principal Investigators, clinical sites, and institutions is kept separately from the Study Protocol and is included in the study Trial Master File. |

**Figure 1: Study Flowchart**



## COMMONLY USED ABBREVIATIONS AND DEFINITIONS OF TERMS

| | |
|---|---|
| ADD | Plus Power Required For Near Use |
| ADE | Adverse Device Effect |
| AE | Adverse Event/Adverse Experience |
| BCVA | Best Corrected Visual Acuity |
| BSCVA | Best Spectacle Corrected Visual Acuity |
| CFR | Code of Federal Regulations |
| COAS | Complete Ophthalmic Analysis System |
| COM | Clinical Operations Manager |
| CRA | Clinical Research Associate |
| CRF | Case Report Form |
| CRO | Contract Research Organization |
| CT | Center Thickness |
| [redacted] | [redacted] |
| CVS | Computer Vision Syndrome |
| D | Diopter |
| DES | Digital Eye Strain |
| DESMD | Digital Eye Strain Manchester Device |
| DMC | Data Monitoring Committee |
| eCRF | Electronic Case Report Form |
| EDC | Electronic Data Capture |
| ETDRS | Early Treatment Diabetic Retinopathy Study |
| FDA | Food and Drug Administration |
| GCP | Good Clinical Practice |
| HIPAA | Health Insurance Portability and Accountability Act |
| IB | Investigator's Brochure |
| ICF | Informed Consent Form |
| ICH | International Conference on Harmonization |
| IDE | Investigational Device Exemption |
| IEC | Independent Ethics Committee |
| IRB | Institutional Review Board |
| ISO | International Organization for Standardization |
| ITT | Intent-to-Treat |
| JJVC | Johnson & Johnson Vision Care, Inc. |
| LC | Limbus Center |
| LogMAR | Logarithm of Minimal Angle of Resolution |
| MOP | Manual of Procedures |
| NIH | National Institutes of Health |
| OD | Right Eye |
| OHRP | Office for Human Research Protections |
| OHSR | Office for Human Subjects Research |
| OS | Left Eye |
| OU | Both Eyes |
| PD | Protocol Deviation |
| PHI | Protected Health Information |

| | |
|---|---|
| PI | Principal Investigator |
| PIG | Patient Instruction Guide |
| PQC | Product Quality Complaint |
| PRO | Patient Reported Outcome |
| QA | Quality Assurance |
| QC | Quality Control |
| SAE | Serious Adverse Event/Serious Adverse Experience |
| SAP | Statistical Analysis Plan |
| SAS | Statistical Analysis System |
| SD | Standard Deviation |
| SOP | Standard Operating Procedure |
| UADE | Unanticipated Adverse Device Effect |
| USADE | Unanticipated Serious Adverse Device Effect |
| VA | Visual Acuity |
| DES | Digital Eye Strain |

## 1. INTRODUCTION AND BACKGROUND

Acuvue® Oasys MAX 1-Day is a new contact lens technology, which has been developed to offer improved clinical performance over existing contact lens designs. This study seeks to assess the clinical performance of this new lens type in comparison with the Dailies Total 1 contact lens. This comparison will focus on acceptable fit rates, with other clinical metrics assessed including slit lamp biomicroscopy findings and tear film stability.

### 1.1. Name and Descriptions of Investigational Products

This clinical study will evaluate two soft contact lens types: Acuvue® Oasys MAX 1-Day (JJVC) daily disposable contact lenses, and Dailies Total 1 (Alcon) daily disposable contact lenses. These lens types are CE marked. 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 CE marked contact lens products is for correcting myopia. During the study, each study lens type will be worn bilaterally in daily wear, daily disposable modality for at least 8 hours per day for a period of 7 to 14 days. No more than two days of missed lens wear are allowed on the days between fitting and follow-up.

Subjects will wear Acuvue® Oasys MAX 1-day contact lenses for 7 to 14 days and Dailies Total 1 contact lenses for 7 to 14 days in a randomized order.

### 1.3. Summary of Findings from Nonclinical Studies

Not Applicable – Marketed product only.

### 1.4. Summary of Known Risks and Benefits to Human Subjects

This study will use approved marketed products. The following risks/adverse events can be associated with the use of any marketed contact lens:

- Discomfort, pain, watering or unusual secretions of the eyes
- Redness of the eyes
- Reduced vision and sensitivity to light
- In very rare instances corneal infection, scarring or permanent loss of vision may occur

The key invasive procedures in this work and their associated risks are outlined below:

Staining of the ocular surface with sodium fluorescein

- Some temporary discomfort on application
- Very rarely, anaphylaxis with topical application

There is no direct benefit to the subjects enrolled other than being able to try lens types that they have not had the opportunity to try before. The information obtained from this study may aid in the development of improved contact lenses in the future.
In order to minimize the likelihood of adverse events, subjects will undergo an ocular examination before and after the clinical investigations. Subjects will also be trained on what to do if they develop ocular discomfort, redness, or reduced vision and what to do if they need to be seen outside of the Eurolens Research clinic opening hours.

For the most comprehensive risk and benefit information regarding Acuvue® Oasys MAX 1-Day, and Dailies Total 1 refer to the latest version of the package insert of the marketed products (Appendix C).

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

Acuvue® Oasys MAX 1-Day, and Dailies Total 1 are CE marked/approved and marketed products (APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT).

## 2. STUDY OBJECTIVES, ENDPOINTS AND HYPOTHESES

### 2.1. Objectives

Assess lens fit acceptance of the Acuvue® Oasys MAX 1-day contact lens and the Dailies Total 1 daily disposable contact lens.

### 2.2. Endpoints

**Primary Endpoint(s):**
Lens Fit Acceptance
Lens fit acceptance will be assessed at dispensing and follow-up visits for each subject eye. Acceptable fit is a binary response where Y=1 if lens fit is deemed acceptable by the

investigator and Y=0 otherwise. An unacceptable fit is deemed by one or more of the following criteria:

- limbal exposure at primary gaze or with extreme eye movement
- edge lift
- excessive movement with blink in primary gaze
- insufficient movement with blink in upgaze
- insufficient movement in push-up test

**Other Observations:**

Slit Lamp Findings

The slit lamp findings (biomicroscopy) will be assessed for each subject eye across all study visits (including scheduled and unscheduled visits). The Efron grading scale will be used to quantify the slit lamp observations.

Tear Film Stability

Tear film stability (tear film surface quality) will be assessed in the left eye (OS) only. The Digital Eye Strain Manchester Device (DESMD) system uses an off-axis infrared ring projection illumination system to produce a reflected mire pattern on the tear film surface. Image processing will then be used to assess tear film surface quality and calculate the tear film break-up time. Tear film break-up time will be assessed three times, with a five-minute break between measurements.

Patient Reported Outcomes

Subjective impressions of the study lenses will be assessed using the CLDEQ-8 questionnaire, and two additional questions regarding the subject's opinion of the lenses.

CLDEQ-8 is a validated patient-reported outcome measure assessing patient-experience of symptoms relating to contact lens dryness.[5] The sum of the item scores of CLDEQ-8 ranges from 0 to 37 where higher scores indicate more dryness with respect to contact lens wear.

### 2.3. Hypotheses

**Primary Hypothesis:**

Lens Fit Acceptance

Acceptable fit rate will be calculated by visit for each lens type. No statistical hypotheses will be tested.

## 3. TARGETED STUDY POPULATION

### 3.1. General Characteristics

The study population will be healthy contact lens wearers aged 18-40 years of age from a single site in the United Kingdom (UK).

### 3.2. Inclusion Criteria

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

Inclusion Criteria following Screening:

1. The subject must read, understand, and sign the STATEMENT OF INFORMED CONSENT and receive a fully executed copy of the form.
2. Appear able and willing to adhere to the instructions set forth in this clinical protocol.
3. Between 18 and 40 (inclusive) years of age at the time of screening.
4. They agree not to participate in other clinical research while enrolled on this study.
5. They have worn the same brand of soft daily disposable silicone hydrogel contact lenses at least eight hours per day for at least four days per week over the past 4 weeks.
6. They own a wearable pair of spectacles if needed for distance vision correction (by self-report).

Inclusion Criteria at Baseline Evaluation:

7. They can attain a best-corrected logMAR distance visual acuity of at least 0.20 in each eye.
8. They have spherical contact lens prescription in the range -1.00 to -6.00 DS (based on the calculated ocular refraction).
9. They have up to maximum of 1.00 DC of refractive astigmatism (based on the calculated ocular refraction).

### 3.3. Exclusion Criteria

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

Exclusion Criteria following Screening:

1. Currently pregnant or lactating.
2. Any systemic disease (e.g., Sjögren's Syndrome), allergies, infectious disease (e.g., hepatitis, tuberculosis), contagious immunosuppressive diseases (e.g., HIV), autoimmune disease (e.g., rheumatoid arthritis), or other diseases, by self-report, which are known to interfere with contact lens wear and/or participation in the study or may pose a risk to study personnel.
3. They have an ocular disorder which would normally contraindicate contact lens wear.
4. They have had cataract surgery.
5. They have had corneal refractive surgery.
6. They are using any topical medications such as eye drops or ointments.
7. Any known hypersensitivity or allergic reaction to sodium fluorescein.
8. Use of systemic medications (e.g., chronic steroid use) that are known to interfere with contact lens wear. See section 9.1 for additional details regarding excluded systemic medications.

9. Participation in any contact lens or lens care product clinical trial within 2 weeks prior to study enrollment.
10. Employee or immediate family member of an employee of clinical site (e.g., Investigator, Coordinator, Technician).

Exclusion Criteria at Baseline Evaluation:

11. They have any corneal distortion resulting from previous hard or rigid lens wear or have keratoconus.
12. Any Efron Grade 3 or greater slit lamp findings (e.g., edema, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival injection),
13. They have a pre-corneal tear film break-up time less than five seconds when evaluated on the DESMD tear film imaging system.

### 3.4. Enrollment Strategy

Study subjects will be recruited from the Eurolens Research (The University of Manchester) subject database and/or utilizing Independent Ethics Committee (IEC) or Institutional Review Board (IRB) approved materials.

## 4. STUDY DESIGN AND RATIONALE

### 4.1. Description of Study Design

This is a subject-masked, randomized, bilateral, 2x2 crossover dispensing clinical investigation.

Visit 1 – Screening/Baseline/Lens Fitting #1
Up to 16 subjects will be enrolled, with recruitment ceasing once 10 subjects have successfully completed the study.

At study Visit 1, subjects will be consented and screened for inclusion/exclusion criteria. If a subject is found to meet all eligibility criteria, they will be fitted with the first study lens based on the randomization scheme; otherwise, the subject will be discontinued from the study. The subject will then be dispensed with the study lenses to wear on a daily disposable basis for a period of 7 to 14 days.

Visit 2 - Assessment 1/Lens Fitting #2
Subjects will attend after having worn the study lenses for at least 6 hours. At this visit, DESMD tear film stability will be assessed during a period of extended eye opening (three times on the left eye only, with a 5-minute break between measurements). The second lens type will then be fitted. The subject will then be dispensed with the study lenses to wear on a daily disposable basis for a period of 7 to 14 days.

Visit 3 – Assessment 2
Subjects will attend after having worn the study lenses for at least 6 hours. At this visit, DESMD tear film stability will be assessed during a period of extended eye opening (three times on the left eye only, with a 5-minute break between measurements). Subjects will then be exited from the study.

### 4.2. Study Design Rationale

The purpose of this study is to evaluate the performance of Acuvue® Oasys MAX 1-Day daily disposable contact lenses compared to Dailies Total 1 daily disposable contact lenses. A 2×2 crossover design is used. Crossover designs are a well-established study design in which subjects are exposed to multiple treatments during different time periods. This design is cost effective and more efficient since it eliminates part of the inter-subject variability from the treatment comparisons. Subjects will be randomized into the two lens wear sequences. 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

Up to 16 subjects will be enrolled, with a target of 10 subjects successfully completing the study.

The study will last approximately 3 months. Once the informed consent has been signed the subject will be considered enrolled. Subjects who are discontinued prior to the final evaluation will be replaced. Study recruitment will cease once 10 subjects have completed all study visits.

## 5. TEST ARTICLE ALLOCATION AND MASKING

Subjects will wear Acuvue® Oasys MAX 1-day contact lenses for 7 to 14 days and Dailies Total 1 contact lenses for 7 to 14 days in a randomized order.

### 5.1. Test Article Allocation

Subjects will wear Acuvue® Oasys MAX and Dailies Total 1 sequentially in a random order. Subjects will be randomly assigned to one of the two lens wear sequences: Acuvue® Oasys MAX 1-Day/Dailies Total 1 or Dailies Total 1/Acuvue® Oasys MAX 1-Day.

The randomization scheme will be provided by the study responsible biostatistician and will be generated using the Statistical Analysis System (SAS) software Version 9.4 or higher (SAS Institute, Cary, NC).[4]

The clinical site will follow the randomization scheme provided and will complete enrollment according to the randomization list and will not pre-select or assign subjects.

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.

### 5.2. Masking

This is a single masked study where subjects are masked to the identity of the study contact lenses during the study. The investigators and technical personnel involved in the data collection may be aware of the study lenses based on a slight difference in lens color (the Test lens will be slightly more turquoise in color than the Control lens).

### 5.3. Procedures for Maintaining and Breaking the Masking

The identity of the investigational products will be masked by over labelling the contact lens blister packs with a label containing the study number and expiration date.

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.

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

When conducting the visit, the following steps should be followed to maintain randomization codes:

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

## 6. STUDY INTERVENTION

### 6.1. Identity of Test Articles

The following contact lenses will be used in this study:

Table 1: Test Articles

| | Test | Control |
|---|---|---|
| Name and Description | Acuvue® Oasys MAX 1-Day | Dailies Total 1 |
| Manufacturer | Johnson & Johnson Vision | Alcon |
| [redacted] | Marketed Product | Marketed Product |
| Lens Material | senofilcon A | delefilcon A |
| Nominal Base Curve @ 22°C | 8.5 mm | 8.5 mm |
| Nominal Diameter @ 22°C | 14.3 mm | 14.1 mm |
| Nominal Distance Powers (D) | -1.00 to -6.00 | -1.00 to -6.00 |
| Oxygen Permeability (Dk, edge corrected) | 103 | 140 |
| Wear Schedule in Current Study | Daily disposable | Daily disposable |
| Replacement Frequency | Daily | Daily |
| Packaging Form (vial, blister, etc.) | Blister | Blister |

It is estimated that if 10 subjects are enrolled and use up to 42 lenses per subject, a total of approximately 420 lenses will be used.

### 6.2. Ancillary Supplies/Products

The following solutions will be used in this study:

Table 2: Ancillary Supplies (locally sourced by research site)

| | Solution | Supplies |
|---|---|---|
| Solution Name/Description | Saline pods | Fluorescein Strips |
| Manufacturer | Any Sponsor approved manufacturer of sterile, preservative free, single use saline (0.9% w/v sodium chloride solution) | Contacare Ophthalmics and Diagnostics (or Alternative Sponsor approved product) |
| Preservative | None | None |
| Other distinguishing items (dye, packaging, approval status, etc.) | CE marked | CE marked |

### 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-labelled to mask the subjects to the identity of the lens. The test articles will be in investigational cartons sealed with a tamper evident seal as the secondary packaging form. The sample study label is shown below:

Primary Packaging:


Secondary packaging:


### 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

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 test articles may be retained by the Investigator for future JJVC research studies or disposed of at the mutual agreement of the Sponsor and Investigator.

