Myopia Assessment of Two Manufacturing Processes for Myopia Management Lenses (MAPLE)

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Sponsor: SightGlass Vision, Inc.

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Protocol Approval:

Joe Rappon, Chief Medical Officer
SightGlass Vision, Inc.

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Date

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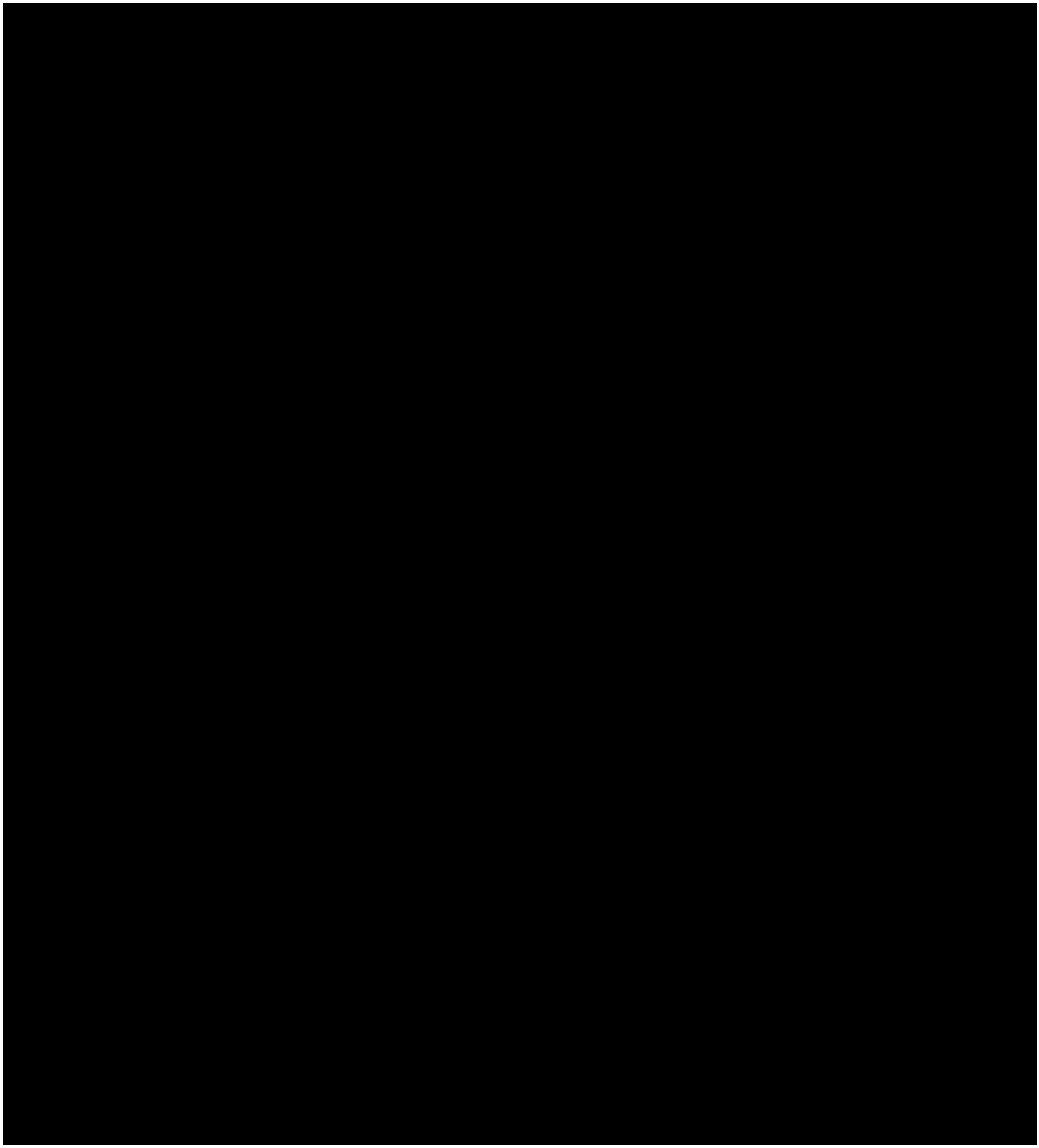

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1 PROTOCOL SUMMARY

1.1 SYNOPSIS

Title: *Myopia Assessment of Two Manufacturing Processes for Myopia Management Lenses (MAPLE)*

Study Description: *This is a randomized, controlled, multisite, subject- and observer-masked, contralateral clinical trial of 6-month duration to compare two SightGlass Vision Diffusion Optics Technology (DOT) spectacle lens manufacturing processes in reducing the progression of juvenile myopia.*

Objectives: **Primary Objective:** *To demonstrate that DOT lenses manufactured by method A are non-inferior to DOT lenses manufactured by method B in terms of axial length progression over a 6-month time period.*

[redacted]

Endpoints:

Primary Endpoint

Test vs. control axial length change from baseline at 6 months.

[redacted]

Study Population:

Approximately 50-60 children between the ages of 6 and 14 years old (inclusive) with myopia.

Inclusion/Exclusion Criteria:

Inclusion criteria:

[redacted]

2. *Best corrected visual acuity by manifest refraction of +0.10 logMAR (20/25 Snellen equivalent) or better in each eye;*
3. *The difference in spherical equivalent power between the two eyes (anisometropia based on manifest refraction) must be less than or equal to 0.75 D;*

[redacted]

[redacted]

Exclusion criteria:

1. *Current use of any myopia control treatment such as atropine, multifocal contact lenses, or orthokeratology (NOTE: Prior bilateral usage acceptable as long as treatment stopped at least 6 months before screening visit. Any subject with a history of unilateral myopia control treatment is excluded.);*

[redacted]

6. *Any ocular or systemic conditions that could influence refractive development or status [e.g., keratoconus, congenital glaucoma, ocular trauma, diabetes, Marfan syndrome or other connective tissue disorder, Down's syndrome, family history of poor night vision (to prevent against enrolling subjects with congenital stationary night blindness)];*

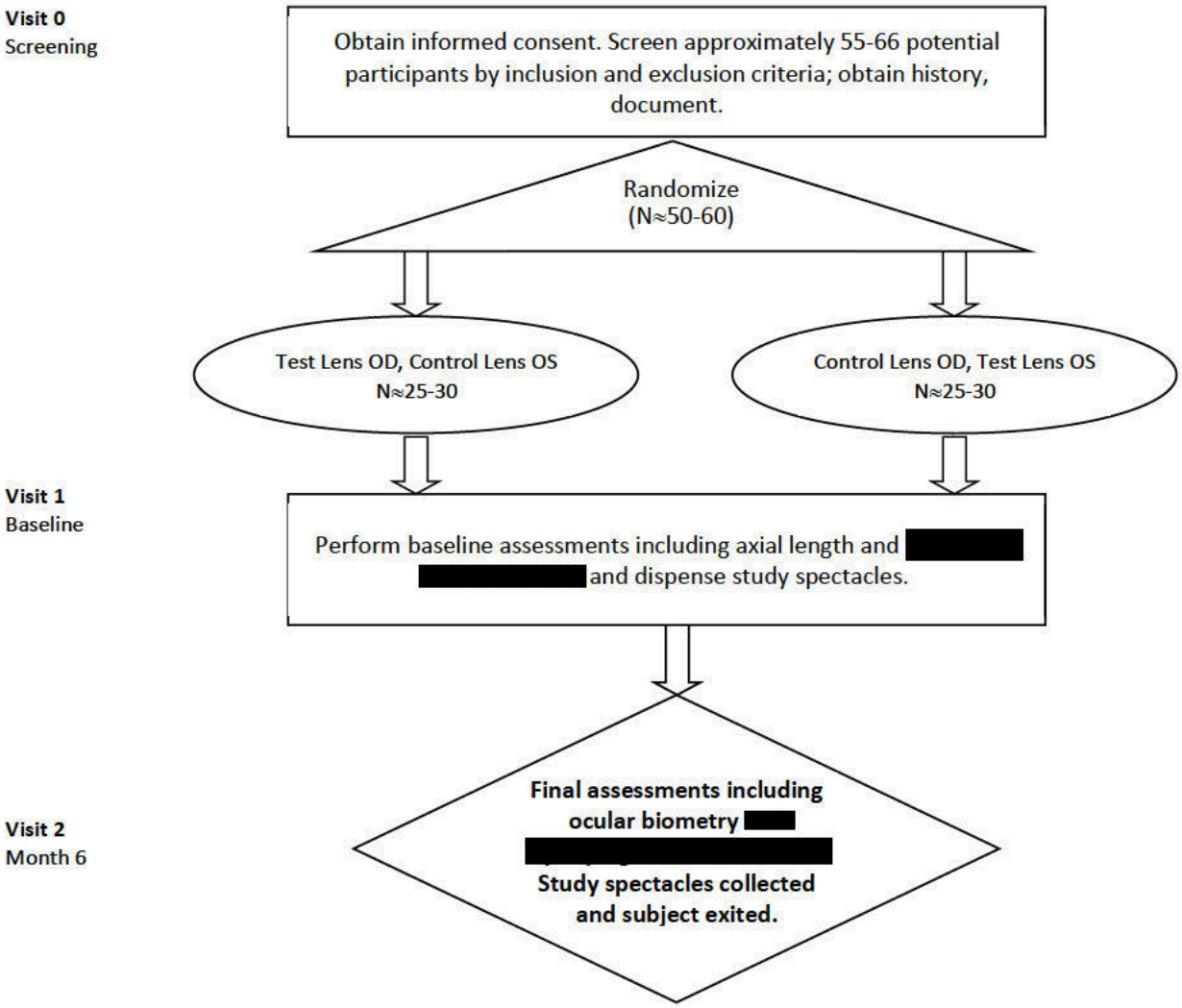
[redacted]

Description of Sites/Facilities Enrolling Participants:	*Approximately five investigational sites will be utilized for this study. It is expected that all sites will be located in the United States. Each site will be asked to enroll 10-12 eligible subjects.*

Description of Study Intervention:	*There will be two different investigational spectacle lenses utilized in this study as follows:* • ***Test:*** *DOT-20-365-090 – Single vision, impact-resistant spectacle lenses with SightGlass Vision DOT 0.2* [redacted] *nd a 5 mm clear aperture. Manufacturing method A* [redacted] • ***Control****: DOT-03-365-130 – Single vision, impact-resistant spectacle lenses with SightGlass Vision DOT 0.2* [redacted] *and a 5 mm clear aperture. Manufacturing method B* [redacted]
Study Duration:	*The total duration of the trial is expected to be approximately 10 months, which includes a 4-month allotment for subject enrollment.*
Participant Duration:	*Subjects will be on the study for 6 months.*

