CooperVision

Performance of Avaira Vitality Toric (Fanfilcon A toric) after at least One Month wearing Avaira Toric (Enfilcon A toric)

[redacted]

Sponsor Study Code:	EX-MKTG-67
Protocol Date:	July 2016
Sponsor Company:	CooperVision, Inc.
Document Type:	Protocol
Study Category:	Post Market
Start Date:	Sept 2016
Finish Date:	March 2017
Clinical Site:	Multicenter
Protocol Sponsor:	[redacted]
	CooperVision
CRO Centre for Contact Lens Research:	[redacted]

Revision History

Document number	Date	Comments
EX-MKTG-67	8/29/2016	First draft (v 1.0)
EX-MKTG-67	8/31/2016	Second draft (v 2.0)
EX-MKTG-67	9/13/2016	Third draft (v 3.0)

PERSONNEL & FACILITIES

STUDY SPONSOR:

CooperVision Inc.
6150 Stoneridge Mall Road, Suite 370
Pleasanton, CA 94588
USA

[redacted]

STUDY INVESTIGATORS:

Site A Spokane Eye Clinic
Dr. Jennifer Kerns

Site B Hospital Contact Lens Service
Mr. Bill Winegar

Site C West Village Eyecare
Dr. Hakim Serhrouchni

Site D Debbie Kim, O.D.
Dr. Debbie Kim

CRO: Centre for Contact Lens Research, Waterloo, Canada
School of Optometry & Vision Science | University of Waterloo
200 University Ave West, Waterloo, Ontario, N2L 3G1 | Canada

Protocol Synopsis

Protocol Number	EX-MKTG-67
Title	Performance of Avaira Vitality Toric Lenses after at least One Month wearing Avaira Toric Lenses
Name of Device(s) and (by USAN material)	Avaira Vitality Toric (Fanfilcon A) Avaira Toric (Enfilcon A)
Indications for Use	**Approved for use:** • Avaira Vitality Toric (Fanfilcon A). (Daily wear) • Avaira Toric (Enfilcon A). (Daily wear) **Indication for use in this study:** • 1 month of daily wear, each lens
Study Design	Prospective, multi-center, subject-masked, bilateral, daily wear, two-month dispensing study.
Purpose	The aim of this study is to determine if adapted contact lens wearers of Avaira Toric (Enfilcon A) lenses can be confidently refit into Avaira Vitality Toric (Fanfilcon A) lenses and can be successful after one month of daily wear.
Study Duration	The anticipated timeline for this study is as follows: • Subject enrolment begins: Sept 2016 • Last subject visit anticipated: Jan 2017 • Visits: V1: Screening & optimize prescription for Avaira toric V2: Dispense new or optimized prescription Avaira Toric - *this visit may not be necessary if subjects habitually wear optimized power Avaira Toric* V3: Baseline Avaira Toric & Avaira Vitality Toric dispense V4: 2 week follow-up wearing Avaira Vitality Toric V5: 1 month follow-up wearing Avaira Vitality Toric & Exit
Patient Population	Habitual toric contact lens wearers that provide written informed consent and meet protocol entry criteria.
Sample Size	Target enrollment of 48 subjects with the hope of at least 44 subjects being in the analysis cohort.
Study Center Location (US)	USA
Number of Centers	Multi-Center, 4 sites.

Patient Follow-up	Patients enrolled in this study will be followed up after the each lens dispensing session. Follow-ups at: o at least 1 month lens wear of Avaira Toric o 2-week and 1 month wear of Avaira Vitality Toric
Primary Endpoints	• Visual acuity with contact lenses, • Lens fit performance (centration, rotation, blink movement) • Investigator's fit acceptability
[redacted]	[redacted]

Table of Contents

1 Introduction

The utilization of soft toric contact lenses has increased significantly over the past few years. CooperVision (CV) produces a number of toric contact lens products including the Avaira toric brand (Enfilcon A) and Avaira Vitality brand (Fanfilcon A). All Enfilcon A toric lenses and Fanfilcon A toric lenses feature CooperVision's exclusive Aquaform® Technology and PEG (Polyethylene Glycol). This combination of material technologies provides a contact lens with high oxygen permeability that is naturally wettable and offers unique comfortable experience.

This study is designed to evaluate how adapted contact lens wearers of Enfilcon A toric lenses will perform following a refit with Fanfilcon A toric lenses, a novel soft contact lens with optimized lens geometry and enhanced water content and UV protection, over one month of daily wear. Overall lens wear experience, including visual quality, lens fit and subjective responses will be assessed.

2 Study Objective

The aim of this study is to determine if adapted contact lens wearers of Enfilcon A toric lenses can be confidently refit into Fanfilcon A toric lenses and be successful after at least one month of daily wear.

Primary outcomes:

- High contrast distance visual acuity (Snellen) with contact lenses
- Lens fit performance (centration, corneal coverage, post blink movement)
- Investigator's fit acceptability

3 Study Hypothesis

3.1 Study Hypothesis

- Null hypothesis (Ho): There is no difference in lens performance between Enfilcon A toric and Fanfilcon A toric lenses for the key variables measured.
- Alternative hypothesis (H1): There is a difference in lens performance between Enfilcon A toric and Fanfilcon A toric lenses for the key variables measured.

