Clinical investigation plan

C24-748 (EX-MKTG-160)

A multisite investigation of the wearing compliance of spectacles for myopia control

A clinical evaluation for CooperVision Inc.

Principal Investigator
Philip Morgan

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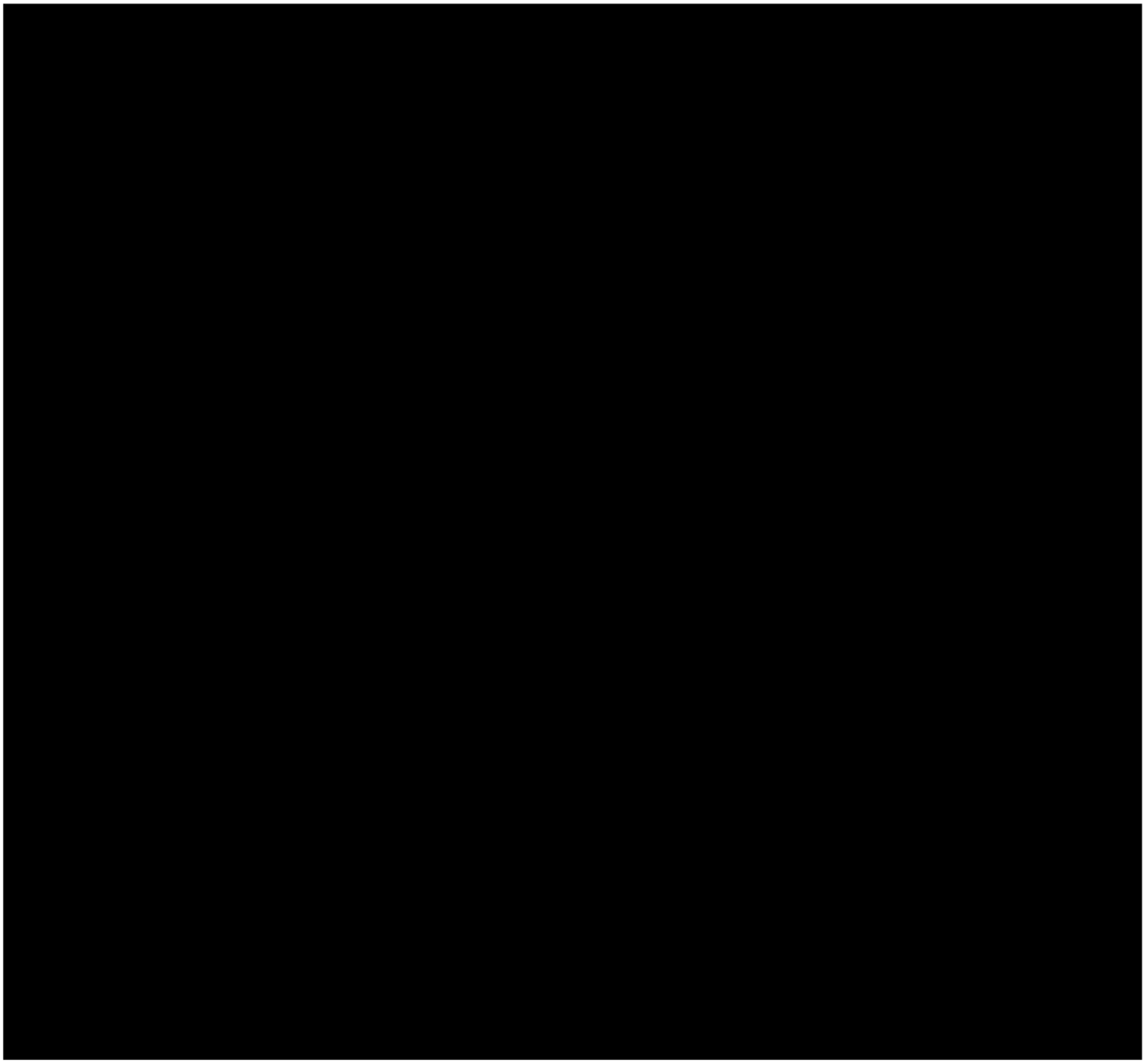
Contents

[redacted]

Document control



Study summary

This multi-centre study will compare the wearing patterns of spectacles prescribed for myopia control at about four optometry practices. Up to 60 established (use of ≥3 months) juvenile wearers will be recruited and their wearing patterns over one week of a month's wear will be evaluated. A study summary is shown in Table 1.

Visit	Procedures
[redacted]	[redacted]
Visit 1	Subject attends their own optometry practice Questions about the study answered Consent form and assent forms signed Temperature sensor fitted to frame (or side with sensor fitted)
Visit 2	Subject attends optometry practice [redacted] Subject discharged from study

Table 1: Study summary.

