[redacted]

EVALUATION OF THE CLINICAL ACCEPTANCE OF SOFT CONTACT LENSES FOR MYOPIA CONTROL

CLINICAL INVESTIGATIONAL PLAN

Sponsor:	CooperVision Inc. (CV)
Study Sponsor Number:	CV20-51
[redacted] Study Number:	ID20-28
Version:	1.0
Issue Date:	3rd September 2020

[redacted]

Clinical Investigational Plan

Evaluation of The Clinical Acceptance of Soft Contact Lenses for Myopia Control

[redacted] Number and Version: ID20-28 Version 1.0

Study Sponsor Number: ***CV-20-51***

Issue Date: 03 September 2020

Protocol Signature Page

As Chief Investigator, I agree to conduct this study in accordance with all applicable laws and regulations and in compliance with the provisions of this Clinical Investigational Plan.

I am responsible for ensuring that the investigation is conducted according to this plan and for protecting the rights, safety, and welfare of the research participants.

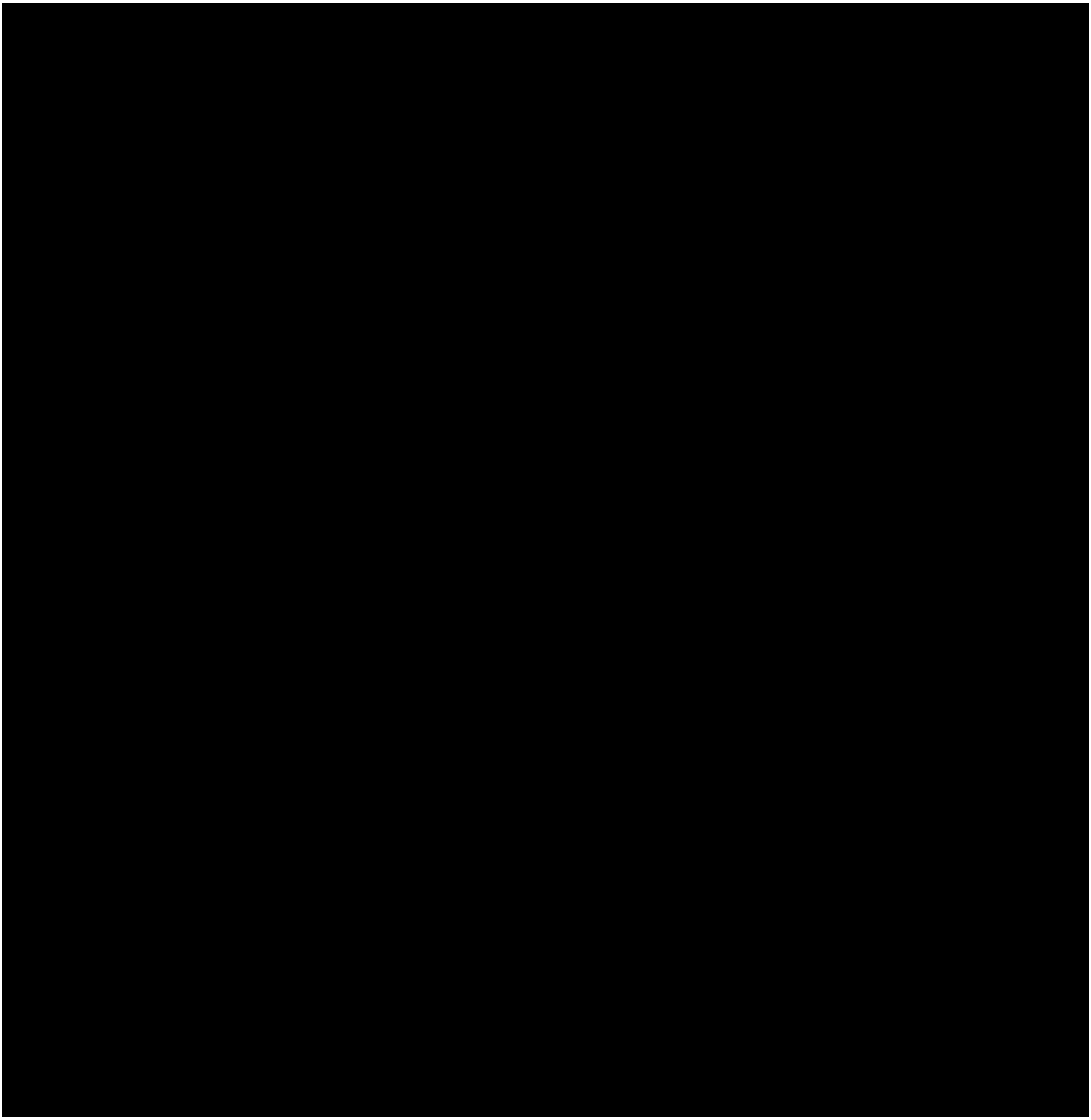
Chief Investigator Name (printed)	Signature	Date

Confidentiality Statement

The information in the following document is provided to you as an investigator, potential investigator, or consultant, for review by you, your staff, and applicable Ethics Committee or Institutional Review Board, and is considered confidential. It is understood that the information will not be disclosed to others without written authorization from [redacted] except to the extent necessary to obtain informed consent from the study participants.

DOCUMENT CHANGE HISTORY

Revision	Originator	Description of Change(s)	Date



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1 Overall Synopsis

Study Sponsor	CooperVision Inc. [redacted]
Title of Study	Evaluation of The Clinical Acceptance and Performance of Soft Contact Lenses for Myopia Management
Protocol Number	[redacted] ID20-28 / CVI: 20-51
Type of study	Single arm, prospective, 10 days wear of each study contact lenses (three contact lens types), randomized order of lens types usage, crossover study with investigator and participant masking.
Study Population	Required: 20 completed participants as per protocol (cohort). Planned: Up to 40 screened, with the aim of enrolling up to 30 participants.
Duration of study treatment	10 (±3) days of daily lens wear per study contact lens type.
Inclusion Criteria	In order to be enrolled, each participant shall meet the following criteria: i. Age 10 to 16 years; ii. Spectacle refraction: -0.75 to -6.00D spherical equivalent, maximum anisometropia 1.25D, cylinder up to -1.00DC iii. Best corrected visual acuity of at least 20/25 in each eye. iv. Parents/guardians and participant have read and understood the Participant Information Sheet; v. Parents/guardians and participant have read, signed and dated the Informed Consent; vi. Have normal eyes with the exception of the need for visual correction; vii. Be willing and able to adhere to the instructions set in the clinical protocol and maintain the appointment schedule.
Exclusion Criteria	The following are specific criteria that exclude a candidate from enrolment in this study: i. Ocular anterior segment infection, inflammation, abnormality, or active disease that would contraindicate contact lens wear; ii. Newly prescribed use of some systemic or ocular medications for which contact lens wear could be contraindicated as determined by the investigator; iii. Monocular participants (only one eye with functional vision) or participants fit with only one lens; iv. Subjects with slit lamp findings greater than grade 1 (e.g. edema, infiltrates, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival, anterior segment inflammation) as per ISO 11980, any previous history or signs of a contact lens related corneal inflammatory event (past corneal ulcers), or any other ocular abnormality that may contraindicate contact lens wear at the enrolment visit; v. History of herpetic keratitis, ocular surgery or irregular cornea; vi. Enrolment of the family members of the investigator, family members of the investigator's staff, or individuals living in the households of these individuals.
Planned Start Date	1 Septmeber 2020
Overall Study Duration	Six months. This includes the study enrolment period, lens wear period of approximately three months and study close out.
Objective(s)	The primary objective of the study will be to: i. determine the level of overall visual satisfaction achieved with each contact lens type tested; ii. determine the habitual daily wearing time; The secondary objective will be to: i. measure the visual performance achieved with each contact lens types tested;

