CLINICAL STUDY PROTOCOL

Title: A clinical validation study to evaluate the performance of a hand-held device supported by a mobile application compared with standard eye care diagnostic devices in measuring refractive error of the eye

Sponsor:	EyeQue Corporation 39608 Eureka Drive Newark, CA 94560
Protocol Number:	EYEQUE-001
Investigational Device:	EyeQue VisionCheck
Investigational Device Exemption:	Not applicable
Protocol Version:	Version 3.0 (17 June 2019)
Authorized Signatory:	John Serri Chief Technology Officer/Chief Operating Officer
Study Contact:	Paul TanPiengco Director of Product Management 818-564-5414

PROTOCOL APPROVAL - SPONSOR SIGNATORY

Study Title	A clinical validation study to evaluate the performance of a hand-held device supported by a mobile application compared with standard eye care diagnostic devices in measuring refractive error of the eye
Protocol Number	EYEQUE-001
Protocol Version	Version 3.0
Protocol Date	17 June 2019

Protocol accepted and approved by:

John Serri

Chief Technology Officer/Chief Operating Officer

EyeQue Corporation
39608 Eureka Drive
Newark, CA 94560

_____

Signature

_____

Date

INVESTIGATOR'S AGREEMENT

Study Title	A clinical validation study to evaluate the performance of a hand-held device supported by a mobile application compared with standard eye care diagnostic devices in measuring refractive error of the eye
Protocol Number	EYEQUE-001
Protocol Version	Version 3.0
Protocol Date	17 June 2019

My signature indicates my commitment to do the following:

- Conduct the investigation in accordance with the agreement, the investigational plan, 21 CFR Part 812, and other applicable regulatory requirements, and conditions of approval imposed by the reviewing institutional review board/independent ethics committee and appropriate regulatory agencies.
- Supervise all testing of the device involving human subjects.
- Ensure that the requirements for obtaining informed consent are met.

_____

Printed Name of Investigator

_____

Signature of Investigator

_____

Date

PROCEDURES IN CASE OF EMERGENCY

Emergency contact information is provided below.

Role in Study	Name	Address and Telephone Number
Sponsor Main Contact	Paul TanPiengco	EyeQue Corporation 39608 Eureka Drive Newark, CA 94560 Cell: 818-564-5414
Sponsor Secondary Contact	Noam Sapiens	EyeQue Corporation 39608 Eureka Drive Newark, CA 94560 Cell: 408-630-5086
Medical Monitor	Jack Modell, MD Vice President and Senior Medical Officer, or on-call medical monitor	Address as of 08 April 2019: Rho, Inc. 2635 E NC Hwy 54 Durham, NC 27713 Phone: 919-595-6461 (Medical Monitor Hotline) 8:00 am - 8:00 pm ET, Monday - Friday Email: MedicalMonitorSupport@rhoworld.com, with cc to jack_modell@rhoworld.com

2. SYNOPSIS

Name of Sponsor/Company: EyeQue Corporation

Name of Investigational Device: EyeQue VisionCheck

Title of Study: A clinical validation study to evaluate the performance of a hand-held device supported by a mobile application compared with standard eye care diagnostic devices in measuring refractive error of the eye

Study Number: EYEQUE-001

Study center(s): 1

Studied period (years):

Estimated date first patient enrolled: Q2 2019

Estimated date last patient completed: Q3 2019

Objectives:

Primary:

- The primary objective of this study is to determine whether EyeQue VisionCheck is statistically non-inferior to the phoropter as assessed by best corrected visual acuity (BCVA) for each eye independently, measured using trial lens frames that correct the refractive error measured by each device, for the age stratum 45 through 65 years.

Secondary:

The secondary objectives include:

- Assessing similarity of refraction values (sphere, cylinder, axis) from the EyeQue VisionCheck compared with the phoropter through comparative plots and Pearson correlations
- Determining whether EyeQue VisionCheck is statistically non-inferior to the autorefractor as assessed by BCVA measured using trial lens frames that correct the refractive error measured by each device
- Assessing similarity of refraction values (sphere, cylinder, axis) from the EyeQue VisionCheck compared with the autorefractor through comparative plots and Pearson correlations
- Determining whether EyeQue VisionCheck is statistically non-inferior to the phoropter as assessed by BCVA measured using trial lens frames that correct the refractive error measured by each device, for the age stratum 30 through 65 years.

Exploratory:

- The exploratory objective of this study is to assess subject preference among the 3 trial lens frames that correct the refractive error measured by the EyeQue VisionCheck, phoropter, and autorefractor.

Safety:

- To evaluate the safety of EyeQue VisionCheck compared with the phoropter and the autorefractor

Study design: This is a single-center, open-label, prospective study in healthy volunteers desiring refraction for correction of visual acuity to compare the EyeQue VisionCheck with the phoropter and autorefractor.

Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects. Subjects will be enrolled to obtain a population of approximately 35% in the age range of 30 through 44 years and approximately 65% in the age range of 45 through 65 years. Subjects will be screened for study participation and, if enrolled, will complete the testing procedures at the same visit. Subjects will not undergo any study-specific screening or testing procedures until written informed consent is obtained. A subject will be enrolled in the study after confirming that the subject has met all of the inclusion criteria and none of the exclusion criteria.

Screening procedures

The subject will complete the following assessments and procedures at Screening to confirm eligibility:

- demographics/medical history/concomitant medication review,
- slit-lamp biomicroscopy,
- laser retinal scan or fundoscopy,
- optical coherence tomography (OCT) (retina and anterior chamber),
- tonometry (non contact),
- Ishihara color test,
- cover test,
- retinoscopy
- phoropter refraction, and
- visual acuity with phoropter correction.

During the OCT and laser retinal scan/fundoscopy, images will be taken of the retina, anterior chamber, and fundus. All eye procedures will be completed without dilation using standard procedures.

Retinoscopy will be used as a basis for further refinement by phoropter refraction. Refraction values (sphere, cylinder, axis) for oculus dexter (OD, right eye) and oculus sinister (OS, left eye) will be recorded for each subject using the phoropter. These values will be used to adjust the lenses in the phoropter while the subject is looking through the device at an Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart to determine BCVA, as subjects are eligible to participate in the study only if their vision (oculus uterque [OU]; both eyes) can be corrected to 20/20 (logarithm of the minimum angle of resolution [LogMAR] 0.0).

The Screening procedures will be used to confirm that the subject does not have an exclusionary diagnosis (see exclusion criteria below).

Testing procedures

Once eligibility is confirmed, the subject will be enrolled and proceed with study testing procedures. The refraction values (sphere, cylinder, axis) for each subject (OD and OS) will be assessed using 2 additional devices: autorefractor and the EyeQue VisionCheck. Subjects will be assessed with the autorefractor using standard device methodology. The refraction values generated from the EyeQue VisionCheck, the autorefractor and the phoropter (during screening) will be used to prepare 3 sets of trial lens frames. Pupillary distance, measured using the autorefractor, will be recorded for all subjects and will be used for preparation of trial lens frames.

All subjects will be trained on how to use the EyeQue VisionCheck device prior to initiating testing. In order to obtain refraction values using the EyeQue VisionCheck, the subject will be required to take 1 practice test followed by a minimum of 3 saved tests for each eye using the EyeQue VisionCheck device and mobile application (app). After completion of a set of tests (1 test for each eye), the subject may elect to save or discard that set of tests. They may choose to discard for any reason which may include not following instruction, pressing the wrong button in error, etc. Each test consists of the subject looking through the VisionCheck device and using the app controls to fully overlap red and green bars at 9 different angles. After completion of all tests (1 practice test and 3 saved tests with each eye), the refraction values will be displayed on the mobile app. These values will be used for preparation of the trial lens frames. If the EyeQue system determines that the overall test results are unreliable, subjects may have to complete 3 additional tests per eye before the system may be able to provide refraction values. Subjects will not be allowed to complete more than 6 saved tests and 1 practice test with each eye. If the EyeQue system determines that the overall test results are unreliable, no values will be provided.