4 Study Design

This is a prospective, multi-center, subject-masked, bilateral wear, two month dispensing study comparing the clinical performance of the Fanfilcon A toric lenses following a refit and adaptation with Enfilcon A toric lenses (Table 1). The subjects will be fit bilaterally into the Enfilcon A toric lenses at the first visit (or continue wearing their habitual Enfilcon A toric lenses) which will be worn for a minimum of one month and then subjects will be re-fit bilaterally with a pair of Fanfilcon A toric lenses for another month of daily wear. After the dispensing Fanfilcon A toric lens, subjects will return for follow up evaluations after 2 weeks, and 1 month.

The subjects will be advised that they may be dispensed with either Enfilcon A toric lenses OR Fanfilcon A toric lenses, however all subjects will be refit with Fanfilcon A toric lenses. The participant will not be informed on which study lens he/she is wearing during the second month but the investigator will have this information.

5 Study Population

5.1 Sample Size Calculation

A sample size calculation was provided based on the 'subjective comfort just before lens removal' (0-10 scale) data on file at CooperVision from study EX-MKTG-63, which gave a standard deviation of 2.4. For an alpha level of 0.05 and power of 0.8, a sample size of 44 will detect a difference of 1.04, which has been confirmed as acceptable by the sponsor.

We recommend dispensing lenses to at least 48 subjects to be sure to have 44 subjects in the eligible analysis population ie. 12/13 at each of the 4 sites.

6 Investigational Sites

6.1 Number of Sites

This study design considers 4 sites within the U.S.

6.2 Investigator Recruitment

The principal investigator and co-investigators at each site will be required to fulfil the following criteria:

- Licensed Optometrist or experienced clinician with at least two years of contact lens fitting experience.
- Experienced Investigators who will be trained in Good Clinical Practice (GCP) by the principal investigator.
- In-office email and either document scanning capabilities or fax.
- Willingness to follow the study protocol and to co-operate with the study monitors.

This clinical study is designed to be in conformance with the ethical principles in the Declaration of Helsinki, with the ICH E6 guidelines for Good Clinical Practice (GCP) and all the applicable local guidelines.

7 Ethics Review / Statement of Compliance

7.1 Relevant Standards / Guidelines

This implementation document has been developed in accordance with the following:

- ICH E6- International Conference on Harmonization: Good Clinical Practice (GCP)
- Declaration of Helsinki

7.2 Institutional Review Board

This study will be conducted in accordance with Institutional Review Board regulations (U.S. 21CFR Part 56.103) or applicable IEC regulations. Copies of all IRB/IEC correspondence with the investigator/sponsor will be kept on file. The study will commence upon approval from the following Institutional Review Board: Sterling Institutional Review Board; Telephone number: (888) 636-1062 and email address: info@sterlingirb.com.

7.3 Clinical Trial Registration

This study will be registered with clinical trials.gov in accordance with section 801 of the Food and Drug Administration (FDA) Act which mandates the registration of certain clinical trials of drugs and medical devices.

7.4 Informed Consent

Informed consent (App 18) shall be obtained in writing from the subject and the process shall be documented before any procedure specific to the clinical investigation is carried out.

8 Potential Risks and Benefits to Human Subjects

There may be direct benefits to the subjects in this study, such as improved vision and/or comfort. Participation in a study may contribute to scientific research information that may be used in the development of new contact lens products. In addition, subjects will receive an examination of the front part of their eyes and may have the opportunity to try a different type of soft contact lenses and/or different lens care products at no cost to them. The contact lens materials used in this study are commercially available as daily wear. This study will investigate subjects' wearing schedule intended for daily wear (NOT extended wear), similar to the average wearing time of 10-16 hours for daily wear lenses.

This study is considered to be a non-significant risk study based on United States Food and Drug administration (FDA) and International Standards Organization (ISO) guidelines, because the study devices used as intended in this study (1) do not represent a potential for serious risk to the health,

safety or welfare of the subject, and (2) are not implants, (3) are not used to support or sustain human life, (4) are not of substantial importance in diagnosing, curing, mitigating or treating disease or otherwise prevents impairment of human health.

Complications that may occur during the wearing of contact lenses include discomfort, dryness, aching or itching eyes, excessive tearing, discharge, hyperemia and variable or blurred vision. More serious risks may include pain, photophobia, iritis, corneal edema or eye infection. Although contact lens-related infections are very infrequent, the possibility does exist. The incidence of infection due to day-wear soft lenses is 0.035%. Almost always an infection will occur only in one eye. This risk is assumed by 35-million Americans who currently wear contact lenses and only current soft lens wearers will be recruited for this study.

Routine clinical procedures including auto-refraction, auto-keratometry, visual acuity, anterior ocular health assessment, and contact lens fitting will be used. In addition, high magnification imaging of the lens fit may be made using 35 mm or digital cameras. Patients will be monitored until the end of the study to reduce the occurrence of adverse or potential adverse events. Patients will be given instructions from their investigator regarding early symptoms and signs of adverse events (also in App 18, Statement of Informed Consent).

9 Materials and Methods

9.1 Subjects

Approximately 48 astigmatic subjects will be enrolled with the aim of at least 44 subjects successfully completing the study and being part of the analysis population. Subjects will either be adapted wearers of Avaira Toric lenses, or they will be refit for a minimum of one month lens wear before being refit to Avaira Vitality Toric. Each subject will be required to attend up to five scheduled study visits over a period of approximately two months.

Each subject will be given a unique ID number. All subjects who sign a consent document will be included in the subject enrollment log which will include; subject ID, date of consent, date of screening, date of study completion, date of discontinuation (if req'd), reason for discontinuation (if req'd). (App 20)

Additionally, all subjects must meet the study inclusion and exclusion criteria listed below.