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

[redacted]

# 7. STUDY EVALUATIONS

## 7.1. Time and Event Schedule

Table 3: Time and Events

| Visit Information | Visit 1 Screening, Baseline, Treatment 1 Lens Fitting | Visit 2 Treatment 1 Follow-up/ Treatment 2 Lens Fitting | Visit 3 Treatment 2 Follow-up |
|---|---|---|---|
| Time Point | N/A | 7 to 14 days from Visit 1 | 7 to 14 days from Visit 2 |
| Estimated Visit Duration | 2 hours | 2 hours | 1.5 hours |
| Statement of Informed Consent | x | | |
| Demographics | x | | |
| Medical History/Concomitant Medications | x | x | x |
| Habitual Contact Lens Information | x | | |
| Inclusion/Exclusion Criteria | x | | |
| Adverse event review | x | x | x |
| Subjective Sphero-Cylindrical Refraction | x | | |
| LogMAR Visual Acuity | x | x | x |
| Slit Lamp Biomicroscopy | x | x | x |
| Corneal topography | x | | |
| Lens application | x | x | |
| Over Refraction (with lenses) | x | x | |
| Lens Fit Assessment | x | x | x |
| DESMD tear film assessment | x | x | x |
| Dispense study lenses | x | x | |
| Exit LogMAR Visual acuity | x | x | x |
| Final Evaluation | | | x |

## 7.2. Detailed Study Procedures

### VISIT 1

It is preferred that subjects attend Visit 1 without their habitual contact lenses in situ. If possible, subjects should not wear lenses for 24 hours prior to the study visit in order to reduce the risk of biomicroscopy signs being a cause of ineligibility for the study.

The visit can still go ahead if the subject is wearing their habitual lenses and it can take place at any time of the working day.

| Visit 1: Screening | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.1 | Statement of Informed Consent | Each subject must read, understand, and sign the Statement of Informed Consent before being enrolled into the study. The Principal Investigator or his/her designee conducting the informed consent discussion must also sign the consent form.<br><br>**NOTE: The subject must be provided a signed copy of this document.** | |
| 1.2 | Demographics | Record the subject's date of birth, gender, race and ethnicity. | |
| 1.3 | Medical History and Concomitant Medications | Questions regarding the subjects' medical history and concomitant medications. | |
| 1.4 | Habitual Contact Lens Information | Questions regarding the subject's habitual lens type and parameters. | |
| 1.5 | Habitual Contact Lens Wear Schedule | Record the duration of wearing this contact lens type and power (number of years and months).<br>During the past 4 weeks, what is the minimum number of days per week that the subject has worn their lenses for at least 8 hours. | |
| 1.6 | Subject Information | In the subject's opinion, what is the average number of hours per day that they are looking at digital displays (eg. computer screen, phone, tablet).<br><br>In the subject's opinion, what is the average number of hours per day (while awake) that they spend in an air conditioned environment. | |

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

| Visit 1: Baseline | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.8 | Subjective Sphero-cylindrical Refraction | Subjective sphero-cylindrical refraction will be performed on both eyes. | |
| 1.9 | Entrance LogMAR Visual Acuity | Distance high contrast visual acuity will be measured OD, OS and OU with the subjective refraction in place. | Appendix E: Eurolens Research SOP # 12A |
| 1.10 | Slit Lamp Biomicroscopy | Grades will be scored to the nearest 0.1 in the best judgment of the investigator using Efron Grading Scales.<br>If any slit lamp findings are Efron Grade 3 or greater (e.g., corneal edema, corneal neovascularization, tarsal abnormalities, conjunctival injection), 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.<br><br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | Appendix F: Eurolens Research SOP # 13 |
| 1.11 | Corneal topography | Corneal topography using the Medmont topographer will be carried out on each eye. Simulated K readings (mm) will be documented. | Eurolens Research SOP # 16 |

| Visit 1: Baseline | | | |
|---|---|---|---|
| Step | Procedure | Details | |
| 1.12 | DESMD environmental conditions | Record the room temperature and humidity | Appendix G |
| 1.13 | DESMD system tear film measurements (extended eye opening) without study contact lenses | Pre-corneal tear film stability will be assessed using the DESMD system during a period of extended eye opening. Subjects will be asked to keep their left eye open for as long as they can (maximum of 30 seconds), with the subject's right eye occluded during the test. Tear film stability will be assessed on three occasions with a 5-minute break between measurements.<br><br>If the median pre-corneal tear film break-up time is less than 5 seconds, the subject is not eligible to continue in the study. | Appendix G |
| 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.<br><br>*If subject is deemed to be ineligible after baseline, proceed to Final Evaluation and complete all forms.* | |
| 1.15 | Randomization | Subjects will be randomized to follow one of two possible lens wear sequences. | |

| Visit 1: Treatment 1 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.16 | Lens application | The first assigned lens type (as per the randomization table) will be applied to each eye. The first choice lens power will be determined based on the refraction findings and contact lens history at the investigator's discretion. BVP and lot number will be recorded. If a lens is damaged, a Product Quality Complaint Form will be completed. The lens will be stored in a labeled vial with unpreserved saline and clearly differentiated from any other lenses. | |

| Visit 1: Treatment 1 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 1.17 | Lens Settling | Lenses will settle for approximately 5 minutes. | |
| 1.18 | Lens Fit Assessment | Evaluate lens centration, movement on blink, and push-up test for each eye.<br><br>An unacceptable fit is defined by one or more of the following criteria:<br>• limbal exposure at primary gaze or with extreme eye movement<br>• edge lift<br>• excessive movement with blink in primary gaze<br>• insufficient movement with blink in upgaze<br>• insufficient movement in push-up test<br><br>**Note:** if lens fit is unacceptable for either eye, the subject will be discontinued from the study. | [redacted] |
| 1.19 | LogMAR visual acuity & over-refraction, with option for lens modification | Distance high contrast visual acuity will be measured for each eye as well as binocularly before and after over-refraction.<br><br>The lens power of one or both lenses may be modified based on the over-refraction at the investigator's discretion. Up to TWO power modifications are allowed (repeat steps 1.15 to 1.18).<br><br>N.B Minimum acceptable logMAR VA is 0.20 in each eye. | Appendix E: Eurolens Research SOP # 12A |
| 1.20 | Exit LogMAR Visual Acuity | Distance high contrast visual acuity will be measured OD, OS, and OU with the study lenses in place. | Appendix E: Eurolens Research SOP # 12A |
| 1.21 | Dispensing criteria | The lens fit and VA must be acceptable in order for a subject to be dispensed lenses.<br><br>Minimum acceptable logMAR VA is 0.20 in each eye.<br><br>*If subject is discontinued, proceed to Final Evaluation and complete all forms.* | |

| Visit 1: Treatment 1 Lens Fitting | | | [redacted] |
|---|---|---|---|
| Step | Procedure | Details | |
| 1.22 | Dispense lenses | The subject will be instructed to wear the lenses on a daily disposable basis and informed that no other contact lens types should be used until the next study visit. Subjects will be instructed to try to wear the study lenses for at least 8 hours per day on the days between today's visit and the scheduled follow-up visit. No more than 2 days of missed lens wear between visits is allowed.<br><br>A patient instruction guide will be issued. Subjects should also be instructed to return any unopened lenses to the investigator at the next visit. Subjects do not need to keep any worn lenses, but are asked to keep and return any lenses which are associated with a suspected product quality issue. | |
| 1.23 | End of Visit 1 and Instructions | Subject are discharged and asked to return 7 to 14 days later for the next visit. On the day of the scheduled follow-up visit, they are asked to come to the visit wearing the study lenses, having worn them for a minimum of 6 hours that day. | |

**VISIT 2**

Subjects will be asked to attend Visit 2 after having worn the lenses for a minimum of 6 hours.

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | [redacted] |
|---|---|---|---|
| Step | Procedure | Details | |
| 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. | Contact lens wear time | On the days between visits (ie. not including the day of fitting and day of follow-up) when contact lenses were worn, what was the average wearing time and comfortable wearing time per day? | |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.3. | Compliance | Confirm compliance with the prescribed wear schedule. | |
| 2.4. | Subject Reported Ocular Symptoms | Subjects will respond to a verbal open-ended symptoms questionnaire. | [redacted] |
| 2.5. | Entrance LogMAR Visual Acuity | Distance high contrast visual acuity will be measured OD, OS, and OU with the study lenses in place | Appendix E: Eurolens Research SOP # 12A |
| 2.6. | Patient Reported Outcomes | Subjects will complete the follow-up questionnaire (CLDEQ-8, MRD). | [redacted] |
| 2.7. | Slit Lamp Biomicroscopy (white light only, with lenses in) | Grades will be scored to the nearest 0.1 in the best judgment of the investigator using Efron Grading Scales.<br>If any slit lamp findings are Efron Grade 3 or greater (e.g., corneal edema, corneal neovascularization, tarsal abnormalities, conjunctival injection) or < Efron Grade 3, which in the investigator's opinion would contraindicate contact lens wear, the subject may not continue at this time. Document any Adverse Events as appropriate.<br><br>Please note: This will not include assessment with sodium fluorescein. | Appendix F: Eurolens Research SOP # 13 |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.8. | Lens Fit Assessment | Evaluate lens centration, movement on blink, and push-up test for each eye.<br><br>An unacceptable fit is defined by one or more of the following criteria:<br>• limbal exposure at primary gaze or with extreme eye movement<br>• edge lift<br>• excessive movement with blink in primary gaze<br>• insufficient movement with blink in upgaze<br>• insufficient movement in push-up test<br><br>**Note:** if lens fit is unacceptable for either eye, the subject will be discontinued from the study. | |
| 2.9. | DESMD environmental conditions | Record the room temperature and humidity | Appendix G |
| 2.10. | DESMD system tear film measurements (extended eye opening) with study contact lenses | Pre-lens tear film stability will be assessed using the DESMD system over a period of extended eye opening. Subjects will be asked to keep their left eye open for as long as possible (maximum of 30 seconds), with the subject's right eye occluded during the test. Tear film stability (breakup time in seconds) will be assessed on three occasions with a 5-minute break between measurements. | Appendix G |
| 2.11. | Lens removal | The contact lenses will be removed. Worn lenses may be discarded if there is no associated adverse event or product quality complaint. | |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.12. | Slit Lamp Biomicroscopy | Grades will be scored to the nearest 0.1 in the best judgment of the investigator using Efron Grading Scales.<br>If any slit lamp findings are Efron Grade 3 or greater (e.g., corneal edema, corneal neovascularization, tarsal abnormalities, conjunctival injection), the visit may not continue at this time, but may continue following the resolution of a reported Adverse Event.<br><br>If the clearance of the fluorescein needs to be expedited, preservative-free rewetting drops or saline may be instilled. | Appendix F: Eurolens Research SOP # 13 |
| 2.13. | Lens application | The second assigned lens type (as per the randomization table) will be applied to each eye. The first choice lens power will be determined based on the refraction findings and contact lens history at the investigator's discretion. BVP and lot number will be recorded. If a lens is damaged, a Product Quality Complaint Form will be completed. The lens will be stored in a labeled vial with unpreserved saline and clearly differentiated from any other lenses. | |
| 2.14. | Lens Settling | Lenses will settle for approximately 5 minutes. | |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.15. | Lens Fit Assessment | Evaluate lens centration, movement on blink, and push-up test for each eye.<br><br>An unacceptable fit is defined by one or more of the following criteria:<br>• limbal exposure at primary gaze or with extreme eye movement<br>• edge lift<br>• excessive movement with blink in primary gaze<br>• insufficient movement with blink in upgaze<br>• insufficient movement in push-up test<br><br>**Note:** if lens fit is unacceptable for either eye, the subject will be discontinued from the study. | |
| 2.16. | LogMAR visual acuity & over-refraction, with option for lens modification | Distance high contrast visual acuity will be measured for each eye as well as binocularly before and after over-refraction.<br><br>The lens power of one or both lenses may be modified based on the over-refraction at the investigator's discretion. Up to TWO power modifications are allowed (repeat steps 2.13 to 2.16).<br><br>N.B Minimum acceptable logMAR VA is 0.20 in each eye. | Appendix E: Eurolens Research SOP # 12A |
| 2.17. | Exit LogMAR Visual Acuity | Distance high contrast visual acuity will be measured OD, OS, and OU with the study lenses in place. | Appendix E: Eurolens Research SOP # 12A |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.18. | Dispensing criteria | The lens fit and VA must be acceptable in order for a subject to be dispensed lenses.<br><br>Minimum acceptable logMAR VA is 0.20 in each eye.<br><br>*If subject is discontinued, proceed to Final Evaluation and complete all forms.* | |
| 2.19. | Dispense lenses | The subject will be instructed to wear the lenses on a daily disposable basis and informed that no other contact lens types should be used until the next study visit. Subjects will be instructed to try to wear the study lenses for at least 8 hours per day on the days between today's visit and the scheduled follow-up visit. No more than 2 days of missed lens wear between visits is allowed.<br><br>A patient instruction guide will be issued. Subjects should also be instructed to return any unopened lenses to the investigator at the next visit. Subjects do not need to keep any worn lenses, but are asked to keep and return any lenses which are associated with a suspected product quality issue. | |

| Visit 2: Treatment 1 Follow-Up / Treatment 2 Lens Fitting | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 2.20. | End of Visit 2 and Instructions | Subject is discharged and asked to return 7 to 14 days later for the next visit. On the day of the scheduled follow-up visit, they are asked to come to the visit wearing the study lenses, having worn them for a minimum of 6 hours that day.<br><br>Subject is asked to bring their spectacles or contact lenses with them to the next scheduled visit, as these will be used for exit acuity. | |

**VISIT 3**

Subjects will be asked to attend Visit 3 after having worn the study lenses for a minimum of 6 hours.

| Visit 3: Treatment 2 Follow-Up | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.1. | Adverse Events and Concomitant Medications Review | Review any changes to the subject's medical history or concomitant medications from the previous study visit. Record any changes and any adverse events. | |
| 3.2. | Contact lens wear time | On the days between visits (ie. not including the day of fitting and day of follow-up) when contact lenses were worn, what was the average wearing time and comfortable wearing time per day? | |
| 3.3. | Compliance | Confirm compliance with the prescribed wear schedule. | |
| 3.4. | Subject Reported Ocular Symptoms | Subjects will respond to a verbal open-ended symptoms questionnaire. | [redacted] |
| 3.5. | Entrance LogMAR Visual Acuity | Distance high contrast visual acuity will be measured OD, OS, and OU with the study lenses in place | Appendix E: Eurolens Research SOP # 12A |
| 3.6. | Patient Reported Outcomes | Subjects will complete the follow-up questionnaire (CLDEQ-8, MRD).. | [redacted] |

| Visit 3: Treatment 2 Follow-Up | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.7. | Slit Lamp Biomicroscopy (white light only, with lenses in) | Grades will be scored to the nearest 0.1 in the best judgment of the investigator using Efron Grading Scales.<br>If any slit lamp findings are Efron Grade 3 or greater (e.g., corneal edema, corneal neovascularization, tarsal abnormalities, conjunctival injection) or < Efron Grade 3, which in the investigator's opinion would contraindicate contact lens wear, the subject may not continue at this time. Document any Adverse Events as appropriate.<br><br>Please note: This will not include assessment with sodium fluorescein. | Appendix F: Eurolens Research SOP # 13 |
| 3.8. | Lens Fit Assessment | Evaluate lens centration, movement on blink, and push-up test for each eye.<br><br>An unacceptable fit is defined by one or more of the following criteria:<br>• limbal exposure at primary gaze or with extreme eye movement<br>• edge lift<br>• excessive movement with blink in primary gaze<br>• insufficient movement with blink in upgaze<br>• insufficient movement in push-up test<br><br>**Note:** if lens fit is unacceptable for either eye, the subject will be discontinued from the study. | [redacted] |
| 3.9. | DESMD environmental conditions | Record the room temperature and humidity | Appendix G |

| Visit 3: Treatment 2 Follow-Up | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| 3.10. | DESMD system tear film measurements (extended eye opening) with study contact lenses | Pre-lens tear film stability will be assessed using the DESMD system over a period of extended eye opening. Subjects will be asked to keep their left eye open for as long as possible (maximum of 30 seconds), with the subject's right eye occluded during the test. Tear film stability (breakup time in seconds) will be assessed on three occasions with a 5-minute break between measurements. | Appendix G |
| 3.11. | Lens removal | The contact lenses will be removed. Worn lenses may be discarded if there is no associated adverse event or product quality complaint. | |

