An evaluation of the LFR-260 against a traditional phoropter in visual acuity testing

Version:	**1.0**
Version Date:	**18-Feb-2022**
Investigational Product:	**LFR-260**
Protocol Number:	**LFR-260-2021**

Sponsor: Evolution Optiks Limited
[redacted]

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Confidentiality Statement

The information provided in this document is strictly confidential and is available for review to investigators, potential investigators, FDA and appropriate Ethics Committees or Investigational Review Boards. No disclosure should take place without written authorization from Sponsor, except to the extent necessary to obtain informed consent from potential subjects.

This document has been developed in accordance with the guidelines for conducting industry sponsored the US Food and Drug Administration trials including the Declaration of Helsinki, the Code of Federal Regulations 21 CFR Part 50- Protection of Human Subjects, 21 CFR Part 54- Financial Disclosure, 21 CFR Part 56- Institutional Review Boards, 21 CFR 812 as well as international standards such as ICH E6 (R2) Good Clinical Practice: Consolidated Guidance.

Version History

Version #	*Version Date*	*Significant Changes from Previous Version*
Version 1	18-Feb-2022	• Original Protocol Version

Table 1: Abbreviations

ADE	Adverse device effect
AE	Adverse event
BCVA	Best Corrected Visual Acuity
CFR	Code of federal regulations
CRF	Case report form
ECP	Eye Care Professional
EDC	Electronic data capture
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
IDE	Investigational Device Exemption
IRB	Institutional Review Board
IWRS	Interactive web response system
LAR	Legally Authorized Representative
MRSE	Manifest Refractive Spherical Equivalent
PHI	Protected health information
SAP	Statistical analysis plan
SAE	Serious adverse event
SCA	Sphere, Cylinder, Axis
SOC	Standard of care
UADE	Unanticipated adverse device effect
VA	Visual acuity

Table 2 Definitions of conditions and materials

Astigmatism	a refractive problem with the eye related to the shape of the lens, which causes blurry vision
Hyperopia	farsightedness
Myopia	nearsightedness
Presbyopia	a condition related to aging that causes lens of the eye to have trouble focusing
Phoropter	Device to perform traditional refraction eye examination

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PROTOCOL SIGNATURE PAGE

The signature below constitutes the approval of this protocol entitled "***An evaluation of the LFR-260 against a traditional phoropter in visual acuity testing"***, and provides the necessary assurances that this trial will be conducted in compliance of all stipulations of the protocol, including all statements regarding confidentiality, and according to local legal and regulatory requirements, the Food and Drug Administration, International Conference on Harmonization Good Clinical Practice E6 R2 (ICH-GCP), and applicable US regulatory requirements.

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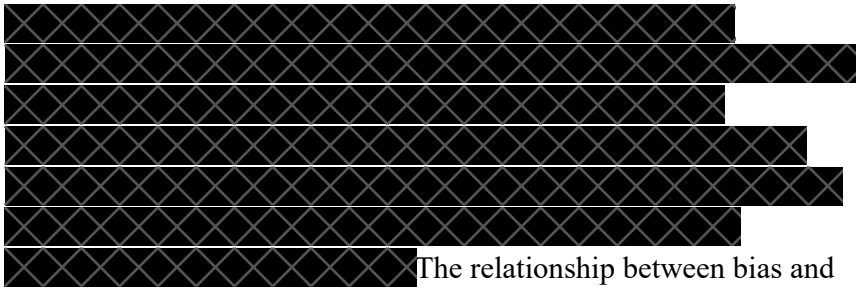
Investigator's Printed Name

_____ _____

Investigator's Signature ***Date***

STUDY SYNOPSIS

Title	An evaluation of the LFR-260 against a traditional phoropter in visual acuity testing
Protocol Number	LFR-260-101
Study Design	2x2 Crossover
Number of Study Sites	2 sites, 3 locations
Number of Subjects	Up to 108 subjects (216 eyes)
Study Population	Healthy volunteers
Investigational Device	LFR-260 in a standard visual acuity test
Comparator Device	Any 510(k) exempt phoropter legally marketed in the US (Refractor, Manual, Non-Powered, Including Phoropter)
Study Objective	To evaluate the agreement of LFR-260 (investigational device) to traditional phoropter (comparator device) when applied in visual acuity test in subjects undergoing a full routine eye examination.
Study Endpoints	The primary effectiveness endpoint is to demonstrate that the LFR-260 is within 0.5D (+/-) in measuring sphere and cylinder results and within 10 degrees for axis results among subjects with low astigmatism and within 5 degrees among subjects with moderate to high astigmatism from the traditional phoropter in a very large proportion of subjects.

Statistical Considerations	The objective of the statistical analysis is to evaluate agreement in sphere, cylinder, and axis measurements between LFR-260 and traditional refraction performed by a traditional phoropter. Specifically, the subjective manifest refraction measured by means of a traditional phoropter will serve as the reference control and is considered to be the gold standard for the purpose of this evaluation. The accuracy of the acuity measurement obtained by the LFR-260 will be evaluated for both cases (uncorrected, corrected) measured with the conventional phoropter. It will be assessed comparing the LFR-260 acuity measurement to the conventional acuity measurement using a Snellen chart (scored to the letter), with similar analyses used for the refractive components. For each measurement, the paired difference will be computed. Good clinical agreement is defined a priori as ≤±0.5 D for sphere and cylinder measurements and ≤±10 degrees for axis measurements for subjects with low astigmatism and ≤±5 degrees for axis measurements for subjects with low astigmatism. The unit of analysis will be the individual eye. Overall device performance will be summarized as the number of and percentage of eyes meeting three of the good clinical agreement criteria listed above.  The relationship between bias and the mean of measurements will characterized. A supporting analysis will evaluate the vector difference between investigational device measurements and the gold standard in terms of sphere and cylinder measurements. The vector differences is square root of (X1-Y1) + (X2-Y2) where the X1 and X2 are measurements of sphere and cylinder using the investigational devices and Y1 and Y2 are the same measurements using the gold standard.