	ii. determine the level of visual satisfaction during specific visual tasks.	
Hypotheses	The primary hypotheses that will be tested will be that: i. overall visual satisfaction with the test contact lens designs is not inferior to the control contact lens design; ii. habitual daily wearing time with the test contact lens designs is not inferior to the control contact lens design. The secondary hypotheses that will be tested will be that: i. the visual performance with the test contact lens designs is not inferior to the control contact lens design; ii. the level of visual satisfaction during specific visual tasks with the test contact lens designs is not inferior to the control contact lens design.	
Efficacy Endpoint (S)	The primary endpoints will be: i. Overall vision satisfaction recorded on a visual analog scale; ii. Daily wearing time in hours. The secondary endpoints will be: i. logMAR visual acuity. ii. Level of visual satisfaction during specific visual tasks recorded on visual analog scales ;	
Efficacy Procedures	The primary efficacy procedures will be: i. Measurement of overall visual satisfaction; ii. Recording of habitual wearing time. The secondary efficacy procedures will be: i. Specialist visual performance measurement. using [redacted]; ii. Measurement of visual satisfaction during specific visual tasks.	
Safety Endpoints:	The safety endpoints will be: i. Preservation of best corrected visual acuity ii. Adverse events rate iii. Slit lamp findings: proportion of grade 3 or higher positive findings compared to baseline.	
Safety Procedure(s)	The procedures to monitor safety will be: i. Identification and prevalence of adverse events; ii. Measurement of Snellen visual acuity; iii. Safety ocular integrity (biomicroscopy); iv. Identification and prevalence of device deficiencies and quality complaints.	
Population Profiling Procedure(s)	The procedures to profile the population's key characteristics will be: i. Demographics and ocular history questionnaire (including concomitant treatment); ii. Manifest spectacle refraction (sphero-cylinder, best sphere); iii. Pupil measurements iv. Ocular dominance measurement.	
Experimental Design	☐ Retrospective ☒ Prospective	☐ Non-Randomized ☒ Randomized
	☐ Single masked (participant) ☐ Single masked (investigator) ☒ Double masked* ☐ Sponsor masked ☐ Open label * Sub-investigators collecting primary and secondary endpoint data and participants will be masked.	☒ Single group ☐ Parallel group ☒ Crossover ☐ Contralateral

Control Product	The control contact lenses will be [redacted] daily disposable multifocal contact lenses in the currently marketed design. The contact lenses are made in omafilcon A by CooperVision Inc. are CE marked for use in children for myopia management in a daily disposable wearing modality.
Test Products	The test contact lenses will be [redacted] daily disposable multifocal contact lenses in alternative designs. The contact lenses are made in omafilcon A by CooperVision Inc. and CE marked for use in children for myopia management in a daily disposable wearing modality: i. Test contact lens 1: [redacted] ii. Test contact lens 2: [redacted]
Study Products Use	The study products will be used as per their CE marking for the correction of myopia in children.
Study Visits	The participants will attend a total of five visits over at most a three-month period. For current contact lens wearers, the visit schedule will be as follow: Visit 1 Screening/ Enrolment / Baseline Visit; Visit 2 Contact Lens Order 1 Dispensing Visit; Visit 3 Contact Lens Order 1 Follow-up & Contact Lens Order 2 Dispensing (V2+ 10±3 days); Visit 4 Contact Lens Order 2 Follow-up & Contact Lens Order 3 Dispensing (V3+ 10±3 days); Visit 5 Contact Lens Order 3 Follow-up Visit and Exit (V4+ 10±3 days). For current spectacle wearers the schedule will be as follow: Visit 1 Screening / Enrolment / Baseline Visit/ Adaptation Contact Lens Dispensing; Visit 2 Adaptation Contact Lens Follow Up & Contact Lens Order 1 Dispensing Visit (V1+ 14 ±7 days); Visit 3 Contact Lens Order 1 Follow-up & Contact Lens Order 2 Dispensing (V2+ 10±3 days); Visit 4 Contact Lens Order 2 Follow-up & Contact Lens Order 3 Dispensing (V3+ 10±3 days); Visit 5 CL Order 3 Follow-up Visit and Exit (V4+ 10±3 days).
Keywords	Myopia, adolescent, contact lenses.
Regulatory Status	Ethics Committee (EC) approval will be obtained prior to the study commencement.
Responsibilities	Sponsor: Name: CooperVision Inc. [redacted]

2 Introduction and Rationale

[redacted]

2.2 *Objectives*

The primary objectives of the study will be to:

i. Determine the level of overall visual satisfaction achieved with the test contact lenses compared with the control contact lens at the follow-up visit;
ii. Determine the habitual daily wearing time with the test contact lenses compared with the control contact lens at the follow-up visit.

The secondary objectives will be to

i. Measure the visual performance achieved with the test contact lenses compared with the control contact lens at the follow-up visit;
iii. Determine the level of visual satisfaction during specific visual tasks achieved with the test contact lenses compared with the control contact lens at the follow-up visit.

2.3 *Hypothesis*

The primary hypotheses that will be tested will be that:

i. visual satisfaction with the test contact lens designs is not inferior to the control contact lens design at the follow-up visit after ten days of wear;
ii. habitual daily wearing time with the test contact lens designs is not inferior to the control contact lens design at the follow-up visit after ten days of wear.

The secondary hypotheses that will be tested will be that:

i. the visual performance with the test contact lens designs is not inferior to the control contact lens design at the follow-up visit after ten days of wear;
ii. the level of visual satisfaction during specific visual tasks with the test contact lens designs is not inferior to the control contact lens design at the follow-up visit after ten days of wear

2.4 *Endpoints*

The primary efficacy endpoints will be

i. Overall visual satisfaction
ii. Daily wearing time in hours.

The secondary efficacy endpoints will be:

i. Mean logMAR visual acuity [redacted]:
ii. Visual satisfaction during specific visual tasks

The other efficacy endpoints of interests will be

i. Visual acuity in the presence of glare
ii. Other Aspects of visual satisfaction.

The primary safety endpoints will be:

i. Preservation of best corrected visual acuity: no loss of visual acuity equivalent or greater than one visual acuity line compared with baseline.
ii. Adverse events rate
iii. Slit lamp findings: proportion of grade 3 or higher positive findings compared to baseline.

3 Study Sponsor and Investigators

3.1 *Study Sponsor*

The Sponsor for this investigation will be CooperVision Inc. 5870 Stoneridge Dr, Suite #1, Pleasanton, CA 94588 USA. [redacted]

[redacted]

[redacted]

[redacted]

[redacted]

3.6 *Independent Ethics Committee*

Before clinical study initiation, this protocol, the informed consent form any other written information given to participants, and any advertisements planned for participant recruitment will be approved by an Independent Ethics Committee (IEC). The Investigator will provide documentation of the IEC approval to the Sponsor. The approval will be dated and will identify the applicable protocol, amendments (if any), informed consent form, all applicable recruiting materials, written information for participants, and participant compensation programs. The IEC will be provided with all information as required by local regulations and/or the IEC. At the end of the study, the Investigator will notify the IEC about the study's completion. The IEC also will be notified if the study is terminated prematurely. Finally, the Investigator will report to the IEC on the progress of the study at intervals stipulated by the IEC.

Voluntary informed consent will be obtained from every participant prior to the initiation of any screening or other study-related procedures. The Investigator has a defined process for obtaining consent. Specifically, the Investigator, or designee, will explain the clinical study to each potential participant and the participant must indicate voluntary consent by signing and dating the approved informed consent form. The participant will be provided an opportunity to ask questions to the Investigator, and if required by local regulation, other qualified personnel.

The Investigator will provide the participant with a copy of the consent form written in a language the participant understands. The consent document will meet all applicable local laws and will provide participants with information regarding the purpose, procedures, requirements, and restrictions of the study, along with any known risks and potential benefits associated with participating, the available compensation, and the established provisions for maintaining confidentiality of personal, protected health information. Participants will be told about the voluntary nature of participation in the study and will be provided with contact information for the appropriate individuals should questions or concerns arise during the study. The participant also will be told that their records may be accessed by appropriate authorities and Sponsor-designated personnel. The Investigator will keep the original, signed copy of the consent and must provide a duplicate copy to each participant.

The study will be submitted to the [redacted] Ethics Service for review. The investigation will not start until approval has been received at the respective site(s).

4 Study Material

4.1 *Study Products*

The study contact lenses will be daily disposable CE marked contact lenses made from omafilcon A material manufactured by CooperVision Inc. Three groups of contact lenses will be used:

i. An adaptation contact lens (pre-investigational phase) ;
ii. One Control contact lens: a currently marketed contact lens design;
iii. Two test contact lenses: new contact lens designs.

4.2 *Control Contact Lenses*

The control contact lenses will be currently marketed MiSight® daily disposable dual focus contact lenses CE marked for myopia control in children and adolescent. [redacted]

[redacted]

[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]
[redacted]	[redacted]

The participants will use the contact lenses during the control contact lens part of the investigational phase as their modality of vision correction. The use of the control contact lenses will be as per their intended use and CE marking.