**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 | Subjective Sphero-cylindrical Refraction | Subjective sphero-cylindrical refraction will be performed on both eyes. | [redacted] |
| F.3 | Best corrected logMAR acuity | Distance high contrast visual acuity will be measured OD, OS and OU with the subjective refraction in place. | Appendix E: Eurolens Research SOP # 12A |
| F.4 | Exit Slit Lamp Biomicroscopy | The Efron slit lamp classification will be used to grade the findings.<br><br>Adverse events will be documented and followed for significant slit lamp findings. | Appendix F: Eurolens Research SOP # 13 |

| Final Evaluation | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| F.5 | Exit Visual Acuity | Record distance high contrast LogMAR visual acuity (OD, OS, and OU) with the subject's own spectacle or contact lens correction in place. | Appendix E: Eurolens Research SOP # 12A |

### 7.3. Unscheduled Visits

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

- 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. | |

| Unscheduled Visit | | | |
|---|---|---|---|
| Step | Procedure | Details | [redacted] |
| U.4 | Entrance VA (if applicable) | Record the distance high contrast LogMAR visual acuity (OD, OS, and OU), and the type of visual correction being worn (study lenses, habitual lenses, distance spectacles or unaided). | [redacted] |
| U.5 | Subjective Sphero-cylindrical Refraction (if applicable) | Subjective sphero-cylindrical refraction will be performed on both eyes. | [redacted] |
| U.6 | Best corrected logMAR visual acuity (if applicable) | Distance high contrast visual acuity will be measured OD, OS and OU with the subjective refraction in place. | Appendix E: Eurolens Research SOP # 12A |
| U.7 | 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. | Appendix F: Eurolens Research SOP # 13 |
| U.8 | 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.9 | Exit Visual Acuity (if applicable) | Record the distance high contrast LogMAR visual acuity (OD, OS, and OU), and the type of visual correction being worn (study lenses, habitual lenses, distance spectacles or unaided). | Appendix E: Eurolens Research SOP # 12A |

**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 completed all study visits.
- Have not withdrawn/discontinued from the study for any reason described in Section 8.2.

### 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 including use of non-study lenses or not reaching the required wear times.
- Subject lost to follow-up.
- Subject no longer meets eligibility criteria (e.g. the subject becomes pregnant).
- Subject develops significant or serious adverse events causing discontinuation of study lens wear (more than 7 days).
- Subjects who have experienced a Corneal Infiltrative Event (CIE).
- Investigator's clinical judgment regarding the subject safety reasons (that it is in the best interest of the subject to stop treatment).
- Subject missed two consecutive study visits.
- Subject not compliant with study lens wear schedule.
- Subject not successfully dispensed due to lack of efficacy and safety including poor vision, poor comfort, or unacceptable fit.

For discontinued subjects, the Investigator will:

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

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

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

## 9. PRE-STUDY AND CONCOMITANT INTERVENTION/MEDICATION

Concomitant medications will be documented during screening and updated during the study. Disallowed medications for this study include: any ocular topical medications (including comfort drops) and any systemic medications that in the view of the investigator may affect the ocular surface or contact lens wear from 24 hours prior to study visits.

Concomitant therapies that are disallowed include: any that the investigator feels may significantly affect contact lens wear.

### 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 medications is shown in Table 4. Subjects taking these medications on a continual, routine basis that have demonstrated successful contact lens wear for at least 6 months will generally be allowed to participate in this study. Subjects taking these medications on a routine basis but for less than 6 months will not be allowed to participate in the study.

**NOTE: That subjects taking these medications on a temporary basis (e.g., antihistamines for seasonal allergy) will be allowed to participate if the medication has sufficient time to leave the body prior to the study. This is dependent on the half-life of the drug, body weight/fat, age, genetics, liver/kidney function, and metabolism of the subject. Given these unknowns, subjects taking the medications on a temporary basis must have ceased that medication at least 2 weeks prior to signing the informed consent.**

Table 4: Disallowed systemic medications (less than 6 months of continual use).

| Class of Drug | Common Indication(s) | Common Examples |
|---|---|---|
| Estrogens* | Menopause, osteoporosis, vaginitis | Vagifem, Estrace, Climara, Vivelle-Dot, Premarin, Minivelle, etc. |
| Antihistamines** | Allergic rhinitis, sedation, hives, allergic conjunctivitis, skin allergy, itching, motion sickness | Hydroxyzine, Promethagan, Phenadoz, Vistaril, Claritin, Zyrtec, Astepro, Astelin, Optivar, Pataday, Allegra, Benadryl, etc. |
| Anticholinergics | Irritable bowel syndrome, Parkinson's disease, peptic ulcer, cystitis, nasal congestion, cold symptoms, overactive bladder, COPD | Bentyl, Spiriva, Atrovent, Hyosyne, Levsin, Symax Fastab, Symax SL, Homax SL, Cogentin, Transderm Scop, etc. |
| Beta-blockers | Hypertension, angina, heart attack, migraine, atrial fibrillation, adrenal cancer, essential tumor, glaucoma | Toprol XL, Lopressor, Tenormin, Propranolol, Timoptic, Trandate, Inderal LA, etc. |
| Psychotropics | Antipsychotic (schizophrenia, mania), antidepression, antiobsessive, antianxiety, mood stabilizer, stimulants (ADHD) | Zoloft, Celexa, Prozac, Lexapro, Effexor, Cymbalta, Ativan, Xanax, Desyrel, Wellbutrin, etc. |

| Class of Drug | Common Indication(s) | Common Examples |
|---|---|---|
| Vitamin A analogs | Cystic acne | Isotretinoin |

*Contraceptive medication not included in this category
**Antihistamines allowed if taken continuously and demonstrated successful wear while taking the medication, or if they stopped taking the medication for at least 2 weeks prior to enrollment

## 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".
Minor deviations have no substantive effect on patient safety or technical integrity of the study. They are often logistical in nature. The informed consent must also not be contradicted by the deviation.

The prescribed visit window for Visit 2 is 7 to 14 days after Visit 1, and for Visit 3 it is 7 to 14 days after Visit 2. If subjects complete Visits 2 or 3 one to six days out of window this will be categorized as a minor protocol deviation. If subjects complete Visits 2 or 3 seven or more days out of window this will be categorized as a major protocol deviation. 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.
Protocol waivers are prohibited.

## 11. STUDY TERMINATION

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

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

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

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

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

## 12. PROCEDURE FOR HANDLING PRODUCT QUALITY COMPLAINTS

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

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

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

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

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

- Date the complaint was received/recorded in the EDC System (Date of Sponsor Awareness).

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

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

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

## 13. ADVERSE EVENTS

### 13.1. Definitions and Classifications

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

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

1. Was not present prior to the study, but appeared or reappeared following initiation of the study.
2. Was present prior to the study but worsened during the study. This would include any condition resulting from concomitant illnesses, reactions to concomitant medications, or progression of disease states.
3. Pregnancy must be documented as an adverse event and must be reported to the clinical monitor and to the Sponsor immediately upon learning of the event.

**Serious Adverse Event (SAE)** – An SAE is any 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."**

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

### 13.2. Assessing Adverse Events

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

- Seriousness/Classifications (see definition in Section 13.1).
- Causality or Relatedness – i.e. the relationship between the test article, study treatment or study procedures and the adverse event (not related; unlikely related; possibly related; related - see definition in Section 13.2.1).
- Adverse Event Severity – Adverse event severity is used to assess the degree of intensity of the adverse event (mild; moderate; severe for all events - see definition in Section 13.2.2).

- Outcome – not recovered or not resolved; recovering or resolving; recovered or resolved with sequelae; recovered or resolved; death related to adverse event; unknown.
- Actions Taken – none; temporarily discontinued; permanently discontinued; other.

### 13.2.1. Causality Assessment

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

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

### 13.2.2. Severity Assessment

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

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

## 13.3. Documentation and Follow-Up of Adverse Events

The recording and documenting of adverse events (ocular and non-ocular) 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. He/she will complete the Adverse Event eCRF.

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

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

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

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

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

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

events related to the test article, study treatment, or study procedures as of the final study visit date, should be followed to resolution of the adverse event or until referral to an appropriate health care provider, as recommended by the Investigator. Non-ocular adverse events that are not related to the test article, study treatment, or study procedures may be recorded as "ongoing" without further follow-up.

## 13.4. Reporting Adverse Events

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

### 13.4.1. Reporting Adverse Events to Sponsor

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

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

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

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

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

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

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

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

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

The Sponsor will report applicable Adverse Events to the local health authorities according 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.

All data summaries and statistical analyses will be performed using the SAS software Version 9.4 or higher (SAS Institute, Cary, NC).[4] Throughout the analysis of data, the results for each subject/eye will be used when available for summarization and statistical analysis. Unscheduled visits will be summarized separately and will be excluded from the statistical analysis.

Summary tables (descriptive statistics and/or frequency tables) will be provided for all baseline variables, efficacy variables, and safety variables as appropriate. Continuous variables will be summarized with descriptive statistics (n, mean, 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

The plan is to complete 10 eligible subjects. This is an early feasibility study and no statistical hypothesis will be tested. Therefore, the sample size was not based on any empirical power analysis. Targeting 10 subjects to complete the study is considered sufficient to assess lens fit acceptance and descriptive summaries of other observations. The data collected for this study may be used to design future clinical trials.

### 14.3. 5Analysis 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 (Per-Protocol Population). Justification of excluding subjects with protocol deviations in the per-protocol population set will be documented in a memo to file.

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

### 14.4. Level of Statistical Significance

No statistical hypothesis will be tested. All planned analysis for this study will be descriptive.

### 14.5. Primary Analysis

Lens Fit Acceptance
Acceptable fit rate will be calculated by visit and lens type for the safety population. No statistical hypotheses will be tested.

### 14.6. Secondary Analysis

Not Applicable.

### 14.7. Other Exploratory Analyses

All other observations will be summarized descriptively by study lens and timepoint.

Further exploratory analysis may be conducted at the discretion of the study responsible clinician.

### 14.8. Interim Analysis

No interim analysis is planned.

### 14.9. Procedure for Handling Missing Data and Drop-Outs

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

### 14.10. Procedure for Reporting Deviations from Statistical Plan

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

## 15. DATA HANDLING AND RECORD KEEPING/ARCHIVING

### 15.1. Electronic Case Report Form/Data Collection

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

External data sources for this study
Data generated from dynamic measurements (e.g. tear film quality) will be collected on specific Microsoft Office Excel format worksheets and video files by the clinical site. At the completion of the analysis, the files will be transferred to JJVC Data Management for data archiving and analysis.
Vendor Name: Eurolens Research
Vendor Address: Carys Bannister building, Division of Pharmacy and Optometry, Faculty of Biology, Medicine and Health, The University of Manchester, Dover St, Manchester M13 9PL, England
[redacted]

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 based on the following: although the study is a pilot study of a new type of clinical measurement, it involves the use of marketed contact lenses and it is being conducted in the United Kingdom.

## 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. Only subjects who are fully able to understand the risks, benefits, and potential adverse events of the study, and provide their consent voluntarily will be enrolled.

### 18.2. Investigator Responsibility

The Principal Investigator is responsible for ensuring that the clinical study is performed in accordance with the signed agreement, the investigational plan, Section 4 of the ICH E6 guidelines on Good Clinical Practice (GCP)[2], and applicable regulatory requirements. GCP is an international ethical and scientific quality standard for designing, conducting, recording, and reporting studies that involve the participation of human subjects. Compliance with this standard provides public assurance that the rights, safety, and well-being of study subjects are protected, consistent with the principles of the Declaration of Helsinki 64$^{th}$ WMA General Assembly 2013[3] and that the clinical study data are credible. The Investigator must maintain clinical study files in accordance with Section 8 of the ICH E6 guidelines on Good Clinical Practice (GCP)[2], and applicable regulatory requirements.

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

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

- Final protocol.
- 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[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 General Data Protection Regulation[6] and other applicable personal data protection and security laws and regulations. Appropriate measures will be employed to safeguard these data, to maintain the confidentiality of the person’s related health and medical information, to properly inform the concerned persons about the collection and processing of their personal data, to grant them reasonable access to their personal data and to prevent access by unauthorized persons.

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

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

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

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

- accurate and, where necessary, kept current.

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

The subject has the right to request through the Investigator access to his/her 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 pilot study of a novel measurement of contact lens wettability. Examples of these new types of study measurements may be published, at the discretion of the study sponsor.