	Homogeneity of treatment effects across sites will be evaluated comparing site level differences between the investigational device and the gold standard separately for sphere, cylinder, and axis and also for the vector analysis of sphere and cylinder. Similarly, differences between measurements from the investigational device and the gold standard device will be summarized by gender, age category, race, and ethnicity to investigate consistency or heterogeneity of the treatment effect across those subgroups, separately for sphere, cylinder, and axis and also for the vector analysis of sphere and cylinder. The primary analysis will be based on the intent-to-treat (ITT) analysis set and will use multiple imputation to address missing values. The multiple imputation (MI) model will include sphere, cylinder, and axis measurements for both the investigational device and the gold standard device and baseline characteristics including age and gender. Analyses will be repeated in a per protocol analysis set that includes eyes with complete data. [redacted] Reliability (repeatability and reproducibility) of LFR-260 will be conducted in a subset of subjects for which measurements will be obtained twice in an office context. This analysis will be repeated in a remote context. Reliability will be evaluated using intraclass correlations for each of the continuous measurements, sphere, cylinder, and axis. .

Study Criteria	**Inclusion Criteria** Participants must fulfill all of the following criteria in order to be eligible for the study: 1. The participant or legal guardian is willing and able to understand, sign and date the Ethics committee approved study specific Informed Consent Form. 2. The participant is a male or female between the ages of 12 and 65 (inclusive). 3. The participant has a history of the following: o No more than mild to moderate far-sightedness or near-sightedness (i.e. Spherical equivalent refraction (SER) between +10 to -15). o an astigmatism of 2.5D or less. o an anisometropia of 1.5D or less. 4. The participant is free of ocular and systemic abnormalities that might affect visual functions. **Exclusion Criteria** Participants will be excluded from participation in the study if any of the following criteria are met at screening: 1. The participant has diabetes mellitus (Type 1 or 2). 2. The participant has an autoimmune condition. 3. The participant is pregnant (self-reported). 4. The participant has an active corneal or conjunctival infection. 5. The participant has an active corneal, conjunctival, or intraocular inflammation (i.e. - uveitis). 6. The participant has diabetic retinopathy. 7. The participant has glaucoma or ocular hypertension. 8. The participant has macular degeneration. 9. The participant has had a previous ocular surgery. 10. The participant has ocular and systemic diseases or abnormalities that might affect visual functions. 11. The participant has a history of amblyopia, strabismus, or any other binocular vision abnormality. 12. The participant has a history of AMD (age macular degeneration).

	13. The participant is a prisoner, a transient or has been treated for alcohol and/or drug abuse in an inpatient substance abuse program within 6 months prior to proposed study enrolment. 14. The participant will not be able to complete questionnaires. 15. The participant is currently in an investigational study for a similar purpose. 16. The participant, in the judgment of the Investigator, may be inappropriate for the intended study procedures.

STUDY FLOWCHART AND FOLLOW-UP ASSESSMENTS

Study Procedure	Screening and Initial Assessment	Repeatability Testing +1 hour (+/- 30 mins)	Reproducibility Testing	Offsite Testing	Remote Testing
		Subset of LFR-260 (n=33)	Subset of LFR-260 (n=33)	Subset of LFR-260 (n=21)	Subset of LFR-260 (n=21)
Informed Consent / Assent (where applicable)	X				
Relevant Medical History	X				
Demographics	X				
Subject Eligibility Verification	X				
Prior Medications	X				
Randomization	X				
Baseline Visual Acuity - Device #1	X				
Refraction (including retinoscopy) - Device #1	X				
Best Corrected Visual Acuity - Device #1	X				
Baseline Visual Acuity - Device #2	X				
Refraction (including retinoscopy) - Device #2	X				
Best Corrected Visual Acuity - Device #2	X				
Repeatability Refraction (including retinoscopy) – LFR-260 only with same ECP		X			
Reproducibility Refraction (including retinoscopy) – LFR-260 only with 2nd ECP			X		
Offsite Refraction (including retinoscopy) – LFR-260 only in offsite location				X	
Remote Refraction (including retinoscopy) – LFR-260 only					X
Additional Best Corrected Visual Acuity – LFR-260 only		X	X	X	X
End of Study	X	X	X	X	X

1.0 Introduction

1.1 Background and Significance

The LFR-260 was designed by comparing its capabilities against an optical bench and physical lenses. Further, it has been tested for quality of image composition and correctness at all the points on the spectrum of settings that we intend to cover.

1.2 Device Name and Intended Use

The LFR-260 is intended to be used for distance vision testing in any environment, may it be in optometric clinics or in the field outside of the clinic, because of its compact form factor and portability.

The LFR-260 is an application-controlled instrument providing capabilities for distance vision testing including sphere, cylinder, and axis. The visual acuity and eye subjective manifest refraction determination will always be administered by an eye care professional (ECP) licensed and registered by the appropriated body in the region intended to be used. The instrument is designed in a way that it will only work with approved personnel and the use of secure credentials.

The device is intended to be used in patients aged from 12-65 years old with healthy visual systems and a refractive error no bigger than (+10 to -15D) and astigmatism no bigger than 2.5D (if any).

1.3 Regulatory Status and Clinical Data

The LFR-260 has not been cleared for use outside of this investigation.

