Clinical investigation plan

C20-688 (EX-MKTG-120)

Using personal face masks with spectacles versus contact lenses

A clinical evaluation for CooperVision Inc.

Study Leader
Aftab Mirza

Principal Investigator
Carole Maldonado-Codina

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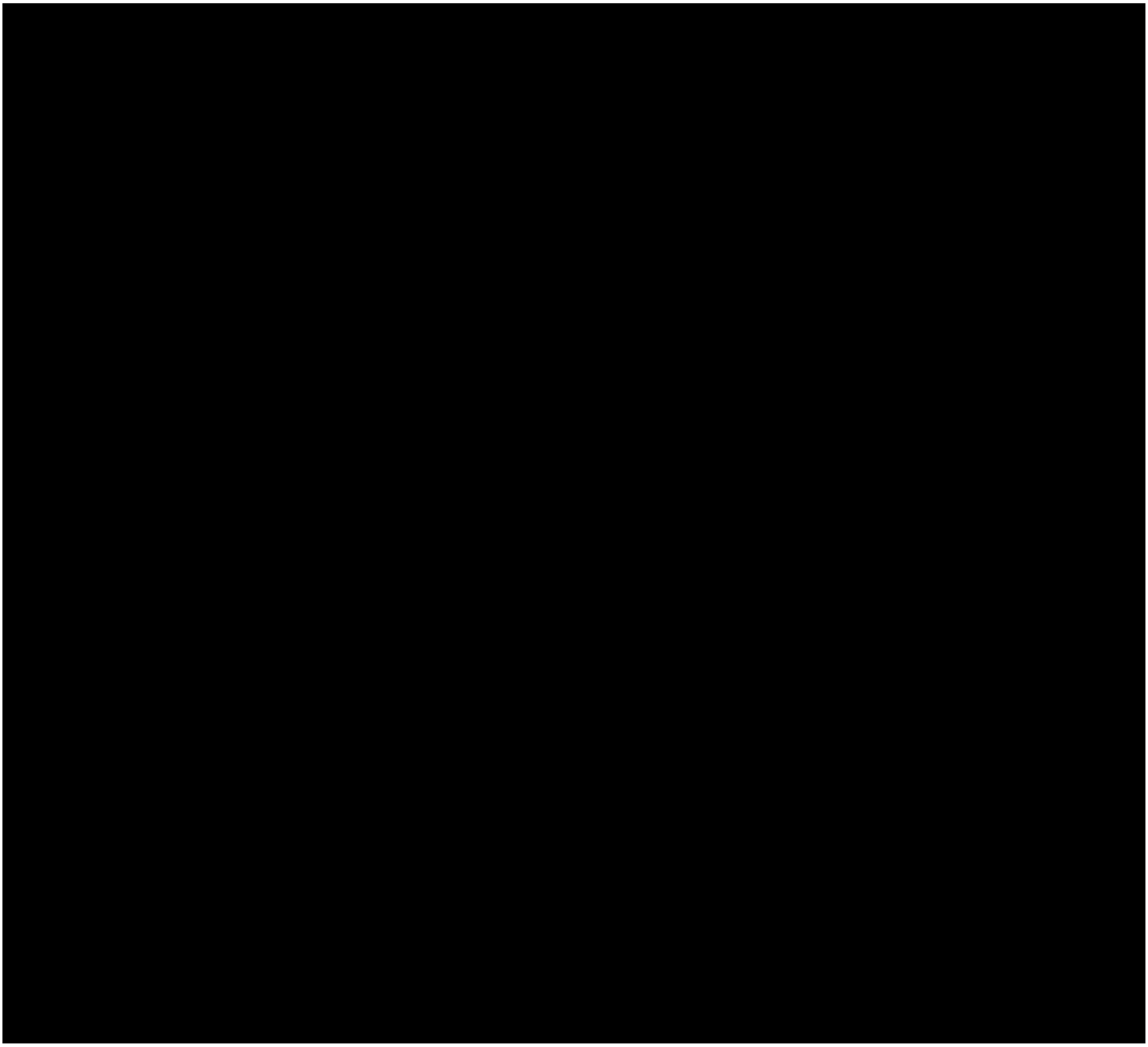

