PROTOCOL CSP-034

A PROSPECTIVE CONTROLLED MULTI-CENTER CLINICAL STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF PERFORMING 0.50 DIOPTER ASTIGMATISM CORRECTION ON THE COMMERCIALLY AVAILABLE RXSIGHT LIGHT ADJUSTABLE LENS (LAL)

RxSight, Inc.
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Aliso Viejo, CA 92656

Version 04
May 23, 2019

I have read and agree to follow the procedures as outlined in this protocol.

This protocol contains confidential proprietary information with respect to RxSight products and clinical trials. I agree to hold this information in confidence and not to disclose it to any third parties for a period of five years from the date of this agreement, or until this information becomes a matter of public knowledge through no action or failure on my part to maintain its confidentiality.

_____
Site Name

_____ _____
Signature *Date*

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[redacted]

RXSIGHT, INC.

PROTOCOL NO. CSP-034

A PROSPECTIVE CONTROLLED MULTI-CENTER CLINICAL STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF PERFORMING 0.50 DIOPTER ASTIGMATISM CORRECTION ON THE COMMERCIALLY AVAILABLE RXSIGHT LIGHT ADJUSTABLE LENS (LAL)

1 STUDY SYNOPSIS

1.1 STUDY OBJECTIVE

The primary objective of this study is to evaluate the safety and effectiveness of performing 0.50 D cylinder correction on the RxSight Light Adjustable Lens (LAL) in patients who have undergone implantation with the FDA approved, commercially available LAL. In preparation for the first LDD light adjustment treatment, all patients undergo manifest refraction. Patients found to have an eye with 0.50 D of manifest cylinder will be invited to participate in the clinical study where they will receive a light adjustment treatment of their spherical refractive error combined with 0.50 D of manifest cylinder (LAL treatment group). Only one eye of a patient may undergo study light treatments. [redacted]

1.2 STUDY POPULATION

The study population will consist of a minimum of 25 eyes in 25 subjects. Each subject will have been implanted with the commercially available LAL, have 0.50 D of manifest cylinder measured in one eye prior to their first light adjustment treatment, and agree to receive a light adjustment treatment of their spherical refractive error combined with 0.50 D of manifest cylinder (LAL treatment group). All study eyes must meet all the applicable inclusion criteria and none of the exclusion criteria. Only one eye of a patient may undergo study light treatments. The historical control groups will consist of all eyes that meet the requirements for inclusion in the respective group and each group will include a minimum of 25 eyes.

1.3 STUDY DESIGN

A prospective, controlled, multi-center, clinical study will be conducted at a maximum of 2 sites located in the United States. Subjects will be followed for a 3 month period as the underlying safety and effectiveness of the LAL and LDD were established in P160055. A minimum of 10 subjects will undergo study light treatment at each participating site.

The study population will consist of patients who have undergone implantation of a commercially available LAL after cataract extraction, who have 0.50 D of manifest cylinder measured in one eye prior to their first light adjustment treatment, who wish to have their 0.50 D of manifest cylinder treated, and who meet all study inclusion/exclusion criteria for study participation. If a subject's first eye receives the investigational light treatment, then this subject's fellow eye immediately becomes ineligible for future study enrollment and investigational light treatment. If a subject enrolls in this study and their first eye does not end up receiving the investigational light treatment, then (1) the subject is exited from this study, and (2) the subject may subsequently re-enroll in this study (and sign a new informed consent form) for evaluation and potential investigational treatment of the fellow eye.

If it is determined that an eye of a patient may be eligible to participate, delegated and trained study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant.

The patient is enrolled upon signing the informed consent and study specific visual testing at the Study Visit #1, including manifest refraction performed by two independent examiners on a 4 meter lane, will be performed.

If at any other time during the Study Visit #1, the subject's eye does not meet inclusion or exclusion criteria, the study exam for that subject should be discontinued and the subject will be exited from the study. Exited subjects will undergo light treatments per the PMA approved labeling. LAL subjects that meet all inclusion/exclusion criteria will receive a first light adjustment treatment (Adjustment #1) at Study Visit #1.