Inclusion criteria

A person is eligible for inclusion in the study if he/she:

- Is between 18 and 40 years of age (inclusive)
- Has had a self-reported eye exam in the last two years
- Is a habitual soft toric lens wearer
- Can be successfully fit with study lenses (≥ grade 2 fit acceptance)
- Has a contact lens spherical prescription between -1.00 to -6.00D with a cylinder between -0.75 and -1.75D (inclusive)
- Has a spectacle cylinder of at least 0.75D in each eye.

- Can achieve best corrected spectacle refraction distance visual acuity of 20/25 (0.10 logMAR) or better in each eye.
- Can achieve a distance visual acuity of 20/30 (0.18 logMAR) or better in each eye with the study contact lenses.
- Has clear corneas and no active ocular disease
- Has read, understood and signed the information consent letter
- Has a contact lens refraction that fits within the available parameters of the study lenses
- Is willing to comply with the wear schedule (at least 5 days per week, > 8 hours/day assuming there are no contraindications for doing so)
- Is willing to comply with the visit schedule.

Exclusion Criteria

A person will be excluded from the study if he/she:

- Has a history of not achieving comfortable CL wear (5 days per week; > 8 hours/day)
- Presents with clinically significant anterior segment abnormalities
- Presents with ocular or systemic disease or need of medications which might interfere with contact lens wear
- Presents with slit lamp findings that would contraindicate contact lens wear such as:
    - Pathological dry eye or associated findings
    - Significant pterygium, pinguecula, or corneal scars within the visual axis
    - Neovascularization > 0.75 mm in from of the limbus
    - Anterior uveitis or iritis (or history in past year)
    - Seborrheic eczema of eyelid region, Seborrheic conjunctivitis
    - History of corneal ulcers or fungal infections
    - Poor personal hygiene
- Has a known history of corneal hypoesthesia (reduced corneal sensitivity)
- Has aphakia, keratoconus or a highly irregular cornea.
- Has presbyopia or has dependence on spectacles for near work over the contact lenses.
- Has undergone corneal refractive surgery.
- Is participating in any other type of eye related clinical or research study.
- Is frequently using rewetting/ lubricating eye drops (more than once per day)

9.2 Study Materials

9.2.1 Contact lens

All subjects will have worn, or be fit with an optimized prescription in Avaira Toric for at least one month before being fit and dispensed the Avaira Vitality Toric. Details of the contact lenses are shown in Table 1.

The Avaira Vitality Toric lenses will be provided by the Sponsor. The sites may be asked to source the Avaira Toric lenses as needed and retain invoices for reimbursement.

Table1: Study lenses

Brand	Avaira Toric lenses **(Control)**	Avaira Vitality lenses **(Test)**
Manufacturer	CooperVision	CooperVision
Material	Enfilcon A	Fanfilcon A
Water Content	46%	55%
Base Curve	8.5	8.4
Lens Diameter	14.5	14.2
Lens Powers Sphere	-1.00 to - 6.00 (0.25 steps)	-1.00 to - 6.00 (0.25 steps)
Lens Power Cylinder	-0.75, -1.25, -1.75	-0.75, -1.25, -1.75
Axis	10^{o} to 180^{o} (10^{o} steps)	10^{o} to 180^{o} (10^{o} steps)
Replacement schedule	Daily wear	Daily wear

9.2.2 Contact Lens care

OPTI-FREE® PureMoist® multipurpose disinfecting solution and lens cases (Alcon, Fort Worth, TX) will be provided to all subjects for care and maintenance of the contact lenses during the study. The sponsor will be providing the lens care solutions to the sites. Subjects will be provided with written instructions on the proper use of this product to clean and disinfect their contact lenses (App 19, Package insert for OPTI-FREE® PureMoist® multipurpose disinfecting solution).

9.2.3 Rewetting/ lubricating eye drops

Subjects will be asked not to use rewetting/ lubricating eye drops during the study.

9.2.4 Storage of Study Medications/Treatments

There are no unapproved investigational products, medications or treatments used in this study requiring special storage accommodations. Room temperature storage is recommended for all study products.

9.2.5 Clinical Supply Inventory

There are no unapproved investigational products used in this study requiring special inventory requirements. Study product will be accounted for using the product accountability forms provided to each site by CooperVision.

9.2.6 Disposal of Consumables

This study dispenses consumables (lenses and lens care product) to subjects for use over 2 months during the study. All study lenses worn by subjects will be collected at their 1 month of wear, respectively. All unused lens care will also be collected and disposed of at the site. Please refer to App 23 for instructions.

9.2.7 Masking and Control of Study Materials

The study contact lenses will be **masked to the subject** only. Study lenses will be inserted from the blister pack after the foil has been removed and transfer to a lens case by the investigators/ assistant to aid masking. The investigator will not be masked.

9.2.8 Ordering and Accountability of Study Materials

The study lenses and solutions will be provided by the sponsor. If additional lenses are required, the study sponsor will re-supply the investigator as requested. The sites are responsible for completing accountability logs for lens dispenses.

9.3 Visit Schedule and Procedures

The visit schedule is shown in Table 2 below.