2.0 Objectives and Study Endpoints

2.1 Objective

The aim of this trial is to establish if LFR-260 (investigational device) is **in agreement with a gold standard** in effectiveness to a traditional phoropter (control device) when applied in visual acuity test in subjects undergoing a full routine eye examination. This will be demonstrated by measuring that the LFR-260 is within 0.5D (+/-) in sphere and cylinder results and within 10 degrees for axis results from the traditional phoropter measurements.

2.2 Rationale

The purpose of this test is to evaluate the agreement to a gold standard of the refraction results provided by LFR-260 compared to a traditional refraction assessment conducted using a traditional phoropter (commonly used at optometry offices as the standard device used for measuring refraction).

Refraction test is part of a routine eye examination and from now on we will use the terms refraction test and vision test indistinctly. We propose the use of LFR-260 to provide information of the visual capabilities of the patient. The test will be provided and supervised by a qualified ECP appropriately registered and licensed in the region where the test.

2.3 Primary Endpoints

The primary effectiveness endpoint is to demonstrate that the LFR-260 is within 0.5D (+/-) in measuring sphere and cylinder results and within 10 degrees for axis results from the traditional phoropter. Precision testing will also be conducted to confirm repeatability and reproducibility of the LFR-260.

2.4 Secondary outcomes

2.4.1 Secondary Endpoints

- Patient satisfaction with LFR-260 device Quad view
- Eyecare provider satisfaction with LFR-260 related to usability, convenience

2.5 Hypotheses

2.5.1 Primary Effectiveness Hypothesis

The primary hypothesis for this study is that the probability of simultaneously achieving good clinical agreement for sphere, cylinder, and axis exceeds a performance goal (PG) for measurements made by the LFR-260 compared to those obtained using traditional phoropter. The *a priori* PG is 0.80. Good clinical agreement is defined as a sphere and cylinder measurements that are within +/- 0.5 D and within 10 degrees for axis among subjects with low astigmatism and within 5 degrees among subjects with moderate to high astigmatism.

3.0 Subject Selection

3.1 Number of Sites / Investigators

Investigators responsible for the conduct of this study in compliance with this protocol will be qualified ECPs (licensed optometrist or ophthalmologist) who are skilled in refraction testing via a traditional phoropter. Two (2) sites at 3 locations (one site has multiple satellite locations) in the United States will be selected for participation in this study. Each location will have 2 ECPs available for testing/evaluation for a total of 6 different ECPs for the study.

3.2 Number of Subjects

Accounting for lost to follow-up, a total of up to 108 subjects (216 eyes) will be enrolled in the study. To control any effect of the instrument induced myopia, we expect to enroll an age tiered distribution of participants of the following approximate percentages:

- Approximately 45% Pediatrics (age from 12 until ≤21 years)
- Approximately 55% Adults/Geriatrics (age between 22-65)

A large portion of the subjects belongs to pediatric population such distribution will address the presence or absence of induced instrument myopia.

3.3 Study Arms

All subjects will be randomized by treatment order to the following refractor testing methods:

- Group I: LFR-260
- Group II: Traditional Phoropter

3.4 Inclusion criteria

Participants must fulfill all of the following criteria in order to be eligible for the study:

1. The participant or legal guardian is willing and able to understand, sign and date the Ethics committee approved study specific Informed Consent Form.
2. The participant is a male or female between the ages of 12 and 65 (inclusive).
3. The participant has a history of the following:
    - No more than mild to moderate far-sightedness or near-sightedness (i.e. Spherical equivalent refraction (SER) between +10 to -15).
    - an astigmatism of 2.5D or less.
    - an anisometropia of 1.5D or less.
4. The participant is free of ocular and systemic abnormalities that might affect visual functions.

3.5 Exclusion criteria

Participants will be excluded from participation in the study if any of the following criteria are met at screening:

1. The participant has diabetes mellitus (Type 1 or 2).
2. The participant has an autoimmune condition.
3. The participant is pregnant (self-reported).
4. The participant has an active corneal or conjunctival infection.
5. The participant has an active corneal, conjunctival, or intraocular inflammation (i.e. - uveitis).
6. The participant has diabetic retinopathy.
7. The participant has glaucoma or ocular hypertension.
8. The participant has macular degeneration.
9. The participant has had a previous ocular surgery.
10. The participant has ocular and systemic diseases or abnormalities that might affect visual functions.
11. The participant has a history of amblyopia, strabismus, or any other binocular vision abnormality.
12. The participant has a history of AMD (age macular degeneration).
13. The participant is a prisoner, a transient or has been treated for alcohol and/or drug abuse in an inpatient substance abuse program within 6 months prior to proposed study enrolment.
14. The participant will not be able to complete questionnaires.
15. The participant is currently in an investigational study for a similar purpose.
16. The participant, in the judgment of the Investigator, may be inappropriate for the intended study procedures.

4.0 Study Overview

4.1 Study Design

This study is organized as multicenter, randomized cross-over study trial. There are two groups involved in the trial, the investigational group and the active control group. The comparison with a placebo group is not part of the trial for ethical reasons.

4.2 Investigational group

The LFR-260 is a portable digital refractor which allows for determination of refractive error as well as for fully remote refractions while social distancing. The device offers a solution that embodies all the aspects that are typically associated with a refraction evaluation in a mobile approach while giving the practitioner full control, ease of use and patient comfort.