After collection of refraction values from each device (phoropter, autorefractor, and EyeQue VisionCheck), the 3 trial lens frames will be prepared and given to the subject in a masked fashion. Best corrected visual acuity will be assessed using the ETDRS eye chart. For each subject, BCVA LogMAR scores will be collected for OD, OS, and OU for each of the 3 trial lens frames. Subjects will also be asked a question regarding overall satisfaction with visual acuity using each of the 3 trial lens frames. Subjects will be monitored for adverse events (AEs) and adverse device effects (ADEs) during the study.

Number of subjects (planned): Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects. An initial cohort of 39 subjects will be excluded from the analysis populations due to a software error identified in the EyeQue app that has since been corrected; therefore, approximately 160 additional subjects will be enrolled in the study. Subjects will be enrolled to obtain a population of approximately 35% in the age range of 30 through 44 years and approximately 65% in the age range of 45 through 65 years.

Diagnosis and main criteria for inclusion:

Inclusion criteria:

1. Male or Female

2. Age 30 through 65 years at the time of consent
3. Binocular vision
4. Subject desires refraction for correction of visual acuity and vision (OU) can be corrected to 20/20 (LogMAR 0.0)
5. Willing and able to give informed consent and follow all study procedures and requirements
6. Ability to speak and understand the English language

Exclusion criteria:

1. Spherical correction > +8 or < -10
2. Using anticholinergic medications (including first-generation antihistamines) or other medications known to affect visual acuity within the greater of 3 days or 5 half-lives prior to enrolling in this study
3. Using an investigational drug or approved therapy for investigational use within the greater of 3 days or 5 half-lives prior to enrolling in this study
4. Has initiated any new medication in the past 2 weeks that, in the best medical judgment of the investigator, would impact their participation in the study or ability to use the EyeQue VisionCheck device
5. Eye disease, including but not limited to:
    - Glaucoma (≥ 22 mmHg intraocular pressure)
    - Cataracts (≥ 1+ nuclear sclerotic cataract, ≥ 1+ cortical, posterior subcapsular cataract [any grade using the Lens Opacities Classification System III])
    - Macular degeneration (retinal pigmented epithelium mottling and/or any drusen within 500 µm of macula)
    - Eye infection (corneal ulcer, corneal infiltrates, superficial punctate keratitis)
    - Keratoconus
    - Diabetic neuropathy/retinopathy (≥ mild nonproliferative diabetic retinopathy)
    - Cytomegalovirus retinitis
    - Color blindness (any color deficiency)
    - Diabetic macular edema (evidence of fluid)
    - Amblyopia
    - Chronic or acute uveitis (cells and/or flare in anterior chamber)
    - Strabismus (exotropia, esotropia, and hypertropia)
    - Abnormal astigmatism (mild to severe, > 5 diopters)
    - Macular hole

6. Eye surgery within the last 12 months (including Lasik or lens replacement)
7. Subject does not have the physical dexterity to properly operate the EyeQue VisionCheck device or the EyeQue app on the smartphone in the investigator's opinion

Investigational device and mode of administration: The investigational device is the EyeQue VisionCheck, and the intended use is to measure the refractive error of the eye. This is a self-administered, portable, monocular refraction system consisting of 3 main components: a mobile app, a cloud-based processing platform, and the VisionCheck optical device that attaches to a compatible smartphone owned/operated by the end user. The EyeQue app guides the subject through interactive measurements with the EyeQue VisionCheck device in order to determine refractive error.

Study duration: The study duration for each subject will be 1 day. All study-related procedures, including screening, will be completed in 1 visit.

Reference devices and mode of administration: The reference devices will be the phoropter and autorefractor. Prior to enrollment of study subjects, both devices will be calibrated following standard practice. Standard device methodology for refraction tests will be used to obtain refraction values with each device.

Criteria for evaluation:

Efficacy:

Primary Endpoint:

- Statistical non-inferiority of EyeQue VisionCheck compared with phoropter assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device analyzed with age stratum 45 through 65 years.

Secondary Endpoints:

- Comparison of raw refraction values produced using the EyeQue VisionCheck and the phoropter analyzed with age strata 30 through 65 years and 45 through 65 years.
- Statistical non-inferiority of EyeQue VisionCheck compared with autorefractor assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device analyzed with age strata 30 through 65 years and 45 through 65 years.
- Comparison of raw refraction values produced using the EyeQue VisionCheck and the autorefractor analyzed with age strata 30 through 65 and 45 through 65 years.
- Statistical non-inferiority of EyeQue VisionCheck compared with phoropter assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device analyzed with the age stratum 30 through 65 years.

Exploratory Endpoint:

- Subject preference of trial lens frames that correct the refractive error measured by

each of the 3 devices: EyeQue VisionCheck, phoropter, and autorefractor.

Safety:

If any AEs occur during the study, the safety endpoints will include the frequency and severity of AEs, ADEs, and serious adverse events (SAEs).

Statistics:

Analysis Populations

Modified Intent to Treat Population: All subjects that perform BCVA for trial frames with test lenses based on both phoropter and EyeQue VisionCheck.

Safety Population: All subjects that meet the screening criteria and are enrolled in the study.

After enrollment in this study was initiated, a software error was identified in the EyeQue app used with the EyeQue VisionCheck. The error was corrected and the algorithm for the EyeQue app was updated. An initial cohort of 39 subjects was enrolled in the study prior to these changes being implemented. Due to these EyeQue app updates, this initial cohort of 39 subjects will be excluded from the analysis populations and any safety information for these subjects will be listed separately.

Power and Sample Size

Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects to assess the effectiveness and safety of the EyeQue VisionCheck. The initial cohort included 39 subjects; therefore, approximately 160 additional subjects will be enrolled in the study. Based on prior study data, rejection of non-inferiority bounds of 0.1 LogMAR (one line) and 0.05 LogMAR (one-half line) would require approximately 10 and 40 subjects, respectively, with 90% power on the BCVA from the resulting lens from each approach. This assumes the devices are roughly equivalent and the standard deviation (SD) is 0.077; these data are based on a previous version of the EyeQue VisionCheck device tested against an autorefractor. The proposed sample size has been inflated to allow for the possibility that a larger standard deviation will be observed in the current study, as well as to allow for comparisons within each stratum.

When the software error in the EyeQue app was identified, the algorithm for the EyeQue app was updated with more stringent parameters which may also impact the number of evaluable subjects. Due to the updates to the parameters, there may be additional subjects for which EyeQue VisionCheck refraction values are not produced, leading to an increase in the number of subjects that will not be evaluated for the primary endpoint. Of the approximately 160 additional subjects that will be enrolled in the study, it is anticipated that approximately 60 subjects will not be evaluable due to failing screening or not having refraction values produced with the EyeQue VisionCheck. Additionally, the larger sample size provides a sufficiently robust database for investigations of the secondary outcomes and descriptions of the EyeQue VisionCheck's performance characteristics.

Efficacy Analysis

Best corrected visual acuity will be assessed independently for each eye and the worse value for

each test lens set and subject will be selected for the primary analysis. Each subject's BCVA LogMAR score from the phoropter-based lenses will be subtracted from the BCVA LogMAR score from the EyeQue VisionCheck-based lenses. The mean, SD, and two-sided 95% confidence interval (CI) will be reported across all subjects for worst eye, OD, OS, and OU, and if the upper bound (one-sided 95% CI) does not include the value 0.1 for the worst eye comparison, then non-inferiority will be declared. This will be repeated using BCVA scores from the autorefractor-based lenses and EyeQue VisionCheck-based lenses.