Study summary

The aim of this study is to explore (a) satisfaction with vision correction and (b) ease of use of personal face masks (PFM) in a group of spectacle wearers and a group of newly-fitted contact lens wearers. This will be a two-arm, parallel-group, randomised study. Up to 35 single vision spectacle wearers will be recruited to participate in the study. Subjects will be randomised to either continue to wear their spectacles or to be fitted with the study daily disposable (DD) contact lens (clariti 1 day, CooperVision Inc.), for a period of two weeks. [redacted]

A study summary is shown in Table 1.

V s t	Procedures
In t a v s t	Informat on and consent forms s gned Med ca and ocu ar h stor es [redacted] v sua acu ty Subject ve scores and quest onna res [redacted] Conf rmat on of e g b ty Random sat on to treatment type V s on, sub ect ve scores, [redacted] (contact ens group on y) Contact ens app cat on/remova /educat on sess on (contact ens group on y)
[redacted]	[redacted]
2 week v s t	Med ca and ocu ar h stor es Subject ve scores and quest onna res V sua acu ty [redacted] Study ex t and payment ssued

Table 1: Study summary.

Section 1. Overview

1.1 Background

The transmission of COVID-19 is thought to occur mainly through small droplets released after coughing, sneezing and through contact with contaminated surfaces. Use of personal face masks (PFM) is considered to be one of the most important strategies for protecting the wearer from this and other infectious diseases.

Although PFM is aimed to protect the user, it has the potential to negatively impact upon day to day tasks as well as individual work performance. Face protection such as masks, goggles and face shields are often worn for hours at a time and anecdotal evidence suggests that use of prescribed spectacles in combination with PFM can be difficult. One of the most common problems encountered is fogging of spectacles whilst wearing a face mask. This can result in significantly impaired vision which may interfere with the performance of daily activities. Furthermore, the use of spectacles with masks and other forms of PFM is physically uncomfortable. One way to potentially overcome these issues is to fit contact lenses.

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

The aim of this study is to explore (a) satisfaction with vision correction and (b) ease of use of PFM in a group of spectacle wearers who will be randomised to continue wearing spectacles or be fitted with daily disposable contact lenses.

1.4 Study design

This will be a two-arm parallel-group, randomised study. Thirty-five single vision spectacle wearers will be recruited to participate in the study. Subjects will be randomised to either continue to use their spectacles or to be fitted with the study daily disposable (DD) contact lens (clariti 1 day, CooperVision Inc.). Subjects will attend the clinic for two visits.

At the initial visit, subjects will sign the consent form and be screened according to the inclusion/exclusion criteria. [redacted]

[redacted]. Subjects will be randomised to either continue to wear their spectacles or to the study contact lens for two weeks. Subjects randomised to the contact lens group will be fitted with the study DD contact lens and will receive a training/education session on contact lens application and removal. All subjects will be supplied with disposable surgical masks (Type I or II) and asked to wear them for the majority of the time that they need to wear PFM and for at least one hour per day. After two weeks, subjects will return to the clinic for a final visit, where the clinical assessments will be repeated.

1.5 Statistical considerations

The principal hypothesis to be tested in this work is that subjective scores for the spectacle group and contact lens group will be the same.

Visual acuity, [redacted] and subjective responses will generate data that are likely to be continuous and normally distributed. As 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.

1.5.1 [redacted]

[redacted]

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 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 Senate Committee on the Ethics of Research on Human Beings (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 14155:2011 ‘Clinical investigation of medical devices for human subjects’.

Section 2. Resources

2.1 Subject selection

In this work, up to 35 subjects will be consented with the aim of 15 subjects completing the study in each group.