Figure 1: Image of the LFR-260

A standard phoropter on the market is comprised of a set of lenses which can be adjusted by an ECP to guide a patient through different settings as in "do you see better now?" format. In contrast, the objective device, LFR-260, achieves the same functionality but relies on a digital approach based on a micro lens array, a high-density embedded display, and a tunable lens. The device was developed taking a different approach that allows a significant reduction in the number of lenses, allowing higher portability and smaller footprint. The lower number of lenses does not compromise functionality compared to other traditional solutions. With these components, the LFR-260 provides the same capabilities as traditional lens systems, however in a portable, lightweight format.

The instrument will be able to perform traditional refractive tests with the standard optotypes (Snellen, ETDRS, Landolt C, LEA symbols) such as:

- Determining the required spherical correction

- Determining the required astigmatic correction measuring with JCC (Jackson cross-cylinder) – magnitude and direction.

4.3 Control group

The control group is a traditional refraction performed by a phoropter. The results for both refractions will be recorded separating the components Sphere (S), Cylinder (C) and Axis (A). A calculation of the spherical equivalent will be performed at the end of the visit and both values will be recorded in the study documentation. The best corrected visual acuity for each measurement will be recorded.

4.4 Visual Acuity Testing Procedure

All the subjects will undergo the standard visual acuity testing using both the LFR-260 and the traditional phoropter. Both eyes will be tested, always starting with the right eye. Both eyes will be tested with a traditional phoropter and the LFR-260. The subject will be seated on a height adjustable chair to ensure comfort during the test. Once the subject is seating comfortably the examiner will measure the distance between the outer canthus of the eye and the visual acuity to be used. The left eye will be patched while testing the right eye and vice versa. They could be covered with the occlude or using the masking capabilities of the LFR-260.

The following outcomes will be measured (for both eyes):

- Unaided VA
- Aided VA
- Distance for the test

Evaluation of the refractive state should be performed by reading the Snellen chart (or equivalent depending on the patient) at 20 feet (or adjusted to the appropriate distance depending on the dimensions of the actual optometric office). The subject should be informed that the chart only includes letters (or equivalent for patient population).

Outcomes will be recorded. If a line was incomplete, the scored letters should be added to the VA. The goal is to obtain best corrected visual acuity (20/20 Snellen) to ensure that the highest level of visual acuity possible for the patient.

Visual acuity testing will be performed without the use of cycloplegic agents and or pupil dilation at all times. To control the potential effect of instrument myopia we will propose starting the examination using the fogging method to relax any potential accommodation.

4.5 Test sequence

In the traditional refractor procedure of Snellen charts (or equivalent), if the patient cannot see a letter, the practitioner moves the patient closer to the chart 1m at the time. In the case of LFR-260, the letter sizes will adjust to simulate such movement and change of perceived size and recorded accordingly. Such adjustment should take place until the subject can see the top letters. The smallest letter the subject can see clearly would be considered the VA for distance.

Actual test sequence:

a) Screening phase: In which the examiner will initially determine by single letter presentations what would be the smallest Snellen chart (or equivalent) level at which the subject will correctly identify letters.
b) Testing phase: the examiner will start presenting letters of the size determined at the screening phase and smaller ones.
c) Test continuation: if a letter is missed at a level, one level larger will be added to the testing. If a letter is correct at a level, one level smaller will be added to the mix.
d) Acuity determination: Tests of 5 letters at each level until smallest level with 5/5 letters correct and the smallest level with 0/5 correct are determined.
e) Quad view: at any time during a refraction, the ECP may provide a patient with a "quad view". This mode shows four different prescriptions simultaneously and allows the patient to switch from a memory-based decision to a solely vision-based decision.

4.6 Letter scores calculation

With the lens correction obtained and present either on the phoropter or the LFR-260, the subject will be asked to read the Snellen chart (or equivalent) emphasizing that each letter will be scored and will ask the subject to take their time in answering in order to achieve best identification. The examiner will record each letter identified correctly on a score sheet. If a letter is not correctly recognized it will not be recorded, each correct letter is a point. The score of each line, even if zero, and the total score for the eye will be recorded right after the examination and recorded in the patient chart and the case report form.

4.7 Subject Screening and Recruitment

A study coordinator (e.g. research nurse or staff member) designated specifically for this study, investigator, or sub-investigator at each investigative site will approach each potential subject and inquire about their interest and eligibility in participating in this study. If the patient wishes to participate, a member of the research team will go through the informed consent / assent (where applicable) process, which will explain the purpose of the study, the procedures, the risk/benefits, alternatives to participation, and their confidentiality. After the consent process, the subject will be screened to confirm eligibility.

At the baseline visit, each subject choosing to participate will sign and date an informed consent and HIPAA authorization / assent (where applicable). A copy of the consent and authorization will be placed into the subject's medical record.

Study guidelines, aimed at helping guide the subject in their follow-up responsibilities, will include a subject information worksheet and site contact information for advice in case of complications or questions regarding follow-up visits.

4.8 Randomization

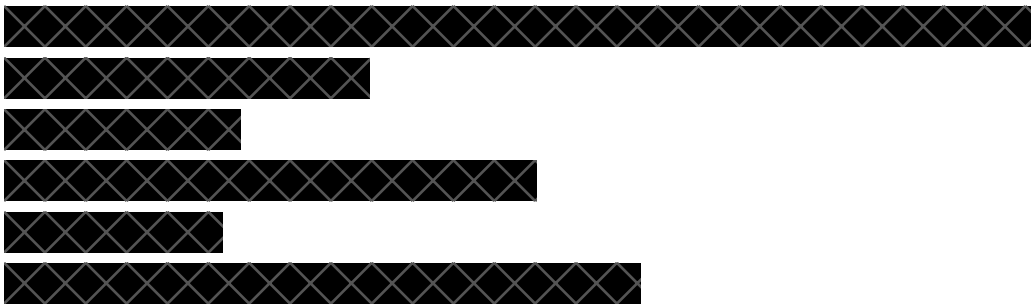
The randomization will be performed between the LFR-260 and the traditional phoropter within site to account for the first system used. Randomization will be carried out according to the blocks procedure to avoid order imbalance of first device used in the trial.