Section 1. Overview

1.1 Background

This study seeks to compare the wearing patterns of spectacles prescribed for myopia control. [redacted]

1.2 Personnel

This work will be managed by Eurolens Research, The University of Manchester under the general direction of Philip Morgan PhD MCOptom FAAO FBCLA. The Principal Investigator for the work is Philip Morgan. Subjects will be recruited by about four UK optometry practices.

1.3 Study objectives

This study aims to compare the wearing patterns of spectacles for myopia control across different ages, different levels of myopia and between males and females.

1.4 Study design

This will be an unmasked multi-centre study which is controlled by cross-comparison. The wearing patterns of up to 60 established spectacle wearers will be evaluated via the use of temperature sensors fitted to the side of their spectacles. [redacted]. Subjects will wear the sensor for approximately one month. The data from the final week of this period will be used for analysis, in an attempt to minimise 'unusual' wear patterns which may occur early in the study as the subject adapts to being on a clinical study.

1.5 Statistical considerations

The principal hypothesis to be tested in this work is that wearing times for young and old wearers will be the same. Wearing time data are likely to be normally distributed and so the impact of age will be explored using linear regression models or other parametric methods.

Deviations from this 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.

1.5.1 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.

1.5.2 Power analysis

Power analysis was conducted based on information from a previous study [redacted], assuming (a) that males vs. females are compared and (b) younger vs. older subjects are compared. For sex, power analysis based on previous data in spectacle wearers shows that for a two-sided two-sample t-test with an alpha of 0.05, assuming standard deviations of 0.95 for females and 2.61 for males, a sample size of 17 subjects in each group is required to detect a 2-hour difference in daily wearing time between groups with 80% power.

For age, power analysis on the same basis, assuming standard deviations of 3.31 for older subjects (> 10 years) and 0.68 for younger subjects (< 10 years), a sample size of 25 subjects in each group is required to detect a 2-hour difference in daily wearing time between groups with 80% power.

Given this, 60 subjects will be recruited to comprise approximately 50% males and 50% females, and with subjects recruited across the full age range. Subjects will be recruited into the following prescription range 'bins' (mean sphere) in approximately equal numbers; 1) plano to -1.50DS, 2) -1.75 to -3.75DS and 3) -4.00DS and above.

1.6 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 Organisation (ISO) guidelines due to the daily wear nature of the study. The work where practical will be conducted in accordance with:

- ICH Good Clinical Practice Guidelines
- BS EN ISO 14155 'Clinical investigation of medical devices for human subjects - Good clinical practice'
- Declaration of Helsinki

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 Senate Committee on the Ethics of Research on Human Beings (hereafter referred to as Manchester UREC).

1.7 Clinical trial registration

This study will be registered with clinicaltrials.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.

Section 2. Resources

2.1 Subject selection

In this work, up to 60 subjects will be recruited – approximately 15 at each of about four UK optometry practices. Note that the subjects will be recruited to comprise approximately 50% males and 50% females, and with subjects recruited across the age range 6-15 years. Subjects will be recruited into the following prescription range 'bins' (mean sphere) in approximately equal numbers; 1) plano to -1.50DS, 2) -1.75 to -3.75DS and 3) -4.00DS and above.

2.1.1 Subject accountability

This study includes an online information meeting where the subject and guardian or parent can ask questions and two clinic visits: one to fit the sensor and one to return the sensor. Once the study consent and assent forms are signed, the subject is considered to be enrolled on the study. 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. If a subject withdraws after signing the consent form, they will not be replaced.

2.1.2 Subject recruitment

Subjects will be recruited directly from the patient bases at the optometry practices, using approved recruitment wording [redacted]

2.1.3 Inclusion criteria

Subjects will only be eligible for the study if:

1. They are aged between six and 15 years old.
2. Their parent or guardian understands the rights of the subject and are willing to sign a statement of informed consent.
3. They understand the study at a level appropriate for their age and are willing to sign a statement of assent.
4. They and their parents or guardians are willing and able to follow the protocol.
5. They currently use spectacle lenses for myopia control and have done so for at least three months.
6. They agree not to participate in other clinical research for the duration of this study.

2.1.4 Exclusion criteria

Subjects will not be eligible to take part in the study if:

1. They have an unusual ophthalmic history, which in the opinion of the site investigator or Principal Investigator might impact on the successful conduct of the study.
2. They are amblyopic.

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, lack of motivation, discomfort, repeated refusal to follow instructions or the use of non-study products. Subjects will be discontinued if a serious adverse event occurs or if they miss the study visit on two scheduled occasions. 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 responsibilities

The investigators will be appropriately qualified, have suitable resources to conduct the study, have study training, ensure subject safety and data integrity. At all times they 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 their participation in the clinical study.