2.1.1 Subject withdrawal and replacement

This study includes two clinical visits. 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 completed the dispensing visit 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 subjects 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 aged between 18 and 40 years.
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 are a 'neophyte' (i.e. someone who has not worn contact lenses previously, with the exception for the purposes of a trial fitting).
5. They have a contact lens spherical prescription between +8.00D and -10.00D (inclusive) based on the ocular refraction.
6. They have a cylindrical correction of -0.75DC or less in each eye based on the ocular refraction.
7. They own and habitually wear single vision spectacles.
8. They are willing to be fitted with contact lenses and understand they may be randomised to either group.

9. They are willing to wear the contact lenses (if relevant) or spectacles for at least 8 hours per day, 5 days per week.
10. They are able to wear the supplied surgical masks for the majority of time that they need to wear PFM and will wear the PFM for at least one hour a day for at least four days per week.
11. They can attain at least 0.20 logMAR distance high contrast visual acuity in each eye with the study lenses (if relevant) or spectacles.
12. They agree to not participate in other clinical research while enrolled on this study.

2.1.4 Exclusion criteria

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

1. They have an ocular disorder which would normally contra-indicate contact lens
2. wear.
3. They have a systemic disorder which would normally contra-indicate contact lens wear.
4. They are using any topical medication such as eye drops or ointment.
5. They have had cataract surgery.
6. They have had corneal refractive surgery.
7. They have any corneal distortion resulting from previous hard or rigid lens wear or have keratoconus.
8. They are pregnant or breastfeeding.
9. They have any ocular abnormality which would, in the opinion of the investigator, normally contraindicate contact lens wear.
10. They have any infectious disease which would, in the opinion of the investigator, contraindicate contact lens wear or pose a risk to study personnel; or they have any immunosuppressive disease (e.g. HIV), or a history of anaphylaxis or severe allergic reaction.
11. They require significant ocular/face personal protective equipment beyond a personal face mask.
12. They have taken part in any other contact lens or care solution clinical trial or research, within two weeks prior to starting this study.
13. They have spectacles which are not within ±0.50D of their refractive error.

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. 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 adverse events listed in [redacted] (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 any ocular adverse event will be recorded on the eCRF and reported to the Sponsor using CVI report forms, and those ocular adverse events 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

In the case of a 'serious' or 'significant' adverse event, the Principal Investigator will notify the Industrial Contact Person 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 Industrial Contact Person 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

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

2.5.1 Protocol amendments

Any amendments will be agreed between the Industrial Contact Person 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.

2.6 Study resources

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

2.6.1 Lenses

Details of the study lens are provided in Table 2. The lens is CE marked. Initial lens selection will be as indicated by the manufacturer fitting guidelines.

Name	c ar t 1 day
Manufacturer	CooperV s on Inc
Mater a	somof con A
EWC (%)	56
BOZR (mm)	8.6
D ameter (mm)	14.1
Spher ca powers (D)	+8.00D to -10.00D (0.50D steps after +6.00D and -6.00D)

Table 2: Study lenses.

2.6.1.1 Use of lenses

Study contact lenses will be worn on a daily wear, daily disposable basis (i.e. removed at end of day and discarded). Lenses should be worn for a minimum of eight hours per day, five days per week. The lenses are also to be worn for a minimum of two hours before attending the follow-up visit.

2.6.2 Care regimen

No care system will be used on this study.

2.6.3 Surgical masks

Subjects will be supplied with disposable surgical masks (Type I or Type II). Surgical masks should be worn for a minimum of one hour per day, four days per week. Subjects will be asked to wear the surgical mask for the majority of time that they need to wear PFM. Surgical masks should not be reused and should be discarded after use.

2.6.4 Inventory control

All study lenses will be supplied by CooperVision Inc. All worn and unworn lenses will be discarded. There will be an accurate accounting of the study test product at the completion of the study. All used study test products will be documented (Lot number; Expiry date etc.) in the study paperwork or CRF.

2.6.5 Clinical equipment

Clinical equipment is regularly maintained and calibrated as required. Standard operating procedures and international standards are used where appropriate.

2.7 Study control

Bias will be minimised by randomising the treatment allocation. Eligible subjects will be randomly assigned to one of two treatment groups (contact lens or spectacles) using computer-generated random numbers.