1.2 SCHEMA

Figure 1: *Study Flow diagram*



1.3 SCHEDULE OF ASSESSMENTS

[redacted]

Screening – Visit 0: Day -21 to -7

- Informed consent/assent
- Demographics
- Ocular and medical history, and number of myopic parents
- Concomitant medications/therapies
- Ocular biometry [redacted]

[redacted]

- Stereopsis
- Color vision
- Monocular (right eye) scotopic, low mesopic, and high mesopic pupil size
- Manifest refraction
- Monocular BCVA (logMAR)
- Slit-lamp examination
- Inclusion/exclusion criteria
- Randomization
- Parent questionnaire
- Participant questionnaire
- Monocular pupillary distance (PD) and optical center (OC) height measurements [redacted]
- Order study spectacles [redacted]
- Schedule Visit 1

Baseline – Visit 1: Day 0

- Concomitant medications/therapies review

[redacted]

- Monocular PD and OC height measurements [redacted]
- Collect habitual spectacles
- Dispense new study spectacles

[redacted]

- Slit-lamp examination

[redacted]

- Ocular biometry [redacted]
- Adverse events
- Device deficiencies
- Schedule Visit 2

End-of-Study – Visit 2: Month 6 (± 14 days)

- Concomitant medications/therapies review
- Stereopsis
- Manifest refraction
- Monocular BCVA (logMAR)
- Slit-lamp examination
- Ocular biometry [redacted]
- Parent questionnaire
- Participant questionnaire
- Adverse events
- Device deficiencies
- Collect study spectacles
- Return habitual spectacles
- Exit subject

Additional Spectacle Dispensing Visit

- Collect existing study spectacles
- Dispense new study spectacles
- Adverse events
- Device deficiencies

Unscheduled Visit (minimum required assessments)

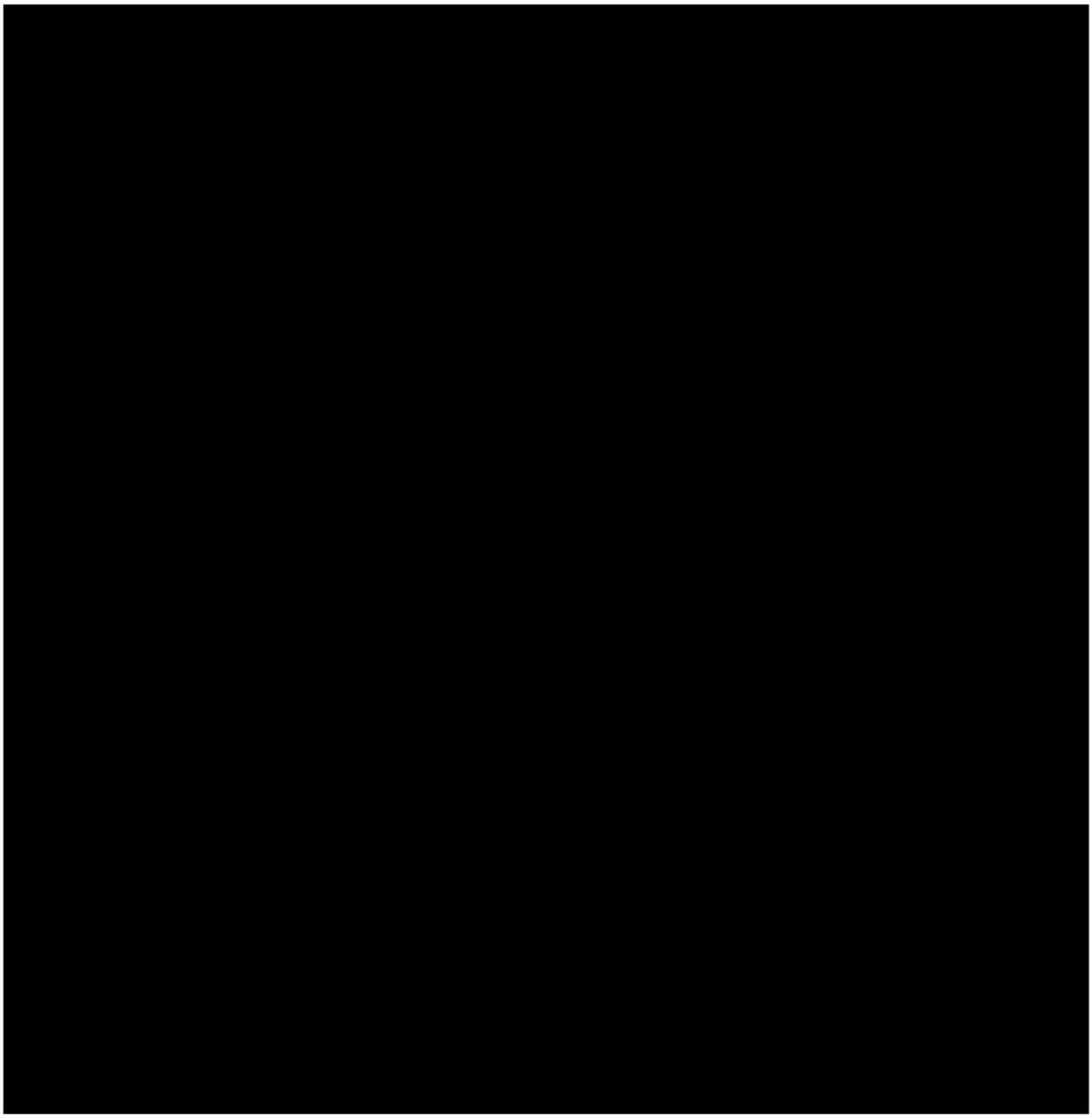
- Concomitant medications/therapies review
- Manifest refraction
- Monocular BCVA (logMAR)
- Slit-lamp examination
- Adverse events
- Device deficiencies

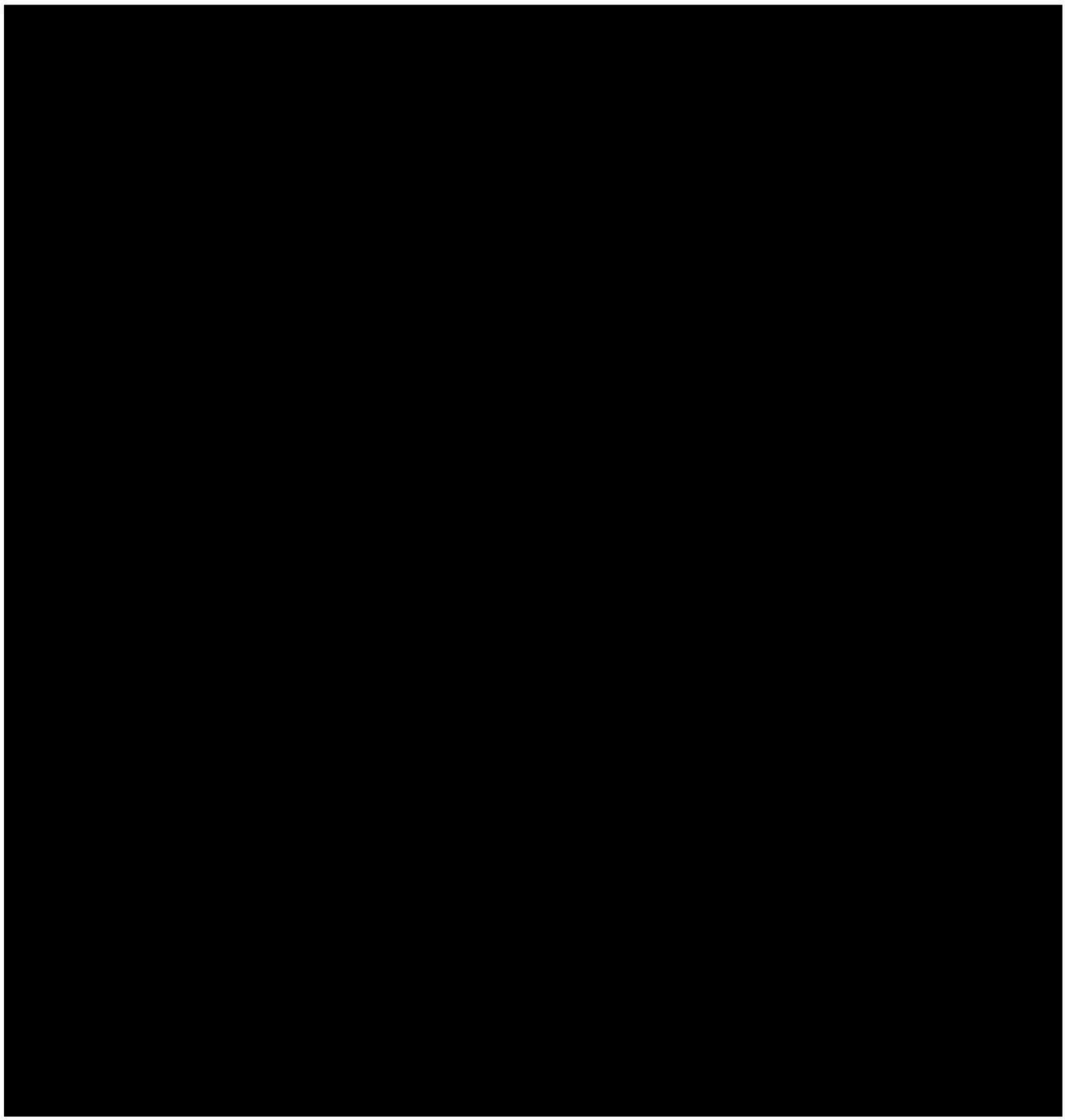
1.4 TABLE OF ASSESSMENTS (TABLE 1)

