VISIONCARE RESEARCH

PROTOCOL

VERSION 1

MULTI-CENTER CROSS-OVER EVALUATION OF AVAIRA VITALITY™ SILICONE HYDROGEL CONTACT LENS AND TWO HYDROGEL LENSES IN DAILY WEAR

SPONSOR:	CooperVision Inc.
STUDY NUMBER:	AVAR-402 (EX-MKTG-103)
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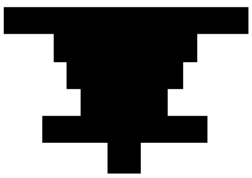

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Multi-center cross-over evaluation of Avaira Vitality™ silicone hydrogel contact lens and two hydrogel lenses in daily wear

AVAR-402 (EX-MKTG-103)

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Multi-center cross-over evaluation of Avaira Vitality™ silicone hydrogel contact lens and two hydrogel lenses in daily wear

AVAR-402 (EX-MKTG-103)

PERSONNEL AND FACILITIES

SPONSOR:

Multi-center cross-over evaluation of Avaira Vitality™ silicone hydrogel contact lens and two hydrogel lenses in daily wear

AVAR-402 (EX-MKTG-103)

SYNOPSIS

STUDY OBJECTIVES: To evaluate the comparative clinical performance of the Avaira Vitality™ silicone hydrogel lens used in daily wear and to compare this with competitive hydrogel lens products.

STUDY DESIGN: This will be an 8-week, single-masked, bilateral, two-part, cross-over evaluation of hydrogel and silicone hydrogel lenses in daily wear with approx. 100-120 subjects. Lenses will be replaced either on a 2-weekly or 4-weekly basis, depending on control lens group.

MASKING: Subjects will be masked to lens type. Investigators will be unmasked.

STUDY LENSES: The following lenses will be used:

	Avaira Vitality™	**Biomedics 55 Premier**	**Acuvue 2**
Test / control	Test	Control	Control
Manufacturer	CooperVision	CooperVision	Johnson & Johnson
Material / water content (%)	fanfilcon A 55%	oculfilcon D 55%	etafilcon A 58%
Diameter/ base curve (mm)	8.40/14.2	8.60/14.2	8.40/14.0
Sphere powers (D)	-1.00 to –6.00D (-0.25D steps)		
Recommended replacement period	Monthly	Monthly	2-weekly
Other	Light blue handling tint UV blocker	UV blocker	Light blue handling tint UV blocker 3-2-1 indicator

LENS CARE PRODUCTS: Alcon Opti-Free PureMoist care system, unless subject intolerant in which case an alternative will be selected by the investigator.

STUDY POPULATION: Volunteer subjects with a sphere requirement in the range -1.00D to -6.00D and with astigmatism of 1.00D or less in both eyes. Subjects will be current daily wear contact lens wearers not using any of the study lenses.

NO. SITES: Approximately six sites (up to 22 subjects/site) in US.

STUDY VISITS: There will be a minimum of 3 or 5 scheduled visits, depending on control lens (see below):

Lens Type	Visit 1	Visit 2 2-week FU	Visit 3 4-week FU	Visit 4 6-week FU	Visit 5 8-week FU
Biomedics 55 Premier	Dispense BM55 (control)	2 weeks evaluate BM55	4 weeks evaluate BM55 + dispense Avaira Vitality	2 weeks evaluate Avaira Vitality	4 weeks evaluate Avaira Vitality + Exit
Time (days)	0	14 days after V1 (-1/+3)	28 days after V1 (-1/+3)	14 days after V3 (-1/+3)	28 days after V3 (-1/+3)
Acuvue 2	Dispense AV2 (control)	2 weeks evaluate AV2 + dispense Avaira Vitality	2 weeks evaluate Avaira Vitality + Exit	NA	NA
Time (days)	0	14 days (-1/+3)	14 days after V2 (-1/+3)		

KEY VARIABLES:

Comfort: comfort reported at visit [0-10 scale]

Wearing time: average & comfortable WT [hrs]

Surface wetting: Pre-lens tear film quality [0-4]

Deposits: Film deposits [0-4]

White spot deposits [no.]

Overall lens fit acceptance [0-4].

OTHER VARIABLES:

Comfort throughout the day on selected days (Days 3, 7, 12, and 26, day 26 for B55 control only) [0-10] using text messaging reminders and responses.

Symptoms

[redacted]

Lens fit: Centration [0-4], corneal coverage [Y/N], post-blink movement [mm], tightness on push-up [%].

[redacted]

[redacted]

1 INTRODUCTION

There has been a trend over the last 20 years of moving from hydrogel to silicone hydrogel contact lenses.[1] In 2018, three-quarters (76%) of prescribed soft lenses in the US were silicone hydrogel lenses and this trend is likely to continue.[2] With existing hydrogel users, an impediment to refitting to silicone hydrogels is the concern that the comfort and wetting performance may be inferior, thus, mitigating the obvious benefits of improved oxygen availability.

The Avaira® Vitality™ (fanfilcon A) soft contact lens is a silicone hydrogel lens indicated for the correction of myopia and hyperopia. This was launched recently (FDA 510k approval: 2016) and has, therefore, been the subject of few clinical studies. The 510k application reported a 3-month comparative clinical study involving 90 subjects and in which the lens was found to be substantially equivalent to the control lens (stenfilcon A).[3]

This study aims to simulate the switching of hydrogel lens wearers to Avaira Vitality silicone hydrogel lenses. Two of the most commonly used hydrogels are Acuvue 2 (Johnson & Johnson) and Biomedics 55 Premier (CooperVision). Acuvue 2 is a well-established hydrogel lens and has been tested in a wide range of clinical studies.[4-7] Biomedics 55 Premier is an improved version of the Biomedics 55 lens which has also been tested in a number of clinical studies.[8-12]

The purpose of the proposed study, therefore, is to evaluate the clinical performance of Avaira Vitality in comparison with hydrogel lenses in subjects switched from hydrogel to silicone hydrogel contact lenses.

2 STUDY OBJECTIVES

The aim of this study will be to evaluate the comparative clinical performance of the Avaira Vitality™ silicone hydrogel lens used in daily wear and to compare this with competitive hydrogel lens products, Biomedics 55 Premier and Acuvue 2.

3 STUDY DESIGN & RATIONALE

3.1 Study Design

An approx. 100-120 subject, 8-week, single-masked, bilateral, two-part, cross-over evaluation of hydrogel and silicone hydrogel lenses in daily wear. Lenses will be replaced either on a 2-weekly or 4-weekly basis, depending on control lens group.

3.2 Study Rationale

In order to compare the comfort, wetting and deposition, it is necessary to make a within-subject comparison. A cross-over study is therefore seen as the most appropriate comparison. Switching from hydrogel to silicone hydrogel lens simulates the common sequence of events in current clinical practice. However, this does not allow a randomized comparison and may be subject to sequence bias.

3.3 Primary Outcome Hypothesis

Subjective comfort reported at the visit will be better with Avaira Vitality than the control contact lenses at the final visit.

3.4 Secondary Outcome Hypotheses

i. Average wearing time will be longer with Avaira Vitality than the control contact lenses at the final visit.

ii. Comfortable wearing time will be longer with Avaira Vitality than the control contact lenses at the final visit.

iii. Pre-lens tear film quality will be better with Avaira Vitality than the control contact lenses at the final visit.

iv. Film deposits will be better with Avaira Vitality than the control contact lenses at the final visit.

v. White spot deposits will be fewer with Avaira Vitality than the control contact lenses at the final visit.

vi. Overall lens fit acceptance will be better with Avaira Vitality than the control contact lenses at the final visit.