The contact lenses will be worn on a daily disposable modality, that is the contact lenses will be worn during the day, removed and discarded at the end of each day before sleep, a similar new pair of contact lenses being used each day as per the user instructions [redacted]

4.3 *Test Contact Lenses*

The test contact lenses will be daily disposable dual focus contact lenses CE marked for myopia control in children and adolescent. [redacted]

[redacted]

	MiSight® Design 2A	MiSight® Design 2B
[redacted]	[redacted]	[redacted]

The participants will use the contact lenses during the test contact lens part of the investigational phase as their modality of vision correction. The use of the test contact lenses will be as per their intended use and CE marking.

The contact lenses will be worn on a daily disposable modality, that is the contact lenses will be worn during the day, removed and discarded at the end of each day before sleep a similar new pair of contact lenses being used each day as per the use instruction [redacted].

4.4 *Adaptation Contact Lenses*

The participants who are non-contact lens wearers at enrolment, will wear CE marked single vision contact lenses made form Omafilcon A for approximately two weeks during the pre-investigation phase to get adapted to contact lens wear.

[redacted]

	[redacted]
[redacted]	[redacted]

The participants will use the contact lenses during the test contact lens part of the investigational phase as their modality of vision correction. The use of the adaptation contact lenses will be as per their intended use and CE marking.

The contact lenses will be worn on a daily disposable modality, that is the contact lenses will be worn during the day, removed and discarded at the end of each day before sleep a similar new pair of contact lenses being used each day [redacted]

4.5 *Labelling*

4.5.1 Test & Control Contact Lenses

The test and control contact lenses will be dispensed in a masked manner so that the participants cannot see the lens label and remain masked to the details of the study lenses worn. The sub-investigators carrying out the visual acuity measurements will be masked with respect to the identity (tests vs. control) of the study contact lenses being worn.

A printed sticker will be placed over the study contact lenses blister package with the following labelling:

i. FOR STUDY USE ONLY
ii. Study CV20-51[redacted]ID20-28
iii. Lens code
iv. Lens power
v. Lot number
vi. Expiry date
vii. STORE BETWEEN 15^{O}C AND 25^{O}C
viii. CE mark number
ix. Sterile symbol

4.5.2 Adaptation Contact Lenses

The adaptation single vision contact lenses will be used by the non-contact lens wearers at the time of enrolment, the contact lenses will be dispensed for the participants to adapt to contact lens wear before the study phase.
The adaptation contact lenses will be used, unmasked as per their CE marking in their standard packaging.

5 Study Population

5.1 *Recruitment Procedure*

The study population needs to be an adolescent population as the visual activity and vision quality acceptance are different from those of adults and, therefore, cannot be predicted reliably using an adult population. The contact lenses intended target population for this lens will be children as young as seven years of age, but in order to gain more reliable vision satisfaction information, the test population will be adolescent of at least ten years of age.

[redacted] The participants fulfilling the criteria for inclusion and none of the exclusion criteria will be invited in a random fashion to participate in the study until the test population is achieved.

The prospective participants will initially be contacted by telephone, the investigation will be explained in detail and if interested the screening / enrolment visit will be scheduled. A copy of the Participant Information Sheet

and Informed Consent will be sent to the prospective participants for information at least 24 hours prior to the enrolment visit.

The prospective participants will be given a Participant Information Sheet to read and an Informed Consent to sign prior to any evaluation.

5.2 *Number of Participants*

Up to 40 participants will be screened, with the aim to enrol up to 30 with a view to achieve a cohort (participants completing the study as per protocol) sample size of at least 20 which was determined to be optimal, balancing the need for sufficient discrimination and limiting inconvenience to participants by not inflating the study sample (see section 7.1).

5.3 *Inclusion and Exclusion Criteria*

5.3.1 Inclusion Criteria

There are no requirements as to participant race or gender.

In order to be enrolled, each participant shall meet the following criteria:

i. Age 10 to 16 years;
ii. Parent/guardian and participant have read and understood the Participant Information Sheet;
iii. Parent/guardian and participant have read, signed and dated the Informed Consent;
iv. Best corrected visual acuity of at least 20/25 in each eye;
v. Have normal eyes with the exception of the need for visual correction;
vi. Spectacle refraction:
    Distance: -0.75 to -6.00D Spherical equivalent (maximum anisometropia 1.25D)
    Astigmatism: up to -1.00DC
vii. Be willing and able to adhere to the instructions set in the clinical protocol and maintain the appointment schedule.

5.3.2 Exclusion Criteria

To be eligible as a participant, each candidate shall be free of any ocular or medical condition that may affect the results of this study.

The following are specific criteria that exclude a candidate from enrolment in this study:

i. Ocular anterior segment infection, inflammation, abnormality, or active disease that would contraindicate contact lens wear;
ii. Newly prescribed (within the past 30 days) use of some systemic medications (such as antihistamines, decongestants, diuretics, muscle relaxants, tranquilizers, stimulants, anti-depressants, anti-psychotics, oral contraceptives) or new prescription eyedrops which is not rewetting/lubricating eyedrops for which contact lens wear could be contraindicated as determined by the investigator;
iii. Monocular participants (only one eye with functional vision) or participants fit with only one lens;
iv. Subjects with slit lamp findings greater than grade 1 (e.g. edema, infiltrates, corneal neovascularization, corneal staining, tarsal abnormalities, conjunctival, anterior segment inflammation) as per ISO 11980, any previous history or signs of a contact lens related corneal inflammatory event (past corneal ulcers), or any other ocular abnormality that may contraindicate contact lens wear at the enrolment visit;
v. History of herpetic keratitis, ocular surgery or irregular cornea;
vi. Enrolment of the family members of the investigator, family members of the investigator's staff, or individuals living in the households of these individuals.

5.4 *Premature Withdrawal*

A participant will be withdrawn from the investigation before completion if:

i. The participant/parent/guardian withdraws his/her consent to be included in the trial;
ii. An adverse event takes place that is considered by the participant/parent/guardian or the investigator to warrant withdrawal;
iii. Any event that leads the investigator to believe that it is not in the best interest for the participant to continue in the study;
iv. The study is prematurely terminated by the Principal Investigator, local research ethics committee or the Sponsor;
v. The participant is lost to follow-up;
vi. The participant no longer meets the eligibility criteria;
vii. The participant dies.

5.5 *Informed Consent*

Each participant and parent/guardian will give written consent according to local requirements after the nature of the study has been fully explained. The consent form will be signed before performance of any study-related activity. The consent form will have received approval by both the Sponsor and by the reviewing IEC before its use. The informed consent will be in accordance with principles that originated in the Declaration of Helsinki, current ICH and GCP guidelines, applicable regulatory requirements, and sponsor policy.

Before entry into the study, the investigator or an authorized member of the investigational staff will explain to potential participants and parents/guardians the aims, methods, reasonably anticipated benefits, and potential hazards of the study, and any discomfort it may entail. Participants and parents/guardians will be informed that their participation is voluntary and that they may withdraw consent to participate at any time. They will be informed that choosing not to participate will not affect the care the participant will receive. Finally, they will be told that if needed their records may be accessed by health authorities and authorized sponsor staff without violating the confidentiality of the participant, to the extent permitted by the applicable law(s) or regulations.

The participants and parents/guardians will be given sufficient time to read the informed consent form and will have the opportunity to ask questions. After this explanation and before entry into the study, consent will be appropriately recorded by means of the participants' dated signature. After having obtained the consent, a copy of the informed consent form will be given to the participants and to the parents/guardians.

6 Study Design & Procedures

6.1 *General Description*

The study will be conducted as a single arm, prospective, randomized (order of testing for the three study contact lens types), cross-over, double masked (participants and research staff carrying out the response measurements) of approximately ten days (range 7 to 13 days) wearing each of the study contact lenses.

The participants not wearing contact lenses at the time of enrolment will be wearing pre-study adaptation contact lenses for approximately two weeks (range 7 to 21 days) during the pre-study phase included for the participants to adapt to contact lens wear prior to the study phase

Participants satisfying all of the inclusion criteria and none of the exclusion criteria will wear the three study contact lens types (two test designs and one control design) in a randomized three-way crossover design (Diagram 1).

The time required by participants who are current contact lens wearers at the time of enrolment into the study will be a total of 9.25 hours for the five visits (Table 2A) and for those who are non-contact lens wearers 10.00 hours (Table 2B).