## 22. REFERENCES

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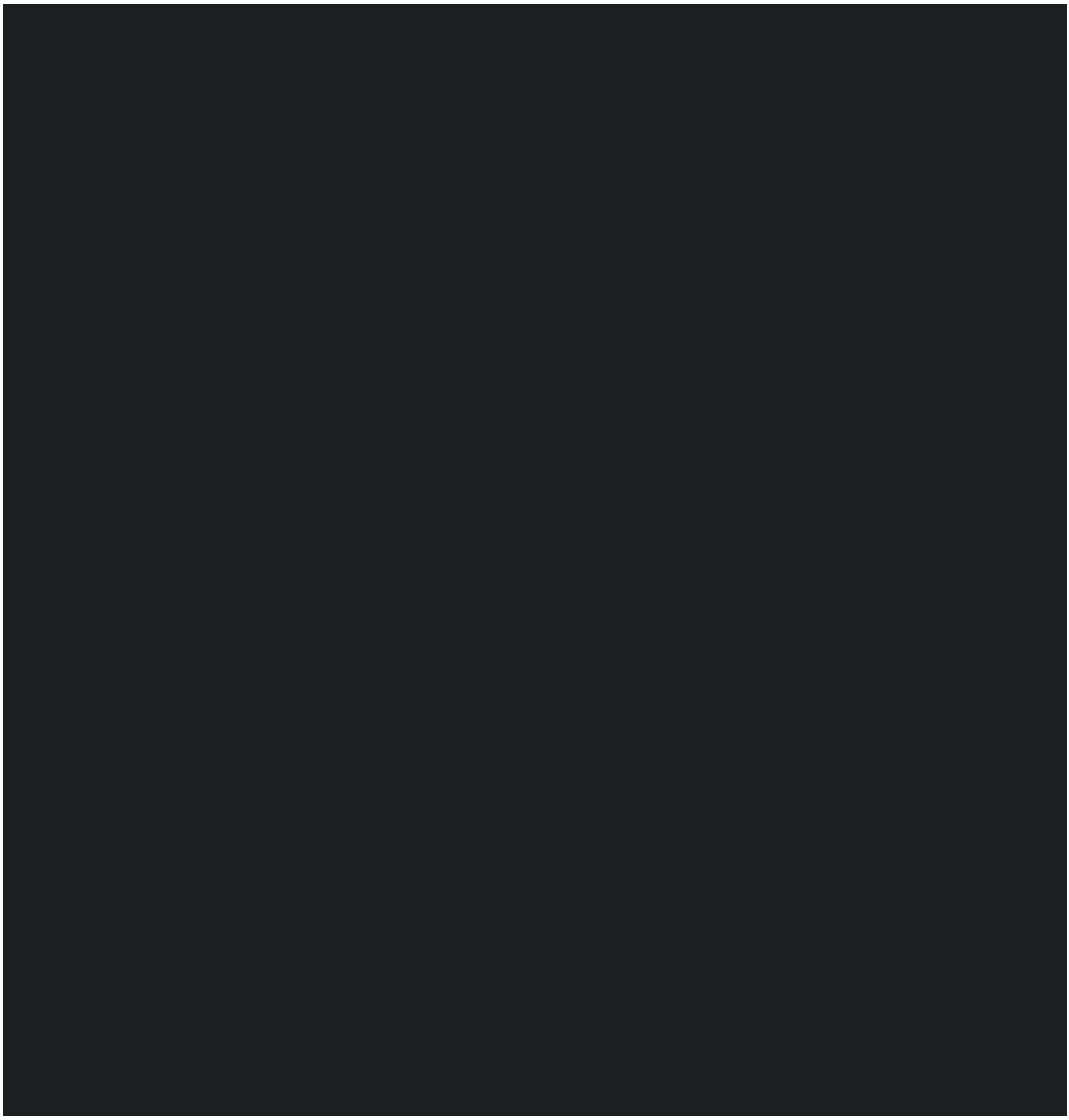
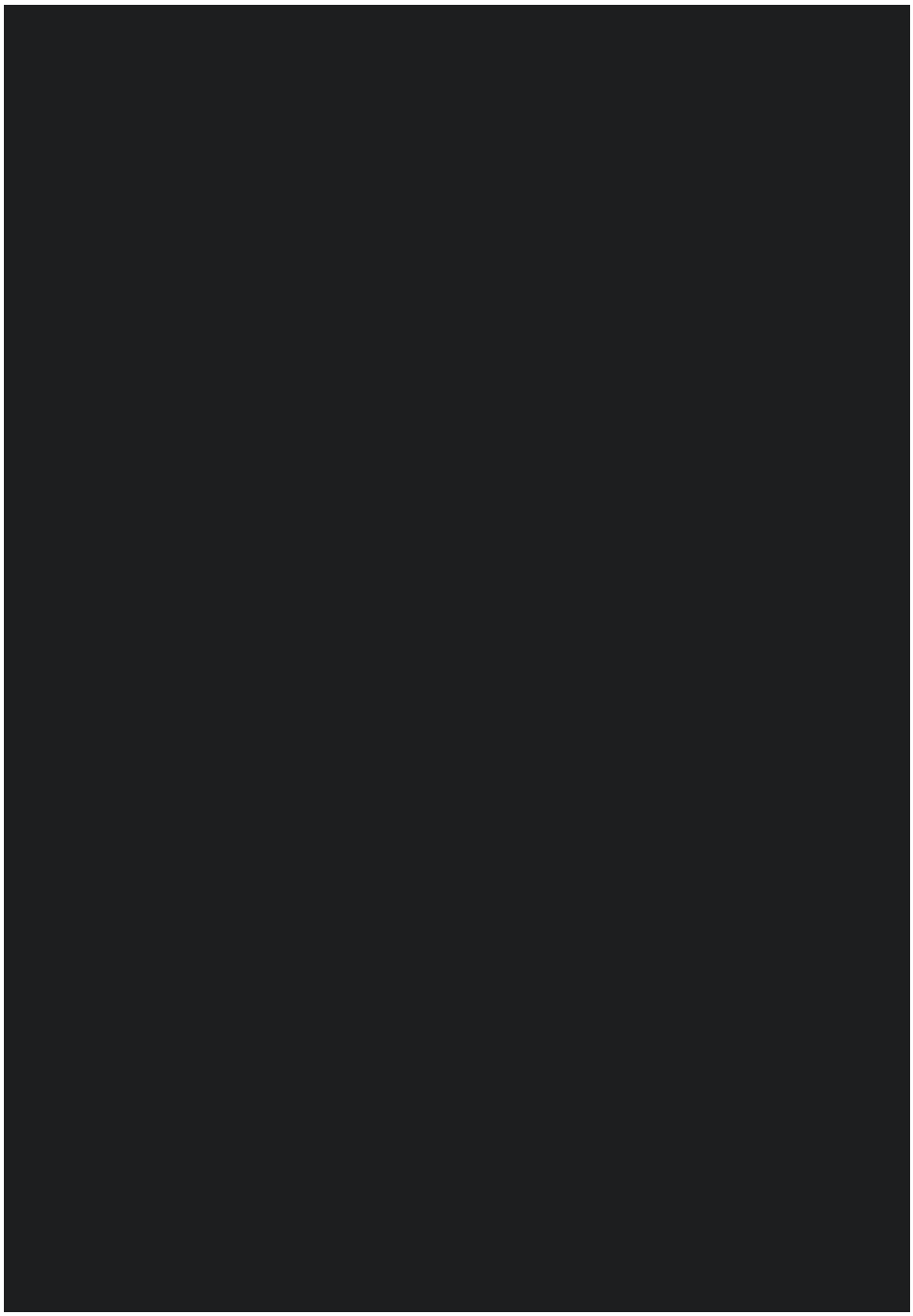
2. Declaration of Helsinki - Ethical principles for Medical Research Involving Human Subjects. Available at: https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects/
3. United States (US) Code of Federal Regulations (CFR). Available at: https://www.gpo.gov/fdsys/browse/collectionCfr.action?collectionCode=CFR
4. SAS Institute Inc: SAS® 9.4 Statements: Reference, Third Edition. Cary, NC: SAS Institute Inc; 2014.
5. Chalmers RL, Begley CG, Moody K, Hickson-Curran SB. Contact Lens Dry Eye Questionnaire-8 (CLDEQ-8) and opinion of contact lens performance. Optom Vis Sci. 2012 Oct;89(10):1435-42. doi: 10.1097/OPX.0b013e318269c90d. PMID: 22960615.
6. Data Protection Act. Available at: http://www.legislation.gov.uk/ukpga/1998/29/contents

## APPENDIX A: PATIENT REPORTED OUTCOMES





## APPENDIX B: PATIENT INSTRUCTION GUIDE

N/A

## APPENDIX C: PACKAGE INSERT (APPROVED PRODUCT)

Acuvue® Oasys MAX 1-Day / Dailies Total 1 Contact Lenses

EN

# Instructions For Use
# Daily Disposable ACUVUE® Contact Lenses

CE 2797

IN000649

**PLEASE READ CAREFULLY AND RETAIN FOR FUTURE REFERENCE. ACUVUE® CONTACT LENSES ARE MEDICAL DEVICES AND SHOULD ALWAYS BE FITTED BY AN EYE CARE PROFESSIONAL. ALWAYS FOLLOW YOUR EYE CARE PROFESSIONAL'S DIRECTIONS AND THE INSTRUCTIONS CONTAINED IN THIS LEAFLET.**

| Brand Name | Material | Packaging Solution | Wearing Schedule |
|---|---|---|---|
| 1-DAY ACUVUE® Brand Contact Lenses | etafilcon A | 1 | 1 Day |
| 1-DAY ACUVUE® MOIST Brand Contact Lenses | etafilcon A | 3 | 1 Day |
| ACUVUE® OASYS Brand Contact Lenses with HydraLuxe™ 4 | senofilcon A | 2 | 1 Day |
| 1-DAY ACUVUE® TruEye® Brand Contact Lenses 4 | narafilcon A | 2 | 1 Day |
| 1-DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® | etafilcon A | 3 | 1 Day |
| 1-DAY ACUVUE® MOIST Brand Contact Lenses for ASTIGMATISM | etafilcon A | 3 | 1 Day |
| ACUVUE® OASYS Brand Contact Lenses for ASTIGMATISM with HydraLuxe™ 4 | senofilcon A | 2 | 1 Day |
| 1-DAY ACUVUE® MOIST Brand MULTIFOCAL Contact Lenses | etafilcon A | 3 | 1 Day |
| ACUVUE® OASYS MAX 1-Day Contact Lenses 4 5 | senofilcon A | 2 | 1 Day |
| ACUVUE® OASYS MAX 1-Day MULTIFOCAL Contact Lenses 4 5 | senofilcon A | 2 | 1 Day |

Key: **Packaging Solution:** 1 Borate buffered saline 2 Borate buffered saline with methyl ether cellulose 3 Borate buffered saline with povidone. **Material content:** 4 Lens material contains silicone and meets Class 1 UV absorbing standards with transmissibility of less than 1% UVB (280-315nm) and less than 10% UVA (315-380nm) radiation. All other ACUVUE® products meet Class 2 UV absorbing standards with transmissibility of less than 5% UVB and 50% UVA radiation. 5 Lens material contains a light absorbing chromophore that reduces transmittance in the range from 380 nm to 450 nm.

Borates (boric acid & sodium borate) are defined as CMR 1B substances in a concentration above 0.1% weight by weight and are safe when the product is used according to label instructions.

Not all of the listed products might be available at your country.
Please check which product is available in your country. www.acuvue.com

## 1. PRODUCT DESCRIPTION and INTENDED USE

This leaflet refers to Daily Disposable ACUVUE® contact lenses that are intended to be worn for less than 24 hours while awake. Your Eye Care Professional should prescribe the lenses and determine your wearing schedule. Your lenses do not require cleaning or disinfection and should be discarded upon removal.

- Daily Disposable ACUVUE® Spherical Brand Contact Lenses are intended for Daily Wear for the optical correction of myopia (short-sightedness) and hyperopia (long-sightedness) in persons with healthy eyes that may have 1.00D or less of astigmatism.
- 1-DAY ACUVUE® DEFINE® Brand Contact Lenses with LACREON® are also intended to alter/enhance the appearance of the eye.
- Daily Disposable ACUVUE® Brand Contact Lenses for ASTIGMATISM are intended for Daily Wear and for the optical correction of myopia (short-sightedness) and hyperopia (long-sightedness) in persons with healthy eyes that may have astigmatism.
- Daily Disposable ACUVUE® Brand Contact Lenses for PRESBYOPIA are intended for Daily Wear for the optical correction of myopia (short-sightedness) and hyperopia (long-sightedness) in presbyopic persons with healthy eyes who have 0.75D or less of astigmatism.

DO NOT WEAR YOUR LENSES WHILE SLEEPING.

All Daily Disposable ACUVUE® contact lenses contain a UV blocker to help provide protection against transmission of harmful UV radiation to the cornea and into the eye.
**WARNING: UV ABSORBING CONTACT LENSES are not substitutes for protective UV absorbing eyewear such as UV absorbing goggles or sunglasses because they do not completely cover the eye and surrounding area. You should continue to use UV absorbing eyewear as directed.**

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

## 2. CONTRAINDICATIONS (When Not to Use)

When wearing contact lenses for REFRACTIVE AMETROPIA USE, **DO NOT USE** these lenses when any of the following conditions exist:

- Inflammation or infection in or around the eye or eyelids
- Any eye disease, injury, or abnormality that affects the cornea, conjunctiva, or eyelids
- Any previously diagnosed condition that makes contact lens wear uncomfortable
- Severe dry eye
- Reduced corneal sensitivity (corneal hypoesthesia)
- Any systemic disease that may affect the eye or may be made worse by wearing contact lenses
- Allergic reactions on the surface of the eye or surrounding tissues that may be induced or made worse by wearing contact lenses or use of contact lens solutions
- Any active eye infection (bacterial, fungal, protozoal or viral)
- If eyes become red or irritated
- Irritation of the eye caused by allergic reactions to ingredients in contact lens solutions (i.e. rewetting drops). These solutions may contain chemicals or preservatives (such as mercury, Thimerosal, etc.) to which some people may develop an allergic response.

## 3. WARNINGS - What You Should Know About Contact Lens Wear:

EYE PROBLEMS, INCLUDING CORNEAL ULCERS (ulcerative keratitis), CAN DEVELOP RAPIDLY AND LEAD TO LOSS OF VISION. IF YOU EXPERIENCE ANY OF THE FOLLOWING SYMPTOMS:

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

**YOU SHOULD IMMEDIATELY REMOVE THE LENSES, AND PROMPTLY CONTACT YOUR EYE CARE PROFESSIONAL.**

- These lenses are prescribed for daily wear and are for single use. Studies have shown that daily disposable soft contact lens wear reduces the risk of some complications including discomfort and inflammation that are associated with lens care and handling and reuse can put you at greater risk of these problems.
- Lenses prescribed for daily disposable wear, should not be worn while sleeping. Clinical studies have shown the risk of serious eye problems (i.e.: ulcerative keratitis) is increased when lenses are worn overnight.[1]
- Studies have shown that contact lens wearers who smoke have a higher rate of eye problems (ulcerative keratitis) than nonsmokers.
- Problems with contact lenses or lens care products could result in serious injury to the eye.
- Proper use and care of your contact lenses and lens care products are essential for the safe use of these products.
- The overall risk of serious eye problems (i.e.: ulcerative keratitis) may be reduced by carefully following directions for lens wear and disposal.
- **Do not** expose contact lenses to **water** while wearing them. Water can harbour microorganisms that can lead to severe infection, vision loss, or blindness. If your lenses have been submersed in water when participating in water sports or swimming in pools, hot tubs, lakes, or oceans, you should discard them and replace them with a new pair. Ask your Eye Care Professional for recommendations about wearing your lenses during any activity involving water.

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

## 4. PRECAUTIONS

- **DO NOT** use if the sterile blister package is opened or damaged or after the expiry date.
- When you first get your lenses, be sure that you are able to put the lenses on and remove them (or have someone else available who can remove the lenses for you) before leaving your EYE CARE PROFESSIONAL's office.
- **NEVER** use tweezers or other tools to remove your lenses from the lens container.
- Remember, always start with the same eye.
- Always be sure the lens is in your eye and you see clearly before commencing your removal technique.