3.5 Safety Hypothesis

The study lenses are FDA approved, therefore, no safety end points are required.

However, in order to ensure the continued safety of the subjects in the trial, slit lamp findings will be assessed at all visits and the spectacle refraction and VA will be collected at the start and end of the study. Adverse events will also be recorded and monitored following the procedures listed in Section 8.

3.6 Masking

Subjects will be masked to lens type. When lenses are dispensed, the blister packs will be opened out of sight of the subject. Investigators will be unmasked.

3.7 Randomization

Subjects will be randomly allocated to one of the two control groups. The order of wear of the test and control lenses will not be randomized. A random number generator (Microsoft Excel) using a blocking method and stratified by site will determine the randomization of control lenses to subjects, which will then be incorporated into the Randomization Log. ID numbers will be assigned consecutively to maintain randomization.

The randomized assignment of subjects will be performed at the first assessment. The following must have occurred prior to randomization:

- Informed consent has been obtained
- Subject meets all the inclusion / exclusion criteria
- Subject history and baseline information have been collected

4 STUDY POPULATION

4.1 Number of Sites

Approximately six sites located in the US, each recruiting approximately 22 subjects. Investigators will be contact lens practitioners with at least 3 years post-registration experience of contact lens fitting.

4.2 Investigator Recruitment

Investigational sites will be identified by Visioncare Research. The investigators will be required to fulfil the following criteria:

- Appropriately licensed eye care practitioner or contact lens optician
- At least three years post-registration contact lens fitting experience.
- In-office email.
- Willingness to follow the study protocol and to co-operate with the study monitors.
- Experienced investigators trained in Good Clinical Practice (GCP) and the study protocol prior to commencing the study.
- Computers available to complete CRFs using electronic data capture (EDC).

All of the investigational sites will be trained and evaluated by on-line training modules before enrolling subjects.

This clinical study is designed to be in conformance with the ethical principles in the Declaration of Helsinki, with the ICH guidelines for GCP and all applicable local regulations.

4.3 Number of Subjects

Approximately 100-120 habitual soft contact lens wearers will be enrolled in the study across all sites; approximately 50-60 subjects will use each control lens, Biomedics 55 Premier or Acuvue 2, before using the test lens, Avaira Vitality.

Each subject will be required to attend up to five scheduled study visits over a period of approximately 8-weeks.

The study population has been chosen to represent the range of patients that may use these contact lens types. Subjects will be adapted soft contact lens wearers and will be recruited from the sites' existing patient database or via IRB approved recruitment material. The enrolment period for the study is expected to last approximately 5 weeks.

4.4 Inclusion Criteria

All subjects must satisfy the following conditions prior to inclusion in the study:

i. Be a currently adapted soft contact lens wearer (>1 month of lens wear).

ii. Be at least 18 years of age.

iii. Refractive astigmatism $\leq$1.00D in both eyes.

iv. Have clear corneas and be free of any anterior segment disorders.

v. Be correctable through spherocylindrical refraction to 20/25 or better in each eye.

vi. Contact lens sphere requirement between -1.00D and -6.00D (inclusive).

vii. Require visual correction in both eyes (monovision allowed, no monofit).

viii. Have normal eyes with no evidence of abnormality or disease. For the purposes of this study a normal eye is defined as one having:
   a. No amblyopia
   b. No strabismus
   c. No evidence of lid abnormality or infection
   d. No conjunctival abnormality or infection that would contraindicate contact lens wear
   e. No clinically significant slit lamp findings (i.e. corneal staining, stromal edema, staining, scarring, vascularization, infiltrates or abnormal opacities)
   f. No other active ocular disease.

ix. [redacted].

x. Willing to comply with the wear and study visit schedule.

4.5 Exclusion Criteria

Any of the following will render a subject ineligible for inclusion:

i. Using CooperVision Avaira Vitality, J&J Acuvue 2 or CooperVision Biomedics 55.

ii. Require toric or multifocal contact lenses.

iii. Previously shown a sensitivity to any of the study solution components.

iv. Any systemic or ocular disease or allergies affecting ocular health.

v. Using systemic or topical medications that will in the investigator's opinion affect ocular physiology or lens performance.

vi. Clinically significant (≥Grade 3) corneal staining, corneal stromal edema, corneal vascularization, tarsal abnormalities, bulbar hyperemia, limbal hyperemia, or any other abnormality of the cornea that would contraindicate contact lens wear.

vii. Any corneal infiltrates or any corneal scarring or neovascularization within the central 5mm of the cornea.

viii. Keratoconus or other corneal irregularity.

ix. Aphakia or amblyopia.

x. Have undergone corneal refractive surgery or any anterior segment surgery.

xi. Abnormal lacrimal secretions.

xii. Has diabetes.

xiii. Known/reported infectious disease (e.g., hepatitis, tuberculosis) or an immunosuppressive disease (e.g., HIV).

xiv. History of chronic eye disease (e.g. glaucoma).

xv. Pregnant or lactating or planning a pregnancy at the time of enrolment.

xvi. Participation in any concurrent clinical trial or in last 30 days.

4.6 Subject Identification

Subjects will be identified by a four-digit code made up of the site number and their enrolment number.

The enrolment ID must be assigned to the subjects sequentially and in ascending order for each site. Therefore, the first subject at Site 1 will be allocated ID 01/01, the second subject will be 01/02 and so on. Subject identification is recorded in the Enrolment log and cannot be used more than once.

4.7 Study Withdrawal Criteria

If during the study it becomes evident to either the sponsor (CooperVision) or Visioncare Research that the study contact lenses pose a threat to subject well-being, the study will be terminated and the Institutional Review Board (IRB) will be advised of the reason for termination.

4.8 Subject Replacement

Subjects that are discontinued from the study will not be replaced.

4.9 Medications/Treatments Permitted and Not Permitted During the Study

Preservative free rewetting/comfort drops may be used in this study, as needed, to lubricate and rewet lenses, if agreed by the investigator.

The use of topical ocular medications is contraindicated at all times during this study unless prescribed as part of a treatment for an adverse event. The use of any ocular medications to treat conditions that arise will require temporary suspension of lens wear, an adverse event report, and evaluation of the subject for discontinuation from the study.

For any adverse event where lens wear is suspended, an unscheduled follow-up evaluation of the subject must be performed before allowing the subject to return to lens wear. Subjects may not return to lens wear until all topical ocular medications have been discontinued and a documented exam has verified the resolution of the adverse event.

4.9.1 Concomitant Medications

Changes in concomitant medications from those recorded at the initial visit should be indicated on the follow-up visit forms by checking 'Yes' on the concomitant medication question and recording the change on the appropriate EDC forms.

4.10 Procedures for Monitoring Subject Adherence

To track compliance, subjects will be asked at each follow-up visit about their average contact lens wearing times (typical insertion and removal times) and average number of days lenses are worn per week.