4.9 Visit Summary

4.9.1 Screening/Initial Assessment

The procedures to be completed at Visit 1 are as follows:

- Screening: Talk to the patient to determine if he/she would fit study requirements, and assess likelihood of meeting enrollment criteria.
- Informed Consent / Assent: Obtain subject informed consent or assent for minors. Allow subject or their legally authorized representative (LAR) sufficient time to thoroughly read and understand the consent form and answer any questions he/she may have about the study. If subject provides informed consent, complete the subject enrollment log.
- Inclusion Criteria: Ensure subject meets all inclusion criteria.
- Exclusion Criteria: Ensure subject does not meet any of the exclusion criteria.
- Pre-study assessments: Obtain medical history and demographics from subject.
- Prior medications/therapy: Note any medications or therapy that the subject is currently taking. Medications of note include:



- Randomization: determine the order of system utilized for testing
- Device #1 testing including:
    - Baseline Visual Acuity

  - Refraction (including retinoscopy)
  - Measure Best Corrected Visual Acuity
- Device #2 testing including:
  - Baseline Visual Acuity
  - Refraction (including retinoscopy)
  - Measure Best Corrected Visual Acuity
- Patient satisfaction with LFR-260 device Quad view
- Eyecare provider satisfaction with LFR-260 related to usability, convenience

*Conclusion of Study: Study coordinator will complete the Study Exit Form, which will indicate the conclusion of subject participation in this study.
*For subjects included in the Precision Tests or Remote Testing (4.9.2 and 4.9.3), Study Exit Form to be completed after all testing is completed.

4.9.2 Precision Tests

1. Repeatability Testing (+1 hour post initial testing)

In a subset of 33 patients (11 per location), LFR-260 testing will be repeated by the same ECP to confirm the initial findings. One ECP per location will perform Repeatability Testing for a total of 3 ECPs included for this testing method.

- ECP will complete Refraction with LFR-260 one hour post initial testing
- Measure Best Corrected Visual Acuity
- Conclusion of Study: Study coordinator will complete the Study Exit Form, which will indicate the conclusion of subject participation in this study.

2. Reproducibility Testing

In a separate subset of 33 patients (11 per location), LFR-260 testing will be reproduced by two separate ECP operators at each location for a total of 6 ECPs.

If the patient is randomized to Group I, the steps listed below will be completed at the beginning of the patient visit. If the patient is randomized to Group II, the steps listed below will be completed after the eye exam with use of the traditional phoropter.

1. ECP #1 will complete Refraction with LFR-260.
   a. Best Corrected Visual Acuity will be measured.
2. ECP #1 will leave the room, and ECP #2 will complete Refraction with LFR-260.
   a. Best Corrected Visual Acuity will be measured.

3. Conclusion of Study: Study coordinator will complete the Study Exit Form, which will indicate the conclusion of subject participation in this study.

4.9.3 Offsite Testing

In a separate subset of 21 patients (7 per location), LFR-260 testing will be completed by the ECP operators offsite at each location.

After the initial LFR-260 and traditional phoropter is complete within the clinic, participants in the offsite testing cohort will be taken to a non-clinical setting for the following procedure:

1. An additional LFR-260 will be set up in a remote location (room separate from clinic).
2. The patient will be taken to the remote room, and the ECP will perform the refraction.
3. Best Corrected Visual Acuity will be measured and collected.
    a. Results will be captured to compare against the initial LFR-260 refraction results.

4.9.4 Remote Testing

In a separate subset of 21 patients (7 per location), LFR-260 testing will be completed by the ECP operators remotely at each location.

After the initial LFR-260 and traditional phoropter is complete, participants in the remote testing cohort will remain in the clinical setting for the following procedure, while the ECP relocates to an area outside of the exam room:

1. The patient will be shown the LFR-260 and site staff will oversee the telehealth refraction remotely on the LFR-260 by the ECP.
2. Results for the Best Corrected Visual Acuity will be collected.
    a. Results will be captured to compare against the initial LFR-260 refraction results.

4.9.5 Subject Discontinuation or Withdrawal

Subjects may withdraw their consent to participate in the clinical study at any time, for any reason. In addition, it may be necessary to terminate a subject from the clinical study due to medical safety consideration, non-compliance, or administrative concerns. If for any reason a subject is withdrawn or terminated before completing the study, the reasons for withdrawal or termination must be documented. If a subject is withdrawn or terminated due to medical safety considerations because of an adverse event, the adverse event must be followed by medical attention to satisfactory resolution and all study data related to the subject will be reported.

Subjects who withdraw or are withdrawn prior to completion of the study periods will be scheduled a termination visit. At this visit, all study procedures will be completed according to the next

scheduled visit per protocol. All pertinent data will be documented in the source documents and the CRFs including a Study Exit form

If the site is notified that a subject plans to withdraw during a study visit, the site will treat the current visit like the termination visit by completing the current visit (if able), all applicable source documents and the CRFs including the Study Exit CRF.

4.10 Study Duration

All subjects will be followed only for the initial visit as no follow-up assessments are expected after the initial visual acuity testing is complete.

4.11 Clinical and Functional Assessments

Subjects will be clinically evaluated by the Investigator or a qualified individual noted on the Delegation of Authority (DOA) log. Clinical and functional assessments will be measured as follows:

- Patient satisfaction with LFR-260 device Quad view
- Head injury / concussion sub-group assessment (if applicable)
    - Measure any cognitive issues or nauseous experience to refraction.