2.3.2 Investigator reporting responsibilities

In the case of a 'serious' or 'significant' adverse event, the Principal Investigator will notify the Sponsor as soon as possible. Manchester UREC and any regulatory authorities will be informed as required.

2.4 Study termination

If it becomes necessary to terminate the study earlier than planned, the Sponsor will notify the Principal Investigator who will end the study with the cooperation of other staff members. Manchester UREC will be informed.

2.5 Protocol deviations

These are unanticipated or unintentional changes that occur after Manchester UREC approval. Any deviations, major (affect the integrity of the study and/or subject safety) or minor from this protocol will be recorded, and reported to the Sponsor as appropriate. Manchester UREC will be informed as necessary.

2.5.1 Protocol amendments

Amendments will be agreed between the Sponsor and the Principal Investigator with the cooperation of other staff members. Amendments will be recorded, identified and distributed. Approval from Manchester UREC will be obtained as necessary.

2.5.1.1 Use of spectacles

Spectacles should be worn in line with normal wear patterns for the subject.

2.6 Study control

This study is controlled by cross-comparison.

2.7 Documentation

Documents related to this work that require archiving will be kept by Eurolens Research for a period of 20 years after completion of the final report. The Sponsor's permission will be sought before the documents are destroyed.

2.8 Data collection and analysis

Data collected in this work will be recorded on paper case report forms (CRFs), and Excel spreadsheets.

2.9 Study completion

The clinical phase of the study will be considered as complete when all subjects have attended their last visit.

2.10 Subject confidentiality

All matters related to this work will remain confidential within the optometry practices involved, Eurolens Research, the Sponsor and any regulatory authority (e.g. Manchester UREC). The relevant parties will take all reasonable steps to ensure that specific product information is not passed on to study subjects unless this is required for clinical management of an adverse event. Personal subject information will not be made available. To cater for this, subjects will only be referred by their unique identity number in the study report. The data activities of Eurolens Research are registered with the data protection officer at The University of Manchester.

2.11 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. Conduct site visits.
3. Monitor and ensure the safety of the subjects.
4. Ensure that the investigation is being conducted according to the protocol.

5. Monitor and review (or oversee review of) the study records to ensure accuracy.
6. Review study product accountability.
7. Document their observations and make them available to relevant authorised parties (e.g. Manchester UREC).
8. Implement the Eurolens Research clinical monitoring standard operating procedure.

Section 3. Subject management

3.1 Visit scheduling

Subjects will be required to attend an online information meeting followed by two clinic visits – an initial visit (Visit 1) and a follow-up visit (Visit 2), after approximately one month. Acceptable date ranges are shown in Table 2.

Visit	Target	Allowable range
1	N/A	N/A
2	28 days from Visit 1	20 to 40 days from Visit 1

Table 2: Visits and allowable ranges.

3.1.1 Unscheduled visits

An unscheduled visit is an interim visit requested by the subject or investigator due to an unanticipated event. Pertinent data will be collected and will be recorded on the CRF.

3.1.2 Missed visits

Subjects not attending for a visit will be contacted and encouraged to return for assessment. If two scheduled appointments are missed, the subject will be discontinued. It is expected that study personnel at the optometry practices will attempt all reasonable means of communication in this event, including corresponding with the subject's parent/guardian by letter.

3.2 Visit conduct

3.2.1

[redacted]

3.2.2 Informed consent

The subject's parent/guardian will be required to sign an informed consent form, and the subject sign an assent form, prior to enrolment [redacted] and before any procedures

specific to the clinical investigation are performed. A copy of the signed forms will be issued to the subject and their parent/guardian. They are then considered to be enrolled on the study.

3.2.3 Visit 1

Subjects should attend wearing their spectacles. Written assent/consent from the subject and parent/guardian will be obtained as detailed in section 3.2.2.

The following procedures will be performed:

1. The temperature sensor will be fitted to the spectacle frame (or a side with sensor fitted). The frame will be fitted to the face to ensure that the sensor is in comfortable contact with the skin.
2. The subject will be discharged from this clinic visit, and asked to return four weeks later.

3.2.4 Visit 2

Subjects should attend wearing their spectacles. The following procedures will be performed:

1. The temperature sensor will be removed from the spectacle frame (or the old side refitted).
2. Study payment will be issued/processed, and the subject will be discharged from the study.

[redacted].

3.2.5 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 they determine 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(s) by verbal questioning of the subject and parent/guardian by the investigator.

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 in order to make comments and ask for re-drafts. If no comments are received from the Sponsor within eight weeks, a final report will be released with a separate document control page, requesting the Sponsor to sign and return 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 Personnel