Table 2: Visit schedule

Visit code	Visit schedule	Visit Description
1	—	Screening and establish optimum prescription with Avaira Toric lenses.
2	1 to 2 weeks from Visit 1*	Dispense new or modified power Avaira Toric (scheduled when lenses are available)*
3	Greater than 28 days from V2 **	1-month Baseline Data collection wearing Avaira Toric AND dispense Avaira Vitality Toric**
4	2-weeks from Visit 3 (12-16 Days from V3)	2-week progress visit with Avaira Vitality Toric
5	1 month from Visit 3 (27-32 Days from V3)	1-month progress visit with Avaira Vitality Toric AND Study exit

**Note: Visit 2 is only necessary if a change in Avaira Toric power is required, or if a refit into Avaira Toric is required for adaptation*

***Note: This visit will be scheduled when Avaira Vitality Toric lenses are available to be dispensed*

The forms that need to be completed at each visit is outlined in Table below:

Table 2: Study Forms

Forms	Visit 1 / 1R	Visit 2 / 2R	Visit 3	Visit 4	Visit 5
Informed Consent Letter	X				
Inclusion/Exclusion	X				
Avaira Vitality Prescription Form	X*	X			
Avaira Toric Prescription Form	X**	X			
Biomicroscopy	X	X	X	X	X
Avaira Toric Dispense		X			
Avaira Toric Re-Dispense		X			
Baseline Avaira Toric			X		
Avaira Vitality Toric Dispense			X		
2W Avaira Vitality Toric				X	
1M Avaira Vitality Toric					X
Appendix 8 Subjective Assessment			X	X	X
Appendix 25 Subjective Assessment Insertion			X		
Appendix 9 Agreement questionnaire			X	X	X
Appendix 11 Lens Preference questionnaire				X	X
Investigator's preference			X	X	X

Note: Avaira Vitality Prescription Form will be completed at **V1 ONLY for those subjects that are current Avaira Toric wearers and do not require a change in prescription*

***Note: Contact Lens Order Form will be completed at **V1 ONLY** for those subjects that require fit into new or modified Avaira Toric lenses*

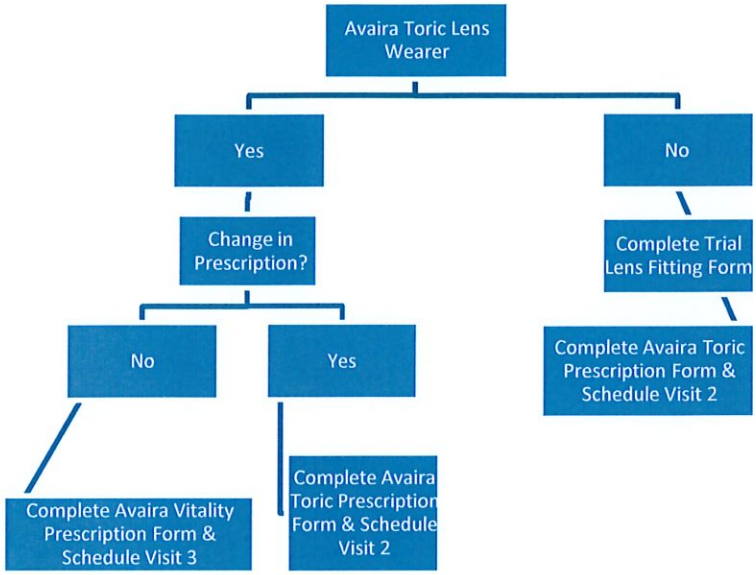
9.3.1 Visit 1: Screening visit & Establish Optimum Prescription

This visit will be performed to assess eligibility and to establish optimum prescription. The subjects should attend the first visit wearing their habitual lenses and having worn them that day for at **least 2**

hours prior to the visit. If they are not wearing their lenses, please reschedule the visit. The following baseline measurements and assessments will be recorded:

- The subject will be required to read and sign an Informed Consent Form prior to enrolment (App 18). When the subject has signed the consent form, the subject will be considered to be enrolled on to the study.
- The person explaining the consent/ the Investigator should also sign the consent form.
- The subject will be provided with a copy of the consent and the original will be kept in the subject's paper chart. It may also be scanned into the subject's electronic medical record (EMR) file.
- The subject is assigned with a Subject ID number. Subjects must be enrolled sequentially.
- The subject enrollment log will be updated (App 20).
- Screening Form (App 1) will be completed to assess eligibility with respect to habitual lens wear, ocular and medical history.
- Subject's age and gender
- Details of current lens:
    - Brand
    - Power(s)
    - Replacement schedule
    - Lens age (days)
- Current lens care used
- Use of rewetting/lubricating drops
- Habitual lens wearing times:
    - Average daily wearing time (hours/day)
    - Average comfortable wearing time (hours/day)
    - Number of days/week (lenses are worn).
- Health history and medications
- Overall habitual lens fit acceptance (0 - 4) and reason if Grade 2 or less and lens orientation
- Habitual high contrast, distance monocular Snellen visual acuity
- Habitual high contrast, distance binocular Snellen visual acuity
- Over-refraction with habitual lenses and Snellen visual acuity with over-refraction
- Remove habitual lenses.
- Automated refraction including keratometry readings
- Subjective sphero-cylindrical refraction and high contrast monocular and binocular Snellen visual acuity
- Determine if subjects need to be scheduled for Visit 2 or Visit 3:
    - For a subject who is a current Avaira Toric wearer and does not require a chance in prescription, please complete Avaira Vitality Prescription Form (App 3). Subject can be scheduled for Visit 3 when Avaira Vitality Lenses are available (≥29 days after screening visit 1).

- For a subject who is a current Avaira Toric wearer but requires a change in prescription, please complete Avaira Toric Prescription Form (App 2B) and schedule Visit 2.
- For a subject who is not a current Avaira Toric wearer, please complete Trial Lens Fitting Form (App 2A) and fit lenses accordingly, after the trial lens fit was successful, complete Avaira Toric Prescription Form (App 2B) and schedule Visit 2.