5 MATERIALS

5.1 Study Lenses

Table 1: Contact Lens Details

	Avaira Vitality™	Biomedics 55 Premier	Acuvue 2
Test / control	Test	Control A	Control B
Manufacturer	CooperVision	CooperVision	Johnson & Johnson
Material / water content (%)	fanfilcon A 55%	oculfilcon D 55%	etafilcon A 58%
Diameter/ base curve (mm)	8.40/14.2	8.60/14.2	8.40/14.0
Sphere powers (D)	-1.00 to –6.00D (-0.25D steps)		
Recommended replacement period	Monthly	Monthly	2-weekly
Other	Light blue handling tint UV blocker	UV blocker	Light blue handling tint UV blocker 3-2-1 indicator

Only lenses distributed by VCR/Sponsor may be used for the study. If additional lenses are required, investigators should contact VCR.

5.2 Lens Care Products and Other Study Products

Subjects will be instructed to use Opti-Free Pure Moist multipurpose solution to clean and store their study lenses at night or when not in use. In the event of subject non-compatibility with this product, an alternative may be dispensed at the discretion of the investigator.

Rewetting/comfort drops given to the subject by the investigator may be used in this study, as needed, to lubricate and rewet lenses.

5.3 Product Accountability

The applicable study initiation documents (including but not limited to: investigator agreement, Statement of Investigator, IRB approval, protocol signature document, financial disclosure form, etc.) must be received by VCR before investigational materials can be shipped to the investigational site. If applicable, approval from the appropriate regulatory authorities must be obtained before shipping lenses to the investigational site.

All study lenses will be sent to each study site by the VCR (see Section 5.1). An initial bank of lenses will be sent to the investigational site for initial dispensing.

All study lenses must be counted upon receipt, recorded on the Lens Accountability Form by the investigational site and stored in a secure area, segregated from any other materials, and issued only as directed in the protocol. The investigational site must document the dispensing and return (unused lenses only) of each investigational lens for each subject using the Lens Dispensing Log and eCRF.

Study sites will not be required to retain any packaging from used lenses.

Study product accountability will be checked by the study monitor (assigned by the sponsor or VCR) during site monitoring. All unused lenses, returned from subjects or never dispensed to the study subjects, must be available to the study monitor for verification of lens accountability at the completion of the study. Any discrepancies in study lens accountability must be explained by the investigator. After the study monitor has verified product accountability, any unused materials will be returned to VCR or to the sponsor unless the investigator is otherwise directed by the VCR. All product returned to VCR or sponsor will be documented on the Lens Accountability Form.

5.4 Lens Wearing Schedule

The subject will be instructed to wear the lenses on daily wear basis, for a minimum of 8 hours a day, 6 days per week and preferably 7 days per week.

5.5 Potential Risks and Benefits for Human Subjects

Potential Risks and benefits for human subjects wearing contact lenses are summarized in the Informed Consent document (separate document).

5.6 Study Documents and eCRFs

The following forms will be completed where appropriate:

eCRFs:

- Baseline forms (including eligibility checklist)
- Trial Fit / Dispensing form
- Follow-up forms (including Unscheduled Visit)
- Adverse Event forms
- Study Exit forms
- Protocol Deviation
- Device Deficiency
- Concomitant medication
- Medical History

Additional Forms

- Statement of Informed Consent
- Participant Information Sheet
- Site Responsibility Log
- Enrolment Log
- Participant Information Guide
- Lens Dispensing Form
- Lens Accountability Form
- Source Document Record Label

6 TREATMENT

6.1 Study Product Formulations

The test lenses will be shipped in blister packs containing a buffered saline packaging solution. The labelling of lenses and packaging will be the standard packaging which will indicate lens power, base curve, diameter, lot number and expiration date.

6.2 Lens Administration

Lenses will be used on a 2-weekly or 4-weekly daily wear basis depending on control lens group, i.e. lenses worn during the day, removed at night and cleaned and stored with Opti-Free PureMoist multipurpose solution.

In the event of lens loss or damage, replacement lens(es) will be issued at an unscheduled visit.

7 METHODS AND ASSESSMENTS

7.1 Subject Recruitment

Recruitment materials (adverts, letters, etc.) must be approved by the Institutional Review Board (IRB). If requested, VCR will provide an advertisement and letter for recruitment purposes. Any changes to these must be submitted back to the IRB via VCR.

The procedures listed below will be conducted on all subjects. Variables must be collected in the order they are listed on the eCRF.

To participate in this clinical study, the Investigator will explain the Statement of Informed Consent to the subject, ensure each subject understands the subject instructions and determine subject eligibility.

The Investigator is required to answer any questions the subject has concerning the study or the information contained in the Statement of Informed Consent and Patient Information Sheet.

A subject is considered enrolled when he or she signs the Statement of Informed Consent. Other study-related activities may not be undertaken prior to obtaining informed consent.

All subjects enrolled should be accounted for, even if they are not dispensed lenses or study product. A signed Statement of Informed Consent constitutes enrolment. After enrolment, a subject is considered active and should be accounted for at every visit until the completion of or discontinuation from the study.

Each site will be expected to enroll approximately 22 subjects.

7.2 Study Visits

7.2.1 Visit Schedule

There will be a maximum of five scheduled visits depending on the lens type:

Biomedics 55 Premier (Control A)

Visit 1: Baseline / Trial Fit / Control A Dispensing
Visit 2: 2-week Follow Up (14 days -1/+3 days from dispensing)
Visit 3: 4-week Follow Up and dispense Test Lens (28 days -1/+3 days from Control Lens dispensing)
Visit 4: 6-week Follow Up (14 days -1/+3 days from Test Lens dispensing)
Visit 5: 8-week Follow-up and Exit (28 days -1/+3 days from Test Lens dispensing)

Acuvue 2 (Control B)

Visit 1: Baseline / Trial Fit / Control B Dispensing

Visit 2: 2-week Follow Up and dispense Test Lens (14 days -1/+3 days from Control Lens dispensing)
Visit 3: 4-week Follow Up and Exit (14 days -1/+3 days from Test Lens dispensing)

A Visit Schedule will be supplied to all sites and this will list the visit windows; this can assist in the scheduling of visits within the appropriate window.

The Investigator should confirm with the subject that they are able to attend the follow-up visit within the visit window before enrolling them in the study. If, in extreme situations (sickness, unforeseen circumstances), the subject can only attend outside the visit window, the Investigator should discuss with VCR whether this visit can be considered a scheduled visit.

A scheduled follow-up visit may only take place when the subject attends wearing the study lenses. If this is not the case and the subject is not experiencing any problems with the lenses, the appointment will be re-scheduled, ideally within the visit window.

See Section 7.5 for instructions regarding unscheduled visits.

7.2.2 Visit 1: Enrolment/ Screening /Baseline

Subjects should attend the first visit wearing their habitual lenses. If they are not wearing their lenses, the visit must be rescheduled.

The following procedures will be conducted on all subjects:

Allow each subject to read the Participant Information and Informed Consent and explain the nature, purpose, risks of the study, etc. If he/she is agreeable, ask the subject to sign the Informed Consent Form, initial and date where appropriate. The person taking consent and the investigator (If they weren't the person obtaining consent) should also sign the consent form. Provide the subject with a copy and retain original.

A subject is considered enrolled when the Statement of Informed Consent has been fully executed. The subject is assigned with a Subject ID number according to the Enrolment Log. Subjects must be enrolled sequentially. Enter details on Enrolment Log as outlined on the form.