Table 2A – Clinical Time Contact Lens Wearers

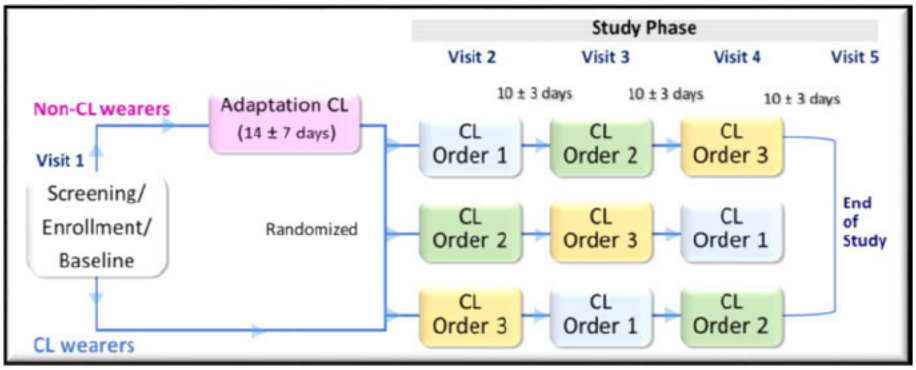
Visit 1	Screening/Enrolment / Baseline Visit	1.75 hours
Visit 2	CL Order 1 Dispensing Visit;	1.25 hours
Visit 3	CL Order 1 Follow-up & CL Order 2 Dispensing (V2+ 10±3days);	2.50 hours
Visit 4	CL Order 2 Follow-up & CL Order 3 Dispensing (V3+ 10±3days);	2.50 hours
Visit 5	CL Order 3 Follow-up Visit and Exit (V4+ 10±3 days).	1.25 hours
	Total	**9.25 hours**

Table 2B – Clinical Time Non-Contact Lens Wearers

Visit 1	Enrolment / Baseline Visit/Adaptation CL Dispensing Visit;	1.75 hours
Visit 2	Adaptation CL Follow Up & CL Order 1 Dispensing Visit (V2+ 14±7days);	2.00 hours
Visit 3	CL Order 1 Follow-up & CL Order 2 Dispensing (V3+ 10±3days);	2.50 hours
Visit 4	CL Order 2 Follow-up & CL Order 3 Dispensing (V4+ 10±3days);	2.50 hours
Visit 5	CL Order 3 Follow-up Visit and Exit (V5+ 10±3days).	1.25 hours
	Total	**10.00 hours**

The investigators carrying out the contact lens fitting, and the safety assessment will not be masked as they will have to follow the contact lenses specific fitting instructions. All the research staff carrying out the response measurements will be masked.

Diagram 1 - Study Design



The participants will not take part in any concomitant investigation of any type or take concomitant medications not allowed by the exclusion criteria.

6.2 *Experimental Routine*

Visit 1 – Screening/Enrolment /Baseline Visit (all participants)

Up to 40 prospective participants will attend the research clinic for the first visit to initially obtain their informed consent and evaluate their suitability to take part in the investigation. They will be asked to attend the clinic wearing their spectacles. After informed consent has been given, the investigator will review the participant's medical history, ocular history (including concomitant treatments), demographics and contact lens wear history (for those already wearing contact lenses). A series of routine optometric assessments and tests will be conducted to determine the participant's prescription and evaluate the participant's ocular health.

- ✓ Once it has been verified that the participants meet the inclusion/exclusion criteria they will be familiarised with the various vision measurements and tasks outlined in the protocol.
- ✓ They will then be fitted with Proclear Single Vision contact lenses. Modification to the lens power (up to three attempts) to determine the optimal lens powers for the specific lens type for the participant will be done according to the fitting guide. The participants will wear these contact lenses for a period of approximately 10-15 minutes to get used to the contact lenses. If after three attempts, no suitable contact lenses can be prescribed, the participants will be discharged from the study.

At the conclusion of the visit:

- ✓ For contact lens wearers, the second study visit will be scheduled.
- ✓ For non-contact lens wearers, the participants and their parents/guardians will be shown how to use the contact lenses and instructed to wear the study contact lenses for at least 8 hours a day, at least 6 days a week and the second study visit will be scheduled within14 ± 7 days.

Visit 2 (for contact lens wearers) – Contact Lens Order 1 Dispensing Visit

The participants will return for the second visit wearing their spectacles. Their concomitant medications will once again be reviewed. The study contact lenses will be randomized to the order in which the two tests and the control contact lenses will be worn (Lens Order 1). The study contact lenses will be selected and fitted according to the manual of procedures, fitting guide and the visual acuity and lens fitting characteristics assessed. Modification to the lens power (up to three attempts) to determine the optimal lens powers for the specific lens type for the participants will be carried out according to the fitting guide. The participants will wear these contact lenses for a period of approximately 15 minutes in order to adapt to the correction and then visual acuity will be measured according to the requirements, lens fitting characteristics will be evaluated. If after two contact lenses modifications (three pairs of contact lenses being tested), no suitable contact lens can be prescribed, the participants will be discharged from the study.

At the conclusion of the visit, the final contact lenses will be dispensed, the participants will be instructed to wear the study lenses for at least 8 hours a day, at least 6 days a week and scheduled for the third study visit to take place 10±3days later.

Visit 2 (for non-contact lens wearers) - Adaption Contact Lens Follow-up / Contact Lens Order 1 Dispensing Visit

The participants will return for the second study visit wearing their adaptation contact lenses. Their contact lens wearing history and satisfaction will be reviewed along with their concomitant treatments. Routine measurements of visual acuity will be carried out and lens fitting characteristics will be evaluated. The adaptation contact lenses will then be removed, and the participant's ocular health be evaluated prior to the insertion of the study contact lens.

The study contact lenses (Lens Order 1) will be dispensed following the same protocol as for the current contact lenses wearers described in the previous section.

At the conclusion of the visit, the final contact lenses will be dispensed, the participants will be instructed to wear the study lenses for at least 8 hours a day, at least 6 days a week and scheduled for the third study visit to take place 10±3days later.

Visit 3 – Contact Lens Order 1 Follow-up / Contact Lens Order 2 Dispensing Visit

Participants will return for their third study visit after having worn the first study contact lenses for 10±3days. They will attend the visit wearing their contact lenses and the following routine will take place:

- ✓ Their medical, ocular and contact lens wearing history will once again be reviewed. Participants will then complete a satisfaction questionnaire. A series of measurements of visual acuity with the study contact

lenses will be conducted for distance and near as required. Lens fitting characteristics will be evaluated, and the first study contact lenses will then be removed.

- ✓ The participants' ocular health will be evaluated prior to the insertion of the second study contact lenses (Lens Order 2). The second study contact lenses will be selected and fitted in the same manner as the first study contact lenses and will follow the same routine.

At the conclusion of the visit, the next pair of contact lenses will be dispensed, the participants will be instructed to wear the study lenses for at least 8 hours a day, at least 6 days a week and scheduled for the fourth study visit to take place 10 ± 3days later.

Visit 4 – Contact Lens Order 2 Follow-up / Contact Lens Order 3 Dispensing Visit

The same routine will be followed as per Visit 3. Contact lens Order 2 performance will be evaluated and Contact Lens Order 3 will be fitted.

At the conclusion of the visit, the final contact lenses will be dispensed, the participants will be instructed to wear the study lenses for at least 8 hours a day, at least 6 days a week and scheduled for the fifth study visit to take place 10±3days later.

Visit 5 – Contact Lens Order 3 Follow-up / Discharge Visit

Participants will return for their last follow-up visit having worn the last study lenses for 10±3days. They will attend the visit wearing their study contact lenses which performance will be assessed. The participants ocular health and vision will then be assessed. At the conclusion of the visit, the participants will be discharged from the study.

6.3 *Measures to Avoid Bias*

6.3.1 Randomization

The order that the three study contact lenses (two tests and one control) worn will be randomised to minimise bias. The randomization scheme will be computer generated using the appropriate software. Upon enrolment, the subjects will be assigned with participant ID number (sequentially) and this number will be linked to the randomization assignment.

6.3.2 Masking

The sub-investigators collecting the subjective responses and carrying out the visual measurements, which constitute the primary and secondary endpoints, will be masked with respect to the identity of the study contact lenses being worn at each visit. The investigators carrying out the contact lens fitting will not be masked as they will have to follow the test and control contact lenses specific fitting manuals.

The participants will be masked via overlabelling of the study contact lenses.

6.3.3 Participant Instructions

Participants will be instructed to wear their study contact lenses daily for 10±3 days, remove the contact lenses at night (prior to sleep), to discard them and to use a new identical pair of contact lenses the following day.

Participants will be advised on normal or adaptive symptoms related to contact lens wear. 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 collect subjective ratings such as comfort, vision, lens handling and symptoms. Responses to these questionnaires will not be considered as Adverse Events, complaints or Device Malfunctions.