- Anterior segment ocular health will be assessment (App 4)
  - External Adnexa anomalies (Present/Absent & Describe)
  - Hyperemia
    - Bulbar (0-4, 0.5 steps)
    - Limbal (0-4, 0.5 steps)
    - Palpebral (0-4, 0.5 steps)
  - Cornea & Anterior eye
    - Infiltrates (0- 4, 1 step)
    - Conjunctival infection (0-4, 1 step)
    - EKC (0-4, 1 step)
    - Corneal ulcers (0-4, 1 step)
    - Lens Adhesions (0-4, 1 step)
    - Recurrent Erosions (0-4, 1 step)
    - Other abnormalities (0-4, 1 step)
  - Staining
    - Corneal Staining (0-4, 0.5 step & Optional sketch of staining)
    - Conjunctival Staining (0-4, 0.5 step)
    - Conjunctival Indentation (0-4, 0.5 step)
  - Other findings
- Eligibility Checklist (App 5) will be completed
- Complete Enrolment Log (App 20). If at this point the subject is found to be ineligible, then complete an Exit form (App 13) and exit the subject from the study.

- If a subject is a current Avaira Toric lens wearer and no change to the lens prescription is required then the subject will be instructed to wear the lenses on a daily wear basis, (at least 5 days/week, >8 hours/day), until Visit 3 appointment can be scheduled, unless they experience a problem which warrants lens removal.
- If a subject requires a new prescription for Avaira Toric lenses, please complete the Avaira Toric Prescription Form (App 2B), order the lenses and schedule Visit 2
- If a subject is not a habitual Aviara Toric wearer, re-fit subject into Avaira Toric lens using the Trial Lens Fitting Form (App 2A). After the fit was successful, please complete the Avaira Toric Prescription Form (App 2B), order the lenses and schedule Visit 2.

In some circumstances a repeated Screening may need to be scheduled. Examples include, but are not limited to:

1. Study procedures unable to be completed in time scheduled for visit;
2. Study products not available at the time of the study visit;
3. A transient health condition which may affect the eye(s) (e.g. a common cold, active allergies, fatigue etc.);
4. The short term use of medications (e.g. antibiotics, antihistamines etc.);
5. Reassessment of ocular conditions (e.g. corneal and/or conjunctival staining, scars etc.).

The maximum total number of repeat screenings permitted will be one (App1R)

9.3.2 Visit 2: Dispense of Avaira Toric Lens

If this visit is required, it will be scheduled when the Avaira Toric lenses are available. This visit will be performed to fit and dispense new or modified power Avaira Toric lenses. Hence, this visit is only necessary if a change in Avaira Toric power is required or if a re-fit into Avaira Toric is required for adaptation. The following measurements and assessments will be recorded:

- Ensure no changes to health/medications and no contraindications for lens wear (App 6A)
- Complete biomicroscopy (App 4)
- A minimum 5 minute washout time after fluorescein insertion is required prior to lens insertion. The performance of the lenses should be assessed after 10-15 minutes settling time. The following variables will be assessed (App 6A)
- Record the parameters of the lenses, lot number, and power, on the Dispensing CRF
- Vision
    - High contrast distance monocular Snellen visual acuity
    - High contrast distance binocular Snellen visual acuity
- Over- refraction and Snellen visual acuity with over-refraction
    - Amendments to the distance sphere power, cylindrical power and/or axis can be made. Record the number of trial lenses required to achieve a successful fit

- Overall lens fit acceptance (0-4) and reason if Grade 2 or less and record lens orientation
- To be successfully dispensed, subjects must show ≥Grade 2 lens fit acceptance with the trial fit lens and must be correctable to 20/30 (0.18 logMAR) or better in each eye with the study contact lenses.
- If the lenses are not a suitable fit to be dispensed then the subject will be discontinued and an Exit Form (App 13) will be completed.
- If successful lens fit and no lens modification is needed, then complete Avaira Vitality Prescription Form (App 3)
- The subject will be instructed to wear the lenses on a daily wear basis, (at least 5 days/week, >8 hours/day), until Visit 3 appointment, unless they experience a problem which warrants lens removal.
- The Investigator or a clinical assistant will review instructions and warnings for lens wear and care, when to remove lenses, and other important issues with the subject.
- Subjects, who appear unable or unwilling to follow instructions to a degree that, in the Investigator's opinion, jeopardizes the subject's wellbeing or the validity of the study, will be discontinued. The reason for discontinuation will be documented.

In some circumstances a repeated Dispensing visit (Visit 2R) may need to be scheduled if an over-refraction was found and lenses in a different prescription need to be ordered. The maximum total number of repeat dispense visit permitted will be one (App 2R)

9.3.3 Visit 3: Baseline with Avaira Toric & Dispense of Avaira Vitality Toric lenses

- If subject is an habitual Avaira Toric wearer with optimum prescription then Visit 3 will be scheduled at least 29 days after **Visit 1**
- If subject was fit into new or modified Avaira Toric lenses then Visit 3 will be scheduled at least 29 days after **Visit 2**
- The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible within the visit window. The following clinical test variables will be recorded on the CRFs as indicated:

Visit 3a: Baseline for Avaira Toric Lenses (App 7A)

- Confirm if any changes to health or medications
- [redacted]

- [redacted]
- Vision
  - High contrast distance monocular Snellen visual acuity
  - High contrast distance binocular Snellen visual acuity
- [redacted]
- Lens fit
  - Lens centration (centered/slightly decentered/substantially decentered)
  - Corneal coverage [Y/N]
  - [redacted]
  - Post-blink movement (0-4 Likert scale)
  - [redacted]
  - Overall fit acceptance (0 - 4) and reason if Grade 2 or less 1 step.
- Remove study lenses and perform slit lamp examination. A minimum 5 minute washout time after fluorescein insertion is required prior to lens insertion.