The following baseline measurements will be recorded on the Baseline eCRF:

Number	Assessment	Procedure	Instructions and gradings
1.1	Subject Demographics	Record age, sex and ethnicity.	
1.2	Medical History	Record medications and associated medical history (such as allergies etc.).	
1.3	Habitual Lens and care system	Record habitual lens type, replacement schedule and parameters (base curve and power).	
1.4	Rewetting Drops	Record current rewetting drop usage (type and frequency).	

Number	Assessment	Procedure	Instructions and gradings
1.5	Habitual Lens Wearing Time	Record the typical insertion & removal times, number of hours worn today, typical time CL comfort deteriorates, maximum wearing time and average number of days per week habitual lenses are worn.	[redacted]
1.6	Subjective Assessments (Comfort, [redacted] – Habitual Lenses	Record subject lens comfort (0-10), [redacted] subjective symptoms [redacted] in the past week with their habitual lenses.	[redacted]
1.7	[redacted]	[redacted]	[redacted]
1.8	Lens Surface Characteristics – Habitual lenses	Assess and grade lens surface wetting (0-4) and lens deposits (film: 0-4; no. of white spots).	[redacted]
1.9	Lens Fit Assessments	Evaluate habitual lens centration (0-2), corneal coverage (Y/N), post-blink movement and primary gaze lag (0-4), tightness on push-up (%) and overall fit acceptance (0-4) and reason if Grade 2 or less. Remove habitual lenses after lens fit assessment.	[redacted]
1.10	[redacted]	[redacted]	
1.11	[redacted]	[redacted]	

Number	Assessment	Procedure	Instructions and gradings
1.12	[redacted]	[redacted]	[redacted]
1.13	Eligibility	Confirm if subject is eligible and complete the eligibility criteria checklist. If at this point the subject is found to be ineligible, then complete an Exit eCRF and exit the subject from the study. The Investigator will also update the Enrolment Log and complete the Source Document Record – see Section 11.5 for further details	

7.2.3 Visit 1: Trial Fit and Dispensing

If eligible, the subjects will undergo a trial fit with the randomly allocated control lens type based on the randomization schedule.

The investigator will complete the Lens Accountability Log. If the appropriate study lenses are not available, an unscheduled visit should be scheduled for dispensing on another day. [redacted]

The following Trial Fit / Dispensing procedures will be conducted on eligible subjects:

Number	Assessment	Procedure	Instructions and gradings
1.17	Lens Parameters	Record the parameters of the lenses (lot number, lens powers). Lens power will be based on subjective sphero-cylindrical distance refraction. **NOTE:** To maintain subject masking, study lens blister packs will be opened out of subject's sight.	Appendix A – Lens Fit Assessments
1.18	Settling Time	Allow the lenses to settle for at least 10-15 minutes	
1.19	Subjective Comfort	Ask subject to grade comfort out of 10 where 0 is "extremely uncomfortable" and 10 is "can't feel the lenses".	Appendix A – Subjective Assessments

Number	Assessment	Procedure	Instructions and gradings
1.20	[redacted]	[redacted]	Appendix A - Vision
1.21	[redacted]	[redacted]	
1.22	Lens Surface Characteristics	Assess and grade lens surface wetting (0-4).	Appendix A – Tear Film Characteristics & Deposits
1.23	Lens Fit Assessments	Evaluate habitual lens centration (0-2), corneal coverage (Y/N), post-blink movement and primary gaze lag (0-4), tightness on push-up (%) and overall fit acceptance (0-4) and reason if Grade 2 or less.	Appendix A – Lens Fit
1.24	Dispensing Criteria	Confirm if vision and lens fit is acceptable. If lens fit is not acceptable, the subject must be discontinued from the study and complete the Exit eCRF.	
1.25	[redacted]	[redacted]	[redacted]

Number	Assessment	Procedure	Instructions and gradings
1.26	Instructions	• The Participant Instruction Guide will be provided to all subjects and it will give instructions regarding lens wear and care. • The Investigator or a clinical assistant will review instructions and warnings for lens wear, when to remove lenses, and other important issues with the participant. Participants who appear unable or unwilling to follow instructions to a degree that, in the Investigator's opinion, jeopardizes the participant's wellbeing or the validity of the study, will be discontinued. • Subject will be instructed to wear the lenses on a daily wear basis (at least 6 days per week and at least 8 hours per day) until the 2-week follow-up appointment, unless they experience a problem which warrants lens removal. In this case, the subject should contact the investigator. [redacted] • In the event of lens loss or damage, replacement lens(es) will be dispensed at an unscheduled visit.	

7.2.4 Visit 2: 2-week Follow-Up

The 2-week follow-up visit will be scheduled approximately 14 days (13-17 days) from the initial lens dispensing date. The subject should attend wearing the study lenses. If the subject attends without the study lenses, the visit should be rescheduled, if possible within the visit window.

The following clinical test variables will be recorded on the Follow-Up Visit eCRF:

Number	Assessment	Procedure	Instructions and gradings
2.1	Concomitant Medications and Medical History Review	Record any changes to concomitant medications or medical history and confirm if the changes are Adverse events	
2.2	Study Lens Wearing Times	Record the typical insertion & removal times, number of hours worn today, typical time CL comfort deteriorates, maximum wearing time and number of days worn since last visit.	[redacted]
2.3	Subjective Assessments (Comfort, [redacted]	Record subject lens comfort (0-10), [redacted] subjective symptoms, [redacted]	[redacted]
2.4	Rewetting Drops	Record current rewetting drops usage (type and frequency)	
2.5	[redacted]	[redacted]	[redacted]
2.6	Lens Surface Characteristics	Assess and grade lens surface wetting (0-4) and lens deposits (film: 0-4; no. of white spots).	[redacted]
2.7	Lens Fit Assessments	Evaluate habitual lens centration (0-2), corneal coverage (Y/N), post-blink movement and primary gaze lag (0-4), tightness on push-up (%) and overall fit acceptance (0-4) and reason if Grade 2 or less. Remove study lenses and store in sterile saline (if Biomedics 55 Premier).	[redacted]

Number	Assessment	Procedure	Instructions and gradings
2.8	[redacted]	[redacted]	[redacted]
2.9	Re-insert study Lenses **(Control A subjects only)**	Re-insert study lenses then continue to step 2.13.	
2.10	Lens Dispense **(Control B subjects only)**	Dispense test lenses to subjects randomized with control B lenses. Repeat steps 1.17 to 1.23 with the test lenses. **NOTE:** To maintain subject masking, study lens blister packs will be opened out of subject's sight.	
2.11	Instructions	• Subject will be instructed to wear the lenses on a daily wear basis (at least 6 days per week and at least 8 hours per day) until the 4-week follow-up appointment, unless they experience a problem which warrants lens removal. In this case, the subject should contact the investigator. • **Control A subjects** – schedule Visit 3, 4-week follow-up, 27-31 days from Visit 1. [redacted] • **Control B subjects** – schedule Visit 3, 2-week follow-up visit within the next 13-17days. • [redacted]	

7.2.5 Visit 3: 4-week Follow-Up

Visit 3 will be scheduled 4 weeks (27-31 days) from Visit 1 for Control A subjects. For Control B subjects, Visit 3 will be scheduled 2 weeks (13-17days) from Visit 2.

The subject should wear the study lenses to the appointment. If the subject attends without the study lenses, the visit should be rescheduled, if possible within the visit window.

