CooperVision™

Study Protocol:

CLINICAL EVALUATION OF INVIGOR TORIC 1-DAY CONTACT LENSES

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Clinical Site:	CORL, Indiana University

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1 Introduction

CooperVision is evaluating the clinical performance of the Invigor toric 1 day (test) compared to clariti toric 1 day (control) over one hour of lens wear.

2 Study Objective

The purpose of this study is to validate the clinical performance of Invigor toric 1 day lenses over a period of one hour of wear.

The primary variable of interest is:

- Toric lens fit

Secondary variable of interest is:

- General lens fit

[redacted]

3 Study Design

This will be a non-dispensing, double-masked, randomized, contralateral study comparing Invigor toric 1 day (Test) against clariti toric 1 day (Control) lenses. Each subject will be randomized to wear the test lens in one eye and the control lens in the other eye for each pair of lenses.

Each subject will be asked to wear four pairs of contact lenses in the study. The order of lens pairs will be randomized. The study may take place over multiple days.

4 Ethics Review / Statement of Compliance

4.1 Relevant Standards / Guidelines

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

- ISO 14155 Clinical Investigation of Medical Devices for Human Subjects
- 21 CFR Part 812 Investigtional Device Exemptions
- Ethical principles of the Declaration of Helsinki
- Principles of US and ICH Good Clinical Practice

4.2 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 conduct of this study will occur at CORL at Indiana University. The conduct of this study will be approved by [redacted] Institutional Review Board prior to commencement.

4.3 Informed Consent

Informed consent 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.

5 Clinical Trial Registration

The Sponsor will register this study with ClinicalTrials.gov in accordance with Section 801 of the Food and Drug Administration Act (FDAA) which mandates the registration of certain clinical trials of drugs and medical devices.

[redacted]

[redacted]

[redacted]

[redacted]r

[redacted].

7 Materials and Methods

7.1 Participants

Approximately up to 15 subjects will be recruited for this study in order to have 10 subjects completed. Each subject will be given a unique ID number. 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:

- Has had a self-reported oculo-visual examination in the last two years.
- Is at least 18 years of age and has full legal capacity to volunteer.
- Has read and understood the information consent letter.
- Is willing and able to follow instructions and maintain the appointment schedule.
- Is correctable to a visual acuity of 20/40 or better (in each eye) with their habitual vision correction or 20/20 best-corrected.
- Currently wears soft contact lenses.
- Has clear corneas and no active ocular disease.
- Has not worn lenses for at least 12 hours before the examination

Exclusion Criteria

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

- Has never worn contact lenses before.
- Has any systemic disease affecting ocular health.
- Is using any systemic or topical medications that will affect ocular health.
- Has any ocular pathology or severe insufficiency of lacrimal secretion (moderate to severe dry eyes) that would affect the wearing of contact lenses.
- Has persistent, clinically significant corneal or conjunctival staining using sodium fluorescein dye.
- Has any clinically significant lid or conjunctival abnormalities, active neovascularization or any central corneal scars.
- Is aphakic.
- Has undergone corneal refractive surgery.
- Is participating in any other type of eye related clinical or research study.

7.2 Study Materials

7.2.1 Contact lens

Subjects will be randomized to receive either the Test or Control lens for each pair of lens per a predetermined randomization schedule. The lenses used in this study will be provided by the Sponsor. [redacted]

Table 1: Study lenses

	Invigor toric 1 day (Test)	clariti toric 1 day (Control)
Manufacturer	CVI	CVI
Material	[redacted]	somofilcon A
Base curve (mm)	8.6	8.6
Diameter (mm)	14.3	14.3
Power (D)	-1.00 -1.75 x 180 -1.00 -1.75 x 090 -6.00 -1.75 x 180 -6.00 -1.75 x 090	-1.00 -1.75 x 180 -1.00 -1.75 x 090 -6.00 -1.75 x 180 -6.00 -1.75 x 090

7.2.2 Contact Lens care

No contact lens care is required for this study as lenses are to be worn for a single day only.

7.2.3 Storage of Lenses and Lens Care Solutions

The study materials must be stored in a secured area. All lenses and lens care solutions should be stored at controlled room temperature (59-86°F).

7.2.4 Clinical Supply Inventory

The investigator must keep an accurate accounting of the study product during the study. A detailed inventory must be completed for study supplies. The study supplies are to be used in accordance with the implementation document by subjects who are under the direct supervision of an investigator.