Light Delivery Device (LDD) Light Treatments
All light treatments will be separated by 3-7 days.

Adjustment #1
The study eye will receive an adjustment #1 light treatment based on the final refraction as determined above.

Adjustment #2 visit
A second adjustment treatment will also be based on the measured manifest refractions performed by two independent examiners. [redacted]

Adjustment #3 (if necessary)
The same refraction process followed by two independent examiners at the Adjustment #2 visit will be followed. [redacted]

Depending on the adjustment(s) performed, subjects will receive two or three adjustments.

Lock-in light treatments
The study eye will receive a minimum of one lock-in treatment and a lock-in #2 may be performed, if necessary.

Examinations will occur at regular intervals over a 3 month period to evaluate the performance of 0.50 D cylinder treatments on the LAL. At the Postop Month 3 visit, two independent examiners will perform the same refraction process as performed at the Adjustment #2 and #3 visits to determine the final refraction.

1.4 INCLUSION CRITERIA

- A patient who has undergone uncomplicated implantation of the PMA approved LAL in a commercial setting in which all surgeons and IDE Investigators:
    - Have received and read the FDA-approved physician labeling (Directions for Use and LDD Operator's Manual);
    - [redacted]
    - Have implanted the LAL in accordance with instructions in the labeling and [redacted] and used the FDA-approved

insertion device (Nichamin III Foldable Lens Inserter with Nichamin II Foldable Lens Insertion Forceps);
    - Have confirmed that the patient was within the intended population as specified in the Indications for Use statement
- The patient received the FDA-approved patient information booklet prior to LAL implantation.
- The patient received and was trained in use of the UV spectacles that are in compliance with all FDA labeling.
- A study eye implanted with the PMA approved LAL that has not undergone any previous LDD treatments.
- A study eye that was implanted with the PMA approved LAL between 17-24 days prior to Study Visit #1/Adjustment #1.
- A study eye with manifest refraction cylinder of 0.50 D measured by two independent examiners at the Adjustment #1 visit prior to the first light adjustment treatment.
- Sign a written Informed Consent form and be willing to receive light treatment for their 0.50 D of cylinder.
- Between the ages of 40 and 80 inclusive on the day the informed consent form is signed.
- Study eye with best corrected distance visual acuity (BCDVA) of 20/20 or better measured at the Adjustment #1 visit prior to the first light adjustment treatment.
- Study eye with clear intraocular media.
- Good vision in the fellow eye with BCDVA 20/40 or better.
- Willing and able to comply with the requirements for study specific procedures and visits.
- Study eye with average dilated pupil diameter of ≥7.0 mm.

1.5 EXCLUSION CRITERIA

- Clinically significant dry eye syndrome (DES) in the study eye.
- Pre-existing macular disease in the study eye.
- Retinal degenerative disorder that is expected to cause future vision loss in the study eye.
- Diabetes with any evidence of retinopathy in the study eye.
- Evidence of glaucomatous optic neuropathy in the study eye.
- History of uveitis in the study eye.
- Significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma in the study eye.
- Corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20 in the study eye.
- Any corneal dystrophy including basement membrane dystrophy in the study eye.

- Keratoconus or suspected of having keratoconus in the study eye.
- Has undergone previous corneal or intraocular surgery in the study eye, except for the cataract surgery and eyes with previous pterygium excision are permitted as long as the pterygium did not extend more than 2mm onto the cornea from the limbus.
- Subjects with serious co-morbid conditions that in the judgment of the investigator makes inclusion in the study not in the best interest of the subject.
- Subjects taking systemic medication that may increase sensitivity to UV light such as tetracycline, doxycycline, psoralens, amiodarone, phenothiazines, chloroquine, hydrochlorothiazide, hypericin, ketoprofen, piroxicam, lomefloxacin, and methoxsalen. LDD treatment in patients taking such medications may lead to irreversible phototoxic damage to the eye. This is only a partial list of photosensitizing medications. Please evaluate all medications that the patient is taking for this effect prior to consideration for implantation.
- Subjects taking a systemic medication that is considered toxic to the retina such as tamoxifen.
- Subjects who the doctor believes will be unable to maintain steady fixation that is necessary for centration of the LDD light treatment in the study eye.
- Irregular astigmatism in the study eye.
- History of ocular herpes simplex virus in the study eye.
- Subject who has participated within another ophthalmic clinical trial within the last 3 months.
- Sutures used at the time of surgery to close the incision wound in the study eye.
- A study eye at time of screening noted with an ocular adverse event that could be negatively impacted by light treatment or negatively impact the effectiveness or safety of a light treatment. This includes corneal edema and superficial punctate keratitis (SPK) (Grade 3 (moderate) or more severe)), retinal conditions including diabetic retinopathy and cystoid macular edema, epithelial defect, and endophthalmitis.
- A study eye with any ongoing ocular adverse event.
- A study eye at time of screening noted with evidence of premature photopolymerization as evidenced as a zone on the lens surface.
- A study eye at time of screening noted with any evidence of posterior capsular opacity (PCO).