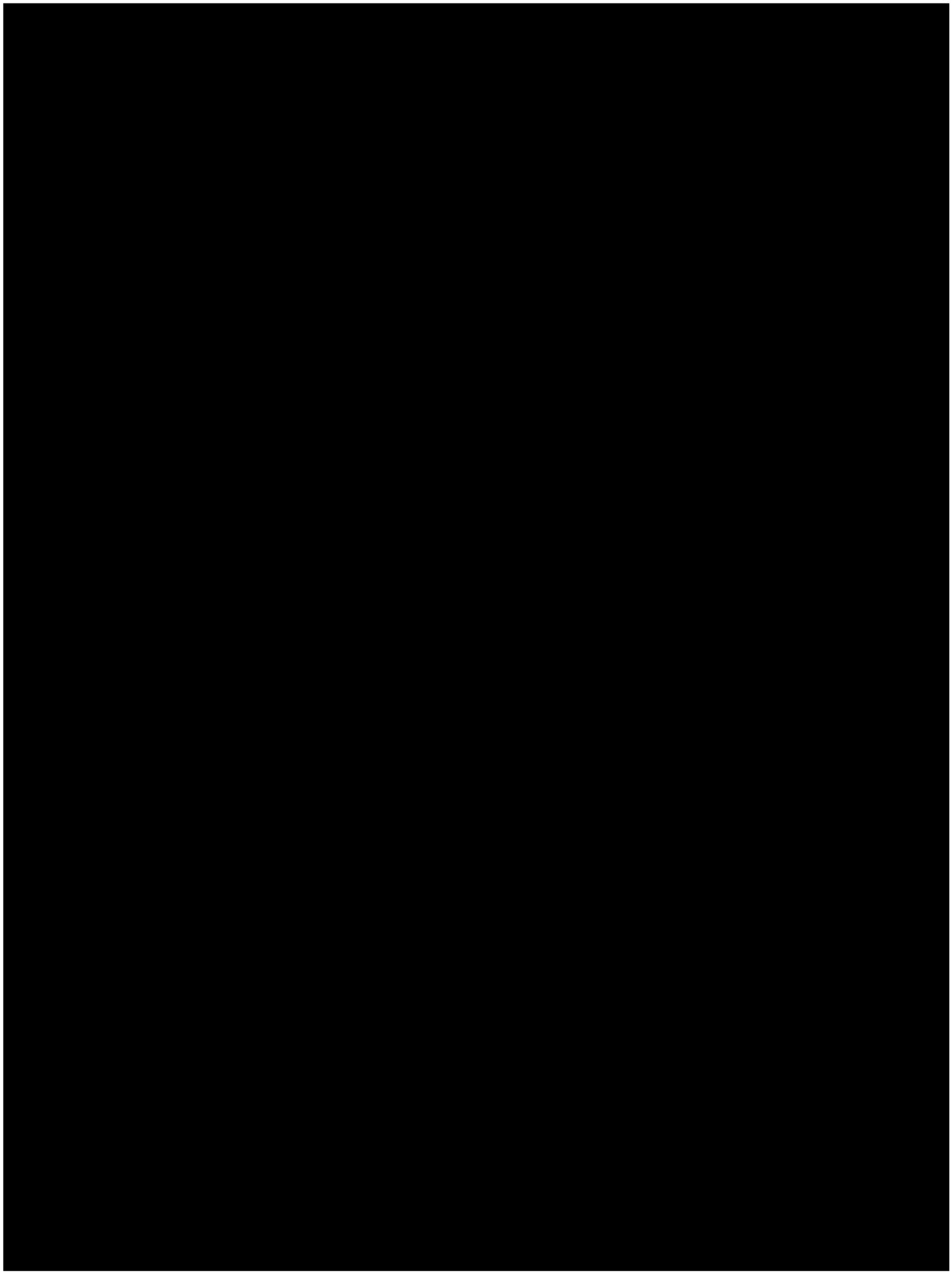
Procedure	Visit 0	Visit 1	Visit 2	U/S visit[1]
	Screening Day -21 to -7	Baseline Day 0	Month 6 [2] +/- 14 days or Exit	As needed
Informed consent/assent	X			
Demographics	X			
Ocular and medical history and # of myopic parents	X			
Concomitant medication/therapy review	X	X	X	X
Inclusion/exclusion criteria	X			
Randomization	X			
[redacted]				
Monocular scotopic, low mesopic, and high mesopic pupil size (OD)	X			
Color vision	X			
Stereopsis	X[3]		X	
Manifest refraction and monocular BCVA (logMAR)	X[3]		X	X
Slit lamp examination	X	X	X	X
PD and OC measurements [redacted]	X	X		
Order study spectacles [redacted]	X			
Collect habitual spectacles		X		
Dispense new study spectacles		X		
[redacted]				
Parent questionnaire	X[3]		X	
Subject questionnaire	X[3]		X	
Adverse events	X	X	X	X
Device deficiencies		X	X	X
Collect study spectacles			X	
Return habitual spectacles			X	
Compliance	*Will be assessed at-home via a telephone or text check-ins around Day 7, Month 2, and Month 4*			

[1] Unscheduled visit – minimum assessments required.
[2] For clarity, Visit 2 is to be scheduled relative to Visit 1 (Day 0). For example, if the Baseline visit occurs on November 1st, 2019, then Visit 2 (month 6 ± 14 days) should be targeted for May 1st, 2020 and occur between April 17th, 2020 and May 15th, 2020.
[3] To be considered baseline assessment.
[redacted]

2 INTRODUCTION







[redacted]

2.5 RISK/BENEFIT ASSESSMENT

2.5.1 KNOWN POTENTIAL RISKS

The known potential risks for the current study are as follows.

General risks related to any spectacles:

- Headache
- Eye strain
- Dizziness
- Eye discomfort
- Eye or face injury (e.g., subject gets hit with an object while wearing study spectacles)
- Discomfort due to the frames of the spectacles
- Allergic reaction to the frames of the spectacles

Possible/potential incremental risks due to the test lenses:

- Glare
- Halos
- Blurred/hazy vision

[redacted]

2.5.2 KNOWN POTENTIAL BENEFITS

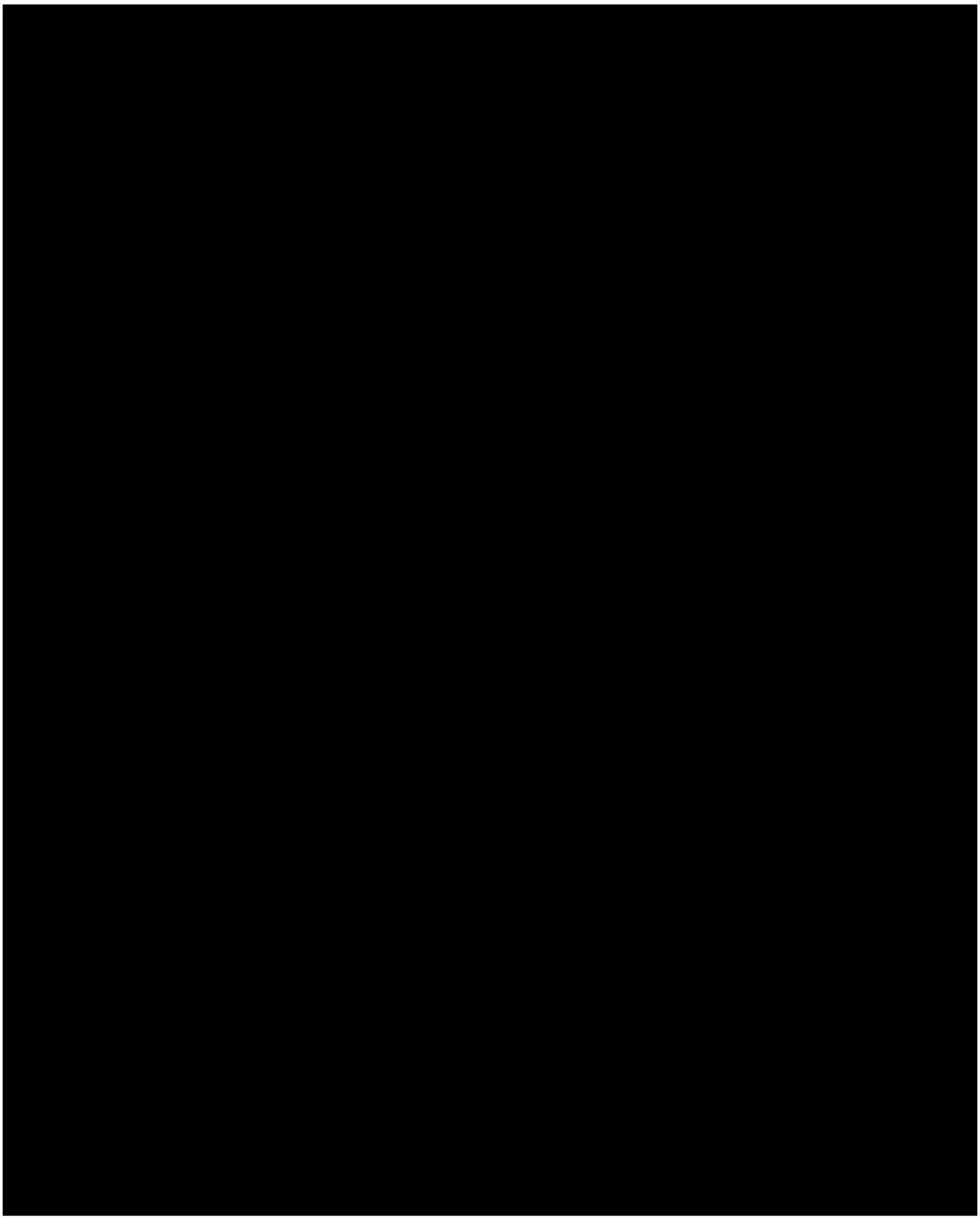
All of the study spectacles will correct refractive ametropia with or without astigmatism and may reduce the rate of progression of myopia in children. Furthermore, the subjects will be provided comprehensive eye care and spectacles at no charge for the duration of the trial.