7.2.5 Disposal of Consumables

This study dispenses consumables (lenses) to participants for use during the study. Study solutions used and/or study lenses worn by participants will be collected and discarded at the completion of the study.

7.2.6 Masking and Control of Study Materials

The contact lenses coding will be masked to both the investigator and subject. If standard labelling does not sufficiently mask the study material then over labelling will be performed.

7.2.7 Ordering and Accountability of Study Materials

The test and control lenses will be provided by the sponsor. The investigator must complete an accurate accounting of the study product at the completion of the study. A detailed inventory must

be completed for study supplies. All unused and used materials will be returned to the Sponsor at the end of the study.

7.3 Visit Schedule and Procedures

7.3.1 Baseline Visit

Procedures to be Performed

The following evaluations will be performed to assess eligibility according to the Inclusion and Exclusion Criteria at the baseline visit only:

- The patient is expected to attend the baseline visit not wearing their habitual contact lens products.
- The subject will be required to read and sign an Informed Consent Form prior to enrolment. When the subject has signed the consent form, the subject will be considered to be enrolled on to the study.
- Baseline visual acuity with spectacles or spectacle refraction.
- Keratometry will be done on subjects.
- Palpebral aperture size and HVID will be measured.
- Slit lamp biomicroscopy will be assessed according to the guidelines set out in the CVI Grading scales.
- The investigator will confirm that the patient meets the criteria set out in the inclusion criteria

7.3.2 Lens Pair 1

Dispensing

- The study contact lenses will be fitted according to the randomization table.
  - [redacted]
- [redacted]
- Lenses will be allowed to settle for at least 15 minutes.
- [redacted]
- Lenses will then be assessed and graded according to the guidelines detailed in CVI Grading scales after settling.

- [redacted]
  - General lens fit assessment
    - Lens centration, movement, push-up, lag
    - General fit acceptance and preference
  - Toric lens assessment
    - Toric mark visibility
    - Lens orientation (3 measurements per lens)
    - Rotational stability (maximal and minimal differences between extreme gazes)
    - Rotational recovery (nasal and temporal)
    - Toric fit acceptance and preference
- The subject will be given a pair of over-spectacles to wear.
- The subject will be discharged and asked to return for a follow-up visit after 1 hour.

One-hour Follow-up

[redacted]

- Lenses will then be assessed and graded according to the guidelines detailed in CVI Grading scales after settling.
  - [redacted]
  - General lens fit assessment
    - Lens centration, movement, push-up, lag
    - General fit acceptance and preference
  - Toric lens assessment
    - Toric mark visibility
    - Lens orientation (3 measurements per lens)
    - Rotational stability (maximal and minimal differences between extreme gazes)
    - Rotational recovery (nasal and temporal)
    - Toric fit acceptance and preference
- The contact lenses will be removed and retained.
- Slit lamp microbiology will be assessed if applicable.

7.3.3 Lens Pairs 2-4

Similar procedures as lens pair 1 (7.3.3) will be repeated for lens pairs 2-4.

If more than one pair of lenses will be evaluated in the same day, there will be a 15-minute wash-out period between the two lens pairs.

If the study takes place over multiple days, biomicroscopy and visual acuity (with habitual spectacles or spectacle refraction) will be assessed before initial lens insertion and after completion of each study day.

7.3.4 Exit

- Slit lamp biomicroscopy will be assessed according to the guidelines set out in CVI Grading scales.
- Exiting visual acuity with spectacles or spectacle refraction.
- The subject will be discharged and will sign the exit statement.

7.4 Adverse Event Definitions

An 'adverse event' refers to any undesirable clinical occurrence in a participant, whether it is considered to be device-related or not. Adverse events (AE) may be classified as 'unanticipated adverse device effects,' 'serious adverse events,' 'significant adverse events,' or 'non-significant adverse events,' as defined below.

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.
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.
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.