2.8 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 company's permission will be sought before the documents are destroyed.

2.9 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.

2.10 Study completion

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

2.11 Confidentiality

All matters related to this work will remain confidential within Eurolens Research, the funding company and any regulatory authority (e.g. Manchester UREC). Eurolens Research will take all reasonable steps to ensure that specific lens-related information is not passed on to study participants unless this is required for clinical management of an adverse event. Personal subject information will not be made available without explicit consent. 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.

2.12 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.

2.13 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 3. Subject management

3.1 Visit scheduling

Subjects will be required to attend two visits – an initial visit and one follow-up visit. Acceptable date ranges are shown in Table 3. Subjects in the contact lens group may need to attend for more than one 'teach' session.

V s t	Target	A owab e range
In t a v s t	N/A	N/A
2 week Fo ow-up	14 days from D spens ng 1	10-20 days from n t a v s t

Table 3: Visits and allowable ranges.

3.1.1 Unscheduled visits

Subjects who attend at their own volition, (or as instructed to do so by the investigator) rather than for a scheduled study visit, will be examined and the visit will be classified as 'unscheduled'. Data collected at these visits will be recorded on the clinical study database.

Should a subject attend for their initial visit and be ineligible for the study owing to a reason which the investigator believes to be transient (for instance slit lamp signs higher than those acceptable according to inclusion/exclusion criteria), a repeat first visit can be conducted a short time later. This visit may involve some or all of the scheduled initial visit procedures, with the exception of the consent process, which would not be repeated.

3.1.2 Missed visits

Subjects not attending for a visit will be contacted and encouraged to return for assessment.

3.2 Visit conduct

3.2.1 Pre-enrolment

The subject will receive a study-specific information form outlining the study at least 24 hours before the consent visit. Each subject will also be sent a short on-line information presentation detailing study visits and procedures. They will be asked to complete several multiple-choice questions to gauge their understanding of the study.

3.2.2 Initial visit

Subjects should attend this visit wearing (or having brought along) their habitual spectacles.

They will then be required to sign an informed consent form prior to enrolment [redacted]. 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 history.
2. Details of general health and medications.
3. Details of PFM use (type of PFM, hours per day, days per week).
4. The BVD of the subject's spectacles by asking the subject to position the spectacles on their own face (if not already being worn).
5. Focimetry will be carried out on the subject's spectacles to ascertain the prescription of the lenses.
6. The investigator will perform refraction and distance and near monocular logMAR visual acuity (both high and low contrast), in accordance with the current Eurolens Research Standard Operating Procedure 'The set up, measurement of visual acuity and procedures for carrying out an over refraction using the Eurolens computerised logMAR VA chart'.
7. The investigator will assess whether or not the subject's single vision spectacles have a mean sphere equivalent within ±0.50D of that found for the refraction after having taken effectivity into account.
8. [redacted]
9. Facemask usability questionnaire [5-point scale from 1 (very unsatisfactory) to 5 (very satisfactory)] will be completed [redacted]
    a. Breathability
    b. Heat
    c. Tightness
    d. Ease in talking
    e. Comfort on ear lobes
    f. Overall comfort

[redacted]

11. Questions about using the mask during day-to-day activities/tasks [redacted]
12. Slit lamp biomicroscopy will be carried out for the signs outlined in Table 4 and in accordance with the current Eurolens Research Standard Operating Procedure 'Examination of the anterior segment using slit lamp biomicroscopy'. Grades will be scored to the nearest 0.1 unit in the best judgement of the investigator using Efron Grading Scales. Corneal staining will be graded for five regions (central, superior, temporal, inferior and nasal) as well as an 'overall' grade. The predominant type of corneal staining present will also be recorded.