**General Precautions:**

- Due to the small number of patients enrolled in clinical investigation of lenses, all refractive powers, design configurations, or lens parameters available in the lens material are not evaluated in significant numbers. Consequently, when selecting an appropriate lens design and parameters, the Eye Care Professional should consider all characteristics of the lens that can affect lens performance and ocular health, including oxygen permeability, wettability, central and peripheral thickness, and optic zone diameter.
- The potential impact of these factors on the patient's ocular health should be carefully weighed against the patient's need for refractive correction; therefore, the continuing ocular health of the patient and lens performance on the eye should be carefully monitored by the prescribing Eye Care Professional.
- If you wear your contact lenses to correct presbyopia using monovision or multifocal correction, you **may not** be able to get the best corrected visual acuity for either far or near vision. Visual needs are different for different people, so your Eye Care Professional should work with you when selecting the most appropriate type of lens for you.
- Eye Care Professionals should instruct the patient to remove lenses immediately if the eyes become red or irritated.
- **Always** contact your Eye Care Professional before using any medicine in your eyes.
- **Be aware** that certain medications, such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, and those for motion sickness may cause dryness of the eye, increased lens awareness (feeling of the lens in the eye), or blurred vision. Always inform your Eye Care Professional if you experience any problems with your lenses while taking such medications.
- **Be aware** that if you use oral contraceptives (birth control pills), you could develop changes in vision or comfort when wearing contact lenses.
- **Do not** change your lens type (e.g. brand name, etc.) or parameters (e.g. diameter, base curve, lens power, etc.) without consulting your Eye Care Professional.
- **Always** have a functional pair of glasses with a current prescription available to use if you become unable to wear contact lenses, or in circumstances where contact lens wear is not advised.
- As with any contact lens, follow-up visits are necessary to assure the continuing health of your eyes. Ask your Eye Care Professional about the recommended follow-up schedule.

## 5. ADVERSE REACTIONS (Side Effects) - Possible Problems and What To Do

**Be aware that problems can occur while wearing contact lenses and may be associated with the following symptoms:**

- Burning, stinging, itchy, and/or dry eyes
- Reduced lens comfort or feeling of something in your eye
- Swelling or inflammation in or around the eyes
- Eye redness
- Eyelid problems
- Watery eyes and/or unusual eye secretions
- Poor or blurred vision
- Rainbows or halos around objects
- Sensitivity to light (photophobia)
- There may be the potential for some temporary impairment due to peripheral infiltrates, peripheral corneal ulcers, and corneal erosion. There may be the potential for other physiological observations, such as local or generalized edema, corneal neovascularization, corneal staining, injection, tarsal abnormalities, iritis and conjunctivitis, some of which are clinically acceptable in low amounts.

When any of the above symptoms occur, a serious eye condition may be present. YOU SHOULD IMMEDIATELY REMOVE THE LENSES, and promptly be seen by your Eye Care Professional, so that the problem can be identified and treated, if necessary, in order to avoid serious eye damage.

**Recognizing Problems and What To Do**

You should conduct a simple 3-part self-examination at least once a day. Ask yourself:

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

If you notice any problems, you should IMMEDIATELY REMOVE YOUR LENS. If the problem or discomfort stops, discard the lens and place a new fresh lens on the eye. If after applying the new lens, the problem continues, IMMEDIATELY REMOVE THE LENS AND CONTACT YOUR EYE CARE PROFESSIONAL.

## DIRECTIONS FOR USE

**When you first get your lenses, be sure that you are able to put the lenses on and remove them (or have someone else available who can remove the lenses for you) before leaving your Eye Care Professional's office.**
**DO NOT** use if the sterile blister package is opened or damaged or after the expiry date.

**Step 1: Getting Started**

It is essential that you learn and use good hygiene in the care and handling of your new lenses. Cleanliness is the first and most important aspect of proper contact lens care. In particular, your hands should be clean, dry, and free of any soaps, lotions, or creams before you handle your lenses.

Before you start:
- **Always** wash your hands thoroughly with warm water, a mild soap, rinse carefully and dry with a clean lint-free towel before touching your lenses to reduce the chance of getting an infection.
- You should avoid the use of any soaps containing cold cream, lotion, or cosmetics before handling your lenses. These substances may come into contact with the lenses and interfere with successful wearing. It is best to put on your lenses before putting on makeup.

**Step 2: Opening the Packaging**

Always confirm the lens parameters (e.g. diameter (DIA), base curve (BC), lens power (D), etc.) printed on the multi-pack and on the individual lens package match your prescription. DO NOT use if there is a mismatch.

**Multi-pack**
Each multi-pack contains individually packaged lenses. Each lens comes in its own foil-sealed plastic package designed specifically to keep it sterile while sealed.

**Lens Package**
To open an individual lens package, follow these simple steps:
1. Shake the lens package and check to see that the lens is floating in the solution.
2. Carefully peel back the foil closure to reveal the lens.
3. Place a finger on the lens and slide the lens up the side of the bowl of the lens package until it is free of the container. Occasionally, a lens may stick to the inside surface of the foil when opened, or to the plastic package itself. This will not affect the sterility of the lens. It is still perfectly safe to use. Carefully remove and inspect the lens following the handling instructions.

**Lens Handling Tips**
- Handle your lenses with your fingertips, and be careful to avoid contact with fingernails. It is helpful to keep your fingernails short and smooth.
- After you have removed the lens from the packaging, examine it to be sure that it is a single, moist, clean lens that is free of any nicks or tears. If the lens appears damaged, DO NOT use it.

**Step 3: Placing the Lens on the Eye**

Once you have opened the lens package and examined the lens, follow these steps to apply the lens onto your eye:
1. BE SURE THE LENS IS NOT INSIDE-OUT by following one of the following procedures:
   - Place the lens on the tip of your index finger and check its profile. The lens should assume a natural, curved, bowl-like shape. If the lens edges tend to point outward, the lens is inside out.
   - Gently squeeze the lens between the thumb and forefinger. The edges should turn inward. If the lens is inside out, the edges will turn slightly outward.
   - Place the lens on the tip of your index finger and, looking up at the lens, locate the numbers 1-2-3. 1-2-3 indicates correct orientation, while a reverse of 1-2-3 indicates the lens is inside out. If the lens is inside out (reverse 1-2-3), invert the lens and locate the numbers again to confirm correct lens orientation. Note that the 1-2-3 marking is not present on all ACUVUE® lenses.
2. With the lens on your index finger, use your other hand to hold your upper eyelid so you won't blink.
3. Pull down your lower eyelid with the other fingers of your "applying" hand.
4. Look up at the ceiling and gently place the lens on the white of the lower part of your eye.
5. Slowly release your eyelid and close your eye for a moment.
6. Blink several times to centre the lens.
7. Use the same technique when applying the lens to your other eye.

There are other methods of lens placement. If the above method is difficult for you, ask your Eye Care Professional for an alternate method.

**Step 4: Centring the Lens**

A lens, which is on the cornea (clear dome at the front of the eye), will very rarely move onto the white part of the eye during wear. This, however, can occur if application and removal procedures are not performed properly. To centre a lens, follow either of these procedures:
- Close your eyelids and gently massage the lens into place through the closed lids.

**OR**

- Gently move the off-centred lens onto the cornea (centre of your eye) while the eye is open, apply light pressure - with a clean finger - on the upper or lower lid margin to maneuver the lens into place.

**Cosmetic Lenses and Visual Symptoms**
Cosmetically tinted contact lenses may let less light through than non-cosmetic lenses. Therefore, you may experience some visual symptoms while wearing them (i.e. seeing the lens pattern in your peripheral vision).

**Hazardous Conditions**
- If you use aerosol (spray) products, such as hair spray, while wearing lenses, keep your eyes closed until the spray has settled.
- **Avoid** all harmful or irritating vapours and fumes while wearing lenses.
- **Never** rinse your lenses in water from the tap. Tap water contains many impurities that can contaminate or damage your lenses and may lead to eye infection or injury.

**Water Activity**
- Do not expose your contact lenses to water while you are wearing them.

**Lubricating/Rewetting Solutions**
- Your Eye Care Professional may recommend a lubricating/rewetting solution for your use. These solutions can be used to wet (lubricate) your lenses while you are wearing them.
- **Do not** use saliva or anything other than the recommended solutions for lubricating or rewetting your lenses. Do not put lenses in your mouth.

**Sharing Lenses**
- **Never** allow anyone else to wear your lenses. Sharing lenses greatly increases the chance of eye infections.

**Adhering to the Prescribed Wearing & Replacement Schedules**
- **Never** wear your lenses beyond the amount of time recommended by your Eye Care Professional.
- **Always dispose** of your lenses as recommended by your Eye Care Professional.
- Any unused product or waste material should be disposed of in accordance with local requirements.

**REMOVING YOUR LENSES**

**CAUTION:** Always be sure the lens is on the cornea (clear dome at the front of the eye) before attempting to remove it. Determine this by covering the other eye. If vision is blurred, the lens is either on the white part of the eye or it is not on the eye at all. To locate the lens, inspect the upper area of the eye by looking down into a mirror while pulling the upper lid up. Then inspect the lower area by pulling the lower lid down.

Wash, rinse, and dry your hands thoroughly. You should follow the method that is recommended by your Eye Care Professional. Below is an example of one method:

**Pinch Method:**
**Step 1.** Look up, slide the lens to the lower part of the eye using the forefinger.
**Step 2.** Gently pinch the lens between the thumb and forefinger.
**Step 3.** Remove the lens.

**NOTE:** For your eye health, it is important that the lens can move on your eye. If the lens sticks (stops moving) on your eye, apply a few drops of the recommended rewetting solution. Wait until the lens begins to move freely on the eye before removing it. If non-movement of the lens continues, you should immediately consult your Eye Care Professional.

**EMERGENCIES:** If chemicals of any kind (household products, gardening solutions, laboratory chemicals, etc.) are splashed into your eyes: FLUSH EYES IMMEDIATELY WITH TAP WATER AND IMMEDIATELY CONTACT YOUR EYE CARE PROFESSIONAL OR VISIT A HOSPITAL EMERGENCY ROOM RIGHT AWAY.

**6. REPORTING OF ADVERSE REACTIONS (Side Effects)**

Any incident experienced whilst wearing ACUVUE® Brand Contact Lenses should be reported to the manufacturer and/or its authorized representative and/or to your national authority.

**Manufactured by:**

**USA:** Johnson & Johnson Vision Care, Inc.,
7500 Centurion Parkway, Jacksonville, Florida, 32256, USA
**IRELAND:** Johnson & Johnson Vision Care Ireland UC, The National Technology Park, Limerick, Ireland

Please refer to carton for country of origin. Full address listed above.

EC REP AMO Ireland, Block B, Liffey Valley Office Campus,
Quarryvale, Co. Dublin, Ireland
www.acuvue.com


**Revision Date: 05/2022**
**The following symbols may appear on the labels or packaging.**

| Symbol | Definition |
|---|---|
| | Caution, Consult Instructions for Use |
| | Manufacturer |
| | Date of Manufacture |
| | Use-by Date (expiration date) |
| LOT | Batch Code |
| STERILE | Sterilized Using Steam Heat |
| | Do Not Re-Use (Single Use) |
| | Do Not Use if Package is Damaged |
| | Fee Paid for Waste Management |
| MD | Medical Device in the European Community |
| | Indicates a Single Sterile Barrier System |
| Rx only | CAUTION: U.S. Federal law restricts this device to sale by or on the order of a licensed practitioner |
| | UV Blocking |
| EC REP | Authorized Representative in the European Community |
| CE 2797 | CE-mark and Identification Number of Notified Body |
| DIA | Diameter |
| BC | Base Curve |
| D | Dioptre (lens power) |
| CYL | Cylinder Power |
| AXIS | Axis |
| MAX ADD | Highest Near Addition That Can Be Corrected |
| LOW / L | "Low" near ADD |
| MID / M | "Medium" near ADD |
| HGH / H | "High" near ADD |
| $S_N$ | NATURAL SHIMMER™ |
| $S_P$ | NATURAL SPARKLE™ |
| N | NATURAL SHINE™ |
| | Lens Orientation Correct |
| | Lens Orientation incorrect (Lens Inside Out) |
| | "Identification mark" for paper containers and wrapping |
| | "Identification mark" for composite materials |
| | Opening Package (Carton) |
| | Contains Hazardous Substances |
| | Importer in European Community |

**APPENDIX D:** [redacted]

[redacted] Lens Fitting Assessment

[redacted] Subject Reported Ocular Symptoms/Problems

[redacted] Determination of Distance Spherocylindrical Refractions

[redacted] Distance and Near Snellen Visual Acuity Evaluation

[redacted] Patient Reported Outcomes

[redacted] **LENS FITTING ASSESSMENT**

[redacted]

NOTE: If the lens is not perfectly centered, the direction of decentration should be recorded on an 8

[redacted]

[redacted]

[redacted]

[redacted]

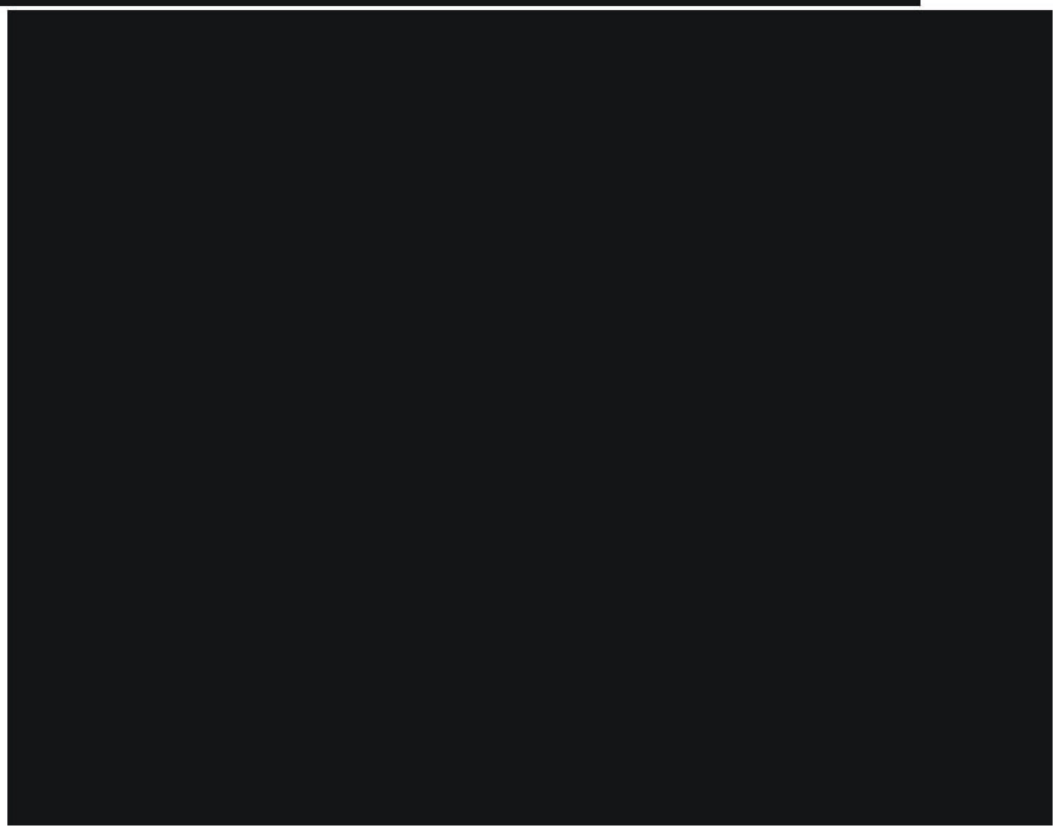
[redacted]