Raw refraction values for the phoropter and EyeQue VisionCheck will be plotted and Pearson correlations calculated. This will be repeated using autorefractor and EyeQue VisionCheck values.

Subject preference data will be tabulated with counts and percentages of subjects that considered the EyeQue VisionCheck trial lenses better as well as the counts and percentages of subjects that considered the EyeQue VisionCheck trial lenses better or equal.

Analyses will be repeated for each age stratum including ages 30 through 65 and ages 45 through 65.

Safety Analyses

Adverse events, ADEs, and SAEs will be reported with counts and percentages. Adverse events that can be associated with a particular device will be reported separately from those without clear attribution. A subject experiencing more than 1 instance of an event will be counted only once for that event. Analyses will be repeated for each age stratum including ages 30 through 65 and ages 45 through 65.

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4. LIST OF ABBREVIATIONS AND DEFINITIONS OF TERMS

Abbreviation	Explanation
AE	adverse event
ADE	adverse device effect
app	application
BCVA	best corrected visual acuity
CFR	Code of Federal Regulations
CI	confidence interval
eCRF	electronic case report form
EDC	electronic data capture
ETDRS	Early Treatment Diabetic Retinopathy Study
EyeQue	EyeQue Corporation
GCP	Good Clinical Practice
ICF	informed consent form
ICH	International Conference on Harmonisation
IEC	independent ethics committee
IRB	institutional review board
LogMAR	logarithm of the minimum angle of resolution
OD	oculus dexter (right eye)
OS	oculus sinister (left eye)
OU	oculus uterque (both eyes)
PHI	protected health information
SAE	serious adverse event
UADE	unanticipated adverse device effect
US	United States

5. INTRODUCTION

Uncorrected refractive errors account for more than 40% of the major causes for visual impairment globally (Pascolini D, 2010; World Health Organization, Blindness and vision impairment fact sheet). The most common types of refractive errors include myopia, hyperopia, presbyopia, and astigmatism. When an individual has an uncorrected refractive error, symptoms may include blurred vision, double vision, haziness, squinting, headaches, and eye strain. Refractive error correction is accomplished through the use of eye glasses, contacts, or refractive surgery. Traditionally, refraction measurements are conducted by an eye care professional during a comprehensive eye exam using diagnostic devices such as a phoropter or autorefractor. However, not all of the population has access to optometrists/ophthalmologists and these diagnostic devices or can afford these exams. Additionally, for some instances it may be more convenient to be able to obtain refraction values outside of the clinic.

The EyeQue Corporation (EyeQue) is developing an inexpensive, portable, self-administered device to measure refraction values that can be used outside of the clinic. The EyeQue VisionCheck device is a monocular refraction system consisting of 3 components: a mobile application (app), a cloud-based processing platform, and the VisionCheck optical device that attaches to a compatible smartphone owned/operated by the end user. The EyeQue app guides the subject through interactive measurements with the EyeQue VisionCheck device in order to determine refractive error.

This is a single center, clinical evaluation study to evaluate the performance of the EyeQue VisionCheck device compared with standard eye care diagnostic devices of phoropter and autorefractor in measuring refractive error of the eye. The intent of this study is to determine whether EyeQue VisionCheck is statistically non-inferior to the phoropter and autorefractor in correcting visual refractive errors. The best corrected visual acuity (BCVA) using trial lens frames prepared using refraction values from each of the 3 devices, raw refraction values from each device, and subject satisfaction with the 3 different trial lens frames will be assessed during the study.

6. STUDY OBJECTIVES

6.1. Primary Objective

The primary objective of this study is to determine whether EyeQue VisionCheck is statistically non-inferior to the phoropter as assessed by BCVA for each eye independently measured using trial lens frames that correct the refractive error measured by each device, for the age stratum 45 through 65 years.

6.2. Secondary Objectives

The secondary objectives include:

- Assessing similarity of refraction values (sphere, cylinder, axis) from the EyeQue VisionCheck compared with the phoropter through comparative plots and Pearson correlations
- Determining whether EyeQue VisionCheck is statistically non-inferior to the autorefractor as assessed by BCVA measured using trial lens frames that correct the refractive error measured by each device
- Assessing similarity of refraction values (sphere, cylinder, axis) from the EyeQue VisionCheck compared with the autorefractor through comparative plots and Pearson correlations
- Determining whether EyeQue VisionCheck is statistically non-inferior to the phoropter as assessed by BCVA measured using trial lens frames that correct the refractive error measured by each device, for the age stratum 30 through 65 years.

6.3. Exploratory Objectives

The exploratory objective of this study is to assess subject preference among the 3 trial lens frames that correct the refractive error measured by the EyeQue VisionCheck, phoropter, and autorefractor.

6.4. Safety Objective

The safety objective of this study is to evaluate the safety of EyeQue VisionCheck compared with the phoropter and the autorefractor.

7. INVESTIGATIONAL PLAN

7.1. Overall Study Design

This is a single-center, open-label, prospective study in healthy volunteers desiring refraction for correction of visual acuity to compare the EyeQue VisionCheck with the phoropter and autorefractor. Prior to enrollment of study subjects, both the phoropter and autorefractor devices will be calibrated following standard practice.

Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects. The initial cohort included 39 subjects; therefore, approximately 160 additional subjects will be enrolled in the study. Subjects will be enrolled to obtain a population of approximately 35% in the age range of 30 through 44 years and approximately 65% in the age range of 45 through 65 years. Subjects will be screened for study participation and, if enrolled, will complete the testing procedures at the same visit. Subjects will not undergo any study-specific screening or testing procedures until written informed consent is obtained. A subject will be enrolled in the study after confirming that the subject has met all of the inclusion criteria and none of the exclusion criteria.

Screening procedures

The subject will complete the following assessments and procedures at Screening to confirm eligibility:

- demographics/medical history/concomitant medication review,
- slit-lamp biomicroscopy,
- laser retinal scan or fundoscopy,
- optical coherence tomography (OCT) (retina and anterior chamber),
- tonometry (non contact),
- Ishihara color test,
- cover test,
- retinoscopy,
- phoropter refraction, and
- visual acuity with phoropter correction.

During the OCT and laser retinal scan/fundoscopy, images will be taken of the retina, anterior chamber, and fundus. All eye procedures will be completed without dilation using standard procedures.

Retinoscopy will be used as a basis for further refinement by phoropter refraction. Refraction values (sphere, cylinder, axis) for oculus dexter (OD, right eye) and oculus sinister (OS, left eye) will be recorded for each subject using the phoropter. These values will be used to adjust the lenses in the phoropter while the subject is looking through the device at an Early Treatment Diabetic Retinopathy Study (ETDRS) eye chart to determine BCVA, as subjects are eligible to

participate in the study only if their vision (oculus uterque [OU]; both eyes) can be corrected to 20/20 (logarithm of the minimum angle of resolution [LogMAR] 0.0).

The Screening procedures will be used to confirm that the subject does not have an exclusionary diagnosis.

Testing procedures

Once eligibility is confirmed, the subject will be enrolled and proceed with study testing procedures. The refraction values (sphere, cylinder, axis) for each subject (OD and OS) will be assessed using 2 additional devices: autorefractor and the EyeQue VisionCheck. Subjects will be assessed with the autorefractor using standard device methodology. The refraction values generated from the EyeQue VisionCheck, the autorefractor, and the phoropter (during screening) will be used to prepare 3 sets of trial lens frames. Pupillary distance, measured using the autorefractor, will be recorded for all subjects and will be used for preparation of trial lens frames.