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

Code	Condition	Reporting
Serious Adverse Events		
01	Presumed infectious keratitis or infectious corneal ulcer	Notify sponsor as soon as possible, **within 24 hours;** IRB reporting as per requirements
02	Permanent loss of ≥ 2 lines of best spectacle corrected visual acuity (BSCVA)	
03	Corneal injury that results in permanent opacification within central cornea (6mm)	
04	Uveitis or Iritis (e.g. presence of anterior segment inflammation as described in ISO 11980, Annex B)	
05	Endophthalmitis	
06	Hyphema	
07	Hypopyon	
08	Neovascularization within the central 6mm of cornea	
00	Other serious event	
Significant Adverse Events		
11	Peripheral (outside central 6mm), non-progressive, non-infectious ulcer	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
12	Symptomatic corneal infiltrative event	
13	Superior epithelial arcuate lesions (SEALs) involving epithelial split	
14	Corneal staining ≥ dense coalescent staining up to 2mm in diameter (e.g. moderate, ISO 11980 grade 3)	
15	Corneal neovascularization ≥ 1.0mm vessel penetration (e.g. ≥ ISO 111980 Grade 2), if 2 grade change from baseline	
16	Any temporary loss of ≥ 2 lines BSCVA for ≥ 2wks	
17	Any sign and/or symptom for which subject is administered therapeutic treatment or which necessitates discontinuation of lens wear for ≥ 2 weeks	
10	Other significant event	
Non-significant Adverse Events		
21	Conjunctivitis (bacterial, viral or allergic)	Notify sponsor as soon as possible, **within 5 working days**; IRB reporting as per requirements
22	Papillary conjunctivitis if ≥ mild scattered papillae/follicles approximately 1mm in diameter (e.g. ISO 11890 Grade 2), if 2 grade change from baseline	
23	Asymptomatic corneal infiltrative events	
24	Any sign and/or symptom for which temporary lens discontinuation for > 1 day is recommended (if not already classified)	
20	Other sign and/or symptom warranting classification as a non-significant adverse event	

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 in the investigator's opinion they are unexpected in nature, severe or have a high rate of occurrence.***

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as Adverse Events.

7.5 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 test device 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.

7.6 Reporting Adverse Events

All potential Serious and Unanticipated Adverse Device Effects that are related or possibly related to subject participation will be reported to the Principal Investigator and the sponsor within 24 hours of the investigator becoming aware of the event. The Principal Investigator will report the event to the IRB as soon as possible (by fax, mail/delivery, phone, or email). 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 as soon as possible, but no later than 5 working days after the occurrence.

Sponsor contact details are:

7.7 Discontinuation from the Study

A subject's study participation may be discontinued at any time if, in the opinion of the sponsor or the investigator it is in the best interest of the subject. All discontinuations will be fully documented on the appropriate study forms and the Discontinuation Form will be completed.

8 Device Malfunctions

A device malfunction means the failure of the device to meet its performance specification or otherwise perform as intended. *Any defective lens that is likely to cause or contribute to a Serious Adverse Event should be reported to the Principal Investigator and the sponsor* ***within 24 hours*** *of the investigator becoming aware of the malfunction.*

Other defective lenses should be reported to the Sponsor as soon as possible.

This clinical study will also ascertain satisfaction or preference with subjective attributes such as comfort, vision, or lens handling. Responses to these subjective questionnaires will not be considered as complaints or Device Malfunctions.

9 Statistical Analysis Plan

9.1 Statistical analysis

Summary statistics will be produced (e.g. mean, standard deviation). Paired t test will be used to compare slit lamp biomicroscopy, lens fit and subjective scores between study lens types. Repeated Measures Analysis of Variance (ANOVA) or paired analysis will be used to compare the variables between study visits. The critical alpha level for statistical significance will be set at $p \leq 0.05$, with adjustment for multiple comparisons.

All participants 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.

10 Data Quality Assurance

[redacted]

10.2 Record keeping

Detailed records of all study visits will be made using the Case Report Forms (CRFs). All data recorded on forms will be in ink. Any corrections to the forms will be initialed and dated at the time they are modified.

10.3 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. 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.

10.4 Data Entry / Data Management

Data will be entered into an electronic spreadsheet. Study staff will only be able to modify the data file via password entry. The investigators will be responsible for the data integrity, and complete data entry for each visit as well as the take home questionnaires. The investigator will send the data collected to the study sponsor within approximately 5 business days after the last subject completes the final visit.

10.5 Confidentiality

This study is confidential in nature. Details of confidentiality are covered within the Master Agreement signed between the sites and the sponsor.

All records will also be handled in accordance with HIPAA (1996) standards.

10.6 Publication

Publication conditions are laid out in the Master Agreement signed between the site and the sponsor.

11 Study Costs

The sponsor will compensate the clinical site and the subjects for their time and participation in this voluntary study.

[redacted]

[redacted]

12 Appendix

[redacted]