[redacted]

3 OBJECTIVES AND ENDPOINTS

3.1 EFFICACY OBJECTIVES AND ENDPOINTS (TABLE 3)

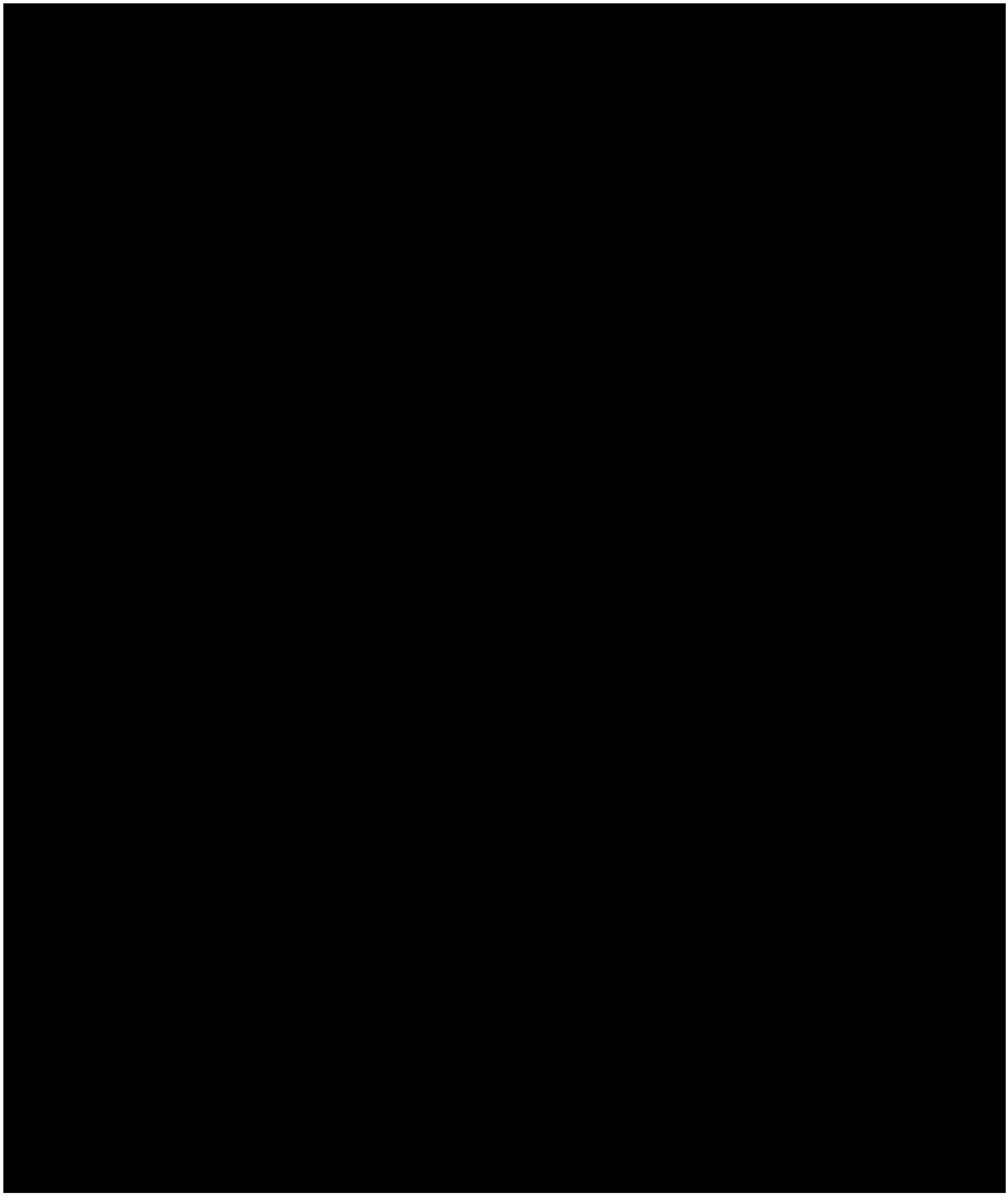
OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary Efficacy		
The primary objective of this study is to demonstrate that DOT lenses manufactured by method A are non-inferior to DOT lenses manufactured by method B in terms of axial length progression over a 6-month time period.	The primary endpoint of this study is to compare test vs. control axial length change from baseline at 6 months.	[redacted]



3.2 SAFETY OBJECTIVES AND EVALUATIONS (TABLE 4)

SAFETY OBJECTIVES	SAFETY EVALUATIONS	JUSTIFICATION FOR SAFETY EVALUATION
Several safety evaluations are being conducted to evaluate the safety performance of this device as well as to monitor individual subject safety during the study.	The safety evaluations of this trial are: • Adverse Events • Device Deficiencies • Stereopsis • Monocular best-corrected visual acuity (BCVA) [redacted]	Adverse events, device deficiencies, and symptoms, problems, and complaints are standard safety assessments for device studies. These may be determined during visits, through questionnaires, through patient diary, or other communication. Best-corrected visual acuity assessment, through a manifest refraction, is standard for ophthalmic clinical trials, is an important assessment for evaluating amblyopia, and is a required for inclusion/exclusion criteria. [redacted]

4 STUDY DESIGN



[redacted]

4.3 END OF STUDY DEFINITION

A participant is considered to have completed the study if he or she has completed all mandatory visits of the study including Visit 2 as shown in the Schedule of Activities (**TABLE 1**), Section 1.4.

The end of the study is defined as completion of Visit 2 (Month 6) or discontinuation by the last participant from all sites.

5 STUDY POPULATION

The study population will include approximately 50-60 children between the ages of 6 and 14 years old (inclusive) with myopia. For clarity, 14-year-old children may be enrolled in this study up until the day before their 15th birthday.

This population has been selected as the incidence of juvenile myopia begins around 5 or 6 years of age. As age of myopia onset is an important determinant in an individual's final (adult) refractive state, the younger a child develops myopia, the more likely that they will develop a higher level of myopia as an adult and are thus at a higher risk of developing a sight-threatening condition. Therefore, intervening early to reduce the overall progression of myopia is important. Given that myopia typically progresses until the mid-teens, children up to 14 years of age will also be included in this trial.

5.1 INCLUSION CRITERIA

In order to be eligible to participate in this study, an individual must meet all of the following criteria:

1. At time of informed consent/assent, child must be 6 to < 15.0 years of age [redacted]
2. Best corrected visual acuity by manifest refraction of +0.10 logMAR (20/25 Snellen equivalent) or better in each eye;
3. The difference in spherical equivalent power between the two eyes (anisometropia based on manifest refraction) must be less than or equal to 0.75 D;

[redacted]

[redacted]

5.2 EXCLUSION CRITERIA

An individual who meets any of the following criteria will be excluded from participation in this study:

1. Current use of any myopia control treatment such as atropine, multifocal contact lenses, or orthokeratology (NOTE: Prior bilateral treatment acceptable as long as treatment stopped at least 6 months before screening visit. However, any subject with a history of unilateral myopia control treatment is excluded.);

[redacted]

6. Any ocular or systemic conditions that could influence refractive development or status [e.g., keratoconus, congenital glaucoma, ocular trauma, diabetes, Marfan syndrome or other connective tissue disorder, Down's syndrome, family history of poor night vision (to prevent against enrolling subjects with congenital stationary night blindness)];

[redacted]

5.3 LIFESTYLE CONSIDERATIONS

During this study, participants are asked to:

- Wear the assigned spectacles constantly except for sleeping, swimming, or other activities in which spectacle wear would be dangerous or otherwise not possible (minimum of 10 hours per day);
- Abstain from contact lens wear of any kind;
- Abstain from using any other myopia control treatments such as atropine eye drops;
- Wear impact-resistant spectacle frames containing single-vision lenses (i.e., sports goggles) for activities in which the study spectacles or standard dress frames would be unsafe, provided that the assigned study spectacles are still worn for at least 10 hours per day;
- Report any study spectacle breakage or problem to their parent or guardian immediately;
- Follow all instructions provided by their investigator including study spectacle cleaning procedures.

During this study, participant's parent(s) or legal guardian(s) are asked to:

- Respond to at-home check-ins via a telephone or text messages around Day 7, Month 2, and Month 4
- Alert the investigator about any study-related problems reported by their child, including study spectacle breakage;

- Follow-up with all study visits as instructed;
- Follow any other instructions provided by the investigator.

5.4 SCREEN FAILURES

Screen failures are defined as participants who consent to participate in the clinical trial but are not subsequently randomly assigned to the study intervention or entered in the study. A minimal set of screen failure information is required to ensure transparent reporting of screen failure participants and to respond to queries from regulatory authorities. Minimal information includes demography, screen failure details, eligibility criteria, and any serious adverse event (SAE).

5.5 STRATEGIES FOR RECRUITMENT AND RETENTION

It is anticipated that approximately 55-65 subjects will have to be screened to enroll approximately 50-60 eligible subjects for this trial. There will be approximately 5 sites utilized for this trial and each site will be expected to enroll approximately 10-12 subjects, which is approximately one subject per site per week on average to meet the expected enrollment period of less than 4 months.

In general, it is expected that sites will be able to recruit an approximately even number of subjects per site. However, competitive enrollment will be utilized provided that no single site enrolls more than 15 subjects (approximately 25-30% of the total number of study subjects).

Sites will be selected based on their ability to adequately conduct the trial. Additionally, sites will be selected to ensure that a diverse population of subjects are enrolled, including representative proportions of relevant racial and ethnic subgroups consistent with the intended use population of the device.

Recruitment strategies will include contacting established site patients who may be eligible, and may also include local advertising, social media, developing a study specific website, and potentially include help from patient advocacy groups. All advertising will be IRB/EC approved prior to usage.

Given the intended use, all subjects in the study will be children between 6 to 14 years of age at the time of enrollment. In addition to the Statement of Informed Consent Form that the subject's parent(s) or legal guardian(s) must read, understand and sign, an Informed Assent document will be prepared for appropriate subjects (likely 7 to 14 years of age) to help safeguard this pediatric population.