Visit 3b: Fitting and Dispensing of Avaira Vitality Toric Lens (App 7B)

The performance of the lenses should be assessed after 10-15 minutes settling time and the following variables will be assessed:

- Record the parameters of the lenses, lot number, and power, on the Dispensing CRF (App 7B).
- Vision
  - High contrast distance monocular Snellen visual acuity
  - High contrast distance binocular Snellen visual acuity
- [redacted]
- [redacted]
- Lens fit
  - Lens centration (centered/slightly decentered/substantially decentered)
  - Corneal coverage [Y/N]
  - [redacted]

- Post-blink movement (0-4 Likert scale)
- [redacted]
- Overall fit acceptance (0 - 4) and reason if Grade 2 or less.

- [redacted]

- To be successfully dispensed, subjects must show >Grade 2 lens fit acceptance with the trial fit lens and must be correctable to 20/30 (0.18 logMAR) or better in each eye with the study contact lenses.
- If the lenses are not a suitable fit to be dispensed then the subject will be discontinued and an Exit Form (App 13) will be completed.
- The subject will be instructed to wear the lenses on a daily wear basis, (at least 5 days/week, >8 hours/day), until Visit 4 appointment, unless they experience a problem which warrants lens removal.
- The Investigator or a clinical assistant will review instructions and warnings for lens wear and care, when to remove lenses, and other important issues with the subject.
- Subjects, who appear unable or unwilling to follow instructions to a degree that, in the Investigator's opinion, jeopardizes the subject's wellbeing or the validity of the study, will be discontinued. The reason for discontinuation will be documented.
- The subject will be discharged and asked to return for a follow-up visit (V4) after 2-weeks

9.3.4 Visit 4: 2-week follow up for Avaira Vitality Toric

The 2-week follow-up visit for Avaira Vitality Toric lenses will be scheduled 14 ± 2 days after Visit 3. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible within the visit window.

The following clinical test variables will be recorded on the CRFs as indicated:

- Confirm if any changes to health or medications (App 10)
- [redacted]

[redacted]

- Vision
  - High contrast distance monocular Snellen visual acuity
  - High contrast distance binocular Snellen visual acuity
- [redacted]
- Lens fit
  - Lens centration (centered/slightly decentered/substantially decentered)
  - Corneal coverage [Y/N]
  - [redacted]
  - Post-blink movement (0-4 Likert scale)
  - Overall fit acceptance (0 - 4) and reason if Grade 2 or less.
- [redacted]
- Remove study lenses and perform slit lamp examination. A minimum 5 minute washout time after fluorescein insertion is required prior to lens re-insertion.
- The subject will be instructed to wear the lenses on a daily wear basis, (at least 5 days/week, >8 hours/day), until Visit 5 appointment, unless they experience a problem which warrants lens removal.

9.3.5 Visit 5: 1-month follow up on Avaira Vitality Toric Lenses & Study Exit

The 1-month follow-up visit will be scheduled one month (28±3 days) from Visit 4. The subject should wear the lenses for a minimum of 2 hours prior to the appointment. If the subject attends without lenses or with less than 2 hours of lens wear on that day and they are not having any problems with their lenses, the visit should be rescheduled, if possible within the visit window.

Visit 5a: 1-month follow-up for Avaira Vitality Lenses

The following variables will be recorded on the CRFs as indicated:

- Confirm if any changes to health or medications (App 12)
- [redacted]
- [redacted]
- Vision
  - High contrast distance monocular Snellen visual acuity
  - High contrast distance binocular Snellen visual acuity
- [redacted]
- Lens fit
  - Lens centration (centered/slightly decentered/substantially decentered)
  - Corneal coverage [Y/N]
  - [redacted]
  - Post-blink movement (0-4 Likert scale)
  - [redacted]
  - Overall fit acceptance (0 - 4) and reason if Grade 2 or less.
- [redacted]
- Vision

- High contrast distance monocular Snellen visual acuity
- High contrast distance binocular Snellen visual acuity

- [redacted]
- Remove study lenses and perform slit lamp examination.
- Exit subject from the study, see details below.

Visit 5b: Study Exit

- The Study Exit Form (App 13) must be completed when a subject exits the study. This will occur either at study completion, i.e. at Visit 5, or if the subject is discontinues from the study at another time. If there are records entered into the clinics own patient chart system the exit date should also be recorded on these source documents.
- A Study Exit Form must be completed for all subjects who have taken a study ID number. Post-study follow-up visits will be scheduled if the Investigator judges this is necessary.
- At the final study visit, the following measurements are taken:
  - Remove study lenses and perform slit lamp assessment to establish anterior segment ocular health.
  - Monocular high contrast visual acuity with sphero-cylindrical refraction (Snellen)
  - If the VA at the Exit Visit is two or more lines worse than at Screening, repeat a monocular sphero-cylindrical refraction (sphere, cylinder and axis) if the best corrected spectacle vision remains two or more lines worse than at Screening, the Investigator will be required to provide an explanation and complete an adverse event form if needed.
  - Post-study follow-up requirement (Y/N). If yes, the reason and date of the follow-visit must also be recorded.
- If the subject is being exited due to discontinuation, further details need to be recorded on the Study Exit Form (App 13).

