Clinical investigation plan

C23-747
(EX-MKTG-154)

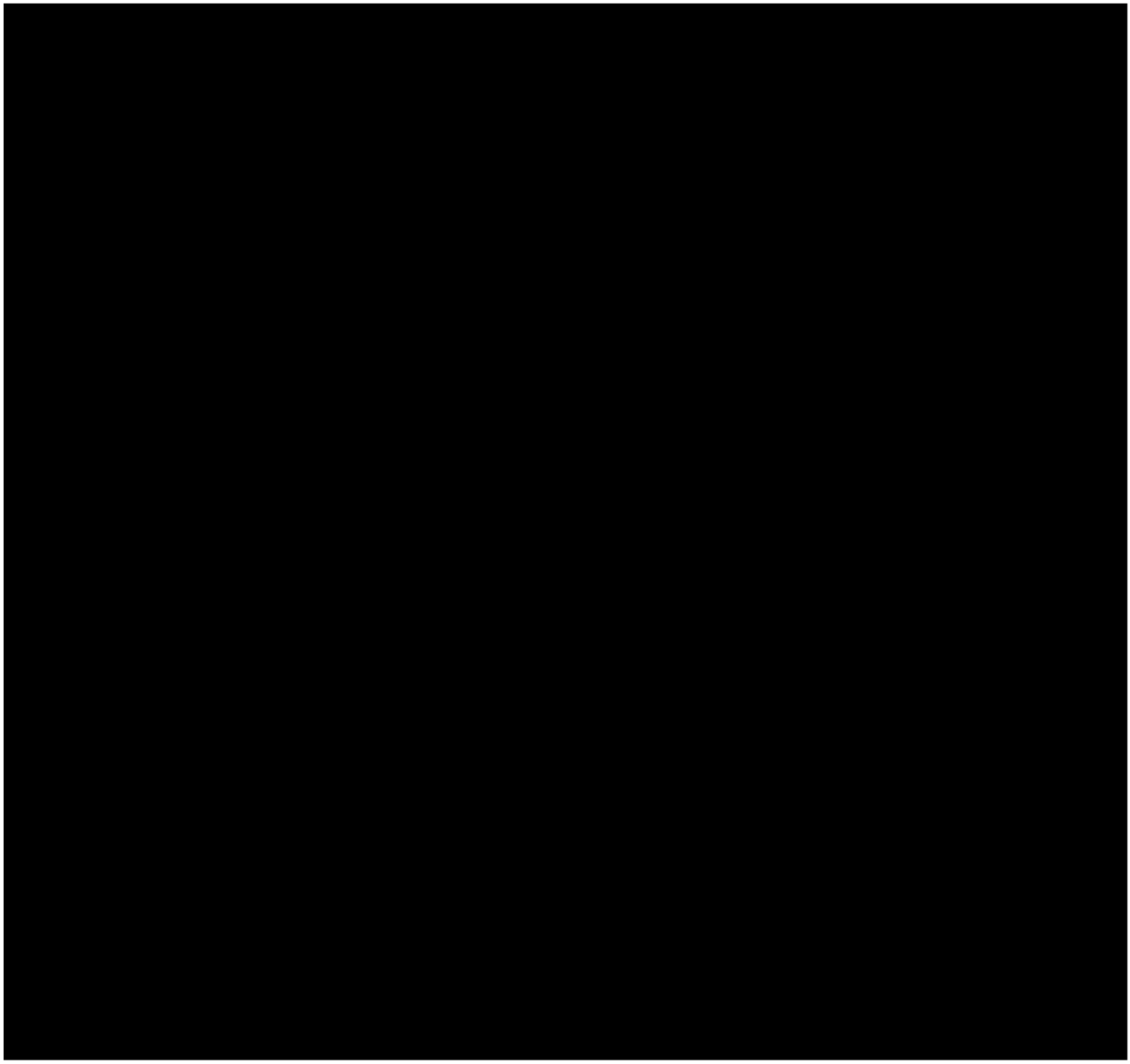
A clinical comparison of two soft contact lenses
(iteration under umbrella protocol C19-678)

A clinical evaluation for
CooperVision Inc.

Principal Investigator
Carole Maldonado-Codina

November 2023

Contents



Study summary

This subject-masked, non-randomised, crossover controlled non-dispensing study will compare the performance of Live Daily Disposable and Clariti 1day lenses, in a single study visit. Up to 50 subjects will be consented with the aim of completing at least 44 subjects. All subjects will first be fitted with the Live Daily Disposable lens and secondly with the Clariti 1day lens.

A summary of the study visit and procedures is provided in Table 1.