6 STUDY INTERVENTION

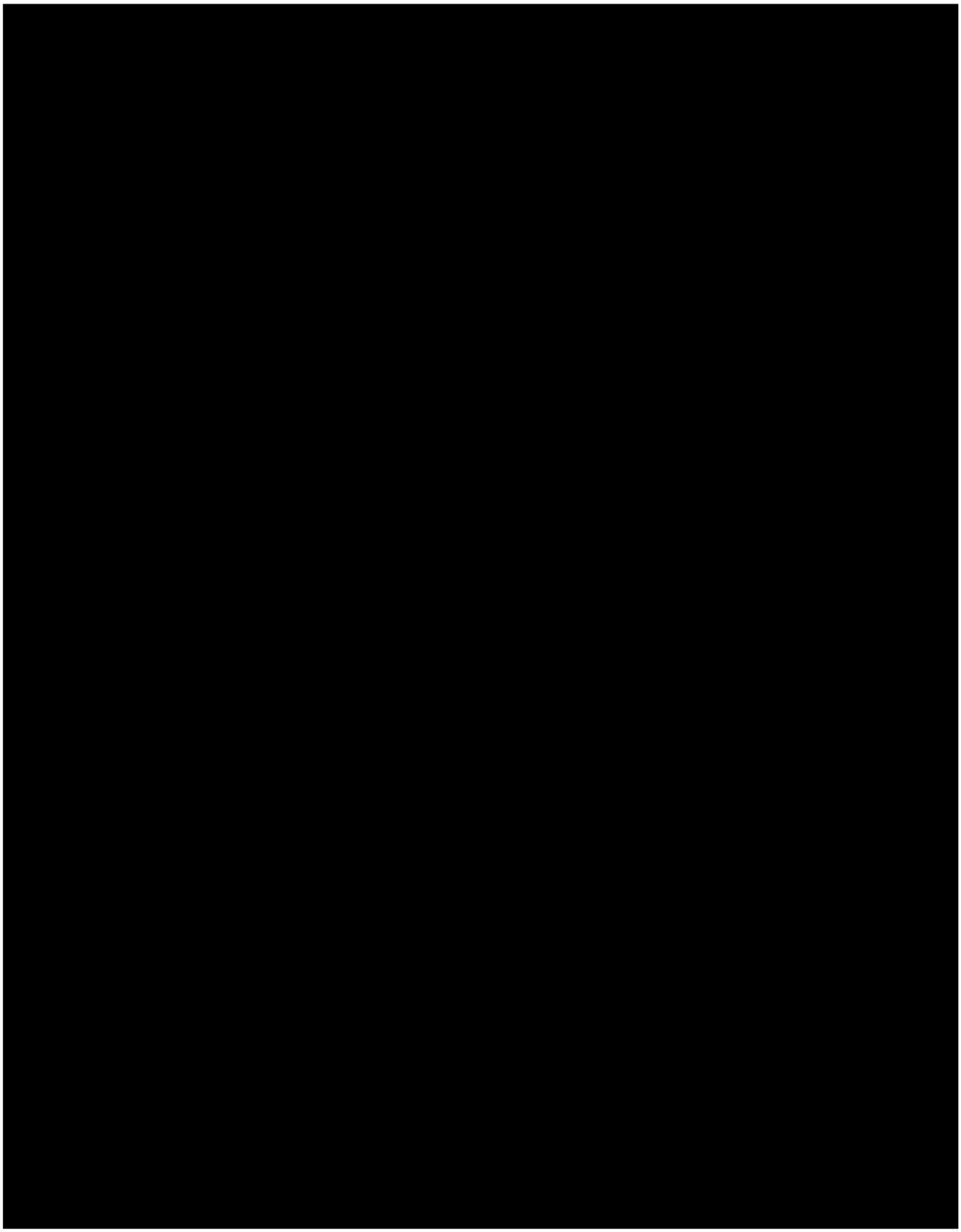
6.1 STUDY INTERVENTIONS ADMINISTRATION

6.1.1 STUDY INTERVENTION DESCRIPTION

The study spectacles will comprise the following:

- Standard, commercially available, pediatric or adult ophthalmic spectacle frames. While a selection of frames will be provided to the sites to facilitate speed of manufacturing, exceptions can be made in the case that none of the available frame options work for a particular subject
- Single vision, [redacted] commercial finished, spectacle lenses used as base lens to be edged and mounted to spectacle frames.

[redacted]



6.3 MEASURES TO MINIMIZE BIAS: RANDOMIZATION AND MASKING

The investigators will be unmasked during the study. However, to minimize potential bias, subjects will be randomized to treatment group. The study randomization codes will be maintained by unmasked Biostats/Data Management study personnel. Given the contralateral nature and short duration of this study, CRO personnel and Sponsor staff masking is not necessary for this study.

Subjects will be randomized to one of two treatment orders: test/control or control/test in the left and right eyes. The randomization will be a stratified block randomization scheme with a block size of two and stratified by investigational site.

Subjects and their parents will be masked during the trial.

Objective measurements are being used for all primary [redacted] endpoints. Additionally, a masked observer at the site will take all biometry [redacted] measurements. To facilitate this masking, the subject will be led into the room(s) containing the biometer [redacted] without their study spectacles. After the masked observer takes the necessary measurements, the subject will be led back out of the room by site personnel.

Any unintended unmasking of study participants, their parents, or masked site personnel should be documented by the investigator.

6.4 STUDY INTERVENTION COMPLIANCE

Subject compliance with wearing the study spectacles will be assessed via a questionnaire at Visit 2. Furthermore, there will be at-home check-up telephone calls/text messages that occur at approximately Day 7, Month 2, and Month 4. Should the investigator become aware of non-compliance, all reasonable efforts should be made to alleviate the circumstance and educate the subject and parent(s) about the importance for wearing the study spectacles as directed.

6.5 CONCOMITANT THERAPY

At the baseline visit (Visit 1), the investigator should collect the subject's habitual spectacles. This is being done to avoid subject non-compliance and the parents and subjects will be notified of this requirement during the Informed Consent/Assent process. At the conclusion of the trial, these spectacles will be returned to the subjects.

[redacted]

7 STUDY INTERVENTION DISCONTINUATION AND PARTICIPANT DISCONTINUATION / WITHDRAWAL

7.1 DISCONTINUATION OF STUDY INTERVENTION

Study participants who discontinue wearing the study spectacles or who fail to wear the study spectacles for 10 hours a day should not necessarily be discontinued from the study. The investigator should discuss any situation of this kind with the study's Medical Monitor and determine if the subject should remain enrolled in the trial. Should the subject remain enrolled despite study spectacle discontinuation, the remaining study procedures should be completed as indicated by the study protocol unless the subject or parent decides to completely withdraw from the study. If a clinically significant finding is identified (including, but not limited to changes from baseline) after enrollment, the investigator or qualified designee will determine if any change in participant management is needed. Any new clinically relevant finding will be reported as an adverse event (AE).

The data to be collected at the time of study intervention discontinuation will include all study procedures, data collection, and follow-ups as described in this protocol.

7.2 PARTICIPANT DISCONTINUATION/WITHDRAWAL FROM THE STUDY

Participants are encouraged to complete the study but are of course free to withdraw from participation in the study at any time upon request.

An investigator may discontinue or withdraw a participant from the study for the following reasons:

- Significant study intervention non-compliance;
- Insufficient visual acuity with the study spectacles (see below);
- If any clinical adverse event (AE) or other medical condition or situation occurs such that continued participation in the study would not be in the best interest of the participant;
- If the participant doesn't meet an inclusion criterion and/or meets an exclusion criterion (either newly developed or not previously recognized) that precludes further study participation.

The reason for participant discontinuation or withdrawal from the study will be recorded on a Case Report Form (CRF). Subjects who sign the informed consent form and are randomized but do not receive the study intervention may be replaced. Subjects who sign the informed consent form, are randomized, and receive the study intervention, and then subsequently withdraw, or are withdrawn or discontinued from the study, will be replaced if study enrollment has not yet ceased.