10 Adverse Events and their Reporting

10.1 Adverse Response Definitions

Adverse Event (AE): An AE refers to any untoward medical occurrence (sign, symptom or disease) in a trial subject that does not necessarily have a causal relationship with the study device. AEs may be classified as 'unanticipated adverse device effects,' 'serious AEs,' 'significant AEs,' or 'non-significant AEs,' as defined below. Adverse events can be ocular or non-ocular.

Classification	Definition

Serious Adverse Event	Those events that are life-threatening, or result in permanent impairment of a body function, or permanent damage to a body structure or necessitate medical (therapeutic) or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure.
Unanticipated Adverse Device Effect	Adverse events in a clinical trial that were not previously identified in the protocol in terms of nature, severity, or degree of incidence. An Unanticipated Serious Adverse Device Effect is an unanticipated adverse event that is serious in nature and caused by or associated with the device and is considered reportable.
Significant Adverse Event	Those non-serious adverse events that occur with contact lens usage that are not sight-threatening but are usually symptomatic and may warrant therapeutic management and /or temporary or permanent discontinuation of contact lens wear.
Non-Significant Adverse Events	Those less severe non-serious adverse events that occur with contact lens usage that are not sight-threatening, may or may not be symptomatic and may warrant palliative management, such as ocular lubricants or temporary interruption of contact lens wear.

AE classification, coding (for reporting to the sponsor) and examples are provided in the following table of Contact Lens Adverse Event Classification and Reporting:

Code	Condition	Potential AE Classification	Reporting
01	Presumed infectious corneal ulcer	SERIOUS	Notify sponsor as soon as possible, **within 24 hrs;** IRB reporting as per requirements
02	Permanent loss of ≥2 lines of best spectacle corrected visual acuity (BSCVA)	SERIOUS	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	SERIOUS	
04	Neovascularization within the central 6mm of cornea	SERIOUS	
05	Uveitis or Iritis	SERIOUS	
06	Endophthalmitis	SERIOUS	
07	Hyphema	SERIOUS	
08	Hypopyon	SERIOUS	
09	Persistent epithelial defect	SERIOUS	
00	Other serious event	SERIOUS	
11	Peripheral non-infectious ulcer (outside central 6mm)	SIGNIFICANT	Notify sponsor as soon as possible,

12	Symptomatic corneal infiltrative events	SIGNIFICANT	within 5 working days; IRB reporting as per requirements
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	SIGNIFICANT	
14	Any temporary loss of ≥2 lines BSCVA for ≥2wks	SIGNIFICANT	
15	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (i.e. moderate staining)	SIGNIFICANT	
16	Corneal neovascularization ≥ 1.0mm to 1.5mm vessel penetration (if 2 Grade change from baseline)	SIGNIFICANT	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	SIGNIFICANT	
10	Other significant event	SIGNIFICANT	
21	Conjunctivitis: bacterial, viral, allergic	NON-SIGNIFICANT	
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (if 2 Grade change from baseline)	NON-SIGNIFICANT	
25	Asymptomatic corneal infiltrative events	NON-SIGNIFICANT	
26	Localized allergic reaction	NON-SIGNIFICANT	
27	Contact dermatitis	NON-SIGNIFICANT	
28	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended	NON-SIGNIFICANT	
20	Other non-significant sign and/or symptom	NON-SIGNIFICANT	

Normal or adaptive symptoms

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 they are unexpected in nature, severity or rate of occurrence.***

10.2 Procedures for Adverse Events

Treatment of an adverse event will depend on its nature and severity. Based on the clinical judgment of the investigator the subject may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the study device/procedure or a result of other factors.

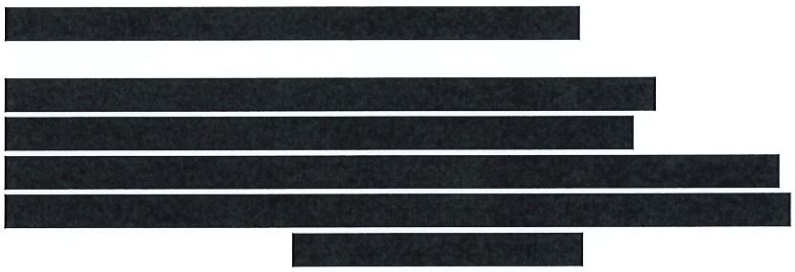
An Adverse Event Form will be completed for each adverse event. If both eyes are involved, a separate Adverse Event Form will be completed for each eye. Whenever possible, the adverse event will be photo-documented.

Expenses incurred for medical treatment as part of study participation will be paid by the sponsor (bills and prescription receipts kept). The subject must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

10.3 Reporting Adverse Events

All potential **Serious and Unanticipated Adverse Device Effects** that are related or possibly related to subject participation in the investigation will be reported to the Principal Investigator and to the designated medical monitor of the sponsor within 24 hours of the investigator becoming aware of the event (Appendix 2-AE). The Principal Investigator will report the event to the EC/IRB as soon as possible (by fax, mail/delivery, phone, or email), but within 10 business days of becoming aware of the problem. *All fatal or life threatening events will be reported immediately to the IRB.*

Significant and Non-Significant Adverse Events will be reported to the sponsor and the study coordinator as soon as possible, but no later than 5 working days after the occurrence (Appendix 2-AE).