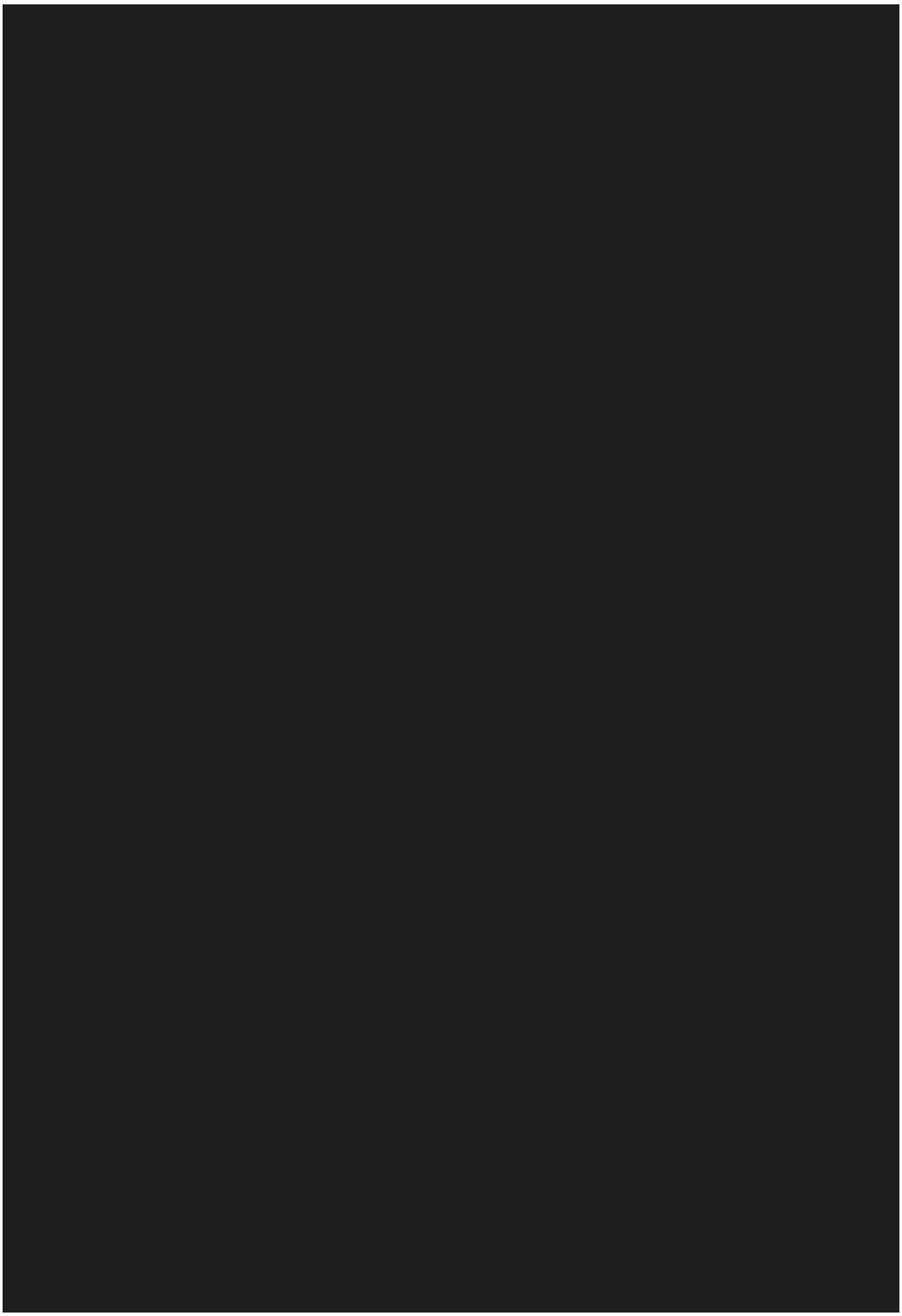
[redacted] SUBJECT REPORTED OCULAR SYMPTOMS/PROBLEMS

[redacted]

[redacted] DETERMINATION OF DISTANCE SPHEROCYLINDRICAL REFRACTIONS

[redacted]





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[redacted]

[redacted]

[redacted] DISTANCE AND NEAR SNELLEN VISUAL ACUITY EVALUATION

[redacted]

[redacted]

[redacted]

[redacted]

[redacted] PATIENT REPORTED OUTCOMES

[redacted]

## APPENDIX E: EUROLENS RESEARCH SOP #12A LOGMAR ACUITY

# Eurolens Research

# Clinical
# Standard Operating Procedure

# The set up, measurement of visual acuity and procedures for carrying out an over refraction using the Eurolens computerised logMAR VA chart

**Neil Chatterjee**
Research Optometrist

**First issued: v0; July 8, 2009**
**Reviewed (with changes): v1; February 7, 2014**
**Reviewed (no changes): v1; February 2, 2016**
**Reviewed (with changes): v2; December 19, 2017**
**Reviewed (no changes): v2; November 19, 2019**

## Document control

| | |
|---|---|
| Title: | The set up and measurement of visual acuity using the Eurolens computerised logMAR VA chart |
| Document type: | Clinical standard operating procedure |
| Number of pages: | 11 |

Document author: _____ Date: 19 Dec 2017
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Document reviewed by: _____ Date: 19 Dec 2017
Gillian Howarth,
Research Optometrist

Document reviewed and approved by: _____ Date: 22 Dec 2017
Michelle Inwood,
Project Officer

Document approved by: _____ Date: 12-Jan-2018
Philip Morgan,
Director

## Summary

This document contains details of:

1. Overview of chart design.
2. The procedure of calibration and set up of the Eurolens computerised logMAR chart.
3. A method of measurement of VA using the Eurolens chart.
4. A method of carrying out an over refraction for clinical study contact lenses when visual performance is being measured using the Eurolens chart at 6m.

## Responsibilities

GOC-registered study investigators/research optometrists.

## Definitions/Acronym

*logMAR* - logarithmic value of the minimum angle of resolution.

The MAR relates to the resolution required to resolve the elements of a letter. logMAR is the $\log_{10}$ of the MAR. (**Table 1**)

| Snellen | Decimal | MAR | logMAR |
|---|---|---|---|
| 6/60 | 0.10 | 10 | 1.00 |
| 6/24 | 0.25 | 4 | 0.602 |
| 6/12 | 0.50 | 2 | 0.301 |
| 6/6 | 1.00 | 1 | 0.000 |
| 6/4 | 1.50 | 0.667 | -0.176 |

Table 1. The relationship between different acuity measurements

*Optotype* – A standardised symbol for testing vision.

*Over refraction* – the amount, in Dioptres (D), that will be accepted by a subject over a contact lens in order to obtain the optimum visual performance when viewing a visual acuity test chart.

## Chart design

1. The Eurolens computerised logMAR visual acuity chart (hereafter referred to as Eurolens chart) is a logMAR chart designed to run on an Apple Macintosh with

Microsoft Excel software. The chart is displayed through an external monitor connected to the Apple Mac via its monitor socket and appropriate cable.

2. The Eurolens chart is similar in design to the traditional Bailey-Lovie logMAR chart, however it uses a reversed Sloan font as the optotype. The need for the reversed font is due to the chart being viewed indirectly in a mirror in a 3m consulting room. The chart is mounted on an adjustable mount, above the subject's head.
3. The indirect viewing makes the effective distance of the chart 6m from the subject. This 6m distance is the standard testing distance in optometric practice.
4. High (100%) and low (10%) contrast VA measurements can be taken with the chart.
5. The VA measurement from the Eurolens chart is intended to be equivalent to that obtained from the traditional Bailey-Lovie logMAR charts at 6m. The Eurolens chart has two advantages over the Bailey-Lovie. The Eurolens chart does not fade or discolour (which reduces legibility). Further, unlike the fixed Bailey-Lovie chart, the letters can be randomised on the Eurolens chart, which reduces the effect of memory influencing the subject's VA score.

## Initial computer set up

1. The Apple Macintosh should have the following installed:
    a. Reversed Sloan font (otf file, which should be copied to the Macintosh HD/Library/Fonts/ folder)
    b. Microsoft Office 2011 or later
    c. Eurolens chart v5 software
2. The external monitor should be connected to the Mac. It will require the use of an appropriate adaptor and cable.
3. The additional monitor should be recognised automatically by the Mac. The Mac should configure the monitor as a second desktop. To verify this, move the mouse pointer across the screen. It should be possible to move the mouse pointer off the edge of the main screen and it should appear on the external monitor.
4. The Eurolens Chart software is an Excel file called Eurolens Research chart.xls. This, for convenience, is located on the desktop.
5. To run the chart, open the Excel file. Click on "enable macros".
6. The chart should be displayed on the external monitor and the chart's control panel should appear on the Mac's main screen (**Figure 1**).

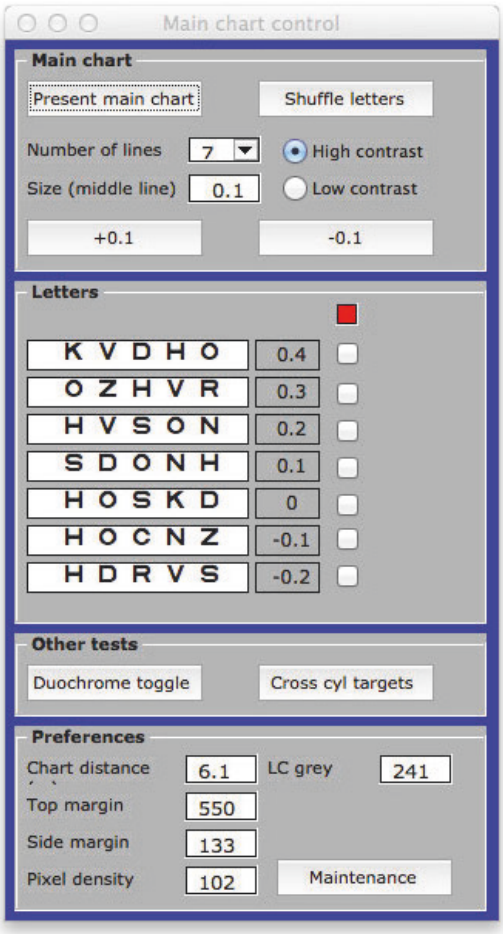


Figure 1. Chart control panel

7. If the letter chart appears on the Mac's main screen, it will need to be "dragged" onto the external monitor. To do this the chart control box must be closed. The main chart can now be dragged onto the second screen and maximised.
8. To restart the control panel, click on the Excel icon in the dock. Then in Excel's menu, select.: Tools -> Macro-> Macros. A macro box should appear, select the macro entitled 'showform' and click on run. The chart's control panel can be reopened if closed (e.g. accidentally) by repeating this step.

## Chart calibration procedure

1. It is important the charts are calibrated before first use, to ensure the optotypes are of the correct size and contrast. Minute adjustments of monitor contrast or brightness can affect the contrast of the letters (especially low).

2. If the chart distance is set to 6m, the 0.8 letter on the computer chart should be the same height as that on the Bailey-Lovie chart, measuring just under 55mm high.
3. The chart distance should then be set to the distance of the subject's head to the chart.
4. The monitor should be inclined downwards at an angle of approximately five degrees from the vertical. The reason being the contrast of an LCD monitor can vary with tilt. At five degrees of inclination, the monitor will be 'straight on' for the subject sat on the chair below. (see Appendix A)
5. The monitor should then be calibrated using a Datacolor Spyder 4. Whilst calibrating, the room lights should be on full illumination and the monitor set to factory default values (all setting "standard"). The corresponding monitor profile file generated should be saved and then used as the profile for the external monitor.
6. The contrast of the low contrast chart should be measured. The test spreadsheet (low contrast grey test.xlsx) should be displayed on the monitor with room lights on. Measurements of the luminance of the grey and white halves are taken with the spyder. The luminance measurements are then averaged. The contrast of the grey to white backgrounds is calculated as follows:

$$\% \text{ contrast} = \frac{\text{white lum} - \text{grey lum}}{\text{white lum}} \times 100$$

7. The RGB vales of the grey background should be altered until the contrast is calculated to be approximately 10%. This value is usually between 240 and 245 units.
8. Acuity measurements on the freshly calibrated chart should then be compared to those taken with two already calibrated charts. This is done by measuring high and low contrast visual acuity with all three charts (in a randomised order on around eight subjects). The acuity measurements of the three charts should all agree within two letters (0.04 logMAR) for high and low contrast acuity.
9. If the high contrast acuity on the test chart does not agree with that of the control charts, then the "chart distance" value should be altered on the test chart, until it is in agreement with the controls.
10. Once the high contrast acuity values are in agreement, the test chart's low contrast acuity should be in agreement with the control. If not then the "LC grey" value should be altered on the test chart until agreement is reached.

11. Final settings for each monitor on 11 October 2017 are contained in Appendix B.

## Measurement of VA using the Eurolens chart

### General instructions

1. The subject should be seated in the chair 3m from the mirror. This will place the chart at a 6m testing distance.
2. The default test chart for standard testing should be a 7-line chart ranging from 0.4 to -0.2 (Figure 1).
3. The subject's acuity can be tested monocularly and/or binocularly according to the study protocol.
4. If the subject cannot read the top line then increase letter size in 0.1 steps until the subject can see the top line.
5. Adjusting the "number of lines" box can alter the number of rows of letters displayed on the chart. Please note to display larger letters (over 0.4), then only one or three rows should be selected.
6. Letters can be increased in size by 0.1 steps, by clicking on the "+0.1" box. Letters can be increased in size to a maximum of 1.0.
7. Letters can be decreased in size by clicking on "-0.1".
8. The control panel displays information on the optotypes currently displayed on the chart and their size in logMAR.
9. The VA score is calculated using the same method as a traditional Bailey-Lovie chart, with each letter scoring 0.02 units and each complete line scoring 0.1 (see below).
10. To display the high contrast chart select "high contrast", similarly to display the low contrast chart select "low contrast". This will display letters of 100% and 10% contrast respectively
11. The Mac generates the sequence of letters used in the chart randomly. Clicking on "shuffle letters" can change the sequence of letters.
12. Letters should be shuffled after each VA measurement to avoid the subject learning the chart.
13. As the chart is at 6m, any over-refraction performed can be considered to be equivalent to that performed on a 6m Snellen chart i.e. at infinity.

14. The 6m testing distance should also be taken into account when comparing logMAR scores obtained with the Bailey-Lovie chart at 3m. The Bailey-Lovie scores should differ by -0.3.

**Subject instructions (standard chart display)**

After positioning the subject at the desired test distance, initiate the testing as follows:

1. Ask the subject to read the smallest line where they feel they can easily read all the letters. If the subject reads all the letters on the initial line, encourage them to continue reading the smaller lines until three or more letters on a 5- letter line are incorrectly identified.
2. If the subject identifies one letter incorrectly on the initial line, ask them to read the line(s) above until one complete line has been identified correctly. Then encourage the subject to continue reading the smaller lines/letters until three or more letters on a 5-letter line are incorrectly identified*. Note: The subject is to be encouraged to read and even guess at the letters until three or more letters are incorrectly identified.*

**Scoring**

To determine the VA unit score for a given line: Take the maximum VA for the last line read (i.e. the line on which three or more letters were missed) and add +0.02 for every letter missed on the chart.