C ass f cat on	Pr mary s gns	Secondary s gns
S gns	Con unct va redness L mba redness Cornea neovascu ar sat on Ep the a m crocysts Cornea oedema Cornea sta n ng Locat on of sta n ng Conjunct va sta n ng Pap ary conjunct v t s	B ephar t s Me bom an g and dysfunct on Muc n ba s
Sca e	Efron Grad ng Sca es (scored to nearest 0.1)	Efron Grad ng Sca es (scored to nearest 0.1) (except muc n ba s, where the number s recorded.

Table 4: Biomicroscopic signs. Staining assessed with sodium fluorescein.

The presence of any adverse events will be recorded [redacted]

13. 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.
14. The subject will be randomised to one of the two treatment groups. For subjects assigned to the spectacle group, proceed to step 22.

15. For those assigned to the contact lens group, the study lenses will be fitted and allowed to settle for five minutes or until tearing stops (whichever is the longer).
16. Monocular logMAR visual acuity (high contrast) will be recorded before performing an over-refraction, and then monocular logMAR visual acuity (high and low contrast) will be carried out with the over-refraction in place, and in accordance with the current Eurolens Research Standard Operating Procedure 'The setup, measurement of visual acuity and procedures for carrying out an over refraction using Eurolens computerised logMAR VA chart'.

[redacted]

21. Subjects will be trained on contact lens application, removal and best practice immediately at the end of the visit or at a later date if required. More than one visit is possible for this 'teaching' session if there are problems with handling. Subjects will be dispensed with contact lenses only once the investigator is satisfied with their ability to successfully apply and remove lenses.
22. For both groups: Subjects will be supplied with disposable surgical masks (Type I or II) and will be asked to wear them for the majority of time that they need to wear PFM (for at least one hour per day for at least four days per week). Subjects will receive instructions on how to wear the surgical mask.

[redacted]

Subjects will then be discharged and asked to return for the two-week follow-up visit.

a. Subjects in the contact lens group will be asked to attend the follow-up visit after having worn the study lenses for at least two hours. They should be asked to wear their lenses for a minimum of eight hours per day, five days per week. No formal 'building up' of wearing time will take place, instead subjects will asked to wear their contact lenses for as long as they are comfortable until they have achieved the required 8 hour minimum wear time. Some subjects may achieve this on the first day of wear, others may take a few days before they are happy to wear for 8 hours, but all subjects should progress to a minimum of 8 hours per day as soon as they are able.
b. Subjects in the spectacle group will be asked to wear their spectacles for a minimum of 8 hours per day, 5 days per week. They should attend the follow-up visit having worn spectacles for a minimum of 2 hours on the day of the visit.
c. Subjects should use PFM for at least one hour per day for at least four days per week.

3.2.3 Follow-up visit

For the contact lens group, subjects should attend wearing the study lenses which should have been in situ for at least two hours. Subjects who attend without lenses in situ for at least two hours will usually be rescheduled. For the spectacle group, subjects should attend wearing their spectacles. Spectacles should have been worn for a minimum of two hours on the day of the visit.

The following procedures will be performed:

1. Any medical or ocular issues since the last visit.
2. Spectacle or contact lens wearing times since the previous visit (hours per day, days per week and comfortable hours per day).
3. Spectacle or contact lens wearing time on study visit day.
4. Surgical mask wearing times since the previous visit (hours per day, days per week and comfortable hours per day).
5. [redacted]
6. Facemask usability questionnaire will be completed [redacted]
7. [redacted]

[redacted]

8. Questions about using the mask during day-to-day activities/tasks [redacted]

9. [redacted]

11. For spectacle wearers, monocular logMAR visual acuity (high contrast) will be recorded. Proceed to step 15.

12. For contact lens wearers, monocular logMAR visual acuity (high contrast) will be recorded before performing an over-refraction, and then monocular logMAR visual acuity (high and low contrast) will be carried out [redacted] as described in section 3.2.2.

13. [redacted]

15. The subject will be issued with their payment and discharged.

3.2.4 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(s) 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 Industrial Contact Person in order to make comments and ask for re-drafts. If no comments are received from the Industrial Contact Person within eight weeks, a final report will be released with a separate document control page (in duplicate), requesting the Industrial 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 funding company.

4.3