10.4 Discontinuation from the Study

All discontinuations will be fully documented on the appropriate CRF Exit (Appendix 2-EX) and Adverse Event forms (Appendix 2-AE) as needed. Subjects will be followed until resolution and they are free of the study-related complications or other ocular pathology, where possible. When possible, the study lenses involved in an Adverse Event will be returned to the sponsor in a new tightly sealed contact lens case, and labeled with the subject's study ID number and stored in multipurpose solution.

11 Statistical Analysis

11.1 Statistical analysis

Descriptive statistics will be provided on information regarding baseline variables (e.g., age, gender). Differences between lenses and over time will be compared using Paired t-tests. Paired t-tests

/analysis of variance for normal (interval/continuous) data. The appropriate test will be selected based on tests of normality. Means and standard deviations will be provided for each variable.

A Binomial test will be used to analyze the results for the count data of subjective preferences. The number of "no preference" will be evenly distributed to the two options on the basis they would be equally likely to choose either. All subjects who were evaluated will be used in the analysis. In the event of missing data, individual data points will be excluded in the analysis and not extrapolated from the collected data.

12 Data Quality Assurance

12.1 Study monitoring

A site visit or discussion may be conducted during the course of the study as appropriate. Prior to final data lock, a close-out visit/discussion may be warranted to check for accuracy and completeness of records. Prior to data export for analysis there will be a discussion to confirm the cohort to be analyzed, with specific discussion around the data integrity in cases of protocol deviations and adverse events. 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.

12.2 Record keeping

Detailed records of all study visits will be made using the paper Case Report Forms (CRFs). Each subject will be identified on the CRFs with a study ID number which will not contain any identifying information such as initials and date of birth.

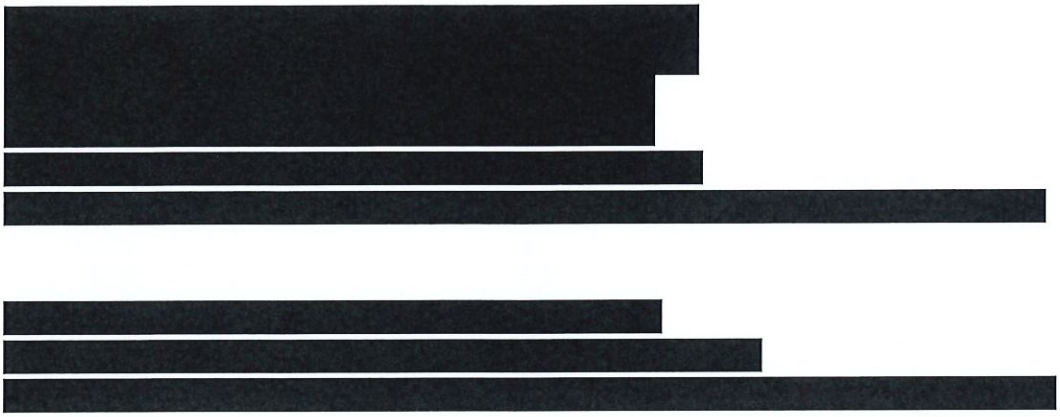
12.3 Record retention

Following study completion, data will be available in electronic and/or paper format for audit, sponsor use, or subsequent analysis. The original clinical raw data (including completed CRFs and Informed Consent forms) will be retained according to guidelines set forth in the general work agreement with the site. After the study closeout visit, the sites will send the original CRFs to the sponsor. The Sponsor will be notified and consulted if ever the files are to be destroyed. In the event that this implementation document is indicated for design verification and validation purposes, as indicated on the title page, all original raw data forms and completed CRF's will be forwarded to the sponsor at completion of the final report.

12.4 Data Entry / Data Management

Data will be entered on paper CRFs. The clinical investigators will be responsible for the data integrity and the completeness of data entry for each visit. The sites will make an attempt to scan/email or fax all the paper CRFs to the Centre for Contact Lens Research within ONE BUSINESS DAY of the visit date (Appendix 12, Fax cover sheet). The CCLR personnel will review all CRFs for integrity and

completeness and email or fax data queries back to the site as necessary. The site should make an attempt to answer all data queries within TWO business days of receipt. The CCLR will review and enter all data into a database and study staff will only be able to modify these data via password entry.



12.5 Confidentiality

All information gathered during this study is proprietary and should be made available only to those directly involved in the study. Information and reports arising from this project are the property of the sponsor.

All records will also be handled in accordance with HIPAA (1996). No identifying information will be collected on the CRFs or any of the documentation provided to the Centre for Contact Lens Research or to the sponsor.

12.6 Publication

The investigators will not be permitted to publish or present at scientific meetings results obtained from the clinical study without prior written consent from the sponsor.

13 Study Costs and Subject Compensation

CVI will compensate the Investigators, (principal investigators), and the subjects, (each a "Subject" and together the "Subjects"), for their time and participation in this voluntary study. Payments to the Clinical Investigator are per visit with a total of 5 visits for 48 subjects.

Clinical Site will receive the payment for the subjects and are responsible for distributing each subject's compensation (checks). Complete outline/details of the payment compensation are detailed in the Clinical Study Agreement with each Clinical Site.

There will be no payments to the Clinical Site for unscheduled visits, unless Subjects are visiting regarding an adverse event. Data from unscheduled office visits, if mandated by your clinic, can be collected and entered using the unscheduled visit form (Appendix 2-US).

Expenses incurred for medical treatment as part of study participation will be paid by CVI (bills and

prescription receipts kept). The subject must be followed until resolution and a written report is completed indicating the subsequent treatment and resolution of the condition.