For example:

| | | | |
|---|---|---|---|
| i) | 0.00 line | 3 letters missed | logMAR score +0.06 |
| ii) | +0.20 line | 0 letters missed | |
| | +0.10 line | 2 letters missed | |
| | 0.00 line | 3 letters missed | logMAR score +0.10 |
| iii) | -0.20 line | 0 letters missed | |
| | -0.30 line | 2 letter missed | |
| | -0.40 line | 4 letters missed | logMAR score –0.28 |

## Over-refraction

Unless the clinical study protocol states otherwise the following procedures should be carried out:

1. Visual acuity using the Eurolens chart will be measured with no over-refraction in place. The study protocol may require that this be carried out monocularly or binocularly.
2. A binocular over-refraction should be carried out using the chart at 6m. This procedure will control accommodation and allow accurate assessment of the subject's visual status. These results will allow the Investigator to judge whether or not the contact lens BVP is acceptable.

### Bailey Lovie chart

LogMAR visual acuity can also be measured on a card-based Bailey-Lovie chart. The use of this chart is covered in more detail in the relevant SOP[1]. In summary the differences are:

1. Unless specified the Bailey-Lovie chart is used at a testing distance of 3m as it is viewed directly.
2. The font used (5x5 sans-serif font)[2] is that defined in the British Standard: BS 4274.
3. If the Bailey-Lovie is used at 3m, then it should not be used as a target to determine over-refraction. Instead an alternative chart (e.g. Snellen) positioned at 6m should be used.

## References

1. Eurolens Research Standard Operating Procedure. Assessment of visual performance using the Bailey-Lovie logMAR visual acuity test chart and procedures for carrying out an over-refraction.
2. BS 4274-1:2003. Visual acuity test types. Test charts for clinical determination of distance visual acuity – Specification.

## Appendix A. Screen inclination calculation

To calculate chart inclination

$$\text{Tan (angle of chart inclination)} = \frac{\text{Subject's distance below chart}}{\text{Subject to chart distance (parallel to floor)}}$$

| Room | 1.015 | 1.014 | 1.013 | 1.012 |
|---|---|---|---|---|
| Subject's distance below chart (eye to top of monitor) (cm)* | 50 | 65 | 65 | 65 |
| Subject to chart distance (parallel to floor) (cm) | 600 | 605 | 610 | 600 |
| Calculated chart inclination (degrees) | 4.7 | 6.1 | 6.1 | 6.2 |

Table 2: Eurolens clinic room screen inclination.

* Subject with Eurolens ID 2023 of average UK male height (175cm, ONS data) was used

## Appendix B. Example of chart settings (11 October 2017)

| | | | | | |
|---|---|---|---|---|---|
| Clinic room | 1.012 | 1.013 | 1.014 | 1.015 | 1.018 |
| Monitor number | 4 | 5 | 3 | 1 | 2 |
| Chart distance (m) | 6.0 | 6.1 | 6.05 | 6.0 | 6.1 |
| LC grey | 240 | 240 | 243 | 240 | 237 |

Table 3: Eurolens clinic room chart settings

All monitors calibrated were a BenQ G2255 displaying the chart at native resolution (1920x1080).

## Appendix C. Revisions to chart software

2008

Initial clinic version of computer chart software

01/02/2013 v5

2013 version of chart software was rewritten for compatibility with Office 2011 and Mac OSX10.8. Contains the following amendments:

- Colours of the control box have been altered for better legibility with office 2011
- Chart letter display was updated for 16:9 monitors
- Letter size is calculated correctly for chart distance
- Low contrast letters contrast adjustable from chart control panel.

## APPENDIX F: EUROLENS RESEARCH SOP #13 SLIT LAMP BIOMICROSCOPY

# Eurolens Research

# Clinical
# Standard Operating Procedure

## Examination of the anterior segment using slit lamp biomicroscopy

Carole Maldonado-Codina
Associate Director

**First issued: v0; May 20, 2002**
**Reviewed (with changes): v2; June 26, 2009**
**Reviewed (no changes): v2; October 14, 2011**
**Reviewed (with changes): v3; March 4, 2014**
**Reviewed (with changes): v4; February 2, 2016**
**Reviewed (no changes): v4; February 5, 2018**
**Reviewed (no changes): v4; April 21, 2020**

## Document control

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| Title: | Examination of the anterior segment using slit lamp biomicroscopy |
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| Number of pages: | 4 |

Document author: Carole M-Codina Date: 2 Feb, 2016
Carole Maldonado-Codina
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Document reviewed by: G Howarth Date: 2 feb 2016
Gillian Howarth
Research Optometrist

Document reviewed and approved by: Michelle Inwood Date: 2 Feb 2016
Michelle Inwood
Project Officer (Business Systems)

Document approved by: P Morgan Date: 2 Feb 2016
Philip Morgan
Director

## Summary

The slit lamp biomicroscope is a high quality illuminating observation system which allows the external and internal ocular structures to be assessed in detail. The Efron Grading Scales for Contact Lens Complications[1] will be used to quantify most of the observations made. If an alternative grading scale is to be used this will be detailed in the study protocol.

## Definitions

*External ocular structures* in this procedure refer to the following structures: conjunctiva, sclera, limbus and associated blood vessels, cornea, lids, lashes and tear film.

*Internal ocular structures* in this procedure refer to the anterior chamber.

*Wratten 12 filter* – A yellow filter which enhances the contrast of fluorescein staining when viewed using cobalt blue light.

## Procedure

1. Using the recommended settings for slit width, magnification and filter, examine the external and internal ocular structures[2]. The following primary signs should be graded using the Efron Grading Scales: conjunctival redness, limbal redness, corneal neovascularisation, epithelial microcysts, corneal oedema and corneal infiltrates. The following secondary signs are also usually graded using the Efron Grading Scales: blepharitis and meibomian gland dysfunction. The number of mucin balls present are counted and recorded.
2. Instil sodium fluorescein (using a fluorescein ophthalmic strip wetted with saline) in both eyes and using cobalt blue light and a Wratten 12 filter or similar yellow filter, examine and grade the following: corneal and conjunctival staining. The location and 'type' of any staining is also usually recorded. Corneal staining type is usually divided into the following categories: no staining, toxicity, SEAL, foreign body/abrasion, inferior dehydration and non-specific.
3. The upper eyelid should then be everted and examined both with cobalt blue light (with the yellow filter in place) and with white light (no filter in place). The grading of upper palpebral conjunctivitis should then be made with the Efron Grading Scales.
4. If a soft contact lens needs to be applied after the examination, irrigate the eye with unpreserved sterile saline once the examination has been completed in order to remove excess sodium fluorescein.

## Recording slit lamp findings

Grades for the appearance of the ocular structures are recorded and classified according to Table 1 using Efron Grading Scales. Grades are scored to the nearest 0.1 in the best judgment of the investigator, with the exception of mucin balls where the number is counted. Location of staining is categorised as either superior, inferior, central, nasal or temporal.

| C ass f cat on | Pr mary s gns | Secondary s gns |
|---|---|---|
| S gns | Conjunct va redness<br>L mba redness<br>Cornea neovascu ar sat on<br>Ep the a m crocysts<br>Cornea oedema<br>Cornea nf trates<br>Cornea sta n ng<br>Locat on of sta n ng<br>Con unct va sta n ng<br>Pap ary conjunct v t s | B ephar t s<br>Me bom an g and dysfunct on<br>Muc n ba s |
| Sca e | Efron Grad ng Sca es (scored to nearest 0.1) | Efron Grad ng Sca es (scored to nearest 0.1) (except muc n ba s, where the number s recorded). |

**Table 1: Biomicroscopic signs.**

## References

1. Efron Grading Scales for Contact Lens Complications devised by Nathan Efron (2000 Millennium edition).
2. Morris J (2013). Slit lamp biomicroscopy. Optometry in Practice: 14 (3): 85-96.

## APPENDIX G: EUROLENS RESEARCH DESMD SYSTEM SETUP AND MEASUREMENT PROCEDURES

**APPENDIX G: DESMD SYSTEM SETUP AND MEASUREMENT PROCEDURES**

Authors: Michael Read and Maria Nascues-Cornago

Date: 11th July, 2022

Version 3.0

## Table of contents

## 1. Experimental setup

The Digital Eye Strain Manchester Device (DESMD) is designed to assess contact lens performance in a non-invasive manner during use of a digital display. The instrument aims to allow control over environmental conditions (including airflow and humidity), whilst the study participant engages in a range of digital device tasks. The DESMD system is shown in Figure 1. The system is based on an optical breadboard (B6090AX, Thorlabs UK Ltd) mounted on a height adjustable table (Topcon GB). A chin rest (Head Support, SR Research Ltd., Ottawa, Canada) is mounted to one end of the table, to accommodate the study participant who is seated on an office chair. A 7-inch LCD display (FW279S, Wex Photographic Ltd, UK) is mounted on an adjustable arm, at a 60 cm working distance from the participant. The resolution of the display is 1900×1200 pixels and brightness set at 50% (the settings are otherwise the default monitor settings). The monitor is connected via a HDMI cable to a workstation computer (DELL T3620, DELL UK Ltd.), with the visual tasks displayed using MATLAB software (Mathworks Inc., Natick).

The system comprises three digital cameras, with one camera just below the digital display which captures images of both eyes (termed the central camera), one camera imaging the study participant's left eye from the side (termed the side camera) and a third camera capturing the digital display (termed the display camera). These cameras all feed into the Dell workstation, where the three video streams are synchronized for later analysis.

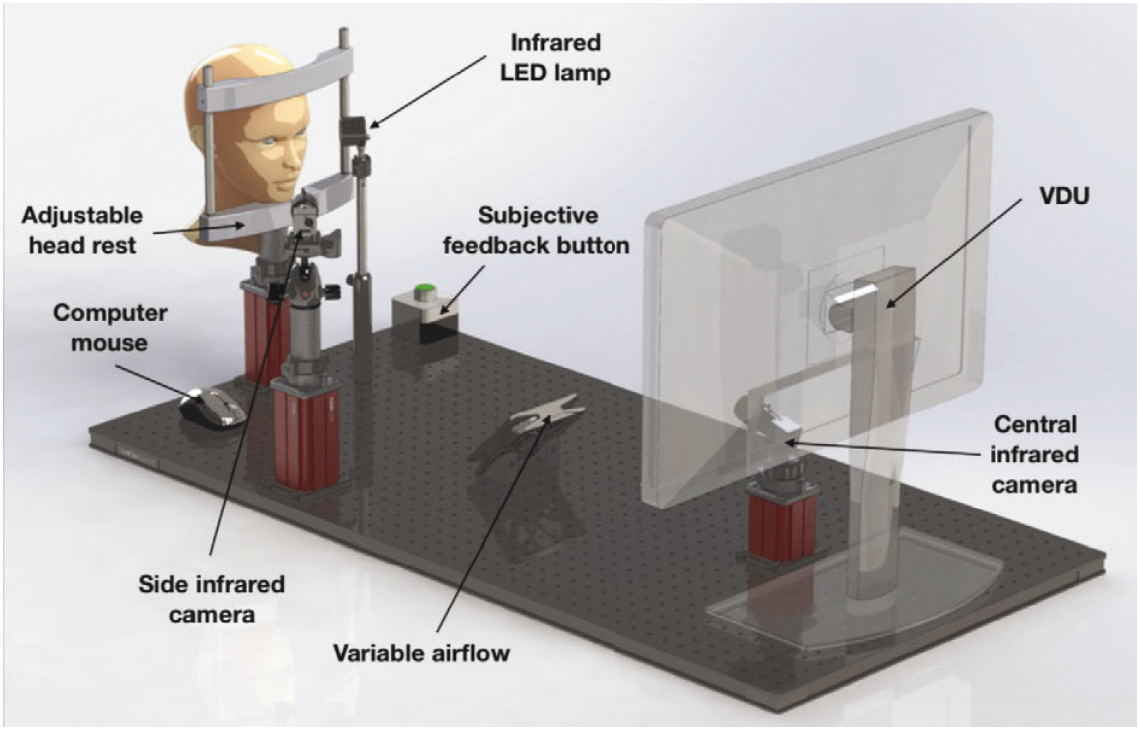


Figure 1. The Digital Eye Strain (DESMD) system

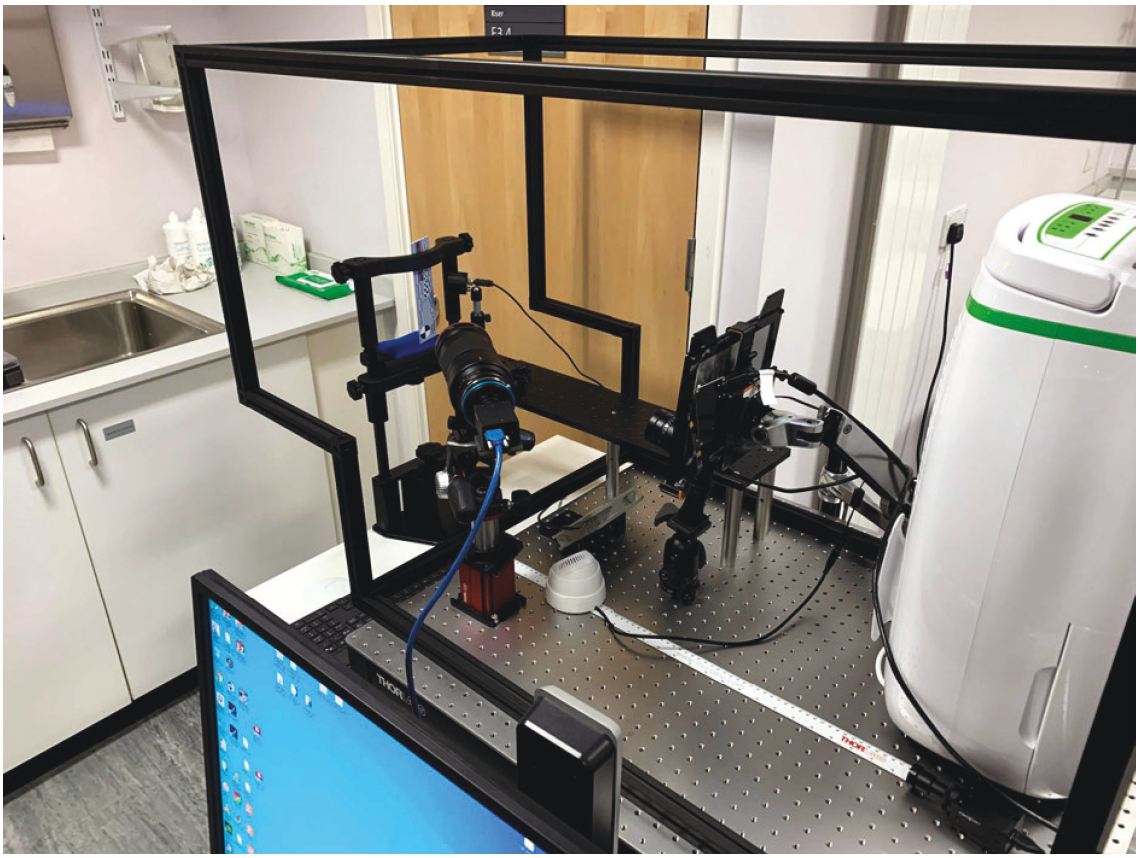

Figure 2. Photograph of the DESMD system.

The central monochromatic camera (MX022RG-CM, Ximea GMbH, Munster, Germany) captures a video feed at 500 frames per second (FPS), with a resolution of 1600×400 pixels and is sensitive to infrared light. The camera is used in conjunction with a MVL50TM23 50mm C-Mount lens (Kowa GmbH, Dusseldorf, Germany) at a working distance of 600mm, giving a horizontal field of view of around 80mm, allowing both of the participants' eyes to be imaged. The camera assembly is mounted on a Manfrotto tripod head (MHXPRO-3W X-PRO, Vitec Imaging Solutions, Cassola, Italy), to allow the camera position to be optimised for video capture.