4.12 Prior, Concomitant, and Excluded Therapy

All concomitant medications/therapies should be collected starting at Visit 1.

5.0 Safety Evaluation

Adverse events are defined as any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users, or other persons, whether or not related to the investigational medical device. See section 8.0 for anticipated risks during the trial.

All adverse events will be collected and recorded, regardless of whether or not they are believed to be related to the device or anticipated. This includes the following:

- Adverse Device Effect (ADE) – adverse event related to the use of an investigational medical device.
- Serious Adverse Events (SAE) – an adverse event that led to death; led to serious deterioration in the health of the subject, that either resulted in: a life-threatening illness or injury; a permanent impairment of a body structure or a body function; in-patient or prolonged hospitalization; medical or surgical intervention to prevent life-threatening

illness or injury or permanent impairment to a body structure or a body function; led to fetal distress, fetal death or congenital abnormality/birth defect.

- Unanticipated Adverse Device Effect (UADE) – any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.
- Device deficiency – inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance.

5.1 Serious Adverse Event Parameters

At any point during the clinical investigation, study termination or unblinding may be considered based on the frequency or severity of serious adverse device effects or serious adverse events. If this occurs, subjects will be notified of the study termination and follow-up requirements, as applicable. Every effort will be made to collect data regarding the subject disposition following such an event.

5.2 AE / SAE Recording and Reporting

Any and all adverse events will be recorded on the Adverse Event Case Report Form. Investigators are required by federal regulations, to report all adverse events that occur during the course of a study to Evolution Optiks or their designee. All adverse events reported on the Case Report Form will be source data verified against the subject record. The site is also responsible for reporting adverse events to the governing IRB in accordance with the requirements of that IRB.

Serious Adverse Events are to be reported to Evolution Optiks or their designee within 24 hours of the investigator's awareness of their occurrence. The Investigator is also required to report any UADEs to Evolution Optiks or their designee within 24 hours. The Investigator is also responsible for reporting these events to the governing IRB in accordance with the requirements of that IRB.

The names and telephone numbers of the contact persons from Evolution Optiks or its designated representative are given in the table below:

SERIOUS ADVERSE EVENT SPONSOR CONTACT INFORMATION			
Name/Title	**Email**	**Office Telephone Number**	**Mobile Telephone Number**
Jennifer Mercuri, MS Project Manager	jennifermercuri@emergentclinical.com	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]	[redacted]

6.0 Clinical Supplies

6.1 Receiving, Storage, Dispensing and Return of Investigational Product

6.1.1 Receipt and Accountability

It is the responsibility of the Investigator to ensure that all product received at the site are inventoried and accounted for throughout the study and recorded in the Product Accountability (inventory) log kept in the site study documents.

6.1.2 Storage and Return or Destruction of Investigational Product

The Investigator will store the investigational product and dispose of remnants per the Sponsor's instructions. Unopened product will be returned to the Sponsor. Product Accountability will be recorded in the source documentation and in the Product Accountability log for monitor review and reconciliation.

6.1.3 Dispensing of Investigational Device

The Investigator will not supply study material to any person except designated staff participating in this study. Study material will only be dispensed from the designated investigational site to eligible study subjects.

7.0 Statistical Analysis

7.1 Study Design and Randomization

The LFR-260-101 study is a multi-center, open-label, 2x2 cross-over design with the aim of investigating the effectiveness of the LFR-260 phoropter device compared to the traditional phoropter.

7.2 Analysis Sets

7.2.1 Intent-to-Treat (ITT)

All randomized patients will be included in the intent-to-treat (ITT) analysis set according to the group to which they were randomized.

7.2.2 Full Analysis Set (FAS)

The Full Analysis Set (FAS) analysis set will be defined similarly to the ITT analysis set except that patients will be analyzed according to the order of devices actually administered. Primary safety analyses will be conducted in the FAS analysis set. If all ITT patients receive their intended device order, the FAS and ITT analysis sets will coincide and will be referred to as the ITT analysis set.

7.2.3 Per Protocol

Primary effectiveness analyses may be repeated in a Per Protocol (PP) analysis set. The PP analysis set will exclude from the ITT analysis set patients that had clinically significant violations of inclusion or exclusion criteria or post randomization protocol violations that may reasonably be predicted to impact on effectiveness endpoints and those that have missing data.

7.3 Primary Effectiveness Endpoint

The primary effectiveness endpoint is to demonstrate that the LFR-260 is within 0.5D (+/-) in measuring sphere and cylinder results and within 10 degrees for axis results among subjects with low astigmatism and within 5 degrees among subjects with moderate to high astigmatism from the traditional phoropter in a very large proportion of subjects.

7.4 Primary Effectiveness Hypothesis

The primary hypothesis for this study is that the probability of simultaneously achieving good clinical agreement for sphere, cylinder, and axis exceeds a performance goal for measurements made by the LFR-260 compared to those obtained using the control device, ***traditional phoropter***.

Symbolically, the null and alternative effectiveness hypotheses are: :

Ho: $\pi \leq PG$
Ha: $\pi > PG$

Where π is the true probability that the LFR 260 is within 0.5D (+/-) in measuring sphere and cylinder results and within 10 degrees for axis results among subjects with low astigmatism and within 5 degrees among subjects with moderate to high astigmatism from the traditional phoropter.

For this study, PG is set to 0.80.

7.5 Sample Size Determination

If the true π is equal to 0.90, then, a 1-sided exact binomial test at alpha=0.05 with 216 eyes (108 subjects) has 99% power.