The participants will be instructed to follow standard recommendations provided to contact lens wearers:

i. Avoid rubbing their eyes, always wash their hands prior to touching their eyes or handling their contact lenses, avoid being in a dusty environment and to use sunglasses when they are outdoors.
ii. Exercise care while washing their face with tap water; avoid splashing tap water into the eyes.
iii. Do not swim with contact lenses whenever possible.
iv. Immediately contact the investigator and scheduled to come in for a check-up within 24 hours if their eyes become red, irritated or painful.

The participants will be provided with instruction sheets (Appendix C)

6.4 *Study Procedures*

6.4.1 Efficacy Procedures

The primary efficacy procedures will be:

i. Recording of overall visual satisfaction on 100point VAS;
i. Recording of duration habitual daily contact lens wear in hours

The secondary efficacy endpoint procedures will be:

i. Measurement of logMAR visual acuities using [redacted] and calculation of the mean acuity
ii. Recording of activities specific visual satisfaction on 100-point VAS questionnaire;

The other endpoints of interests will be:

i. Measurement of visual acuity in the presence of glare using [redacted]
ii. Measurement of other aspects of visual satisfaction.

6.4.2 Safety Procedures

The procedures to monitor safety will be:

i. Identification and prevalence of adverse events;
ii. Measurement of Snellen/LogMAR visual acuity to measure the reservation of best corrected VA no loss of visual acuity equivalent or greater than one visual acuity line compared with baseline
iii. Safety ocular integrity (biomicroscopy) as per ISO 11980 evaluation proportion of Grade 3 or higher positive findings compared with baseline;
iv. Identification and prevalence of device deficiencies and quality complaints recording in the study form and tabled in the report.

6.4.3 Population Profiling Procedures

The procedures to profile the population's key characteristics will be:

i. Demographics and ocular history questionnaire (including concomitant treatment);
ii. Manifest Spectacle refraction (sphero-cylinder, best sphere);
i. Pupil size measurement;
ii. Ocular dominance measurement.

6.4.4 Study Management Procedures

The procedures to ensure that the study protocol is followed will be:

i. Concomitant treatment questionnaire.

6.5 *Contact Lens Wearers (CLW) Study Visit Routine*

CLW Visit 1 – Screening/ Enrolment/ Baseline[1]

The routine below will be followed:

- Explanation of the study[2]
- Signing of the consent form
- Participant demographics and ocular history questionnaire (Questionnaire A)
- Concomitant treatments questionnaire (Questionnaire B)
- Habitual vision satisfaction and wearing history questionnaire (Questionnaire C)
- Manifest Refraction (sphero-cylindrical & best sphere monocular and binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) and near (with +2.00D add) with sphero-cylindrical and best sphere refractions
- Review of inclusion and exclusion criteria
- Ocular dominance measurement
- Pupil size measurements
- [redacted]
- [redacted]
- iPad tasks familiarisation
- Safety ocular integrity examination
- Proclear Spherical CONTACT LENS INSERTION & WEAR 15 MINUTES
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to accept contact lenses or try an alternative prescription
- Contact lens fit clinical evaluation
- Proclear Spherical CONTACT LENS REMOVAL
- Decision to continue with determination of eligibility
- Scheduling

CLW Visit 2 – Lens Order 1 Dispensing

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- STUDY CONTACT LENS INSERTION & WEAR 15 MINUTES (ORDER 1)[3]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[4]
- Contact lens fit clinical evaluation
- Decision to dispense contact lenses[5]
- Dispensing of Study product
- Contact lens usage instruction with participants and parents/guardians
- Scheduling

CLW Visit 3 – Lens Order 1 Follow-up & Order 2 Dispensing (Visit 2 + 10±3 days)

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[1] All participants will attend the visit wearing spectacles

[2] The participants and parents/guardians will be given full details of the investigation at the time of making the appointment for the enrolment visit. The explanation at the time of the visit will be to reinforce the information given during the initial telephone contact and answer any questions the participants and their parents/ guardians may have.

[3] Randomly as per the randomization scheme in place one of the two test contact lenses or the control contact lens

[4] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed.

[5] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (Questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 1)
- Safety ocular integrity examination
- STUDY CONTACT LENS INSERTION & WEAR 15 MINUTES (ORDER 2)[6]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[7]
- Contact lens fit clinical evaluation
- Decision to dispense contact lenses[8]
- Dispensing of Study product
- Contact lens usage instruction
- Scheduling

CLW Visit 4 – Lens Order 2 Follow-up & Order 3 Dispensing (Visit 2 + 10±3 days)

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (Questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 2)
- Safety ocular integrity examination
- STUDY CONTACT LENS INSERTION & WEAR 15 MINUTES (ORDER 3)[9]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[10]
- Contact lens fit clinical evaluation
- Decision to dispense contact lenses[11]
- Dispensing of Study product
- Contact lens usage instruction

[6] Randomly as per the randomization scheme in place; one of the two test contact lenses or the control contact lens.
[7] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed.
[8] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study.
[9] Randomly as per the randomization scheme in place; one of the two test contact lenses or the control contact lens.
[10] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed.
[11] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study.

- Scheduling

CLW Visit 5 – Lens Order 3 Follow-up and Exit (Visit 3 + 10±3 days)

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (Questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 3)
- Preference questionnaire (Questionnaire E)
- Safety ocular integrity examination
- Discharge

6.6 *Non-Contact Lens Wearers (NW) Study Visit Routine*

NW Visit 1 – Screening/ Enrolment /Baseline Visit/ Adaptation Contact Lens Dispensing[12]

The routine below will be followed:

- Explanation of the study[13]
- Signing of the consent form
- Participant demographics and ocular history questionnaire (Questionnaire A)
- Concomitant treatments questionnaire (Questionnaire B)
- Manifest Refraction (sphero-cylindrical & best sphere monocular and binocular) distance and near
- Standard Snellen/LogMAR visual acuity at distance (monocular & binocular) and near (with +2.00D add) with sphero-cylindrical and best sphere refractions
- Review of inclusion and exclusion criteria
- Ocular dominance measurement
- Pupil size measurements
- [redacted]
- [redacted]
- iPad tasks familiarization
- Safety ocular integrity examination
- PROCLEAR SPHERICAL CONTACT LENS INSERTION & WEAR 15 MINUTES[14]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen/LogMAR visual acuity at distance (monocular & binocular) distance and near
- Decision to accept contact lenses or try an alternative prescription[15]
- Contact lens fit clinical evaluation
- Decision to continue with determination of eligibility

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[12] All participants will attend the visit wearing spectacles.

[13] The participants and their parents / guardians will be given full details of the investigation at the time of making the appointment for the enrolment visit. The explanation at the time of the visit will be to reinforce the information given during the initial telephone contact and answer any questions the participants and their parents / guardians may have.

[14] Randomly as per the randomization scheme in place one of the two test contact lenses or the control contact lens

[15] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed

- Contact lens usage instruction with participants and parents/guardians
- Scheduling

NW Visit 2 – Adaptation Contact Lens Follow-up & Order 1 Dispensing (Visit 1+ 14±7 days)

The routine below will be followed:

- Concomitant treatments questionnaire
- Visual satisfaction and contact lens wearing history questionnaire (Questionnaire C)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Contact lens fit clinical evaluation
- PROCLEAR SPHERICAL CONTACT LENS REMOVAL
- Safety ocular integrity examination
- BREAK 15 MINUTES
- STUDY CONTACT LENS INSERTION (ORDER 1) & WEAR 15 MINUTES[16]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen/LogMAR visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[17]
- Contact lens fit clinical evaluation
- Decision to dispense contact lens[18]
- Dispensing of Study product
- Contact lens usage instruction with participants and parents/guardians
- Scheduling

NW Visit 3 – Order 1 Follow-up & Order 2 Dispensing (Visit 2+ 10±3 days)

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 1)
- Safety ocular integrity examination
- STUDY CONTACT LENS INSERTION & WEAR 15 MINUTES (ORDER 2)[19]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[20]
- Contact lens fit clinical evaluation
- Decision to dispense contact lens[21]

[16] Randomly as per the randomization scheme in place; one of the two test contact lenses or the control contact lens
[17] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed
[18] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study
[19] Randomly as per the randomization scheme in place one of the two test contact lenses or the control contact lens
[20] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed
[21] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study

- Dispensing of Study product
- Contact lens usage instruction
- Scheduling

NW Visit 4 – Order 2 Follow-up & Order 3 Dispensing (Visit 2+ 10±3 days)