The following clinical test variables will be recorded on the Follow-Up Visit eCRF:

Number	Assessment	Procedure	Instructions and gradings
3.1	Concomitant Medications and Medical History Review	Record any changes to concomitant medications or medical history and confirm if the changes are Adverse events	
3.2	Study Lens Wearing Times	Record the typical insertion & removal times, number of hours worn today, typical time CL comfort deteriorates, maximum wearing time and number of days worn since last visit.	[redacted]
3.3	Subjective Assessments (Comfort [redacted]	Record subject lens comfort (0-10), [redacted] subjective symptoms [redacted]	[redacted]
3.4	Rewetting Drops	Record current rewetting drops usage (type and frequency)	
3.5	[redacted]	[redacted]	[redacted]
3.6	Lens Surface Characteristics	Assess and grade lens surface wetting (0-4) and lens deposits (film: 0-4; no. of white spots).	[redacted]
3.7	Lens Fit Assessments	Evaluate habitual lens centration (0-2), corneal coverage (Y/N), post-blink movement and primary gaze lag (0-4), tightness on push-up (%) and overall fit acceptance (0-4) and reason if Grade 2 or less.	[redacted]

Number	Assessment	Procedure	Instructions and gradings
3.8	[redacted]	[redacted]	[redacted]
3.9	Subjective Questionnaire (Preference and Likelihood of Purchase) and Study Exit **(Control B subjects)**	Subjects will be asked a number of questions regarding their lens preference and likelihood of purchase. The responses will be entered by the investigator into the eCRF. Study Exit procedures (Section 7.2.8 steps 1-4) will then be completed for Control B subjects.	Appendix A – Subjective Assessments
3.10	Lens Dispense **(Control A subjects)**	Dispense test lenses to subjects who had been randomized to Control A lenses. Repeat steps 1.17 to 1.25 with the test lenses. **NOTE:** To maintain masking, study lens blister packs will be opened out of subject's sight.	
3.11	Instructions **(Control A subjects)**	• Subject will be instructed to wear the lenses for at least 6 days per week, 8 hours per day. • [redacted]	[redacted]

7.2.6 Visit 4: 6-week Follow-Up (**Control A subjects only**)

The 6-week follow-up will be scheduled 13-17 days from Visit 3. Subjects will attend the visit wearing their study lenses. If the subject attends without the study lenses, the visit should be rescheduled, if possible within the visit window.

The same assessments will be followed as at Visit 2, 2-week follow-up (steps 2.1 to 2.9) and will be recorded on the follow-up visit eCRF.

Subjects will be instructed to wear the lenses for at least 6 days per week and at least 8 hours per day. [redacted]

7.2.7 Visit 5: 8-week Follow-Up (**Control A subjects only**)

The 8-week follow-up will be scheduled 27-31 days from Visit 3. Subjects will attend the visit wearing their study lenses. If the subject attends without the study lenses, the visit should be rescheduled, if possible within the visit window.

The same assessments will be followed as at Visit 3, 4-week follow-up (steps 3.1 to 3.11) and will be recorded on the follow-up visit eCRF.

At this visit, the subjects will be asked a number of questions regarding their lens preference and likelihood of purchase. The responses will be entered by the investigator into the eCRF. Once completed, proceed to Study Exit procedures below.

7.2.8 Study Exit

The Study Exit eCRF must be completed when a subject exits the study. This will occur either at study completion, i.e. after Visit 3 or 5, or if the subject is discontinued from the study at another time. A Study Exit eCRF must be completed for all subjects who have a fully executed consent form. The exit date should also be recorded on the subjects named patient notes i.e. the Source Document Record. Post-study follow-up visits will be scheduled if the Investigator judges this is necessary. In this case the Exit eCRF will not be completed until all post-study visits have been completed.

At the study Exit Visit the following measurements are taken and recorded on the Exit eCRF:

Number	Assessment	Procedure	Instructions and grading
1	[redacted]	[redacted]	
2	[redacted]	[redacted]	
3	[redacted]	[redacted]	[redacted]

Number	Assessment	Procedure	Instructions and grading
4	Subject Study Exit	Record if the subject has successfully completed the study. If the subject is being exited due to discontinuation, further details need to be recorded on the Exit eCRF. This is described in Section 7.4.	

[redacted]

7.3 Clinical Variables

Table 2 summarizes the clinical measurements to be taken at each visit.

Table 2: Summary of Clinical Measurements

PROCEDURES	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5	Unscheduled	Exit
	Day 0	2-week Follow-up	2-week* or 4-week+ Follow-up	6-week Follow-up	8-week Follow-up	As required	
Informed Consent	X						
Demographics	X						
Medical history	X						
Concomitant medications review	X	X	X	X	X	X	
Wearing time	X	X	X	X	X		
Subjective Assessments (Comfort, Symptoms inc. dryness and Vision Quality)	X	X	X	X	X	X	
[redacted]	X	X	X	X	X		
[redacted]	X	X	X	X	X		
Lens fit assessment	X	X	X	X	X		
[redacted]	X						
[redacted]	X						X
[redacted]	X					X	
[redacted]	X	X	X	X	X	X	X
Subject questionnaire (Preference and l kelihood of purchase)			X*		X+		
[redacted]							X
[redacted]	X						
Dispense study lenses	X*+ (Control Lens Dispense)	X* (Test Lens Dispense)	X+ (Test Lens Dispense)				
Adverse events & Device deficiencies	As required						

+*Control A subjects* **Control B subjects*

7.4 Subject Discontinuation

Subjects may be discontinued from the study in the event of any of the following occurring:

i. Unacceptable subjective discomfort (i.e. lens cannot be tolerated or worn)

[redacted]

iii. Unacceptable fit (i.e. lens too tight or too loose)

iv. At the discretion of the Investigator or the subject

In the event of discontinuation, the Study Exit eCRF must be completed and the study exit date recorded on the Source Document Record. The Investigator will indicate the primary reason for discontinuation by selecting one of the boxes provided on the Exit eCRF. Comments can be added to the eCRF if necessary.

If a subject is discontinued outside of a visit window, an Unscheduled Visit eCRF must also be completed

7.5 Unscheduled Visits

An unscheduled visit is defined as any follow-up that occurs outside the visit window of the scheduled visit. A visit is also classified as unscheduled if the subject is seen a second time within the scheduled visit window.

Investigators should try as far as possible to schedule follow-up visits within the window. If this is not possible, and the visit falls outside the window, the visit will be an unscheduled visit, unless it has been agreed with VCR that it can be considered a scheduled visit.

Alternatively, the Investigator might judge that a follow-up visit is in the best interest of the subject and schedule two visits within the same window, e.g. follow-up of an adverse event. Unscheduled visits are also made available anytime at the subject's request.

Unscheduled visits will be recorded on the Unscheduled Visit eCRF. All variables listed on the forms must be completed unless the subject exhibits a condition that prohibits the completion of a full visit. If this is the case, a written explanation is required in the comments section (e.g. not wearing lenses due to discomfort).

Presenting VA, slit lamp variables and symptoms including dryness must always be completed and the reason for the visit and any actions taken must be indicated on the forms.

7.6 Site Training and Visits

The study initiation will take place via on-line training modules and a phone call.

The sponsor or VCR may choose to initiate an on-site visit as deemed appropriate. If this occurs, VCR will email prior to the visit to arrange a convenient time. Interim and close-out monitoring visits will be documented in the Monitoring Plan which is a separate document.