The side camera (MQ042MG-CM, Ximea GMbH, Munster, Germany) captures a video feed at 30 frames per second, with a resolution of 2048×2048 pixels and is sensitive to infrared light. The camera assembly is mounted on a Manfrotto tripod head (MHXPRO-3W X-PRO, Vitec Imaging Solutions, Cassola, Italy), itself mounted on a height adjustable 1.5” post holder (LPH200, Thorlabs Inc., New Jersey, US) to allow the camera position to be optimised for video capture.

The display camera (GS3-U3-23S6M-C, PointGrey Inc, Canada) captures a video feed at 15 frames per second, with a resolution of 1920×1080 pixels. The camera assembly is mounted on a Manfrotto tripod head (MHXPRO-3W X-PRO, Vitec Imaging Solutions, Cassola, Italy) allowing the camera position to be optimised for video capture of the digital display.

The DESMD has two LED infrared light sources. The first light source is an infrared LED light (Thorlabs LIU850A) which is diffused by a piece of paper (100GSM) and a custom emulsion film photomask target (JD Photodata Ltd, UK), comprising of multiple concentric rings. The LED lamp is mounted on a height and angle adjustable mount allowing it to be positioned near to the participant's left eye (at a 45-degree angle from the visual axis). The side camera is used to view a reflection of the concentric ring target in the tear film. This light also acts to illuminate the participants left eye for the central camera. The participant's right eye is illuminated with a similar LED lamp on the other side, with the intensity adjusted to create even illumination of the subject's eye on the central camera. This LED is also on an adjustable mount to optimise alignment with the participant’s eyes.

Where required, a handheld pendant button (CompuPhase, Bussum, Netherlands) is also connected to the workstation via a USB cable. Each button press is logged by custom software (see Section 3.4). A linear slide (Motorised linear potentiometer, Tinkerforge GMbH, Germany) is also connected to the workstation via USB. Custom MATLAB software tracks subjective comfort during extended eye opening (see Section 3.6).

Where required, a small USB-powered desk fan (RS PRO Desk Fan, RS Components Ltd., Corby, UK) is positioned in front and below of the participant at a distance of 50cm. When the fan is switched on the airflow is approximately 1.5 meter per second at the participants face.

If required, the environmental humidity surrounding the DESMD device can be modified. To assess the impact of environmental humidity on clinical performance, the environment surrounding the DESMD system can be controlled using either a dehumidifier or humidifier. Two dehumidifiers (2 x Meaco Platinum dehumidifier, Meaco Ltd., Guildford, UK) allow the humidity within the testing environment to be maintained at a relatively low humidity (RH of 30% +/- 10%). Use of the humidifier (Levoit LV600HH, Levoit Inc., Anaheim, CA) allows the testing environment to be maintained at a relatively high humididty (RH of 60% +/- 10%). Both the humidifier and dehumidifier have a humidity feedback system to maintain the desired relative humidity. To allow sufficient time for the room to reach the required humidity, testing days will be allocated to either high or low humidity testing and the required system activated on the evening before clinical testing. To confirm the environmental conditions are at the correct level, a humidity sensor (Humidity and Temperature sensor, Tinkerforge GMbH, Germany) will continuously measure humidity and temperature during testing via custom MATLAB software.

## 2. DESMD preparation and testing

Prior to testing, any surfaces which the investigator or study participant will be touching or in close proximity with will be wiped down with alcohol wipes. The participant will be seated at the instrument and the height of the chair, table and chin rest carefully adjusted to obtain a comfortable position for the participant. The test will be carefully explained to the participant. If required, the response pad and subjective feedback button will be demonstrated, and their use carefully explained to the study participant. The side and central camera will have their position adjusted to centre the region of interest and the focusing will be optimised. The investigator will start the video recording first and then initialise the visual task. Following completion of each task, the participant will be asked to sit back from the instrument. The video filenames will include details of subject ID, visit, vision correction, humidity, airflow and visual

task. Data files of measurements recorded by Matlab software (such as visual acuity, symptomatic events and analogue subjective comfort data) will also include this information. Similarly, output files generated from image analysis of captured videos will include these identification details.

## 3. DESMD analysis metrics

Below are several metrics which can be captured using the DESMD system:

### 3.1 Blink and palpebral aperture height analysis

The videos captured will be processed using MATLAB image analysis software. For the blink analysis and palpebral aperture height, only data from the left eye will be processed and analysed.

This software loads the central camera video file and identifies the pupil location. The software extracts a single column of pixels from the video frame, which crosses through the pupil centre, and the automated process is repeated on subsequent frames, with the columns of pixel values concatenated across all of the frames in the video to produce a space-time plot. From this plot the eyelid blinking episodes can be readily visualised as downward spikes and subsequently marked by the investigator to determine blink frequency. Once this process is completed, a video frame corresponding to the first blinking time point marked on the space-time plot is loaded and the investigator uses the mouse scroll wheel to scroll through the video frames until the point of maximum closure of the eyelid can be identified. The investigator then marks the position of the upper and lower eyelids (in line with pupil centre) at maximum closure to determine the gap between lids (closed palpebral aperture). This process is repeated for the remaining blinks identified. To determine the average palpebral aperture height (PAH), the position of the eyelids is assessed at any interblink interval longer than 2 seconds where no detectable lid movement is observed. The closed palpebral aperture is expressed as a percentage of the average PAH to evaluate blink completeness (with 100% indicating complete lid closure on the blink).

For the 10 most complete blinks, the blink velocity and duration will also be assessed. The blink cycle is divided into a closing phase and opening phase. The investigator marks the position of the upper lid on three specific video frames: (i) 100 frames (0.2 seconds) prior to maximum eyelid closure (ii) at the point of maximum eyelid closure and (iii) 500 frames (1 second) after maximum eyelid closure. The custom software then returns to the space-time plot, with the position of the upper lid prior to the blink and at maximum closure highlighted, in addition to lines indicating the 25% and 75% completeness of lid closure. The investigator then marks on the space-time plot the point at which the upper lid reaches 25% and 75% of total closing amplitude. The relevant video frames are then displayed and the actual position of the upper lid at these time points is accurately marked. The software is then able to calculate the average closing velocity. This process is then repeated for the opening phase. The duration of the closed phase is defined as the time interval between 25% of closing amplitude and 25% of opening amplitude. The total duration of the blink is defined as the time interval between the 75% of closing amplitude and 75% of opening amplitude.

The software will extract the following metrics:

- Blink rate

- Interblink interval (seconds)
- Blink completeness (mm)
- Closing and opening blink speed (mm/s)
- Total blink duration (ms)
- Closed phased duration (ms)
- Palpebral aperture height (mm)

Blink rate, interblink interval, blink completeness and palpebral aperture height metrics will be determined across the 5 minutes and at 1-minute increments. Blink speed and duration metrics will be determined for the 10 most complete blinks.

### 3.2 Tear film surface quality (TFSQ)

The infrared light next to the participants' left eye projects a pattern of concentric rings onto the corneal/tear film surface, which is imaged by the side camera. When the reflected disc pattern is regular, the tear film is considered to be smooth and stable. When the tear film becomes unstable, the reflection of the rings is disturbed. The custom MATLAB algorithm developed for the DESMD system, characterises tear film dynamics by the morphological changes of the reflected pattern reflections, based on the methodology described in Downie et al. (Automated Tear Film Surface Quality Breakup Time as a Novel Clinical Marker for Tear Hyperosmolarity in Dry Eye Disease. IOVS 2015). Prior to analysis of the images, any frames affected by blinking or large eye movements will be detected and removed from the analysis. The central circular ring is then detected allowing the analysis to be centred relative to the reflected mires. The image is then transformed from Cartesian to polar coordinates, converting the concentric rings into broadly horizontal lines. The background of the polar coordinates is then subtracted from the polar image using morphological operations. Global thresholding is then performed to enhance the morphology of the reflected mires. The video is then processed and an index (Tear film Surface Quality -TFSQ) extracted at 1 second intervals. The average and SD of TFSQ will be determined across the 5 minutes and at 1-minute increments.

### 3.3 Tear meniscus height (TMH)

The videos captured will be processed using MATLAB image analysis software. This software loads the side camera video file which captures the inferior tear meniscus of the left eye. Following spatial calibration, a video frame is loaded and the investigator is instructed to mark the upper and lower border of the reflected line of the tear meniscus at approximately 6 o'clock position. The software determines the tear meniscus height and this process is repeated every 30 frames (i.e. 1 second). The average and SD of the tear meniscus height will be determined across the 5 minutes and at 1-minute increments.

### 3.4 Symptomatic events

Subjects will be asked to report episodes of discomfort or lens awareness while undertaking the visual tasks by pressing a handheld subjective feedback button, which will record a time-stamped event. Subjects will be instructed to press the button again after 10 seconds if the symptom is still present. Each button press is logged by custom software, which will extract the number and time of symptomatic events.

### 3.5 Tear film stability during extended eye opening

This test is performed with the right eye closed (either by the participant gently holding their eyelid closed, or with the use of an eye patch). The participant is asked to fixate a Maltese cross displayed on the DESMD screen. The participant is then instructed to take two natural blinks and then avoid blinking for as long as possible (up to a maximum of 30 seconds). During this time the side camera will capture a video of the reflected concentric ring mire pattern. The participant will then sit back from the DESMD and rest for 5 minutes. The testing process will then be repeated on two further occasions with a five-minute recovery period between each test. The video captured by the side camera will subsequently be analysed to extract the TFSQ over the 30 second period. The tear film break-up time will then be calculated for each of the three periods of extended eye opening.

### 3.6 Subjective comfort analogue slider during extended eye opening

A linear slide potentiometer will be used to record subjective discomfort during an extended eye-opening period. After training, subjects will be asked to rate the ocular discomfort with the potentiometer while they look at a visual target and keep the left eye open as long as possible. This test will be performed with the right eye closed, so that the observation relates only to the left eye. The subjective discomfort data will be processed using a custom MATLAB software, which extracts the level of discomfort on a 0 to 10 scale (10 = no discomfort; 0 = very uncomfortable) at approximately 0.1-second intervals for the recorded period. The discomfort data will be plotted against time for visual inspection. The rate of comfort change will be determined. Three measurements of subjective comfort (using the analogue slider) during extended eye opening will be captured.

### 3.7 Continuous acuity testing during extended eye opening

The continuous acuity testing during extended eye-opening task is similar to the continuous VA testing visual task (see Section 10), although once a threshold visual acuity has been reached, the participant is asked to avoid blinking for as long as possible whilst continuing to assess visual acuity. This test is performed with the right eye closed, so that the observation relates only to the left eye. The custom MATLAB software will automatically calculate the moving average and SD of visual acuity prior to and during the extended eye-opening period. Three measurements of continuous acuity testing during extended eye opening will be captured.

### 3.8 Pupil size and Interpupillary distance

The central camera video will be processed using custom MATLAB image analysis software. This software loads the video file and, following spatial calibration, automatically detects the pupil, fitting a circle to the right and left eye pupil. This process is repeated every 50 frames (i.e., 0.1 seconds). The software extracts the pupil diameter for the right and left eye pupil and interpupillary distance in millimetres. The average and SD of pupil diameter and interpupillary distance will be determined across the 5 minutes and at 1-minute increments.

# 4 Visual tasks

## 4.1 Maltese cross

For simple fixation tasks, such as tear film stability testing (see Section 3.5), a Maltese cross is displayed on the DESMD monitor.

## 4.2 Documentary video

Subjects will be instructed to watch a 5-minute video, a wildlife documentary film, whilst the central and side camera capture a video of the participants eyes. All subjects will watch the same wildlife documentary videos during the study, which will be specifically selected to minimise any emotional reaction or changes in emotional state during the video recording. During this task, subjects will be asked to report symptomatic events using the handheld device, as described in Section 8.

## *4.3 Tetris-type game*

Subjects will be required to play a MATLAB version of the classic Tetris game during a 5-minute period. Subjects will be instructed to use their dominant hand to press the arrow keys on a keyboard to move the pieces and the non-dominant hand to use the handheld feedback button to report symptomatic events during the task. All subjects will start playing the game on level 1. If the game is over before the 5-minute time point, the game will be restarted.

## *4.4 Continuous VA test*

Custom MATLAB software will be used to assess continuous visual acuity during a 5-minute period. During the test, the software presents a rotating optotype Landolt ‘C’. The subject is instructed to track the orientation of the ‘C’ by pressing the arrow keys on a keyboard. The starting optotype size is 0.5 LogMAR and increases by 0.02 with a correct response and decreases by 0.02 with an incorrect response. Once a response is made the result is logged by the custom software and a new target is presented. The custom MATLAB software will automatically calculate the moving average and SD of visual acuity will be determined across the 5 minutes and at 1-minute increments. During this task, subjects will be asked to report symptomatic events using the handheld device, as described in Section

## APPENDIX H: [redacted] 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.<br>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).<br>Confirm compliance with the prescribed wear schedule.<br>• Record and discuss the lens wear compliance based on the subject's self-report. For example, the subjects will be asked the time of the day the subject typically puts on the study lenses in the morning and takes off in the evening, the number of days per week lenses were worn, and the number of consecutive days the subject didn't wear the study lenses, etc. |

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

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

## 6.0 STUDY CONDUCT DURING PANDEMIC

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

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

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

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

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

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

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

## 6.1 Monitoring Visits

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

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

### 6.1.1 Study Site Initiation:

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

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

### 6.1.2 Interim Monitoring Visits (if applicable):

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

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

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

6.1.3 Study Site Closure:

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

**Attachment A: Study Site Correspondence**

XXXX XX, 2020

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

Dear <<Principal Investigator>> and Study Team,

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

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

**Protocol:**

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

**Protocol Signature Page:**

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

**Informed Consent:**

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

**COVID-19 Risk Control Checklist for Clinical Studies:**

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

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

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

Please file this letter in your site file study correspondence.

**Attachment B: COVID-19 Risk Control Checklist**

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<br>**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<br>Gloves should be required when working directly with patients and changed between each patient |
| | Have staff thoroughly wash hands for at least 20 seconds or use an alcohol-based hand sanitizer when they arrive, before and after each patient, before eating and after using the bathroom. |
| | Cleaning and disinfection procedures for exam rooms and instruments or equipment between patients with gloves. |
| | Cleaning and disinfection procedures for commonly touched surfaces (doors, chairs, computers, phones, etc.) with gloves. |

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

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

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

Principal Investigator Signature and Date

## RESOURCE LINKS

### US Resource Links

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

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

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

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

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

### OUS Resource Links

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

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

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

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

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

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

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

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

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

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

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

## PROTOCOL COMPLIANCE INVESTIGATOR(S) SIGNATURE PAGE

Protocol Number and Title: CR-6495, Clinical performance of two daily disposable silicone hydrogel contact lenses ([redacted])

Version and Date: 2.0, 19 August 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], the Declaration of Helsinki[2], United States (US) Code of Federal Regulations (CFR)[3], and the pertinent individual country laws/regulations and to comply with its obligations, subject to ethical and safety considerations. I, as the Principal Investigator, am responsible for ensuring that all clinical site personnel, including Sub-Investigators, adhere to all regulations and GCP guidelines regarding clinical trials during and after study completion.

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

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 H 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