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 2)
- Safety ocular integrity examination
- STUDY CONTACT LENS INSERTION & WEAR 15 MINUTES (ORDER 3)[22]
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- Decision to dispense contact lenses or try an alternative prescription[23]
- Contact lens fit clinical evaluation
- Decision to dispense contact lens[24]
- Dispensing of Study product
- Contact lens usage instruction
- Scheduling

NW Visit 5 – Order 3 Follow-up Visit and Exit (Visit 3+ 10±3 days)

The routine below will be followed:

- Concomitant treatments questionnaire (Questionnaire B)
- Visual satisfaction and contact lens wearing characteristics questionnaire (Questionnaire D)
- Over refraction (best sphere monocular & binocular) distance and near
- Standard Snellen visual acuity at distance (monocular & binocular) distance and near
- [redacted]
- [redacted]
- Visual satisfaction questionnaire following iPad use vision activities (Questionnaire D)
- Contact lens fit clinical evaluation
- STUDY CONTACT LENS REMOVAL (ORDER 3)
- Safety ocular integrity examination
- Discharge

7 Statistical Analysis and Sample Size Determination

7.1 *Margins of equivalence*

[22] Randomly as per the randomization scheme in place one of the two test contact lenses or the control contact lens
[23] If an alternative prescription is tried the routine above will be repeated. Up to three attempts will be allowed
[24] If the contact lens fit is not suitable for dispensing the participant will be discharged from the study

For the primary endpoints the margin of equivalence for overall visual satisfaction will be 10 points on the 100-point visual analog scale and for daily wearing time 2.0 hours.

For the secondary endpoints the margin of equivalence for overall visual performance will be 0.05 logMAR and for specific activities visual satisfaction 10 points on the 100-point visual analog scales.

7.2 *Determination of Sample Size*

A sample size estimation has been carried out based upon an interim read in a previous study following a similar protocol

The sample size estimation has been carried out based upon an interim read in a previous study following a similar protocol. The analysis of the initial seven participants in that study produced for overall visual satisfaction after one week of wear a mean standard deviation of the difference between test and control in this study of 16.1 points on a the 100-point visual analog scale. Based upon the results of this previous study a sample size of 23 achieves 80% power and a significance level of 0.025 to detect non-inferiority using a one-sided t-test when the margin of equivalence is -10.0 and the true difference between the mean and the reference is 0.0.

The sample size estimation was carried out on the same data for daily wearing time; the mean standard deviation of the difference in daily wearing time between test and control in this study was 0.8 hours. Based upon these results a sample size of 8 achieves 87% power and a significance level 0f 0.025 to detect non-inferiority using a one-sided t-test when the margin of equivalence is -1.0 hour and the true difference between the mean and the reference is 0.0.

Based upon the above estimates involving only seven participants likely to over-estimate variability, hence the aim in this study will be to achieve a per protocol population of at least 20 participants.

7.3 *Statistical Analysis Plan*

A detailed statistical analysis plan will be developed before database closure.

For all the key parameters recorded, summary tables including descriptive and/or distribution statistics will be given for both the per-protocol analysis and the safety data sets.

All participants who meet the eligibility criteria, adhere to the protocol, and successfully complete the full study assessment will be available for the per-protocol analysis. Participants with missing data will be included in the analysis unless there is some non-response-related reason to exclude them, such as a protocol violation/invalid data.

For continuous variables, the following descriptive statistics will be reported: mean, median, standard deviation, quartiles, minimum, maximum and sample size. For nominal and ordinal variables distribution tables will be produced.

Normality testing will be performed for endpoints variables. All the continuous/ordinal endpoints analysed by way of comparative statistics will be checked for normality. The kurtosis and skewness values will be produced. The Q-Q Probability plot will be used to examine the values against the normal distribution. Statistical testing by Kolmogorov Smirnov and Shapiro Wilk tests will also be considered. If the normality assumption holds, a Linear Mixed Model will be used while, if the normality assumption does not hold, a Generalized Linear Mixed Model will be used.

For the primary analyses, the 2-sided 95% confidence interval for the difference between the test and control lenses will be produced, with non-inferiority being shown if the interval is entirely above -10.0 points for overall visual satisfaction and -2.0 hours for daily wearing time.

For the secondary analyses, the 2-sided 95% confidence interval for the difference between the test and control lenses will be produced, with non-inferiority being shown if the interval is entirely below +0.05 logMAR points for overall visual performance and if the interval is entirely above -10.0 points for specific activities visual satisfaction.

8 Risk Analysis

8.1 *Site Specific Risk Analysis*

[redacted]has conducted a risk and benefit analysis of of this study being carried out at its [redacted]following the site SOPs in place to carry out clinical studies. Details of the analysis is detailed below. [redacted]

8.2 *Benefits*

The direct benefit to the participants, who will all be myopic adolescent, will be the opportunity to try different contact lens types to potentially manage their myopia progression. At the end of the study this direct experience will help them in deciding if wearing multifocal soft contact lenses to manage their myopia progression is an optical correction they would consider using. Contact lenses also offer improved side vision, less optical distortion compared to spectacles and the convenience of not wearing spectacles.

The additional benefit for the myopic adolescent population is the determination of the contact lens types that can be incorporated in a long-term study to identify the most efficient designs to control myopia progression. Children myopia is an underestimated epidemic currently lacking solution to stop that progression, hence, the urgent need to improve upon the current solutions available. In this context, controlling myopia progression is not only to do with making the adolescent less reliant on the need of wearing a refractive correction or wearing a refractive correction of a lesser power. The presence of myopia is associated with an increase of the risks of developing ocular pathology in adulthood[redacted].

In addition, participants will receive an examination of the front part of their eyes and may have the opportunity to try different types of contact lenses at no cost to them.

8.3 *Risks*

All the assessments are routine clinical and specialist procedures, and none present any increased risk to participants compared with normal clinical routine.

All the study lenses are CE marked and approved for daily wear use for the correction of presbyopia in adults. Daily wear modality of soft contact lenses (the lenses will be removed every night and cared for with the lens care solution provided) have demonstrated good safety in decades. To make a valid assessment of the safety of soft contact lenses in children, researchers have compared a number of different studies [4] where the children (age 7 to 17 years old) were wearing contact lenses over one- or two-years period. Four of the six studies [5-8] observed no corneal infiltrative events, but the 95% confidence intervals can still be estimated. The upper limit never exceeds 300 per 10,000 patient years. The summarised incidence of corneal infiltrates in children teenagers and adults showed that the incidence of corneal infiltrative events in children is markedly lower than in adults [10]. The prospective studies of children represent over 2,000 patient years

of soft contact lens wear. Combining the six prospective studies, the estimated incidence of corneal infiltrative events in children is per 54 per 10,000 patient years and the upper 95% limit is 86 per 10,000 patient years. Therefore, each year, no more than 86 cases of corneal infiltrative events per 10,000 patients. In contrast, the expectation will be 300 in adults. The frequency of adverse events is lower in children compared to university students and young adults. The likelihood of microbial keratitis is negligible, with no reported cases in over 2,000 prospective and 400 retrospective patient years of lens wear [redacted].

Vigilance is still needed in spite of the low incidence of microbial keratitis in children. Education is key. All participants will be educated about the importance of good hygiene and list risky behaviours that can have consequences. Participants with an uncomfortable red eye will be seen promptly and managed appropriately. Complications may occur due to non-compliant behaviour. Behaviours related to increased risk of contact lens-related infections were much more common in teenagers and adolescents included showering and sleeping in lenses, with the latter increasing when travelling, drinking, and being away from home. This will be mitigated by the investigator providing information to the participants and parents/guardians reinforcing what they can and cannot do with contact lenses prior to dispensing. The participants will be under the care of the research investigators for the duration of the study period and the investigators will be present to deal with any unexpected event. Further, a medical monitor is appointed for this study. The medical monitor will receive and review any adverse events and may stop the study in the event that he identifies an abnormal trend. The medical monitor will also be available to rapidly treat any adverse event requiring medical management.

Vision with the study contact lenses may not be as good or clear as with spectacles. The participants vision with the study contact lenses will be measured prior to the participants leaving the clinic to ensure that their vision is satisfactory and achieves the required standard for dispensing.

Children 12 years and younger have demonstrated that they can handle contact lenses [redacted]. In this study, some of the participants will be existing contact lens wearers. For non-contact lens wearers, they (including parents/guardians) will be shown how to handle and care for the contact lenses. The use of soft contact lenses in adolescent, either to simply correct myopia with spherical contact lenses or retarding myopia using multifocal contact lenses is part of the management of myopia in [redacted] practice and several contact lenses are CE marked for that application. A contact lens alternative to control myopia is the use of rigid gas permeable contact lenses overnight during sleep; the implementation of the modality of myopia progression control is also approved but carries significant greater risk of unwanted effects than the modality followed in this study.