Procedures
Explanation of study procedures and subject instructions
Informed consent taken
Ocular, medical and contact lens histories
Autokeratometry
Refraction
Distance monocular visual acuity, high contrast
Slit lamp biomicroscopy
Confirmation of eligibility
Lens 1
Application of first lens pair (Live Daily Disposable) based on refraction
As soon as possible (~1 minute after lens application)
[redacted]
Subjective scores for comfort, vision, [redacted] overall score
Lens acceptance (as judged by the investigator)
15 minutes after lens application
[redacted]
Subjective scores for comfort, vision and overall score
Lens acceptance (as judged by the investigator)
Lens removal
Lens 2
Application of second lens pair (Clariti 1day)
As soon as possible (~1 minute after lens application)
[redacted]
Subjective scores for comfort, vision, [redacted] and overall score
Lens acceptance (as judged by the investigator)
15 minutes after lens application
[redacted]
Subjective scores for comfort, vision and overall score
Lens acceptance (as judged by the investigator)
Lens removal
[redacted]
Payment processed

Table 1: study summary.

Section 1. Overview

1.1 Background

This clinical investigation plan describes a clinical contact lens study (iteration) which will run under the umbrella protocol entitled, 'Multiple non-dispensing soft contact lens fitting studies' (C19-678) which received full ethical approval from The University of Manchester Research Ethics Committee 1 on May 20, 2021. The umbrella protocol describes a series of iterations which would recruit up to 50 subjects and compare CE marked contact lenses using routine clinical investigations at a single, non-dispensing visit and at a single study site (Carys Bannister Building, The University of Manchester). This iteration conforms to all of these requirements.

This document provides an outline of the specific details for this particular iteration.

1.2 Personnel

This work will be conducted at Eurolens Research, The University of Manchester, under the general direction of Philip Morgan PhD MCOptom FAAO FBCLA. The Principal Investigator for the work is Carole Maldonado-Codina PhD MCOptom FAAO FBCLA.

1.3 Study objectives

CooperVision Inc. wishes to gather short-term clinical performance data for two of the soft contact lenses which they currently manufacture. This non-dispensing iteration will compare the performance of the Live Daily Disposable and Clariti 1day lenses.

1.4 Study outcome measures

The primary outcome measure for this study is the subjective overall score. Secondary measures are subjective comfort and vision. [redacted]

1.5 Study design

Up to fifty participants will take part in a subject-masked, non-randomised crossover, controlled non-dispensing study, which will be controlled by cross comparison. Subjects will attend for one visit only which will last for approximately 2.0 hours. They will not be given any contact lenses to take away with them.

1.6 Statistical considerations

The principal hypothesis to be tested in this work is that subjective scores will be similar for the two lenses.

[redacted] such, these will

be compared using linear regression models or other parametric methods. [redacted] Deviations from this statistical plan will be discussed in the final report. Deviations may be necessary due to differences between the actual data distribution compared with the anticipated data distribution.

1.6.1 Power analysis

In a previous iteration of this study with soft spherical contact lenses, typical inter-subject standard deviation values on a 0-100 scale for comfort, vision [redacted] (at lens dispensing) were 13.4, 14.1 and 13.7 units, respectively. Assuming an equivalence margin of seven units and an alpha of 0.5, data from 44 subjects are required to provide power of 0.90 or greater for equivalence testing for these three parameters. To allow for any inadequate lens fits, up to 50 subjects will be recruited for this work.

1.7 Risk analysis

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 due to the daily wear nature of the study. With the potential benefit of this study, the work is considered to be ethically justifiable. Ethical approval will be sought from the University of Manchester Research Ethics Committee (hereafter referred to as Manchester UREC). The work where practical will be conducted in accordance with the ICH Good Clinical Practice Guidelines and the international standard BS EN ISO 14155: 'Clinical investigation of medical devices for human subjects'.

1.7.1 Clinical trial registration

This study will be registered on www.clinicaltrials.gov.

Section 2. Resources

2.1 Subject selection

In this work, up to 50 subjects will be enrolled.

2.1.1 Subject withdrawal and replacement

This study is a single clinical visit study. Once the study consent form is signed, the subject is considered to be enrolled on the study. Subjects who have signed the consent form, but who have not had the first lens applied to the eye will usually be replaced. All subject data will be included in the final analyses unless there are strong grounds for exclusion; such grounds will be detailed in the final report.

2.1.2 Subject recruitment

Subjects will be recruited by one or more of following means:

1. Posting study details on The University of Manchester's 'Research Volunteers' website.
2. Correspondence to existing wearers on the Eurolens Research database of subjects.
3. Advertising through a variety of media via a format separately approved by Manchester UREC.