8 ADVERSE EVENTS

An Adverse Event (AE) is defined as any unfavorable or unintended sign (including an abnormal finding), symptom or disease temporarily associated with the use of a study device whether or not related to the study device. All ocular AEs and related (to the study device and/or to the study procedures) non-ocular AEs, will be monitored and reported on throughout the study.

Transient symptoms such as end-of-day dryness, lens awareness, itching or burning or other discomfort may occur with contact lens wear and may occasionally reduce wearing time. These are not reported as adverse events unless in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.

Possible ocular AEs are summarized in Table 3 below.

The Investigator will be required to judge whether or not an AE is device-related. Re-occurring device-related events from the same subject are usually tabulated as separate events. In the

case where more than one diagnostic finding is associated with an AE, the event will be counted as one event and categorized under the most significant of the findings.

The Investigator will be required to report all Ocular and Non-Ocular AEs to VCR and to their IRB as required by the IRB guidelines. The seriousness of an AE is categorized as being serious, significant, or non-significant (see Table 3 for example classification of ocular events).

Table 3: Ocular Adverse Events by Severity

Serious	Significant	Non-significant
Results in, or have the potential to cause either permanent impairment of a body function or damage to a body structure and may necessitate medical or surgical intervention. They include but are not limited to:	Symptomatic and warrant discontinuation of contact lens wear (temporary or permanent). They include but are not limited to:	Usually asymptomatic and do not warrant discontinuation of contact lens wear (temporary or permanent). However, as a precautionary measure the Investigator may decide to take action. They include but are not limited to:
MK – Microbial keratitis Permanent reduction in best spectacle-corrected visual acuity (≥ 2 lines) Central (4mm) corneal opacity Central corneal neovascularization Uveitis Iritis Endophthalmitis Hypopyon Hyphemia Penetration of Bowman's membrane Persistent epithelial defect Limbal cell damage leading to conjunctivalization Any untoward medical occurrence that results in death, is life-threatening, requires hospitalization or prolongation of existing hospitalization, results in persistent or significant disability/incapacity or is a congenital anomaly/birth defect	CLPU – Contact lens peripheral ulcer CLARE – Contact lens associated red eye SIE – Significant infiltrative event SEAL – Superior epithelial arcuate lesion Corneal warpage SLK – Superior limbic keratoconjunctivitis Other significant ≥grade 3 corneal findings (e.g. edema or abrasions) Any corneal event which necessitates lens wear discontinuation of > 2 weeks Non-CL related anterior segment events e.g. EKC – epidemic keratoconjunctivitis Temporary loss of ≥ 2 lines of best spectacle-corrected visual acuity New corneal scar without positive history	CLPC – Contact lens associated papillary conjunctivitis SPK – Superficial punctate keratitis Non-significant infiltrative event Blepharitis Meibomitis Contact dermatitis Localized allergic reactions, including solution-related ocular toxicity Conjunctivitis: Bacterial, Viral, Allergic Keratoconjunctivitis Any corneal event not explicitly defined as a serious or significant event which necessitates lens wear discontinuation <2 weeks Other slit lamp findings requiring treatment

For additional information, questions, or assistance in recording potential AEs, contact VCR.

8.1 Adverse Event Categorization

The Investigator will be required to rate the likelihood of an event being device-related (Possible, Probable, Highly Probable) or non-device-related (unlikely, definitely not) in their AE evaluation.

8.2 Adverse Event Reporting

On finding an AE the Investigator will complete an Adverse Event form (AE form) in EDC to capture the event.

The Investigator must notify Visioncare Research of the AE, so that they are able to provide advice and support to the Investigator on how to proceed.

The Investigator must do this by providing the information on the AE eCRF as soon as possible as and no later than:

- 24 hours from discovery if event is Serious or Significant
- 5 working days from discovery if event is Non-Significant

Once the form is saved, an automatic email will be sent to VCR and the Sponsor to notify them of the event. If the AE form in EDC cannot be completed on the day of discovery of the AE, then the Medical Monitor must be contacted to notify them of the AE.

If applicable, VCR will advise the Investigator to notify the IRB as per the IRB requirements. VCR may notify the IRB on behalf of the Investigator.

The Investigator must notify VCR in writing that the AE has been reported to the IRB.

8.3 Adverse Event Documentation

Investigators are required to document and follow-up all AEs.

All AEs must documented on an AE form in EDC upon event discovery. For all ocular AEs, one AE form is used per eye. For AEs which are non-ocular only one AE form will need to be completed in EDC per AE.

Procedure:

The Investigator has the responsibility to:

1. Complete as much information as possible on the AE form in EDC upon event discovery. This includes:
    - A detailed description of the AE and a diagnosis, including a probable cause.
    - Likelihood of the AE being device-related
    - Lens lot and power details (irrespective of whether lenses were being worn at time of the AE)
2. Include in the patient notes detailed drawings that detail size, location and depth or photographs (if necessary)
3. If serious, collect any contact lenses worn, solutions, and the lens case used at the time.
4. Report the AE to the sponsor (via VCR) and the IRB within the specified timelines (see Adverse Event Reporting section 8.2).
5. Follow study subject until resolution recording all information on an unscheduled visit eCRF, including VA, symptoms, slit lamp findings, resolution, and permanent sequelae if any.
6. Complete all remaining information as required on the AE resolution eCRF. If follow-up of the AE is required, the resolution form can only be completed when all AE follow-up visits are finished. The following additional information will also be completed on the AE resolution form:
    - Outcome, ocular sequelae if any

- Whether the patient is discontinued from the study as a result of the AE

8.4 Adverse Event Follow-up

The Investigator will conduct follow-up examinations until the condition:

- Has returned to pre-event status,
- Is considered stabilized
- Or has been satisfactorily explained.

If the subject is referred for medical attention, they will be tracked by the Investigator until the aforementioned conditions are met.

Follow-up data will be collected on an unscheduled visit eCRF and on the AE form in EDC.

The Investigator should use his/her clinical judgement as to whether or not the subject reporting with an AE should continue in the study.

8.4.1 Device Deficiency

A device deficiency means the failure of the device to meet its performance specification or otherwise perform as intended. A device deficiency would be considered reportable to the Sponsor if considered to be likely to cause or contribute to a Serious Adverse Event.

The Investigator will be required to report all reportable device deficiencies to the VCR/Sponsor via the applicable form in the EDC system.

8.4.2 Sponsor Safety Responsibilities

The sponsor will ensure that all participating Investigators are promptly informed of significant new safety information with respect to the study devices as per regulatory requirements.

To comply with this, the sponsor is responsible for promptly advising (in writing, via VCR) all Investigators conducting clinical studies of any incidents of serious or unexpected adverse events/unanticipated adverse device effects reported for the devices/products involved in those studies.

8.5 Study Completion

The study is completed when all subjects have completed the final visit (Visit 3 or 5 depending on control lens group) or been discontinued, and have been exited from the study.

9 DATA MANAGEMENT

9.1 Electronic Case Report Forms/Data Collection

The clinical data for this study will be entered by designated study site personnel onto electronic report forms (eCRFs) using the electronic data collection (EDC) system Medrio.

Medrio is compliant with all relevant aspects of ICH/Good Clinical Practices and 21 CFR Part 11 (Electronic Records & Electronic Signatures) regulations.