It is possible that the following problems may occur with the use of contact lenses; feeling that something is in the eye such as a foreign body or scratched area; excessive watering (tearing) of the eye; unusual eye secretions; redness of the eye; reduced sharpness of vision, blurred vision, rainbows, or halos around objects; sensitivity to light (photophobia); or dry eyes. These complaints will be closely monitored during the study and if the participant experience any of these, they have been informed that they should contact the study investigator as soon as possible. In rare instances, corneal ulcers, scarring, the growth of blood vessels into the cornea, temporary or permanent decreased vision, iritis and infections of the eye requiring treatment might occur.

In the event of any problem or concern the participants and parents/ guardians will be informed at the time of dispensing that they should contact the clinic during clinic hours or call the 24 hours emergency number they have been given.

The participants will have their vision checked at the onset of the study and prior to exiting the study to ensure that vision with contact lenses remain unchanged.

8.4 *Conclusion*

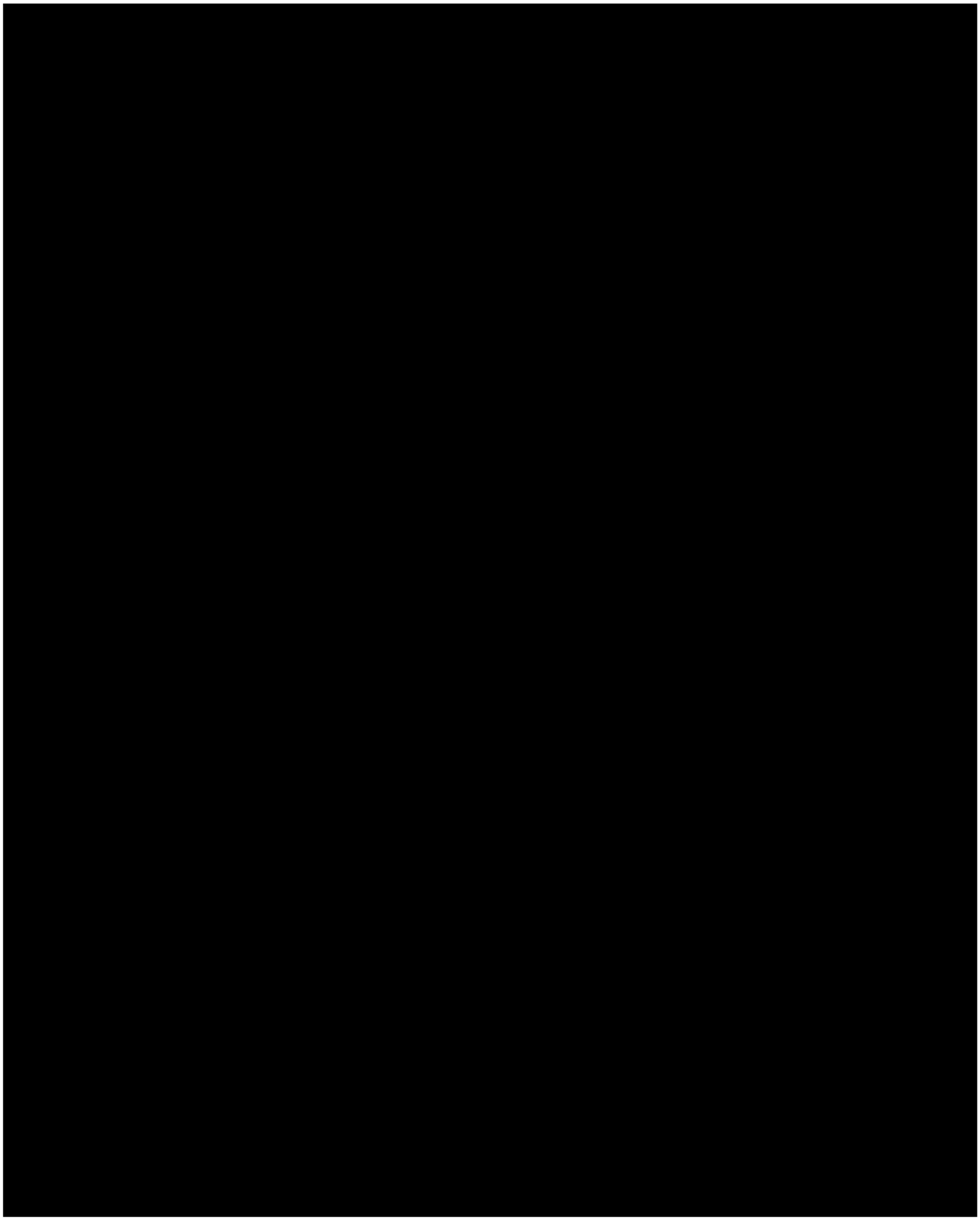
[redacted] the proposed clinical investigation, based on the users and products effectiveness risks and the risk management strategy in place (preventative and corrective), given that the severity of problems will be mostly minor, non-permanent and the likelihood of occurrence is unlikely with likelihood of non-detection if problem occurs being low, this study is justified as the overall potential benefit to the population outweighs its risks.

9 Adverse Events and Reporting

9.1 *Adverse Events*

Adverse events including serious adverse events and quality complaints will be reported in accordance with ICH E6 Guideline for Good Clinical Practice. Adverse event reports to the Independent Ethics Committee and MHRA will be made according to their requirements

[redacted]



9.1.2 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 participative attributes such as comfort, vision, or lens handling. Responses to these participative questionnaires will not be considered as Adverse Events, complaints or Device Malfunctions.

9.1.3 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 participant may be referred to an ophthalmologist for treatment. The investigator will attempt to determine whether the reaction is related to the contact lenses or a result of other factors. An Adverse Event Form will be completed for each adverse event. If both eyes are involved, each eye will be counted as one adverse event and Adverse Event information 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 participant must be followed until resolution and a written report completed indicating the subsequent treatment and resolution of the condition.

[redacted]

11 Investigator, Sponsor and Medical Monitor Responsibilities

11.1 *Investigator Responsibilities*

The investigator is responsible for ensuring participant safety and data quality by: protocol compliance, adherence to GCP and local regulatory requirements, and the Declaration of Helsinki. The investigator should

be appropriately qualified and legally entitled to practice and be trained in the proper method of obtaining informed consent.

The investigator must have the appropriate resources to conduct the clinical trial, be familiar with the protocol and agree to adhere to it, support monitoring and auditing activities, communicate with the Sponsor regarding any clinical trial issues or need for protocol modifications, make the necessary arrangements to ensure proper conduct and completion of the clinical trial, and ensure the protection and welfare of the participant, including arranging any emergency treatment as needed.

The investigator must ensure written Ethics Committee approval is received prior to the start of the clinical trial, that the Ethics Committee and sponsor is kept informed of the clinical trial progress, including serious/adverse events and deviations as required by them, and that any changes to the protocol are notified to the Ethics Committee and review written approval prior to implementation.

The investigator must try to ensure adequate participant recruitment; that all necessary and appropriate information is given to potential participants to ensure informed consent; is taken and documents; and that clinical records indicate the participant is enrolled in a clinical trial. The investigator must ensure that participants are provided with emergency contact details along with a procedure to follow in the case of an emergency, and that participants are kept informed as pertinent new information becomes available that may affect their decision to participate.

The investigator has primary responsibility for the accuracy, legibility and security of all clinical investigation data, video recordings, documents and participant records at the Investigator site during and after the clinical trial. CRFs are to be signed by the investigator, and any alterations to data are to be made by authorized personnel, initialled and dated by same or, in the instance of electronic data, an audit trail will be in place, with no obstruction of the original data.

The investigator must ensure that data be kept for the minimum time as specified by this protocol. The test product must be accounted for (the quantity of the devices received must be reconciled with the quantities of the device used, discarded or returned), and must also be responsible for the supervision and assignment of duties to all responsible for the conduct and evaluation of the clinical trial for the Investigator centre involved

11.2 *Sponsor Responsibilities*

The Sponsor has delegated the selection of the Investigator and study site to the CRO, who should also select and appoint a monitor. The Sponsor has the ultimate responsibility for monitoring. The Sponsor is to supply and keep an up-to-date signed protocol and protocol amendments.