2.1.3 Inclusion criteria

Subjects will only be eligible for the study if:

1. They are of legal age (18) and capacity to volunteer.
2. They understand their rights as a research subject and are willing and able to sign a Statement of Informed Consent.
3. They are willing and able to follow the protocol.
4. They currently wear soft contact lenses, or have done so within the past two years.
5. They are expected to be able to be fitted with the study lenses within the power range available.

2.1.4 Exclusion criteria

Subjects will not be eligible if:

1. They have an ocular disorder which would normally contra-indicate contact lens wear.
2. They have a systemic disorder which would normally contra-indicate contact lens wear.
3. They are using any topical medication such as eye drops or ointment.
4. They are aphakic.

5. They have had corneal refractive surgery.
6. They have any corneal distortion resulting from previous hard or rigid lens wear or have keratoconus.
7. They are pregnant or lactating.
8. They have an eye or health condition including an immunosuppressive or infectious disease which would, in the opinion of the investigator, contraindicate contact lens wear or pose a risk to study personnel; or a history of anaphylaxis or severe allergic reaction.
9. They have taken part in any contact lens or care system clinical research within two weeks prior to starting this study.

2.2 Subject discontinuation

In general, subjects should be discontinued at any time, if it is in their best interests, as judged by the investigator. Reasons for this may include clinical signs of grade 3 or more, lack of motivation, discomfort, repeated refusal to follow instructions or the use of non-study products such as solutions or lenses. Subjects will be discontinued if a serious adverse event occurs or if they miss two or more planned consecutive visits. Subjects who fail to satisfy all the inclusion and exclusion criteria will be discontinued and replaced. Subjects may choose to leave the study at their own request. All discontinuations will be carefully recorded.

2.3 Safety parameters, adverse events and concurrent illnesses

The key safety parameters are the serious and significant ocular adverse events listed in Appendix A (adverse events are classified as 'serious', 'significant' or 'non-significant'). Clinical assessment is made at the study visit(s) for these parameters. The presence of an ocular adverse event will be reported on the case report forms and those described as 'serious' or 'significant' will be detailed in the final report. Similarly, any concurrent illness that is likely to impact on the relevance and quality of the captured data will be noted on the case report form.

2.3.1 Investigator obligations

At all times the investigator will act in the best interest of the subject. Referral or treatment of an adverse event or other clinical finding should be initiated in the best clinical judgement of the investigator, irrespective of the participation in the clinical study.

2.3.2 Reporting obligations

Adverse events will be reported to the sponsor in accordance with their reporting requirements. Manchester UREC and any regulatory authorities will be informed as required.

2.4 Protocol deviations

Any deviations from this protocol will be recorded and reported to the Sponsor Contact Person as appropriate. Manchester UREC will be informed as necessary.

2.5 Study resources

Study products will be stored according to the manufacturer's product instructions.

2.5.1 Lenses

Details of the lenses are provided in Table 2. Both lenses are CE marked and will be used within the terms of their product licence. Each lens pair will be worn for approximately 15 minutes in the clinic only. Lens foils will be overlabelled so that the subject is masked to the lens brand.

	Lens 1	Lens 2
Name	Live Daily Disposable	Clariti 1day
Manufacturer	CooperVision Inc	CooperVision Inc
Material	Somofilcon A	Somofilcon A
EWC (%)	56	56
Base Curve (mm)	8.6	8.6
Diameter (mm)	14.0	14.1
Spherical powers (DS)	-1.00 to -6.00 (0.25 steps)	-1.00 to -6.00 (0.25 steps

Table 2: study lenses.

2.5.1.1 Use of lenses

Subjects will wear the contact lenses in the clinic only. (i.e. lenses will be removed at the end of the study visit and discarded).

2.5.2 Care regimen

No care regimen will be used as the lenses are to be worn in the clinic only.

2.5.3 Inventory control

The sponsor will supply both lens types. All worn lenses will be discarded.

2.6 Data collection and analysis

Data collected in this work will be recorded on a custom-developed database and an established data trail. Data handling will include export of the study information from the clinical database into spreadsheet format for manipulation, followed by export into a statistical package for analysis. Most clinical data will be entered directly onto the electronic case report form and are considered to be source data.

2.7 Study monitoring

In order to provide quality control and quality assurance as part of this work, the study monitor will:

1. Liaise closely with the Principal Investigator.

2. Monitor and ensure the safety of the subjects.
3. Ensure that the investigation is being conducted according to the protocol.
4. Monitor and review (or oversee review of) the study records to ensure accuracy.
5. Document their observations and make them available to relevant authorised parties (e.g. Manchester UREC).
6. Implement the Eurolens Research clinical monitoring standard operating procedure.