All subjects will be trained on how to use the EyeQue VisionCheck device prior to initiating testing. In order to obtain refraction values using the EyeQue VisionCheck, the subject will be required to take 1 practice test followed by a minimum of 3 saved tests for each eye using the EyeQue VisionCheck device and mobile app. After completion of a set of tests (1 test for each eye), the subject may elect to save or discard that set of tests. They may choose to discard for any reason which may include not following instruction, pressing the wrong button in error, etc. Each test consists of the subject looking through the EyeQue VisionCheck device and using the app controls to fully overlap red and green bars at 9 different angles. After completion of all tests (1 practice test and 3 saved tests with each eye), the refraction values will be displayed on the mobile app. These values will be used for preparation of the trial lens frames. If the EyeQue system determines that the overall test results are unreliable, subjects may have to complete 3 additional tests per eye before the system may be able to provide refraction values. Subjects will not be allowed to complete more than 6 saved tests and 1 practice with each eye. The system evaluates the statistical spread of the test results taken by the subject. If the spread is too large, the results are considered to be unreliable and values will not be provided. Such spread can be due to testing error, improper instruction, etc.

After collection of refraction values from each device (phoropter, autorefractor, and EyeQue VisionCheck), the 3 trial lens frames will be prepared and given to the subject in a masked fashion. Best corrected visual acuity will be assessed using the ETDRS eye chart. For each subject, BCVA LogMAR scores will be collected for OD, OS, and OU) for each of the 3 trial lens frames. Subjects will also be asked a question regarding overall satisfaction with visual acuity using each of the 3 trial lens frames. Subjects will be monitored for adverse events (AEs) and adverse device effects (ADEs) during the study.

Appendix 1 presents the schedule of assessments for the study. Section 11 details the study evaluations for screening and testing at the 1 study visit.

7.2. Number of Subjects

Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects. The initial cohort included 39 subjects; therefore, approximately

160 additional subjects will be enrolled in the study. Subjects will be enrolled to obtain a population of approximately 35% in the age range of 30 through 44 years and approximately 65% in the age range of 45 through 65 years.

7.3. Study Endpoints

7.3.1. Efficacy Endpoints

Primary Endpoint:

- Statistical non-inferiority of EyeQue VisionCheck compared with phoropter assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device analyzed with age stratum 45 through 65 years.

Secondary Endpoints:

- Comparison of raw refraction values produced using the EyeQue VisionCheck and the phoropter analyzed with age strata 30 through 65 years and 45 through 65 years.
- Statistical non-inferiority of EyeQue VisionCheck compared with autorefractor assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device, analyzed with age strata 30 through 65 years and 45 through 65 years.
- Comparison of raw refraction values produced using the EyeQue VisionCheck and the autorefractor analyzed with age strata 30 through 65 and 45 through 65 years.
- Statistical non-inferiority of EyeQue VisionCheck compared with phoropter assessed by BCVA (OD, OS, and OU) measured using trial lens frames that correct the refractive error measured by each device analyzed with the age stratum 30 through 65 years.

Exploratory Endpoint:

- Subject preference of trial lens frames that correct the refractive error measured by each of the 3 devices: EyeQue VisionCheck, phoropter, and autorefractor

7.3.2. Safety Endpoints

If any adverse events occur during the study, the safety endpoints will include the frequency and severity of AEs, ADEs, and serious adverse events (SAEs).

7.4. Rationale for Study Design and Control Group

A clinical study based on statistical non-inferiority is the most appropriate means to assess the effectiveness and performance of the EyeQue VisionCheck device relative to the comparator devices, the phoropter and autorefractor, that are standard eye care diagnostic devices used to obtain refraction values.

Masking of the subjects and assessors to the refraction values used to prepare the 3 trial lens frames is appropriate to control and minimize bias in the assessment of BCVA as these LogMAR

scores will be used for determination of statistical non-inferiority. A statistical non-inferiority margin of 0.1 LogMAR has been chosen because the one-line ETDRS difference is an acceptable boundary for corrected visual acuity, with larger differences likely to be unacceptable to patients and smaller differences difficult to reliably detect and/or reproduce.

Based on the intended use for obtaining refraction values, a one-day evaluation is appropriate because standard-of-care eye exams in which refraction values are obtained are typically repeated on a periodic basis, such as yearly, and it is not anticipated that refraction values would change over a short duration where additional repeated measurements would be necessary for this study. Visual acuity may fluctuate often; however, there is no appreciable change over a period of a several months.

The design allows for enrollment of subjects 30 to 65 years because subjects younger than 30 years of age are more likely to have visual accommodation that would add complexity to this comparative study. Younger subjects may be assessed in a separate clinical study.

8. SELECTION AND WITHDRAWAL OF SUBJECTS

8.1. Subject Inclusion Criteria

Subjects must meet all of the following inclusion criteria to be enrolled in the clinical study:

1. Male or female
2. Age 30 through 65 years at time of consent
3. Binocular vision
4. Subject desires refraction for correction of visual acuity and vision (OU) can be corrected to 20/20 (LogMAR 0.0)
5. Willing and able to give informed consent and follow all study procedures and requirements
6. Ability to speak and understand the English language

8.2. Subject Exclusion Criteria

The presence of any of the following exclusion criteria excludes a subject from study enrollment:

1. Spherical correction > +8 or < -10
2. Using anticholinergic medications (including first-generation antihistamines) or other medications known to affect visual acuity within the greater of 3 days or 5 half-lives prior to enrolling in this study
3. Using an investigational drug or approved therapy for investigational use within the greater of 3 days or 5 half-lives prior to enrolling in this study
4. Has initiated any new medication in the past 2 weeks that, in the best medical judgment of the investigator, would impact their participation in the study or ability to use the EyeQue VisionCheck device
5. Eye disease, including but not limited to:
    - Glaucoma (≥ 22 mmHg intraocular pressure)
    - Cataracts (≥ 1+ nuclear sclerotic cataract, ≥ 1+ cortical, posterior subcapsular cataract [any grade using the Lens Opacities Classification System III])
    - Macular degeneration (retinal pigmented epithelium mottling and/or any drusen within 500 μm of macula)
    - Eye infection (corneal ulcer, corneal infiltrates, superficial punctate keratitis)
    - Keratoconus
    - Diabetic neuropathy/retinopathy (≥ mild nonproliferative diabetic retinopathy)
    - Cytomegalovirus retinitis
    - Color blindness (any color deficiency)

- Diabetic macular edema (evidence of fluid)
- Amblyopia
- Chronic or acute uveitis (cells and/or flare in anterior chamber)
- Strabismus (exotropia, esotropia, and hypertropia)
- Abnormal astigmatism (mild to severe, > 5 diopters)
- Macular hole

6. Eye surgery within the last 12 months (including Lasik or lens replacement)
7. Subject does not have the physical dexterity to properly operate the EyeQue VisionCheck device or the EyeQue app on the smartphone in the investigator's opinion

8.3. Subject Withdrawal Criteria

Subjects may be withdrawn from treatment or assessment for the occurrence of an adverse effect or any other conditions that may create a safety risk. Subjects may also be withdrawn at the discretion of the investigator.

Subjects can withdraw consent at any time for any reason without effect on subsequent care. Any enrolled subjects desiring to discontinue prior to study completion should be encouraged to discuss his or her reasons and concerns with the investigator. A subject who discontinues during the study visit prior to completion of all study procedures may be replaced.

8.4. Study Termination

If the study is suspended or prematurely terminated, the appropriate institutional review board (IRB)/independent ethics committee (IEC) and regulatory authority(ies) will be promptly informed of the termination/suspension and will be provided the reason(s) for the termination/suspension. All obligations and responsibilities of the sponsor and the investigator under the United States (US) Code of Federal Regulations (CFR) will remain in force if the study is terminated prematurely.