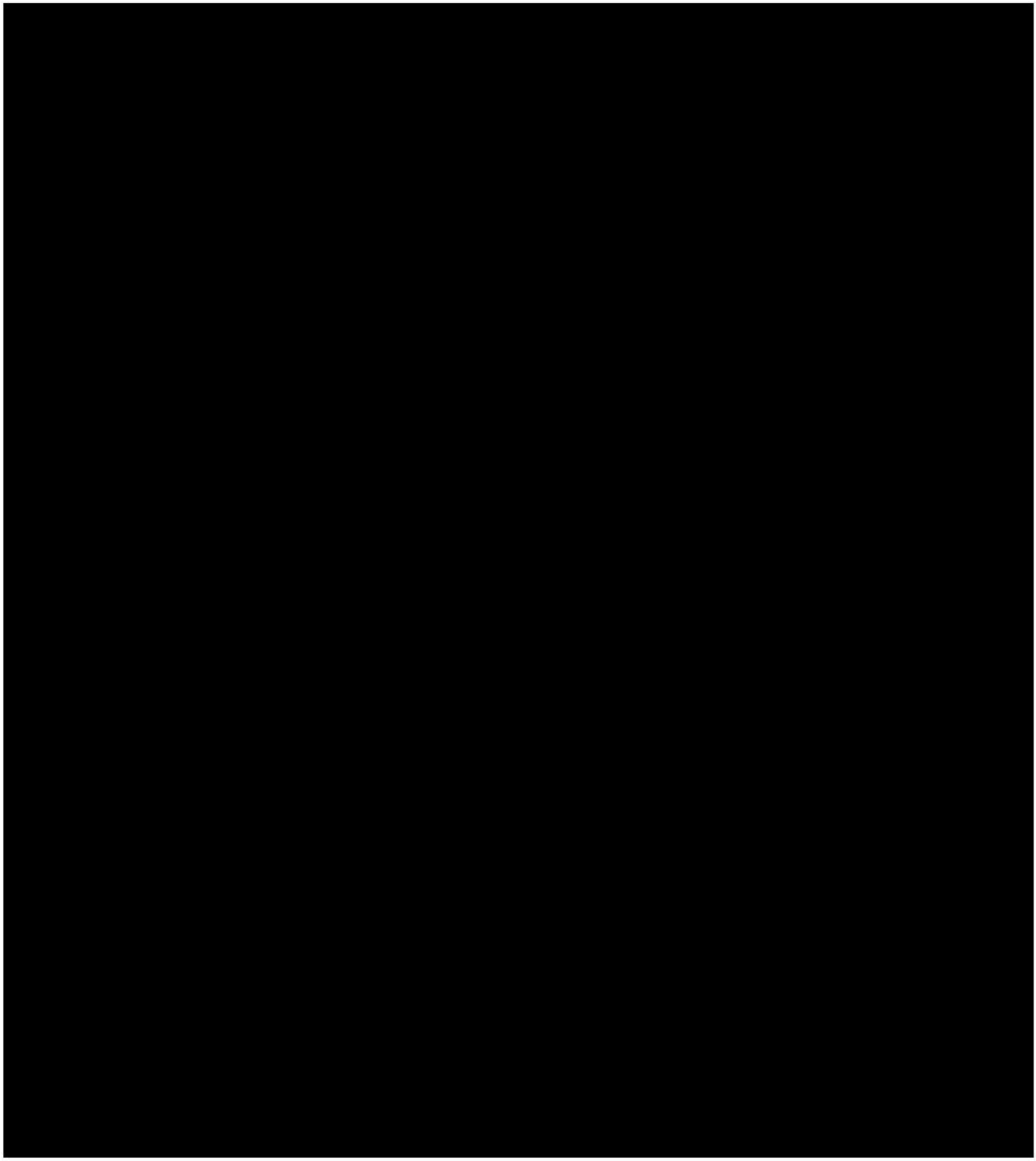
7.3 LOST TO FOLLOW-UP

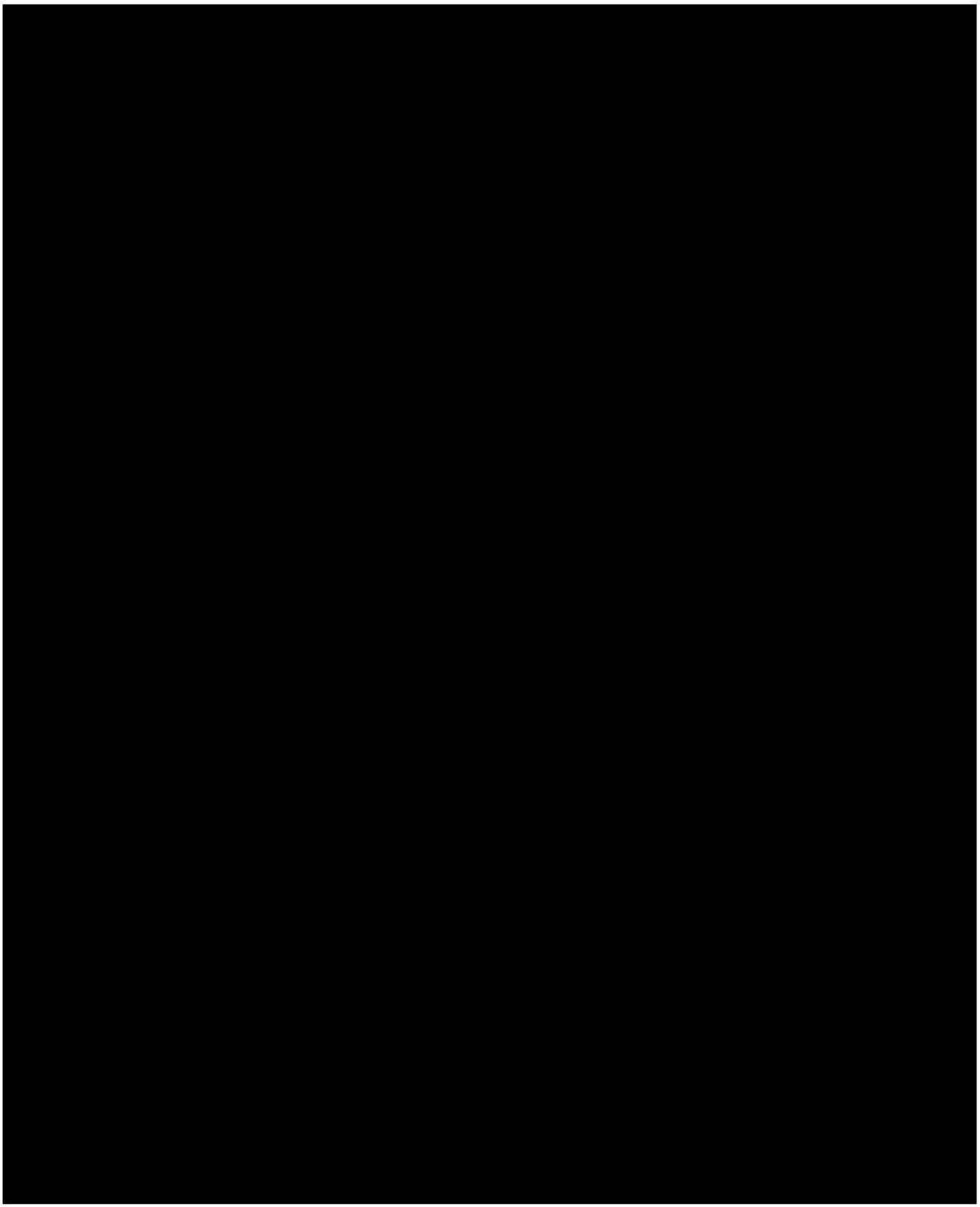
A participant will be considered lost to follow-up if he or she fails to return to a scheduled visit and is unable to be contacted by the study site staff.

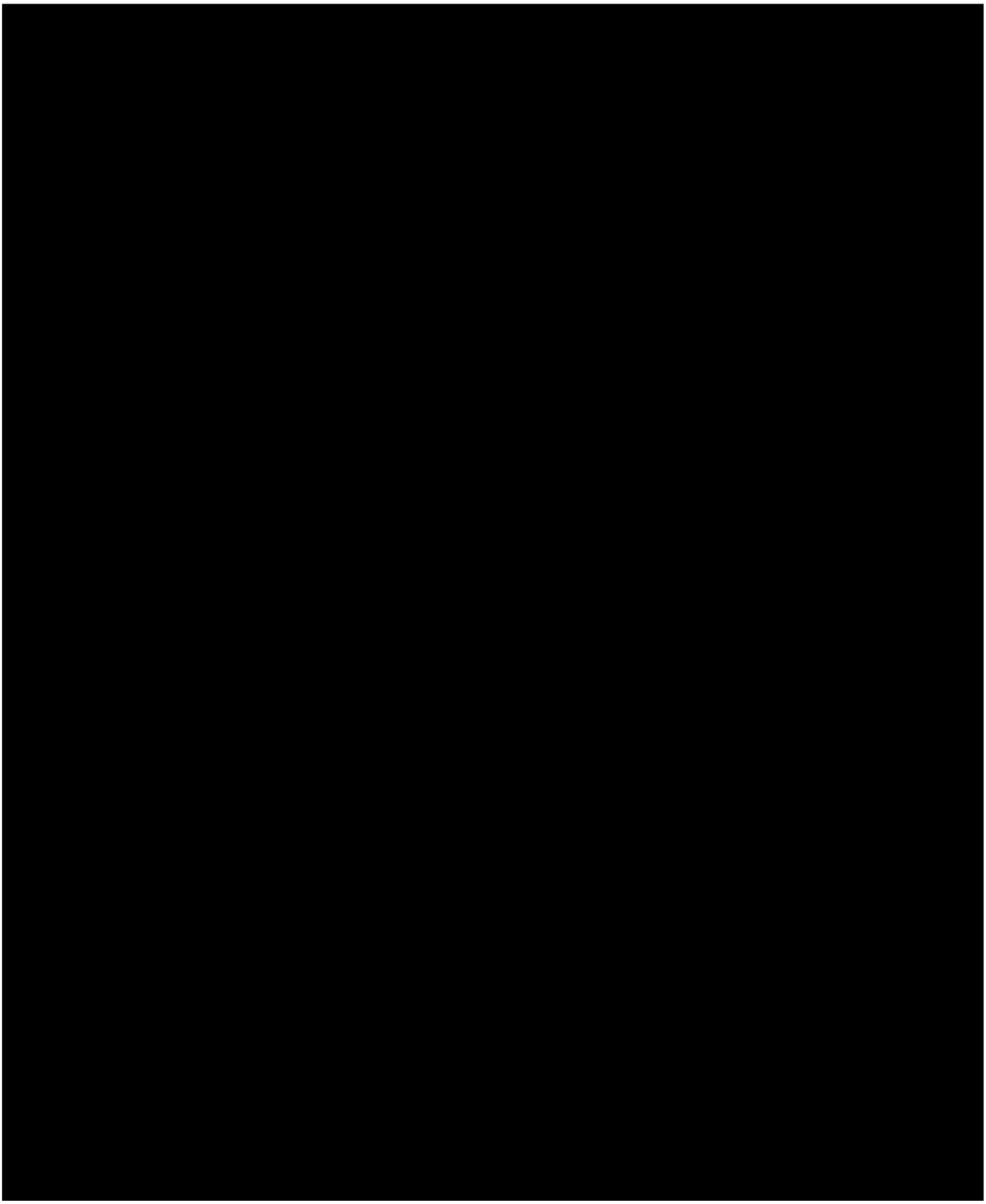
The following actions must be taken if a participant fails to return to the clinic for a required study visit:

- The site will attempt to contact the participant and reschedule the missed visit and counsel the participant on the importance of maintaining the assigned visit schedule and ascertain if the participant wishes to and/or should continue in the study.
- Before a participant is deemed lost to follow-up, the investigator or designee will make every effort to regain contact with the participant (where possible, 3 telephone calls, 3 emails or text messages, and, if necessary, a certified letter to the participant's last known mailing address or local equivalent methods). These contact attempts should be documented in the participant's medical record or study file.
- Should the participant continue to be unreachable, he or she will be considered to have withdrawn from the study with a primary reason of lost to follow-up.

8 STUDY ASSESSMENTS AND PROCEDURES







8.3 ADVERSE EVENTS AND SERIOUS ADVERSE EVENTS

8.3.1 DEFINITION OF ADVERSE EVENTS (AE)

Adverse event means any untoward medical occurrence associated with the use of an intervention in humans, whether or not considered intervention-related (21 CFR 312.32 (a)).

8.3.2 DEFINITION OF SERIOUS ADVERSE EVENTS (SAE)

An adverse event (AE) is considered "serious" if, in the view of either the investigator or sponsor, it results in any of the following outcomes: death, a life-threatening adverse event, inpatient hospitalization or prolongation of existing hospitalization, a persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions, are vision-threatening, or result in permanent impairment of a body function or permanent damage to a body structure.

An example of an ocular SAE would be a permanent decrease of ≥ 2 lines of best corrected visual acuity (BCVA).

8.3.3 CLASSIFICATION OF AN ADVERSE EVENT

8.3.3.1 SEVERITY OF EVENT

For adverse events (AEs) not included in the protocol defined grading system, the following guidelines will be used to describe severity.

- **Non-Significant** – These events are non- vision-threatening and usually do not result in impairment of a body function or damage to a body structure. Examples include: a contact dermatitis from a spectacle frame, a temporary headache, or eye strain.
- **Significant** – These events usually are symptomatic but are non-vision- threatening and result in temporary impairment of a body function or temporary damage to a body structure. An example includes a temporary loss of ≥ 2 lines of BCVA (for ≥ 2 weeks).
- **Serious** – See Section 8.3.2.

[redacted]

8.3.3.2 RELATIONSHIP TO STUDY INTERVENTION

All adverse events (AEs) must have their relationship to study intervention assessed by the clinician who examines and evaluates the participant based on temporal relationship and their clinical judgment. The

degree of certainty about causality will be graded using the categories below. In a clinical trial, the study product must always be suspect.

- **Related** – The AE is known to occur with the study intervention, there is a reasonable possibility that the study intervention caused the AE, or there is a temporal relationship between the study intervention and event. Reasonable possibility means that there is evidence to suggest a causal relationship between the study intervention and the AE.
- **Not Related** – There is not a reasonable possibility that the administration of the study intervention caused the event, there is no temporal relationship between the study intervention and event onset, or an alternate etiology has been established.

8.3.3.3 EXPECTEDNESS

The principal investigator at the site will be responsible for determining whether an adverse event (AE) is expected or unexpected. An AE will be considered unexpected if the nature, severity, or frequency of the event is not consistent with the study population or the risk information previously described for the study intervention.

See the Known Potential Risks (Section 2.5.1) and the IB for the risk information.