Section 3. Subject management

3.1 Visit scheduling

Each subject will attend for a single study visit. Lenses will be worn for a defined period of time, with assessments occurring at various intervals, in accordance with the visit schedule detailed in this protocol. The subject will wear both of the study 'lens pairs' during the single study visit.

3.2 Visit conduct

Visit procedures are carried out in accordance with the relevant, current Eurolens Research Standard Operating Procedures.

3.2.1 Pre-enrolment

The subject will receive a study-specific information form outlining the study at least 24 hours before the initial visit.

3.2.2 Study visit

Subjects should attend wearing their spectacles.

They will then be required to sign an informed consent form prior to enrolment. A copy of the signed form will be issued to the subject. When the subject has signed the consent form, they are considered to be enrolled on the study.

Subjects will be instructed on the following:

1. Lens handling, application and removal, where necessary.
2. Specific study instructions, such as the importance of not using any other contact lens products.
3. General contact lens information such as the management of red eyes.

The following procedures will be performed (any ocular measurement procedures outlined below will be carried out on each eye).

1. Details of the ocular, medical and contact lens-wearing histories of the subject will be noted [redacted]
2. [redacted].
3. [redacted]

4. [redacted]

5. The investigator will confirm that the subject satisfies all the inclusion and exclusion criteria. Subjects who fail to meet all the criteria at this time will usually be discontinued and replaced unless the reason is considered to be transient in which case a further visit can be scheduled.
6. The first lens pair, Live Daily Disposable, will be fitted selecting the closest available lenses for the subject based on refraction from the lens bank.
7. The subject will apply the lenses.
   As soon as possible *(~1 minute after lens application)*, lens fit will be assessed using the following evaluations: horizontal and vertical centration, corneal coverage and movement. Normally, for an acceptable fit, centration and movement will fall within currently accepted clinical criteria [redacted]
8. Distance high contrast monocular logMAR visual acuity will be recorded.
9. The subject will be asked to score the following subjective scores with reference to appropriate vertical visual analogue scales (0-100) [redacted]
   - Comfort
   - Vision
   - [redacted]
   - Overall score
10. [redacted]
11. Fifteen minutes after lens application, lens fit will be assessed (as above).
12. [redacted]
13. [redacted]

15. The subject will be asked to score the following subjective scores with reference to appropriate vertical visual analogue scales (0-100) [redacted]
    - Comfort
    - Vision
    - Overall score
16. [redacted]
17. The contact lenses will be removed and discarded.
18. [redacted]
19. The second lens pair, Clariti 1day, will be fitted selecting the closest available lenses for the subject based on refraction from the lens bank.
20. The same procedures will be carried out for the second lens pair (Clariti 1day) as the first lens pair, points 8 to 18 (above).
21. [redacted]
22. [redacted]
23. At the end of the visit (or if the subject is discontinued earlier in the visit) the subject's payment will be processed and the subject discharged, although they may have been asked by the investigator to attend a post-study follow-up visit. They should continue to use their lenses and solutions as advised, and seek aftercare for their contact lenses.

3.2.3 Post-study follow-up visit

In the case of a subject who exits the study with significant clinical signs or symptoms, the investigator must undertake to examine the subject at intervals he/she determines to be clinically appropriate until the sign or symptom has resolved or returned to a level that is considered to be clinically acceptable. Details from these visits will be recorded on a post-study follow-up visit form.

3.3 Monitoring subject compliance

Subjects are required to adhere to the instructions provided during this clinical investigation. This will be confirmed at the study visit by verbal questioning of the subject by the investigator.

3.4 Missing, unused and spurious data

The absence of any data will be carefully and critically considered. If appropriate, partial datasets will be included in the final analysis. Any data missing from a subject visit will be outlined in the report by indicating the number of subjects included for each analysis. Data that are unused or considered to be spurious will be detailed and discussed in the report.

Section 4. Study co-ordination

4.1 Document processing

All case report forms will be processed and evaluated by Eurolens Research, who will produce the final report with full statistical analysis. A draft report will be sent to the Sponsor Contact Person in order to make comments and ask for re-drafts. If no comments are received from the Sponsor Contact Person within eight weeks, a final report will be released with a separate document control page (in duplicate), requesting the Sponsor Contact Person to sign both copies, one to keep and the other to be returned to Eurolens Research.

4.2 Disclosure

All matters relating to this clinical study are confidential and should only be disclosed to relevant authorised parties. More precise details relating to disclosure are outlined in the Research Agreement. None of the investigators involved in this work owns equity in the sponsor company.

4.3