This study may be discontinued at any time if, in the opinion of the investigator, in consultation with the medical monitor and EyeQue, continuation of the study represents a significant medical risk to participating subjects. All unanticipated ADEs, will be examined to determine whether the ADE presents an unreasonable risk to subjects. If deemed an unreasonable risk, the study will be terminated or suspended.

9. TEST ARTICLE

9.1. Description

The investigational device is the EyeQue VisionCheck, and the intended use is to measure the refractive error of the eye. The EyeQue VisionCheck is a self-administered, portable, monocular refraction system consisting of 3 main components: a mobile app, a cloud-based processing platform, and the VisionCheck optical device that attaches to a compatible smartphone owned/operated by the end user. The EyeQue app guides the subject through interactive measurements with the EyeQue VisionCheck device in order to determine refractive error. The device and mobile app operate on the inverse Shack-Hartmann principle described in patent US 8783871 B2, "Near Eye Tool for Refraction Assessment" (Pamplona V, US Patent, 2014).

The EyeQue VisionCheck device is manufactured for EyeQue Corporation.

9.2. Packaging, Labeling, and Dispensing

All material containers will be appropriately labeled with the study number and product identification as applicable, as well as any other information as required by applicable regulations.

The compatible smartphones and access to the app will be provided to the sites to be used with the EyeQue VisionCheck.

9.3. Storage and Accountability

All test articles will be stored in a secure location at the investigational site.

A log of all test articles received and used during the study will be maintained by the study site. All test articles will be accounted for at the termination of the study and a written explanation provided for any discrepancies. The EyeQue VisionCheck devices and smartphones will be returned to EyeQue. Shipping and handling of all test articles will conform to regulations for investigational devices.

9.4. Device Risk Analysis and Risk Assessment

The device risk analysis and risk assessment were conducted in compliance with 21 CFR 820. Based on this assessment, the EyeQue VisionCheck is non-invasive and considered a low-risk device that requires periorbital surface contact. Even if the EyeQue VisionCheck is misused, the likelihood it will cause harm is low. The comparators in this study, phoropter and autorefractor, are used as part of standard eye exams. Most of the anticipated adverse effects are generally well tolerated and would be expected to occur infrequently. The risk and impact of these adverse effects is low.

Based on the design and the intended use of the EyeQue VisionCheck, and given the low risk of potential adverse effects, this is considered a nonsignificant risk medical device study that is subject to abbreviated investigational device exemption (IDE) regulations, and exempt from the requirement to submit an IDE application.

The following adverse effects may potentially occur with the use of the EyeQue VisionCheck device itself, the comparators, or the procedure used for the device:

- Transient blurred vision
- Transient dizziness
- Headache
- Transient eye irritation
- Superficial eye or periorbital infection

The following approaches have been used to minimize risk in this investigation:

- Subjects will be screened before receiving treatment to ensure they meet the protocol-defined inclusion and exclusion criteria. The inclusion and exclusion criteria have been developed to ensure appropriate subjects are included in the studied population and subjects with confounding conditions or conditions that could put them at risk are excluded from participation.
- The test articles (investigational and comparator devices) are intended for measuring refraction values and/or accessing BCVA. To minimize risk during the evaluations, the site staff will be trained on all devices and subjects will be instructed how to use each device. The phoropter and autorefractor are both operated by the site staff. The EyeQue VisionCheck device will be operated by the subject and subjects will be trained in advance of completing testing with the device. The mobile app provides detailed instructions on how to operate the EyeQue VisionCheck device. Detailed instructions for the site staff to provide to subjects about the EyeQue VisionCheck are provided in the study operations manual.
- To minimize the risk of eye irritation or infection, the devices will be sanitized between users.
- Adverse device effects will be monitored throughout the study by site staff.

If an adverse event occurs, site staff will follow medical procedures appropriate to the type of event.

10. TREATMENT OF SUBJECTS

10.1. Concomitant Medications

Any treatment including all prescription drugs, herbal products, vitamins, minerals, and over-the-counter medications or therapies administered from the time of consent through the end of study participation is considered a concomitant medication. Concomitant medication use will be recorded in the subject source documentation and may include the medication name, dose, frequency, route of administration, and the dates of administration.

10.1.1. Prohibited Concomitant Medications

The following concomitant medications and therapies are prohibited for the duration of the study and cannot be used within the greater of 3 days or 5 half-lives prior to enrolling in this study, unless otherwise specified:

- Anticholinergic medications (including first-generation antihistamines)
- Medications known to affect visual acuity
- Investigational drugs or approved therapies for investigational use

10.1.2. Permitted Concomitant Medications

Other than the prohibited medications and therapies listed in Section 10.1.1, treatment with concomitant medications and therapies is permitted during the study. Concomitant medication deemed necessary for the welfare of the subject during the study may be given at the discretion of the investigator.

10.2. Treatment Compliance

The investigational device will be used on site with the assistance of a study staff member during the study visit and thus is an observed compliance. The number and percentage of subjects not completing assessments on each device will be reported.

10.3. Randomization and Masking

10.4. Randomization

Not applicable to this clinical study.

10.5. Masking

This is an open-label study and the site and subjects will not be masked to the assessment device. Three sets of trial lens frames will be prepared using the refraction values from the 3 devices, including the EyeQue VisionCheck, phoropter, and autorefractor. During the study, the subjects and site personnel performing the BCVA assessments will be masked to the refraction values that are used to prepare each of the trial lens frames. Masking regarding the trial lens frames will

be maintained throughout the study by use of separate site personnel to prepare the frames and perform the BCVA assessment.

If the site personnel performing the BCVA assessments or a subject is unmasked, the subject must be discontinued from the study. Additionally, the sponsor and or designee must be notified.

11. STUDY SCHEDULE AND PROCEDURES

11.1. Study Schedule

The study schedule can be found in Appendix 1. Detailed information on study assessments is provided in Section 12.

11.2. Study Visits

11.2.1. Visit 1

All study-related procedures, including screening, will be completed in 1 visit.

11.2.1.1. Screening Procedures

The subject will complete the following assessments and procedures at Screening:

- Informed consent
- Demographics/medical history/concomitant medication review
- Slit-lamp biomicroscopy
- Laser retinal scan or fundoscopy; images will be taken during this procedure
- Optical coherence tomography; images will be taken during this procedure
- Tonometry (non contact)
- Ishihara color test
- Cover test
- Retinoscopy; results will be used as a basis for further refinement by phoropter refraction
- Refraction values (sphere, cylinder, axis) for OD and OS using the phoropter
- Best corrected visual acuity (LogMAR scores for OD, OS, and OU) assessed using the phoropter refraction values and ETDRS eye chart; subjects are eligible to participate in the study only if their vision can be corrected to 20/20 (LogMAR 0.0)

All eye procedures will be completed without dilation using standard procedures.

11.2.1.2. Testing procedures

Once eligibility is confirmed, the subject will be enrolled and proceed with study testing procedures.

The following testing procedures and assessments will be completed:

- Refraction values (sphere, cylinder, axis) for OD and OS using the autorefractor
- Measurement of pupillary distance using the autorefractor; pupillary distance will be used for preparation of trial lens frames

- Refraction values (sphere, cylinder, axis) for OD and OS using the EyeQue VisionCheck; all subjects will be trained on how to use the EyeQue VisionCheck device prior to initiating testing

In order to obtain refraction values using the EyeQue VisionCheck, the subject will be required to take 1 practice test followed by a minimum of 3 saved tests for each eye using the EyeQue VisionCheck device and mobile app. After completion of a set of tests (1 test for each eye), the subject may elect to save or discard that set of tests. They may choose to discard for any reason which may include not following instruction, pressing the wrong button in error, etc. Each test consists of the subject looking through the VisionCheck device and using the app controls to fully overlap red and green bars at 9 different angles. After completion of all tests (1 practice test and 3 saved tests with each eye), the refraction values will be displayed on the mobile app. If the EyeQue system determines that the overall test results are unreliable, subjects may have to complete 3 additional tests per eye before the system may be able to provide refraction values. Subjects will not be allowed to complete more than 6 saved tests and 1 practice test with each eye. If the EyeQue system determines that the overall test results are unreliable, no values will be provided.