7.6 Testing of Primary Effectiveness Hypothesis

The lower bound (LB) of a 1-sided exact binomial confidence interval will be determined and compared to 0.80. If LB exceeds 0.80, the device will have met the a priori defined performance goal.

7.7 Other Planned Analyses

7.7.1 Bland-Altman Agreement Analysis

Supporting analyses will evaluate the distribution of paired differences between LFR-260 and reference for the three dimensions (sphere, cylinder, and axis) using Bland-Altman agreement analysis. This will include determination of the standard deviation of paired differences, the 95% limits of agreement, and an evaluation of systematic bias. The Bland-Altman plot of paired differences versus the mean of measurements will be provided. The relationship between bias and the mean of measurements will characterized. The same analysis will be applied to the vector difference between LFR-260 measurements and the gold standard in terms of sphere and cylinder measurements. The vector differences is square root of (X1-Y1) + (X2-Y2) where the X1 and X2 are measurements of sphere and cylinder using the investigational devices and Y1 and Y2 are the same measurements using the gold standard.

7.7.2 Poolability and Homogeneity of Treatment Effects

Homogeneity of treatment effects across sites will be evaluated by comparing differences between the LFR-260 and the gold standard separately for sphere, cylinder, and axis and also for the vector analysis of sphere and cylinder.

Similarly, differences between measurements from the investigational device and the gold standard device will be summarized by gender, age category, race, and ethnicity to investigate consistency or heterogeneity of the treatment effect across those subgroups, separately for sphere, cylinder, and axis and also for the vector analysis of sphere and cylinder.

7.7.3 Poolability and Homogeneity of Treatment Effects

The primary analysis will be based on the ITT analysis set and will use multiple imputation to address missing values. The MI model will include sphere, cylinder, and axis measurements for both the investigational device and the gold standard device and baseline characteristics including age and gender. Analyses will be repeated in a per protocol analysis set that includes eyes will complete data. A tipping point analysis will be performed to evaluate the robustness of results with regard to the missing-at-random (MAR) assumption necessary for the validity of the MI analyses.

7.7.4 Reliability and Repeatability Analysis

Reliability of LFR-260 will be conducted in a subset of subjects for which measurements will be obtained twice in an office context. This analysis will be repeated in a remote context. Reliability will be evaluated using intraclass correlations for each of the continuous measurements, sphere, cylinder, and axis and for the vector measurement of sphere and cylinder.

For a subset of 33 subjects (66 eyes), the LFR-260 device will be measured again approximately 60 minutes after the initial assessment in order to measure the repeatability/accuracy of the device.

8.0 Risk Analysis

The subjects in this study will be exposed to minimal increased potential risk. The majority of procedures in this study correspond to the standard of care procedures.

Trial-specific risks include the risks associated with investigational device (LFR-260) and the risks associated with trial-related investigations and data collection.

Clinical investigations performed in this trial include non-invasive diagnostic methods and interview questionnaires. These non-invasive diagnostics represent a minimal risk to the subject.

All adverse events regardless of whether they were investigational device- related will be reported and recorded according to current regulations. See Section 5 for more details.

9.0 Investigator Selection and Regulatory Assessment

9.1 Investigator Responsibilities

Investigators will be identified based on their qualifications to conduct the investigation. Evolution Optiks will further assess the qualifications of each Investigator and their staff by conducting a review of their CV, checking the status of the Investigator within the FDA Debarment List, discussing the availability of the correct subject population at the institution and through a review of the clinical space to ensure that the facility has adequate amenities to conduct the study according to the protocol. The final determination on an Investigator's participation will be made following review of the above criterion and completion of the Site Qualification/Pre-Study Visit.

9.2 Institutional Review Board Approval

Investigators will be responsible for obtaining the initial and continuing review approvals from the governing IRB for the institution at which the proposed clinical investigation is to be conducted. Written certification of approval, and any conditions of approval imposed by the IRB, will be submitted to Evolution Optiks prior to the site's participation in this investigation. Investigational supplies will not be shipped to participating sites until documentation of IRB approval has been provided to Evolution Optiks.

The Investigator and/or his staff is responsible for knowing and complying with any reporting requirements stipulated by their governing IRB.

9.3 Investigator's Agreement

Investigators will be advised of their responsibilities as Investigators in a clinical study. Investigators will also be advised regarding FDA regulations governing clinical studies under IDE regulations, and must abide by record keeping and reporting requirements. This information will be provided to the Investigators via the Investigator Agreement, which must be signed by the Investigator and returned to Evolution Optiks prior to study participation.

9.4 Regulatory documentation and Assessment of Facilities

As part of the study start-up process, the Investigator and their staff will be required to supply documentation of their qualifications to participate in the study as well as a Financial Disclosure Form. Prior to participation in the study, each Investigator is required to submit the following documentation to Evolution Optiks:

- A signed Investigator's Agreement
- A current signed and dated curriculum vitae (current within 2 years)
- A completed Financial Disclosure questionnaire

- Written approval of the study protocol and associated Informed Consent Form / Assent from their governing IRB (This must be provided prior to Investigational product being sent to the site or any subjects being enrolled). The Investigator/site is also required to submit any information required as part of the approval/renewal process for their governing IRB. Reports of any protocol deviations, AEs and Lost-to-Follow-Up subjects should also be provided to the IRB according to their stated requirements.

The Site Qualification Visit or Pre-Study Visit enables the Monitor to review the following with the Investigator and his staff: clinical protocol, the Investigator's Brochure, the Investigational product(s) provided for the clinical study, Investigator responsibilities, data collection and reporting requirements.