9.2 Data Quality Assurance

When eCRFs are reviewed at VCR, they will be subjected to error checking and data queries will be raised electronically via the EDC system for resolution of omissions and discrepancies by the investigator.

Before the final closing of the database, the data will be checked and approved for analysis as per VCR SOPs. This includes checking for missing or erroneous data entries.

9.3 Data Entry and Storage

All study data shall be entered into the study eCRFs. All statistical analyses will be completed by VCR using SAS software (SAS Institute Inc., Version 9.4 or later).

10 SAMPLE SIZE AND STATISTICAL METHODS

10.1 Sample Size Rationale

Assuming a discontinuation rate of 10%, 100 subjects, 50 subjects per group would detect a mean difference in comfort of smaller than 1.0 (0-10 scale).

Table 4: Sample size calculation.

	Comfort		
Scale		0-10	
Type I (a)		5%	
Power (1-b)		80%	
SD of difference between pairs (σ)		1.9	
Minimum detectable difference (T-C) (δ)	0.50	0.75	1.00
Minimum size per group (Inequality)	116	53	31

N.B. Calculations performed using Hintze, J. (2013). PASS 12. NCSS, LLC. Kaysville, Utah, USA. www.ncss.com.

10.2 End-points

Primary:

Comfort reported at visit. Subjects will be asked the following question: "Thinking about the last week of CL wear, how would you assess the overall comfort of your/the study lenses – please rate overall comfort on a 0 to 10 scale, where 10= 'can't feel the lenses' and 0= 'extremely uncomfortable' "

Secondary:

The following variables will be the secondary end-points:

i. Wearing time: Average WT & Comfortable WT [hrs]
ii. Surface wetting: Pre-lens tear film quality [0-4]
iii. Deposits: Film deposits [0-4]
iv. White spot deposits [no.]

v. Overall lens fit acceptance [0-4].

10.3 Statistical Considerations

All statistical analyses will be performed using the SAS software Version 9.4 or later (SAS Institute, Cary, NC).

The final analysis will be completed after all subjects have been exited from the study, all queries have been resolved, and the database has been locked.

The overall type I error rate will be preserved at 5%. All tests will be two-sided. The primary hypothesis must be met in order to satisfy the objective of this study.

From the insertion and removal times the average wearing time will be calculated. If the subject indicates that lens comfort deteriorates during wear, the comfortable wearing time will be calculated from the insertion time and the time that lenses become uncomfortable. If there is no deterioration in comfort then the average wearing time will be used [redacted]

Data from unscheduled visits will not be included in the analysis.

Any deviations from this analysis plan will be detailed in the study report.

10.4 Analysis Population

Statistical analyses will be conducted on all randomized subjects who have successfully completed the study without a protocol deviation that is regarded as impacting the assessment of the primary hypothesis (as per protocol). Missing data will be excluded from the analysis and will not be extrapolated from the collected data.

10.5 Descriptive Statistics

Descriptive statistics will be reported at dispensing and each follow-up visit. Continuous variables will be summarized using mean, standard deviation, and range; and categorical data variables will be summarized using percent frequency distribution, mean, and SD. Nominal variables will be summarized using percentages.

Summaries will be presented by control group for each lens type.

10.6 Data Pooling

Data will be pooled from multiple study sites for this analysis, the basis for pooling comes from three factors:

- The study sites must implement one common protocol.
- VCR must closely monitor study site protocol compliance.
- The study sites must use common data collection procedures.

10.7 Primary Statistical Analysis

Comfort scores at the final follow-up visit will be analysed using a mixed linear model. The model will include the following fixed effects: lens type, control group, site, and the interaction of lens type by control group; and subject nested in site as a random effect. The least-square means and their differences will be reported with 95% confidence intervals for each lens type

by control group. Conclusions will be drawn from the 95% confidence interval of the least-square mean differences.

10.8 Secondary Statistical Analysis

The secondary variables will be analysed using mixed linear models. The models will include the following fixed effects: lens type, control group, site, and the interaction of lens type by control group; and subject nested in site as a random effect. The least-square means and their differences will be reported with 95% confidence intervals for each lens type by control group. Conclusions will be drawn from the 95% confidence interval of the least-square mean differences.

10.9 Additional Statistical Analysis

Other selected variables may be analysed using appropriate statistical methods. A *P*-value less than or equal to 0.050 will be regarded as statistically significant.

10.10 Interim Analysis

There are no planned interim analyses for this study.

11 GENERAL STUDY MANAGEMENT

11.1 Relevant Standards

This protocol has been developed in accordance with the following:

- ISO 14155-1:2011 Clinical Investigation of Medical Devices for Human Subjects
- ISO 11980:2012 Contact Lenses and Contact Lens Care Products – Guidance for Clinical Investigations.
- ICH Harmonized Tripartite Guideline for Good Clinical Practice
- Declaration of Helsinki

The study will also be carried out in accordance with the VCR Quality Management System (ISO 9001:2015) and all the applicable local guidelines.

11.2 Ethics Review

The study protocol, Participant Information Sheet and Informed Consent Form and all other required documents will be submitted to Sterling IRB for each site. A favorable opinion will be received prior to undertaking the study.

If significant protocol changes which require the preparation of an amendment are necessary, written IRB approval will be obtained prior to implementation.

11.3 Protocol Deviations

The Investigators will not deviate from the protocol without written approval from the IRB and VCR.

In medical emergencies, Investigators will use their judgement and remove the subject from immediate hazard. Any significant changes or deviations in the protocol will be the subject of a protocol amendment and must be pre-approved by the IRB.

If an unexpected deviation from the protocol occurs the Investigator must notify the VCR immediately and the deviation from the protocol will be reported on a Protocol Deviation form in EDC and appropriate action taken.

11.4 Premature Termination of the Study

The sponsor reserves the right to terminate the study at any time for any reason including adverse effects. If it is determined that an unanticipated adverse device effect presents an unreasonable risk, then the entire investigation or part of the investigation presenting the risk shall be terminated as soon as possible. A written statement fully documenting the reasons for such termination will be provided to the IRB.

11.5 Source Documentation

Unless otherwise documented, the eCRFs will be considered the source document. The sponsor or sponsor's representatives will be authorized to gain access to the source documentation for the purposes of monitoring and auditing the study (See Sections 11.6, 11.7).

The Source Document Record must be completed to comply with GCP guidelines. It is a permanent record within the patient's chart/notes that documents the subject's involvement in a clinical research study.

Contents of the source document record:

- Study number
- Subject ID
- Confirmation that subject met eligibility criteria
- Confirmation that subject signed the informed consent
- Confirmation that subject received a signed and dated copy of informed consent
- Date enrolled
- Details of lenses worn on study
- General notes
- Adverse events
- Reportable Protocol deviations
- Exit date
- Whether subject completed the study or discontinued
- Investigator's signature

The Source Document Record will be completed for each subject upon enrolment and then updated when required, e.g. when subject exits the study.

11.6 Monitoring

Investigational site monitoring will be performed by a qualified study monitor identified by the sponsor or VCR. On-site visits will be completed at each site. The frequency and procedure of the monitoring visits will be documented in the Monitoring Plan which is in a separate document. The Investigator will allow the study monitor and sponsor representatives or IRB to observe procedures and inspect study records and subjects' medical records throughout the study to verify protocol compliance, case report completeness, and investigational material accountability. Should the Investigator be found to be non-compliant and unwilling or unable to convert noncompliant practices, VCR in consultation with the sponsor will terminate the Investigator's role in the investigation and the IRB will be notified.