- Best corrected visual acuity (LogMAR scores for OD, OS, and OU) assessed using the ETDRS eyechart and trial lens frames produced from:
  - Phoropter refraction values
  - Autorefractor refraction values
  - EyeQue VisionCheck refraction values

    *Subject and assessor will be masked to the refraction values used to produce the trial lens frames
- Subject preference regarding each of the trial lens frames
- Adverse event recording

11.2.1.3. Early Termination

Unless otherwise indicated, subjects will be discontinued from the study if any of the following events occur:

- The subject wants to withdraw from the study.
- The subject is non-compliant with the study protocol
- The subject has no refraction values produced with the EyeQue VisionCheck device
- At the investigator's discretion, continued testing is medically contraindicated.

The reason(s) for premature discontinuation from the study will be recorded.

12. STUDY ASSESSMENTS

12.1. Efficacy Assessments

Results from all efficacy assessments will be recorded on the appropriate eCRF pages.

12.1.1. Best Corrected Visual Acuity

Best corrected visual acuity will be measured using trial lens frames prepared based on the refractive error measured by each device including the EyeQue VisionCheck, phoropter, and autorefractor. Best corrected visual acuity will be assessed using the ETDRS eye chart. For each subject, BCVA logMAR scores will be collected for OD, OS, and OU for each of the 3 trial lens frames.

12.1.2. Refraction Values

Refraction values (sphere, cylinder, axis) for OD and OS will be recorded for each subject using the EyeQue VisionCheck, phoropter, and autorefractor. The refraction values will be used to prepare 3 sets of trial lens frames.

12.1.3. Subject Preference

Subjects will be asked which of the 3 trial lens frames affords them the best overall visual acuity. Subjects will be asked to order the trial lens frames by which frame(s) provides the best vision. A tie is permitted when a subject feels 2 or more frames afford indistinguishable differences in visual acuity.

12.2. Safety Assessments

All subjects who enter the study will be assessed for safety. Safety will be monitored by observation of and direct inquiry regarding AEs during the study visit.

12.2.1. Adverse Events

All AEs, ADEs, and SAEs will be collected from the start of informed consent through the end of the study visit. Details regarding AE definitions, collection, recording, and reporting are found in Section 12.3.

12.2.2. Demographics and Medical History

Demographic information relating to the subject's sex, age, race, ethnicity, and medical history will be collected during the Screening procedures and recorded on the appropriate eCRF page.

12.2.3. Concomitant Medications/Therapies

All concomitant medications/therapies will be recorded in the subject source documentation. The prohibited and/or allowed concomitant medications/therapies for the study are discussed in Section 10.1.

12.3. Adverse Events

12.3.1. Adverse Events, Adverse Device Effects, and Serious Adverse Events

Adverse events will be recorded throughout the study and will be coded using the Medical Dictionary for Regulatory Activities (MedDRA).

The investigator is responsible for the detection and documentation of AEs and ADEs. For all AEs/ADEs, the investigator must pursue and obtain information adequate to determine the outcome of the AE and to assess whether the AE meets the criteria for classification as an SAE requiring immediate notification to the sponsor or its designated representative.

12.3.1.1. Definitions of Terms

12.3.1.1.1. Adverse Events

Any undesirable clinical occurrences observed in subjects during an investigational clinical study. In addition to novel events, an AE may be an exacerbation of a pre-existing medical condition that was present before the subject was assigned to a treatment group.

12.3.1.1.2. Serious Adverse Event

Adverse events considered serious are those that result in one or more of the following

- Death
- Immediately life-threatening

  NOTE: The term "life-threatening" refers to an event in which the subject was at immediate risk of death at the time of the event. It does not refer to an event that hypothetically might have caused death if it were more severe.
- Result in hospitalization or prolongation of an existing hospitalization
- Persistent or significant incapacity or substantial disruption of the ability to conduct normal life functions.
- Results in a congenital anomaly/birth defect
- Important medical events that are not fatal, life-threatening, or require hospitalization may be considered serious when, based upon appropriate medical judgment, they may jeopardize the subject and may require medical intervention to prevent one of the outcomes listed in this definition.

Non-serious adverse events are all other adverse events not deemed serious.

12.3.1.1.3. Adverse Device Effect

An adverse device effect is an AE that is suspected to be related to the device. Adverse device effects can be either anticipated, which means that they have been previously identified in this protocol or the investigator's brochure, or unanticipated.

12.3.1.1.4. Unanticipated Adverse Device Effect

An unanticipated ADE (UADE) is any serious adverse effect on health or safety, 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 application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

12.4. Severity of Adverse Events

The study site will grade the clinical severity of AEs experienced by study participants as either:

- Mild: Causes no limitation of usual activities
- Moderate: Causes some limitation of usual activities
- Severe: Prevents or severely limits usual activities

It is important to distinguish between serious and severe AEs. Severity is a measure of intensity whereas seriousness is defined by the regulatory criteria in Section 12.3.1.1.2.

12.5. Relationship to Test Article

An investigator's causality assessment is the determination of whether there exists a reasonable possibility that the investigational device caused or contributed to an AE and must be provided for all AEs (serious and non-serious).

The sponsor's determination of attribution will be used for reporting to the appropriate health authorities. The relation of an AE to study participation will be determined using the descriptors and definitions provided in Table 1.

Table 1: Attribution of adverse events

Not Related	The AE is clearly/most probably caused by other etiologies such as participant's underlying condition, therapeutic intervention or concomitant therapy, or the delay between administration and the onset of the AE is incompatible with a causal relation, or the AE started before administration (screening phase). Therefore, there is not a reasonable possibility that the AE was caused by the investigational device.
Related	There is a reasonable possibility that the AE was caused by the investigational device. The expression "reasonable possibility" is meant to convey in general that there are facts (evidence) or arguments to suggest a causal relationship.

The investigator should decide whether, in his or her medical judgment, there is a reasonable possibility that the event may have been caused by the investigational device. Any AE that is suspected to be related to the EyeQue VisionCheck, phoropter, or the autorefractor will be classified as an ADE.

12.6. Recording Adverse Events

All AEs, regardless of relatedness to the use of the test article, are to be recorded on the appropriate AE page (either serious or non-serious) in the eCRF throughout the study. All adverse effects during the study will be documented in the subject's medical record. This information will then be transcribed on the AE page of the eCRF by designated study personnel. Required information includes a description of the event, date of onset, date of resolution, the action taken to manage the AE, the subsequent outcome, and severity.

Adverse events resulting from concurrent illnesses, reactions to concurrent medications, or progression of disease states must also be reported.

All AEs/ADEs must be followed to adequate resolution or stabilization. If the AE/ADE has not resolved or stabilized by the time the subject completes the single study visit, the investigator will follow the status of the subject's AE/ADE for at least 7 days beyond the subject's final study visit, unless directed otherwise by the sponsor.