8.3.4 TIME PERIOD AND FREQUENCY FOR EVENT ASSESSMENT AND FOLLOW-UP

The occurrence of an adverse event (AE) or serious adverse event (SAE) may come to the attention of study personnel during study visits and interviews of a study participant presenting for medical care, or upon review by a study monitor.

All AEs including local and systemic reactions not meeting the criteria for SAEs will be captured on the appropriate case report form (CRF). Information to be collected includes event description, time of onset, clinician's assessment of severity, relationship to study product (assessed only by those with the training and authority to make a diagnosis), and time of resolution/stabilization of the event. All AEs occurring while on study must be documented appropriately regardless of relationship. All AEs will be followed to adequate resolution.

Any medical condition that is present at the time that the participant is screened will be considered as baseline and not reported as an AE. However, if the study participant's condition deteriorates at any time during the study, it will be recorded as an AE.

Changes in the severity of an AE will be documented to allow an assessment of the duration of the event at each level of severity to be performed. AEs characterized as intermittent require documentation of onset and duration of each episode.

The investigator will record all reportable events with start dates occurring any time after informed consent is obtained until 7 days (for non-serious AEs) or 30 days (for SAEs) after the last day of study

participation. At each study visit, the investigator will inquire about the occurrence of AE/SAEs since the last visit. Events will be followed for outcome information until resolution or stabilization. If resolution has not occurred within 6 weeks after the study end date, the subject will be exited from the study, but must continue to be followed until the condition has resolved, returned to pre-study condition, or warrants no further follow-up.

8.3.5 ADVERSE EVENT (AE) REPORTING

Any AE observed by the investigator or reported by the subjects shall be documented on an Adverse Event Form. When an AE is initially discovered, the first page of the Adverse Event Form should be completed as well as the 'Treatment / Action' section. Care should be taken to describe the condition accurately.

8.3.6 SERIOUS ADVERSE EVENT REPORTING

The principal investigator at the site shall report all Serious Adverse Events to the Medical Monitor within 24 hours by phone or e-mail (see Section 10.1.5 for Medical Monitor contact information) and submit the Adverse Event Form to the reviewing Institutional Review Board (IRB) as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect.

The study sponsor is responsible for conducting an evaluation of an SAE and shall report the results of such evaluation to the Food and Drug Administration (FDA) and to all reviewing IRBs and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter, the sponsor shall submit such additional reports concerning the effect as FDA requests.

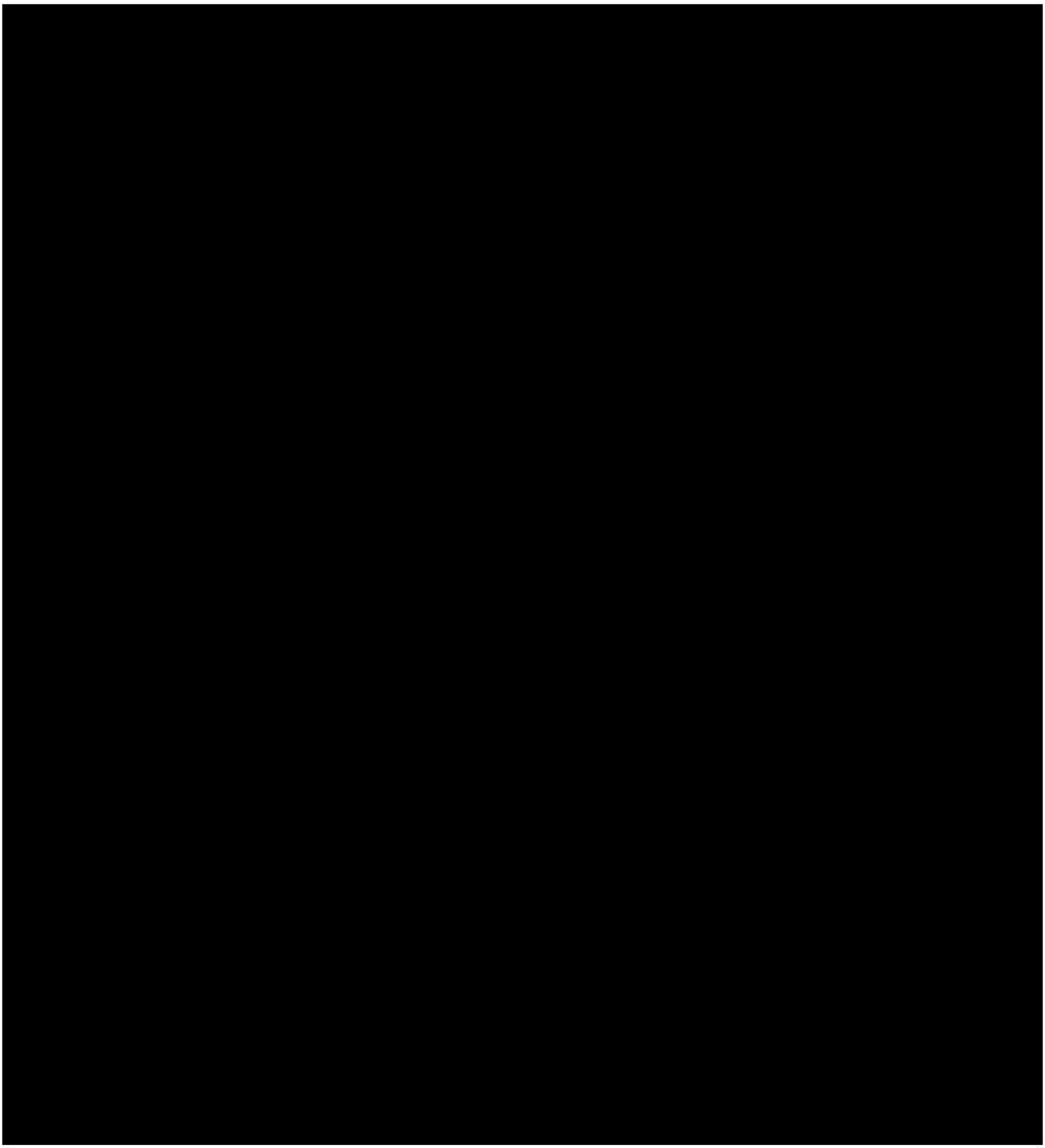
8.3.7 DEVICE DEFICIENCIES

For the purpose of this protocol, device deficiencies are defined as any inadequacy of the study spectacles (i.e., spectacle lenses and spectacle frames) with respect to their identity, quality, durability, reliability, safety, or performance. For clarity, accidental damage should not be considered a device deficiency unless due to a quality issue.

All device deficiencies should be documented on the CRFs. The investigator should assess and document on the CRF whether the device deficiency would have led to a serious adverse event if:

- Suitable action had not been taken;
- Intervention had not been made; or
- Circumstances had been less fortunate.

[redacted]



9 STATISTICAL CONSIDERATIONS

9.1 STATISTICAL HYPOTHESES

The null and alternative primary hypotheses for this study are:

H_0: $\mu_T - \mu_C \geq 0.03$ versus H_A: $\mu_T - \mu_C < 0.03$

Here μ indicates the mean change in axial length between baseline and 6 months.

[redacted]

9.2 SAMPLE SIZE DETERMINATION

The study is sized to ensure an adequate power at an overall alpha level of 0.05 for treatment comparisons in axial length change from baseline at 6 months. [redacted]

Assuming a drop-out rate of 10-20%, a study of 50-60 subjects achieves 80% power to detect non-inferiority [redacted]

[redacted]

9.3 POPULATIONS FOR ANALYSES

The study data will be analyzed in one of the following analysis populations:

The **Per-Protocol (PP)** population will include all randomized subjects who follow the protocol without any major deviation(s) that could impact the integrity of the data. Reasons for exclusion from the PP population may include:

- use of the incorrect study spectacles
- poor compliance with the wearing regimen.

The **Safety** population will include all randomized subjects who use any of the study devices. Subjects will be grouped for analysis based on the actual device used.

9.4 STATISTICAL ANALYSES

9.4.1 GENERAL APPROACH

The analyses will be performed once all data have been entered into the EDC, cleaned and the database has been locked.

Descriptive summaries will include mean, standard deviation, median, and range for continuous variables and counts and percentages for categorical variables. Two-sided 95% confidence intervals (CIs) will be provided for the means and percentages. For key outcome measures, the difference between each of the test arms versus the control and the 95% CI of the difference will be computed.

All statistical analysis will be performed using SAS® (Version 9.4 or higher, SAS Institute Inc., Cary, NC, USA). Some graphical tools (such as EXCEL, PowerPoint) may be used to generate figures.

9.4.2 ANALYSIS OF THE STUDY CONDUCT

The number of subjects who are enrolled, discontinue (early discontinuation of treatment or early termination from the study), and complete the study (through 6 months after randomization) will be tabulated.

Reasons for early discontinuation of the treatment or early termination of from the study will be listed and summarized by treatment arm. Any eligibility criteria exceptions and other protocol deviations will also be summarized by treatment arm.

9.4.3 ANALYSIS OF TREATMENT COMPARABILITY

Demographic and baseline characteristics such as age, gender and race will be summarized for all randomized subjects. Other baseline characteristics such as baseline axial lengths and baseline SER will be summarized for all randomized subjects by treatment.

9.4.4 ANALYSIS OF THE PRIMARY EFFICACY ENDPOINTS

The main analysis of the primary efficacy outcome measures (i.e., change from baseline in axial length) will be on the PP population.

9.4.6 SAFETY ANALYSES

Adverse events will be tabulated by incidence overall, by device related, maximum severity, and those resulting in study discontinuation. Serious adverse events will be listed. Data summarized as well as additional collected data will be provided in supporting line listings. Ocular assessments such as BCVA, biomicroscopic slit lamp, ophthalmoscopy results and other findings will be summarized descriptively.

9.4.7 MISSING DATA

All possible efforts will be made to minimize missing data rate as missing data may potentially bias the outcome of the statistical analyses and the subsequent estimation of the magnitude of the treatment

effect. Due to having only one follow-up visit, it would not be appropriate to impute missing data. Therefore, the efficacy analysis will be completed on the PP population.

9.4.8 PLANNED INTERIM ANALYSES

There will be no interim analyses during this study.

[redacted]

10 SUPPORTING DOCUMENTATION AND OPERATIONAL CONSIDERATIONS

10.1 REGULATORY, ETHICAL, AND STUDY OVERSIGHT CONSIDERATIONS

10.1.1 INFORMED CONSENT PROCESS

10.1.1.1 CONSENT/ASSENT AND OTHER INFORMATIONAL DOCUMENTS PROVIDED TO PARTICIPANTS

Consent forms describing in detail the study, study interventions, study procedures, and risks are given to the participant and written documentation of informed consent is required prior to starting the study or dispensing study interventions.