11.7 Audits

The Investigator shall permit VCR, the sponsor and the IRB to inspect its facilities, equipment, and study-related records, data and other documents upon reasonable notice. In addition, the IRB may conduct such inspections as they deem necessary at any time whether or not advanced notice is given by them. The Investigator agrees to notify the sponsor or VCR within 24 hours (or as soon as reasonably practicable) of the start of any unannounced inspection by the IRB or of the receipt from the IRB of a notice of inspection whether given in writing or orally. If such notice is in writing, a copy with any attachments thereto shall be provided to VCR or the sponsor.

11.8 Records Retention

According to the ICH GCP guidelines the essential documents should be retained until at least two 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 at least two years have elapsed since the formal discontinuation of clinical development of the investigational product. It is the responsibility of the sponsor to inform the Investigator/institution as to when these documents no longer need to be retained. The study lens material is already on the market and therefore the study documents should be kept for a minimum of two years after the end of the study. As the clinical research organization supervising the study, VCR will also retain the written records for the same period of time. Following such retention period, the Investigator or the Clinical Site shall deliver to the sponsor all such Research Results, unless otherwise instructed in writing by the sponsor. Notwithstanding the foregoing, all information provided by or with respect to subjects in the Study will be furnished by Investigator and Clinical Site without patient names.

11.9 Confidentiality and Publication

This study is confidential in nature. The Investigator shall make no public statement, whether in written, oral or electronic form, relating to the VCR, the Sponsor, the substances, materials, products and devices being investigated or the Study itself without obtaining the prior written consent of the VCR or the Sponsor.

All information gathered during this study is proprietary and should be made available only to those directly involved in the study who have a need to know.

Authorized recipients of this data include:

- Investigator and co-investigator(s)
- Other allied health care personnel necessary for the conduct of the study
- IRB personnel
- Sponsor representatives
- Contract Research Organization
- Designated study monitor
- Designated medical monitor
- FDA or other government regulatory agencies

All above personnel who are provided with data concerning this study will be informed of its confidential and proprietary nature. Release of this data (through presentation, publication or other written or oral communication) to other than the above listed personnel requires the prior written permission from the study Sponsor. Study investigators and all office personnel are prohibited from acknowledging participation in the study to individuals and organizations except those listed above. This includes sales representatives and other departments or subsidiaries of the sponsor without the direct written permission of the sponsor.

The study will conform to the requirements of the Health Information Portability and Accountability Act (HIPAA). By signing the authorization to use and disclose protected health information the subject authorizes the sponsor and the sponsor's representatives (VCR) to access their optometric clinical records. This authorization will expire 50 years from the date the subject signs. Subjects will have the right to reverse this authorization at any time.

All patient information will have the patient name (or any information that can identify the patient apart from the mobile phone number) removed before leaving the Principal Investigator's site.

In accordance with the VCR Confidentiality Policy, the data, information, and reports arising from this project are the property of the sponsor company. By signing the Informed Consent Form the subject also understands that their data will be sent to VCR in the UK and the sponsor in the US. VCR will not release to a third party any information arising from this study unless required to do so by a legal or regulatory body. The electronic records will also be handled in accordance with Health Information Portability and Accountability Act (HIPAA).

The study will be registered on the website www.clinicaltrials.gov.

12 REFERENCES

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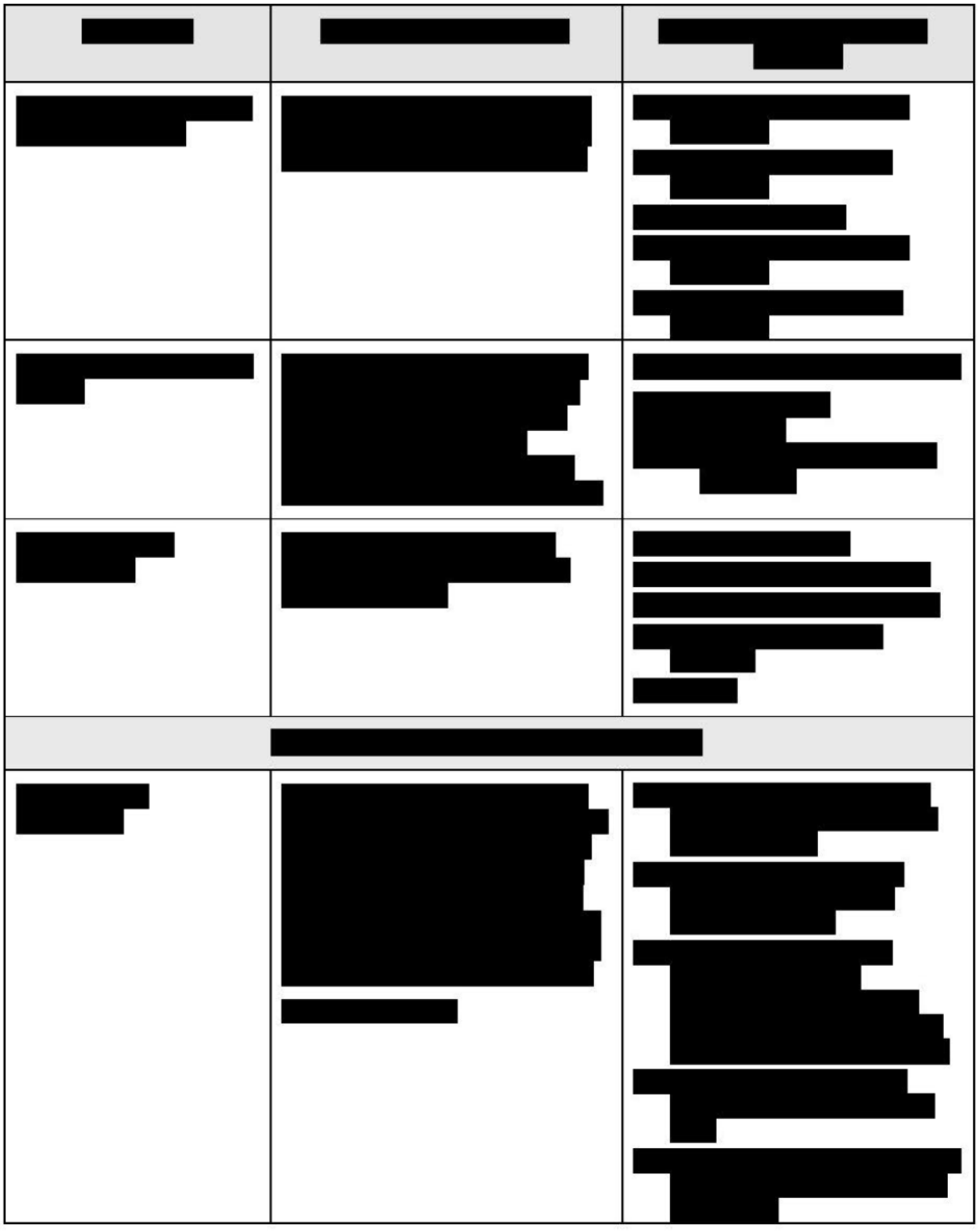
APPENDIX A

[redacted]

[redacted]



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MEASUREMENT INSTRUCTIONS

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