12.7. Reporting SAEs and Unanticipated Adverse Device Effects

For reporting of SAEs and UADEs, the following process ensures compliance with 21 CFR 812 and International Conference on Harmonisation (ICH) guidelines. Investigators and other study center staff must inform Rho Product Safety representatives of any SAE/UADE that occurs (whether or not attributable to the study drug) in the study within 24 hours of when he or she becomes aware of the SAE/UADE. It is the investigator's responsibility to ensure that SAE/UADE reporting procedures are followed appropriately. In addition, the investigator must ensure that these events are entered on the SAE/UADE eCRF via Rave electronic data capture (EDC) or via paper form, if Rave EDC is unavailable. The form will be entered into EDC or faxed to the Rho Product Safety personnel within 24 hours. The following variables will be recorded for each AE: verbatim/AE description, time and date for AE start and stop, maximum intensity, seriousness, causality rating, whether or not the AE caused the subject to discontinue, and the outcome.

Medical Monitor and Emergency Contact Information:
Rho, Inc. Medical Monitor
Email: MedicalMonitorSupport@rhoworld.com

Serious Adverse Event Reporting Contact Information:
Rho, Inc. Safety Group Email: rho_productsafety@rhoworld.com

Serious Adverse Event Help Line: 1-888-746-7231
Serious Adverse Event Fax Line: 1-888-746-3293

The investigator is responsible for informing the IRB of SAEs and UADEs as per local requirements, as well as according to applicable regulations.

12.8. Reporting SAEs and Unanticipated Adverse Device Effects to Health Authorities

The sponsor will forward all reportable SAEs/UADEs to the appropriate regulatory authorities and participating investigators according to 21 CFR 812 and any other applicable regulations.

12.9. Medical Emergency

In a medical emergency requiring immediate attention, study center staff will apply appropriate medical intervention, according to standards of care.

An investigator shall notify the Medical Monitor and the reviewing IRB of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency. Such notice shall be given as soon as possible, but in no event later than 1 business day after the emergency occurred. Except in such an emergency, prior approval by the sponsor is required for changes in or deviations from a plan. All deviations must be documented.

13. STATISTICS

13.1. Power and Sample Size Determination

Approximately 200 subjects will be enrolled in this study to achieve a minimum of 100 evaluable subjects to assess the effectiveness and safety of the EyeQue VisionCheck. The initial cohort included 39 subjects; therefore, approximately 160 additional subjects will be enrolled in the study. Based on prior study data, rejection of non-inferiority bounds of 0.1 LogMAR (one line) and 0.05 LogMAR (one-half line) would require approximately 10 and 40 subjects, respectively, with 90% power on the BCVA from the resulting lens from each approach. This assumes the devices are roughly equivalent and the standard deviation (SD) is 0.077; these data are based on a previous version of the EyeQue VisionCheck device tested against an autorefractor. The proposed sample size has been inflated to allow for the possibility that a larger standard deviation will be observed in the current study, as well as to allow for comparisons within each stratum. A software error in the EyeQue app was identified and the algorithm for the EyeQue app was updated with more stringent parameters which may also impact the number of evaluable subjects. Due to the updates to the parameters, there may be additional subjects for which EyeQue VisionCheck refraction values are not produced, leading to an increase in the number of subjects that will not be evaluated for the primary endpoint. Of the approximately 160 additional subjects that will be enrolled in the study, it is anticipated that approximately 60 subjects will not be evaluable due to failing screening or not having refraction values produced with the EyeQue VisionCheck. Additionally, the larger sample size provides a sufficiently robust database for investigations of the secondary outcomes and descriptions of the EyeQue VisionCheck's performance characteristics.

13.2. Analysis Populations

Two analysis populations are defined for this study.

Modified Intent to Treat Population: All subjects that perform BCVA for trial frames with test lenses based on both phoropter and EyeQue VisionCheck.

Safety Population: All subjects that meet the screening criteria and are enrolled in the study.

After enrollment in this study was initiated, a software error was identified in the EyeQue app used with the EyeQue VisionCheck. The software error was corrected and the algorithm for the EyeQue app was updated. An initial cohort of 39 subjects was enrolled in the study prior to these changes being implemented. Due to these EyeQue app updates, this initial cohort of 39 subjects will be excluded from the analysis populations and any safety information for these subjects will be listed separately.

13.3. Efficacy Analyses

Best corrected visual acuity will be assessed independently for each eye and the worse value for each test lens set and subject will be selected for the primary analysis. Each subject's BCVA LogMAR score from the phoropter-based lenses will be subtracted from the BCVA LogMAR

score from the EyeQue VisionCheck-based lenses. The mean, SD, and two-sided 95% confidence interval (CI) will be reported across all subjects for worst eye, OD, OS, and OU, and if the upper bound (one sided 95% CI) does not include the value 0.1 for the worst eye comparison, then non-inferiority will be declared. This will be repeated using BCVA scores from the autorefractor-based lenses and EyeQue VisionCheck-based lenses.

Raw refraction values for the phoropter and VisionCheck will be plotted and Pearson correlations calculated. This will be repeated using autorefractor and EyeQue VisionCheck values.

Subject preference data will be tabulated with counts and percentages of subjects that considered the EyeQue VisionCheck trial lenses better as well as the counts and percentages of subjects that considered the EyeQue VisionCheck trial lenses better or equal.

Analyses will be repeated for each age stratum including ages 30 through 65 and ages 45 through 65.

13.4. Safety Analyses

13.4.1. Adverse Events

Adverse events, ADEs, UADEs, and SAEs will be reported with counts and percentages. Adverse events that can be associated with a particular device will be reported separately from those without clear attribution. Adverse events will be coded using MedDRA terminology. A subject experiencing more than 1 instance of an event will be counted only once for that event. Analyses will be repeated for each age stratum including ages 30 through 65 and ages 45 through 65. Unanticipated ADEs will be flagged in the by-subject listings of all AEs.

14. DIRECT ACCESS TO SOURCE DATA/DOCUMENTS

The investigator/institution shall provide direct access to source data/documents for study-related monitoring, audits, IRB review, and regulatory inspection.

14.1. Study Monitoring

According to ICH Good Clinical Practice (GCP) guidelines, the sponsor of the study is responsible for ensuring the proper conduct of the study with regard to protocol adherence and validity of data recorded on the eCRFs. The sponsor or its designee is responsible for assigning the study monitor(s) to this study.

The investigator shall permit the study monitor to review study data as frequently as deemed necessary to ensure that data are being recorded in an adequate manner and that protocol adherence is satisfactory.

The investigator shall access medical records for the study monitor so that entries in the eCRFs may be verified. The investigator, as part of his/her responsibilities, is expected to cooperate with the sponsor or designee in ensuring that the study adheres to GCP requirements.

The investigator may not recruit subjects into the study until such time that a site visit has been made by an EyeQue or designee monitor to conduct a detailed review of the protocol and eCRF and study instructions.

14.2. Audits and Inspections

Authorized representatives of EyeQue, a regulatory authority, an IRB or an IEC may visit the site to perform audits or inspections, including source data verification. The purpose of an EyeQue audit or inspection is to systematically and independently examine all study-related activities and documents to determine whether these activities were conducted, and data were recorded, analyzed, and accurately reported according to the protocol, ICH GCP guidelines, and any applicable regulatory requirements. The investigator should contact EyeQue immediately if contacted by a regulatory agency about an inspection.

14.3. Institutional Review Board/Independent Ethics Committee

Prior to the start of the study, the investigator is responsible for ensuring that the protocol and informed consent form (ICF) have been reviewed and approved by a relevant IRB/IEC. The IRB/IEC shall be appropriately constituted and perform its functions in accordance with FDA, ICH GCP, and local requirements as applicable.

The IRB shall approve all protocol amendments (except for logistical or administrative changes), written ICFs and documents updates, subject recruitment procedures (e.g. advertisements), written information to be provided to the subjects, available safety information, information about payment and compensation available to subjects, the investigator's curriculum vitae and/or other evidence of qualifications and any other documents requested by the IRB and regulatory authority (competent authority) as applicable.