For subjects who are 7 to 14 years of age, Assent forms will also be used to describe the study, study interventions, study procedures, and risks and written documentation of assent is required prior to starting study procedures or dispensing study interventions.

10.1.1.2 CONSENT PROCEDURES AND DOCUMENTATION

Informed consent (and assent) is a process that is initiated prior to the individual's agreeing to participate in the study and continues throughout the individual's study participation. Consent and Assent forms will be Institutional Review Board (IRB) approved and the participant and parent/guardian will be asked to read and review the document. The investigator will explain the research study to the participant and parent/guardian and answer any questions that may arise. A verbal explanation will be provided in terms suited to the participant's and parent/guardian's comprehension of the purposes, procedures, and potential risks of the study and of their rights as research participants. Participants and parent/guardian will have the opportunity to carefully review the written consent form and ask questions prior to signing. The participants and parent/guardian should have the opportunity to discuss the study with their family or surrogates or think about it prior to agreeing to participate. The

participant's parent will sign the informed consent document prior to any procedures being done specifically for the study. Participants and parent/guardian must be informed that participation is voluntary and that they may withdraw from the study at any time, without prejudice. A copy of the informed consent document (and assent document if applicable) will be given to the participants and parent/guardian for their records. The informed consent process will be conducted and documented in the source document (including the date) and the form shall be signed prior to the participant undergoing any study-specific procedure. The rights and welfare of the participants will be protected by emphasizing to them that the quality of their medical care will not be adversely affected if they decline to participate in this study.

10.1.2 STUDY DISCONTINUATION AND CLOSURE

This study may be temporarily suspended or prematurely terminated if there is sufficiently reasonable cause. Written notification, documenting the reason for study suspension or termination, will be provided by the study sponsor to the Principal Investigators. If the study is prematurely terminated or suspended, the Principal Investigator will promptly inform study participants, the Institutional Review Board (IRB) and will provide the reason(s) for the termination or suspension. Study participants will be contacted, as applicable, and be informed of changes to study visit schedule.

Circumstances that may warrant termination or suspension include, but are not limited to:

- Determination of unexpected, significant, or unacceptable risk to participants;
- Insufficient compliance to protocol requirements;
- Data that are not sufficiently complete and/or evaluable.

The study may resume once concerns about safety, protocol compliance, and data quality are addressed, and satisfy the sponsor, IRB, and/or Food and Drug Administration (FDA).

10.1.3 CONFIDENTIALITY AND PRIVACY

Participant confidentiality and privacy is strictly held in trust by the participating investigators, their staff, and the sponsor and their interventions. This confidentiality is extended to cover testing of biological samples and genetic tests in addition to the clinical information relating to participants. Therefore, the study protocol, documentation, data, and all other information generated will be held in strict confidence. No information concerning the study or the data will be released to any unauthorized third party without prior written approval of the sponsor.

All research activities will be conducted in as private a setting as possible.

The study monitor, other authorized representatives of the sponsor, representatives of the Institutional Review Board (IRB), or regulatory agencies may inspect all documents and records required to be maintained by the investigator, including but not limited to, the medical records for the participants in this study. The clinical study site will permit access to such records.

The study participant's contact information will be securely stored at each clinical site for internal use during the study. At the end of the study, all records will continue to be kept in a secure location for as long a period as dictated by the reviewing IRB, Institutional policies, or sponsor requirements.

[redacted]

10.1.5 CLINICAL MONITORING

Clinical site monitoring is conducted to ensure that the rights and well-being of trial participants are protected, that the reported trial data are accurate, complete, and verifiable, and that the conduct of the trial is in compliance with the currently approved protocol/amendment(s), ISO 14155:2011 - Clinical investigation of medical devices for human subjects -- Good clinical practice, and with applicable regulatory requirement(s).

Monitoring for this study will be performed by Visioncare Research, Limited following their written Standard Operating Procedures (SOPs). Both on-site and centralized monitoring methods may be used throughout the study as appropriate. A separate monitoring plan will be created for the study and will include more detailed about the following monitoring visits. Furthermore, audits may be conducted by the sponsor to ensure monitoring practices are performed consistently across all participating sites and that monitors are following the monitoring plan. The investigational site will provide direct access to all source data, documents, and reports for the purpose of monitoring and auditing by the CRO, sponsor, and inspection by regulatory authorities.

10.1.5.1 SITE QUALIFICATION VISIT

Qualified personnel or consultants of the sponsor (including the study monitor) will meet with investigators prior to the initiation of the study in order to review the adequacy of the potential subject population, facilities, and equipment with respect to the needs of the study and to familiarize the investigator with the study protocol.

10.1.5.2 SITE INITIATION VISIT

Qualified personnel or consultants of the sponsor (including the study monitor) will review the study procedures with the site before the initiation of subject enrolment to ensure all investigators and study staff are fully trained in ISO 14155:2011 GCP guidelines and the protocol.

10.1.5.3 INTERIM MONITORING VISITS AND CONSULTATION

Interim monitoring visits and telephone, fax, mail and/or email consultation will be performed during the course of the study to ensure the proper progress and documentation of the study findings. The schedule of monitoring visits will be based on the rate of enrolment and number of subjects enrolled at each site and shall ensure that the site is complying with ISO 14155:2011 GCP, that subjects are being properly selected, and that study data are being correctly recorded.

10.1.5.4 CLOSE-OUT MONITORING VISIT

Qualified personnel or consultants of the sponsor (including the study monitor) will visit the clinical site for formal close-out when all subjects have completed the final visit of the study to collect any outstanding forms and to ensure accountability of the study spectacles and all study supplies. An Investigator Study Completion Form will be completed by the investigator.

10.1.6 DATE COLLECTION, HANDLING, AND QUALITY ASSURANCE

Data collection is the responsibility of the clinical trial staff at the site under the supervision of the site investigator. The investigator is responsible for ensuring the accuracy, completeness, legibility, and timeliness of the data reported. All source documents should be completed in a neat, legible manner to ensure accurate interpretation of data. All of the data collection protocols will be standardized through study documentation, uniform study forms and uniform criteria for subject recruitment, including independent confirmation of eligibility by the CRO or Medical Monitor. Study personnel will be trained before collecting study data.

Clinical data, including adverse events (AEs), will be entered into Medrio, a 21 CFR Part 11-compliant data capture system provided by the CRO. The data system includes password protection and internal quality checks, such as automatic range checks, to identify data that appear inconsistent, incomplete, or inaccurate. Clinical data may be entered directly into electronic case report forms (eCRF), which may be then printed, verified and signed by the investigator and used as the source document.

The CRFs will be completed at the time of the visit. All clinical data generated in the study will be submitted to the CRO for quality assurance review and analysis. All forms will be reviewed for completeness and evident recording errors will be rectified by contacting the appropriate clinical site. Computerized editing routines will be used to identify missing, invalid, inconsistent, or questionable data entries for verification prior to data analysis. These data issues will be resolved by contacting the

relevant clinical site. All data files will be backed up routinely, with weekly backups stored at an alternative location.

10.1.6.1 STUDY RECORDS RETENTION

Study records must be retained until the later of: (i) a period of 2 years after the device clearance, or (ii) the period of time required under other Applicable Law. Thereafter, the Institution and Investigator will not destroy any such records unless they have obtained sponsor's prior written permission to do so and, at sponsor's request and expense, will transfer such records to sponsor rather than destroy them.

10.1.7 PROTOCOL DEVIATIONS

A protocol deviation is any noncompliance with the clinical trial protocol, ISO 14155:2011 - Clinical investigation of medical devices for human subjects -- Good clinical practice (GCP), or Manual of Procedures (MOP) requirements. The noncompliance may be either on the part of the subject, the investigator, or the study site staff. As a result of deviations, where appropriate and possible, corrective actions should be developed by the site and implemented promptly.

The site investigator should not make any changes to the study unless necessary to eliminate an apparent immediate hazard to subjects in the study. It is the responsibility of the site investigator to use continuous vigilance to identify and report deviations within 24 hours of identification of the protocol deviation to the CRO and sponsor and within 10 working days to the IRB or otherwise per their policies. The site investigator is responsible for knowing and adhering to the reviewing IRB requirements.

10.2 PUBLICATION POLICY

The sponsor and its designees will have the right to publish or otherwise publicly disclose the information contained in or related to the study in any form without the written consent of the investigators.

At any time following the first publication of the study results from all clinical study sites participating in the study, the investigators may have the right to independently publish or present their portion of the study results after proper review by the sponsor. Investigators should refer to their Clinical Trial Agreement for more detailed information.

10.3 ABBREVIATIONS (TABLE 7)

AE	Adverse Event
AL	Axial Length
BCVA	Best-corrected Visual Acuity
CFR	Code of Federal Regulations
CI	Confidence Interval
cm	Centimeter
CRO	Clinical Research Organization
CRF	Case Report Form
D	Diopter(s)
DC	Diopter(s) Cylinder
DOT	Diffusion Optics Technology
EDC	Electronic Data Capture
eCRF	Electronic Case Report Forms
FDA	Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
IB	Investigator's Brochure
IDE	Investigational Device Exemption
IRB	Institutional Review Board
ISO	International Organization for Standardization
logMAR	Log of Minimum Angle of Resolution
mm	Millimeter
MOP	Manual of Procedures
NIH	National Institutes of Health
OC	Optical Center
OD	Oculus Dexter (right eye)
OS	Oculus Sinister (left eye)
PD	Pupillary Distance
PI	Principal Investigator
QA	Quality Assurance
SAE	Serious Adverse Event
SER	Spherical Equivalent Refraction
SOA	Schedule of Activities
SOP	Standard Operating Procedure
µm	Micron
UP	Unanticipated Problem
US	United States
VA	Visual Acuity

10.4 PROTOCOL AMENDMENT HISTORY

TABLE 8 below is intended to capture changes of IRB-approved versions of the protocol, including a description of the change and rationale. A Summary of Changes table for the current amendment is located in the Protocol Title Page.

Version	Date	Description of Change	Brief Rationale
1.0	04 OCT 2019	Original Version	N/A
1.1	05 AUG 2020	• Date and version number updated throughout document • Reference (#26) in Section 8.2 was added for parent questionnaire [redacted] • Title of Section 9.4.3 corrected to remove the word "arm"	• Version control • Missing bookmark • Typographical error correction

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