Another purpose of this visit is for the monitor to assure that the Investigator:

- Has appropriate training, facilities, patient load, staff, time and willingness to comply with study requirements;
- Understands the requirement to submit the clinical protocol and Investigator's Brochure to the IRB for review and approval;
- Understands the requirement to maintain all study correspondence, study binders, case report forms and subject records on file; and
- Assumes responsibility for oversight of the investigation at his / her center

The monitor will complete a Pre-Study Visit Report to document all activities and topics reviewed during the visit as well as the site personnel present for the meeting. The report will also document any open action items identified as a result of the visit.

9.5 Informed Consent

Subjects expressing an interest in participating in the study will be provided a copy of the IRB approved Informed Consent Form /Assent (where applicable) for review. Any study-related questions posed by the potential subject will be answered by the Investigator or a qualified member of his/her study staff. Potential subjects willing to participate in the study will be required to sign and date the Informed Consent Form. Only those who meet all inclusion and exclusion criteria for the study may be enrolled. Execution of the Informed Consent Form must be obtained prior to initiating any study specific procedures. The signed original informed consent is to be maintained in the site records and the subject should be provided with a copy for their records. The entire Informed Consent process will be documented in the subject's medical record.

9.6 Subject Stipends

Subject stipend or reimbursement will be determined on an Investigator site basis. If subject payments are allowed and warranted, monetary amounts will be reviewed and approved by the governing IRB and documented within each site ICF.

9.7 Confidentiality of Data

Access to subject's records is restricted to the Clinical Investigators, clinical site support staff, and to Evolution Optiks or their designee. Investigators are to instruct their staff in the methods and importance of maintaining subject confidentiality. Case Report Forms will be stored in secure, access-controlled locations at both the clinical sites and Sponsor's locations. Traceability of all forms will be maintained. Subjects will be assigned a subject number by the EDC system at the time of screening. On all CRFs or other reporting forms, study subjects should be identified only by their assigned subject number and initials.

Study results reported by Evolution Optiks will be in aggregate form and individual identities will not be publicly disclosed. It is possible that regulatory authorities (i.e., FDA) may request detailed clinical information regarding specific subjects. In these situations, information will be provided to regulatory authorities by the assigned subject number and subject initials.

The investigator agrees that complete source documents for this study will need to be available to appropriately qualified personnel from Evolution Optiks (or their designated representative) or to country specific health authority inspectors after appropriate notification. The verification of Case Report Form data will be done by direct inspection of source documents (where permitted by law). Record review will be done in compliance with HIPAA and in a manner that protects subject confidentiality.

During the conduct of the study, Investigators must agree not to publicly disclose any study related information including the study design, results or conclusions of the investigation without prior consent of Evolution Optiks.

9.8 Amendments to Protocol

While not expected, it is possible that Evolution Optiks may need to amend the clinical protocol (for example, at the request of the FDA, due to emergence of new information, etc.). In the event that this is needed, the protocol amendment will be reviewed and approved internally by the appropriate Evolution Optiks staff and the FDA. Once finalized, the amendment will be distributed to the participating Investigator sites. Protocol amendments must undergo IRB review and approval at each clinical site, but may undergo expedited review if minor changes are made in the protocol that does not alter subject risk. The written approval from the IRB for the amendment

should specifically refer to the Investigator, the protocol number and title, and reference any amendment numbers that are applicable.

9.9 Protocol Adherence

It is the responsibility of each Investigator and Evolution Optiks to conduct this study in accordance with all aspects of the protocol, Institutional Review Board requirements, the Declaration of Helsinki, the Code of Federal Regulations 21 CFR Part 50- Protection of Human Subjects, 21 CFR Part 54- Financial Disclosure, 21 CFR Part 56- Institutional Review Boards, and 21 CFR 812- Subparts C, Responsibilities of Sponsors, Subpart D, IRB Review and Approval, Subpart E, Responsibilities of Investigators and International Organization for Standardization (ISO) 14155:2020 and general Good Clinical Practice (GCP).

In the event of protocol deviations, both Evolution Optiks and the IRB should be notified of the event via the Protocol Deviation Log as soon as possible. If necessary, corrective actions will be taken to ensure the subject's safety and the integrity of the clinical investigation including, but not limited to site or study termination.

9.10 Change in Investigator

Should the Investigator, during the conduct of the study, resign, relocate or retire, he/she must immediately inform Evolution Optiks and provide an orderly process for study continuation. Should the Investigator, after completion of the study, resign, relocate or retire, he/she must immediately inform Evolution Optiks and provide an orderly process for record retention.

9.11 Records Retention

The types of records to be created and maintained for the clinical trial are dictated by the study protocol, Institutional Review Boards, and Federal regulations. U.S. Federal law requires maintenance of records of device disposition, signed consent forms, study data forms (CRFs), adverse event reports, all correspondence, dates of monitoring visits, and supporting information for a period of two years following the date of marketing clearance or until two years following notification by Evolution Optiks that the study has been discontinued. The Investigator has the responsibility to retain all study records, including the protocol, case report forms, IRB correspondence, letters to and from Evolution Optiks and any other applicable study documentation for the applicable period.

At the completion of the required retention period, it is requested that the Investigator contact Evolution Optiks and allow Evolution Optiks the option of permanently retaining the Investigator's study records. If the Investigator retires or relocates, he/she must identify an individual at their site who will hold responsibility for maintaining the study records. The name and title of this

individual should be provided to the Clinical Affairs Department at Evolution Optiks. Under no circumstances will anyone remove study records from the original study site without prior notification of, and approval by Evolution Optiks.

Investigators may release responsibility to maintain records and transfer custody to any other person who accepts such responsibility. A notice of transfer must be given to FDA no later than ten working days after the transfer occurs.