The sponsor should ensure appropriate information is provided to the Investigators to conduct the clinical trial; that deviations are reviewed with the Investigator as needed and included in the final report. Adverse events are reported by the investigator, and the sponsor in turn will then notify their applicable regulatory authorities, and other investigators as appropriate. The Sponsor is to maintain Sponsor-specific clinical trial documentation as required by the regulatory authorities and to ensure the investigator is aware of their record keeping responsibilities.

11.3 *Medical Monitor Responsibilities*

The Medical Monitor will be a physician specializing in ophthalmology. To reduce study bias concerns, the Medical Monitor will not have any real or potential conflict of interest with the Sponsor, Study Investigator or participating Investigative site.

The primary purpose of the Medical Monitor is to ensure an independent review all Serious Adverse Events (SAE), device-related Adverse Events and AE related to the safety endpoints. When reviewing SAE and

device-related adverse events, the Medical Monitor will report the relationship between the AE and the study device and the study procedure. The results of all events reviewed by the Medical Monitor will be documented.

[redacted]

12 General Clinical Management

12.1 *Data Recording*

The clinical data will be recorded on dedicated electronic case report forms (eCRFs) specifically designed to match the testing routine for each visit. [redacted]. The eCRFs will be reviewed for accuracy and comprehensiveness once completed and signed by the investigator. A summary of the data will also be recorded in the participants' clinical records. These constitute the participants' source documents, which will be signed by the investigator. The content and structure of the eCRFs are compliant with ISO14155:2011.

12.2 *Clinical Monitoring*

[redacted] the study in a manner consistent with ICH GCP E6, EN ISO 14155:2011 and the Declaration of Helsinki. The study monitor will maintain close contact with the Principal Investigator and the Investigator's designated staff. The monitor's responsibilities will include:

i. Ensuring that the investigation is being conducted according to the protocol;
ii. Ensuring the rights and wellbeing of participants are protected;
iii. Ensuring that protocol deviations are documented with corrective action plans, as applicable;
iv. Clarifying questions regarding the study;
v. Resolving study issues or problems that may arise;
vi. Reviewing the study records to ensure completeness and accuracy;
vii. Study and participant source document records reviewed will include:
    a. The Information and Consent Form
    b. Source documentation including consenting, medical history, concomitant medications and adverse event information as applicable.
    c. Study related Regulatory documents as per ICH E3 section 8

The clinical monitor will review study data and will perform, at a minimum, one Interim and one Close-Out Visit on site.

12.3 *Study Product Accounting*

Study product records include the study contact lens shipping orders, dispensing logs and the physical count and disposition of the remaining unused study contact lenses. Used worn lenses collected at the study visits will be discarded by the study site personnel. The clinical monitor will ensure product is reconciled and any discrepancies are investigated and either corrected or documented. At study conclusion all study contact lenses will be reconciled.

12.4 *Participant Compliance Monitoring*

Throughout the course of the study the clinical monitor will review study data for participant compliance to the protocol. Non-compliances will be documented as protocol deviation(s). If a deviation is determined to be major, the deviation will be reported to the Ethics Committee as per their requirements.

12.5 *Unmasking of Study Information*

Masked information on the identity of the assigned study product(s) should not be disclosed during the study unless there are medical or safety reasons to do so, for example knowledge of the product may be necessary for the treatment of some adverse advents. The randomisation and masking data is under the control of a designated unmasked member of staff. In the event of any adverse event requiring unmasking, the identity of the product can be requested by the Investigator, Medical Monitor or any medical personnel. In the event that unmasking occurs, the following should be recorded:

i. The ID of the unmasked participant,
ii. The reason for unmasking,
iii. The study staff person responsible for unmasking,
iv. A list of person(s) who have been unmasked.

12.6 *Participant Payments*

For participants who are eligible and successfully enrolled in the study, financial compensation will be made in return for participants and parents/guardians time and travel expenses and for those who fail the screening visit payment will be pro-rated to their participation. In the event that participation ends prior to completing all the study visits, payment will be made according to the visits undertaken [redacted]

13 Administration Management

13.1 *Relevant Standards*

This clinical study will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, and in compliance with the International Conference on Harmonization (ICH) E6 Good Clinical Practice (GCP) Consolidated Guideline, the International Standards Organization (ISO) Clinical investigation of medical devices for human participants – Good clinical practice (ISO 14155:2011(E)), Ophthalmic optics – Contact lenses and contact lens care products – Guidance for clinical investigations (ISO 19980:2012 (E)) and other regulations as applicable. The Investigator and all clinical study staff will conduct the clinical study in compliance with the protocol. The Investigator will ensure that all personnel involved in the conduct of the study are qualified to perform their assigned responsibilities through relevant education, training, and experience.

13.2 *Deviations from the Protocol*

Protocol deviations are unanticipated or unintentional changes to a study after it has received prior sponsor approval and ethics clearance. Protocol deviations can be major or minor.

If the deviation affects participant's rights, safety and wellbeing, or the scientific integrity of the clinical investigation, the ethics committee must be contacted with requests for deviations, and reports of deviations. Under emergency circumstances, deviations from the clinical investigational plan to protect the rights, safety and well-being of participants may proceed without prior approval of the sponsor and the ethics committee. Such deviations shall be documented and reported to the sponsor and the ethics committee as soon as possible.

13.2.1 Major Protocol Deviations

Major protocol deviations may impact the research protocol, information consent document or other study materials, usually cannot be anticipated ahead of time and are often necessary to ensure the safety and welfare of the participants.

[redacted]

i. Changes in procedures initiated to eliminate immediate risks/hazards to participants;
ii. Enrolment of participants outside the protocol inclusion/exclusion criteria whether agreed to or not by the sponsor;
iii. Inadvertent deviation in specific research intervention procedures or timing of the research intervention which could impact upon the safety or efficacy of the study-related intervention or upon the experimental design;
iv. Information consent documentation violations: no documentation of informed consent; incorrect version of, or incomplete, informed consent documentation used.

13.2.2 Minor Protocol Deviations

Protocol deviations caused by or which originate with research participants are generally considered minor, and normally are not reported to the Independent Ethics Committee unless these result in increased risk to the participants). [redacted]

i. Logistical or administrative aspects of the study (e.g., study participant missed appointment, change in appointment date);
ii. Inadvertent deviation in specific research intervention procedures or timing of the research intervention which would *not* impact upon the safety or efficacy of the study-related intervention or upon the experimental design (i.e., missing a measurement during a session that is not considered critical for the study).

13.3 *Modifications to the Clinical Investigational Plan*

Any modifications to the clinical investigational plan that are considered necessary can only be effected after approval from the principal investigator and the Independent Ethics Committee. In an emergency situation, as indicated in ISO14155, the clinical investigator will exercise his judgement to safeguard the participant's interest and may deviate from the clinical investigation plan without the prior approval of the Independent Ethics Committee. In that case, the deviation will not be considered as a breach of agreement but will be reported to the ethics committee.

13.4 *Termination of the Study*

The Sponsors reserve the right to terminate the study at any time for any reason. The principal investigator has the discretion to initiate stopping the study based on participant safety or if information indicates the study's results may be compromised. The Investigator should promptly notify the IEC of the termination or suspension and of the study and the reason.

13.5 *Data Protection*

All information obtained during the course of the investigation will be regarded as confidential and will be handled in accordance with the Data Protection Act and the General Data Protection Regulation (GDPR) guidelines. All personal data gathered in this trial will be treated in strictest confidence by investigators, monitors, [redacted], the sponsor and the independent ethics committee. No data will be disclosed to any third party without the express permission of the participant [redacted] personnel (monitor, auditor), the sponsor, the independent ethics committees and regulatory organisations in

the context of their investigation related activities which, as part of the investigation will have access to the CRFs and source documents.

13.6 *Data Handling and Record Keeping*

[redacted]

All records, including CRFs, will be kept in the files of the Principal Investigator site for the latter of the two dates a period of two years after the date on which the investigation is terminated or completed, or the date that the records are no longer required for legal clinical requirements.

[redacted]

13.8 *Publication Policy*

The study data will be wholly owned by the Sponsor. The results of the study may not be used in publications or presentations without the written permission of the Sponsor.

13.9 *Compensation*

The Sponsor will compensate the Contract Research Organisation for work carried out as agreed prior to the study and will supply or pay for consumables for use in the study as detailed in the contract.

13.10 *Indemnity/Insurance*

The Sponsor will take out indemnity to cover the participants and research staff involved in the study and the ethics committee. This will NOT cover the research staff for clinical negligence. Investigators will have their own professional indemnity.

[redacted]