When required, the IRB and regulatory authority must be notified of completion or termination of this study, and sent a copy of the study synopsis in accordance with necessary timelines.

15. QUALITY CONTROL AND QUALITY ASSURANCE

The sponsor will implement and maintain quality control procedures to ensure that this study is conducted and data are generated, documented, and reported in compliance with the protocol, and applicable regulatory requirements.

The sponsor or designee will routinely conduct monitoring and/or auditing visits to the study site to verify the adherence to the study protocol, the protection of the rights and well-being of the subjects; and the accuracy and completeness of reported study data recorded on the source documentation. A suitable qualified representative will monitor the clinical investigation as follows:

- Conduct pre-study evaluation visits to verify site qualifications.
- Conduct site initiation visit after IRB/IEC approval and at or before first subject visit.
- Conduct periodic monitoring visits.
- Compare eCRFs to source documents for accuracy, completeness, legibility, and logic.
- Review investigator's files for accuracy, currency, and completeness.
- Conduct ongoing review of site for continued ability to conduct the study.
- Ensure that informed consents are obtained.
- Ensure that IRB/IEC review is current.
- Ensure protocol compliance and document any deviations or violations.
- Assure untoward effects are reported.
- Conduct closeout visit after all subject visits are complete and data in eCRFs are confirmed.
- Follow-up with all ongoing issues, as necessary.
- Prepare reports of visits.

16. ETHICS

16.1. Ethics Review

The protocol and supporting documents for this study will be reviewed and approved by an appropriately constituted IRB/IEC prior to study initiation. The investigator will not start this study before providing EyeQue with evidence of IRB approval.

The investigator will promptly report to the IRB all changes in the research activity and all unanticipated problems involving risks to subjects. The investigator will not make any changes in the research without IRB approval, except where necessary to eliminate apparent immediate hazards to the subjects.

The investigator is responsible for informing the IRB of any amendment to the protocol in accordance with local requirements. In addition, the IRB or IEC must approve all advertising used to recruit patients for the study. The protocol must be re-approved by the IRB or IEC upon receipt of amendments and annually, as local regulations require.

A progress report will be submitted by the investigator to the IRB or IEC at intervals specified by the IRB/IEC, but not less than annually. A copy of this progress report will be sent to EyeQue. After completion of the study, the investigator will submit a final report to the IRB/IEC.

16.2. Ethical Conduct of the Study

The study will be conducted in accordance with GCP as contained in the US CFR governing the protection of human subjects (Title 21, Part 50).

EyeQue is responsible for the ongoing safety evaluation of the product and will expedite the notification of all participating investigators and regulatory authorities of findings that are reportable, or could alter the IRB/IEC approval to continue the study.

16.3. Written Informed Consent

The investigator will ensure that written informed consent is obtained from each participant in accordance with applicable regulations.

Subjects will be interviewed at the initial screening visit by qualified staff at the site and will be provided with a full description of the nature and purpose of the study. The subject will be given adequate time to consider the risks and benefits associated with participation in the study. Each subject will provide written informed consent prior to participating in any study procedures. The original signed consent forms will be retained on file at the clinical site and a copy will be given to the subject. Case histories (subject charts) will also document that informed consent was obtained prior to the subject's participation in the study.

16.4. Authorization to Disclose Protected Health Information

If required under Health Insurance Portability and Accountability Act regulations, or other applicable regulations subjects will be informed of the following information:

- the sponsor of the study;
- any contractors that may be involved in the study;
- the purpose of the protected health information (PHI) being collected;
- the possibility that the PHI may be re-disclosed;
- the duration of the authorization;
- the subject's rights to revoke the authorization; and,
- the right of the subject to refuse signature and limit access to PHI during the conduct of the study (US 21 CFR Title 45, Parts 160 and 164).

Authorization to disclose PHI must be obtained before the subject enters the study.

17. DATA HANDLING AND RECORDKEEPING

17.1. Electronic Case Report Forms/Source Data Handling

The investigator shall be provided with standardized eCRFs and shall ensure that all data from subject visits are promptly entered into the eCRFs in accordance with the specific instructions given. The investigator must sign each eCRF to verify the integrity of the data recorded.

The investigator must maintain all source documents.

17.2. Inspection of Records

The investigator agrees that EyeQue or its designated agents, the IRB/IEC, and the FDA (or other governmental regulatory entity) will have reasonable access to study source documentation for audit and review both during and after completion of the study. These monitoring visits provide EyeQue with the opportunity to evaluate the progress of the study; to verify the accuracy and completeness of eCRFs; to assure that all protocol requirements, applicable regulations, and investigator's obligations are being fulfilled; and to resolve any inconsistencies in the study records. All participating subjects will be required to signify their approval to permit inspection of their medical records by representatives of EyeQue, the IRB/IEC, and regulatory agencies, as needed.

17.3. Retention of Records

The investigator shall maintain adequate records for the study including copies of eCRFs for individual subjects, medical records, consent forms, test article disposition records, safety reports, information regarding participants who discontinued, and other pertinent data. The investigator shall maintain these records for a period of at least 2 years after the last approval of a marketing application and until there are no pending or contemplated marketing applications, or at least 2 years have elapsed since the formal discontinuation of clinical development of the test article. These records should be retained for a longer period if required by the applicable regulatory requirements or by an agreement with the sponsor. The sponsor will inform the investigator/institution as to when these records no longer need to be retained.

18. PUBLICATION POLICY

This research may be submitted for publication. Details of any publication and disclosure terms are addressed in a separate agreement with investigators.

19. LIST OF REFERENCES

Pascolini D, Mariotti SP. Global estimates of visual impairment: 2010. Br J Opthalmol. 2012 May; 96(5): 614-8.

Pamplona V., Menezes de Oliveira Neto M., Mohan A., Raskar R. U.S. Patent No.

US8783871 B2. 2014.

World Health Organization (WHO). Blindness and vision impairment fact sheet. 11 October 2018. Online.

20. APPENDICES

APPENDIX 1. SCHEDULE OF ASSESSMENTS

	Assessment	Visit 1 (Screening and Testing)
Screening	Informed consent	**X**
	Demographics/medical history/concomitant medication review	**X**
	Slit-lamp biomicroscopy	**X**
	Laser retinal scan or fundoscopy [1]	**X**
	Optical coherence tomography[1]	**X**
	Non-contact tonometry	**X**
	Ishihara color test	**X**
	Cover test	**X**
	Retinoscopy[2]	**X**
	Refraction values using the phoropter	**X**
	BCVA[3] assessed using the phoropter and eye chart	**X**
Testing	Refraction values using the autorefractor	**X**
	Measurement of pupillary distance	**X**
	Refraction values using the EyeQue VisionCheck[4]	**X**
	BCVA[3] using trial frames[5] produced from: • phoropter refraction values • autorefractor refraction values • EyeQue VisionCheck refraction values	**X**
	Subject preference regarding each of the trial lens frames	**X**
	Adverse event recording	**X**

BCVA = best corrected visual acuity; ETDRS = Early Treatment Diabetic Retinopathy Study; OD = oculus dexter, right eye; OS = oculus sinister, left eye; OU = oculus uterque, both eyes

Note: All eye procedures will be completed without dilating the eye.

[1] Images will be taken during this procedure.

[2] Results will be used as a basis for further refinement by phoropter refraction.

[3] Best corrected visual acuity will be measured using the ETDRS eye chart; values will be recorded for OD, OS, and OU.

[4] All subjects will be trained on how to use the EyeQue VisionCheck device prior to initiating testing.

[5] Trial frames prepared from refraction values from each of the 3 devices will be provided to the subjects in a masked fashion and BCVA for each trial lens frames will be measured.