1.6 OUTCOME PARAMETERS

Effectiveness Parameters:

- Manifest refraction cylinder (MRCYL)
  Mean MRCYL of the LAL treatment group at Postop Month 3 will be compared to Mean MRCYL of the LAL historical control group and Monofocal IOL historical control group at Postop Month 6.
- Change in manfiest refraction cylinder (MRCYL)
  Mean change in MRCYL between baseline (Visit #1/Adjustment #1) and Postop Month 3 for the LAL treatment group will be compared to Mean change in MRCYL between baseline (Adjustment #1 (LAL)/17-21 days postop (Control)) and Postop Month 6 of the LAL historical control group and Monofocal IOL historical control group.

The comparison will be made by descriptive statistics only.

Safety Parameters:

- Incidence of ocular serious adverse events including persistent and cumulative events defined per ISO 11979-7

The incidence of all other adverse events will also be presented.

1.7 EXAMINATION SCHEDULE

Evaluation	
Study Visit #1/Adjustment #1	Day 0 (17 to 24 days post-implantation with the LAL)
Adjustment #2	3 to 7 days post Adjustment #1 Visit
Adjustment #3, if needed	3 to 7 days post Adjustment #2 Visit
Lock-in #1	3 to 7 days post final adjustment Visit
Lock-in #2, if needed	3 to 7 days post lock-in #1 Visit
Post Lock-In	7-14 days post final lock-in Visit
Postop Month 3	Days 75 to 120 post-implantation with the LAL

Unscheduled visits falling outside the designated ranges for scheduled visits will be considered "interim" visits for data recording purposes and a report form will be completed.

1.8 CLINICAL PARAMETERS:

Clinical assessments when indicated will be performed in the following order:

1. Demographics
2. Ocular history including medications
3. Subjective symptoms/complaints (subject reported)

4. Compliance with UV spectacles
5. Autorefraction
6. Corneal Topography
7. Monocular UCDVA
8. Manifest Refraction
9. Monocular best corrected distance visual acuity (BCDVA)

[redacted]

12. Intraocular pressure
13. Slit Lamp Examination
14. Fundus Examination
15. Dilated pupil diameter
16. Spectral Domain OCT (if needed)
17. Adverse Event

ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
BCDVA	Best Corrected Distance Visual Acuity
CCC	Continuous Circular Capsulorhexis
CDRH	Center for Devices and Radiological Health
CFR	Code of Federal Regulations
CI	Confidence Interval
CRF	Case Report Form
CRO	Contract Research Organization
CTS	Clinical Trial Suite
D	Diopter
DD	Device Deficiency
DES	Dry Eye Syndrome
DEQ	Defocus Equivalent
EDC	Electronic Data Capture
ETDRS	Early Treatment Diabetic Retinopathy Study
EV	Error Vector
FDA	Food and Drug Administration
GCP	Good Clinical Practice
ICD	Informed Consent Document
IDE	Investigational Device Exemption
IOL	Intraocular Lens
IOP	Intraocular Pressure
IRB	Institutional Review Board
IRC	Intended Refractive Correction
ISO	International Organization for Standardization
ITT	Intent To Treat
LAL	RxSight Light Adjustable Lens
LDD	Light Delivery Device
MR	Manifest Refraction
MRCYL	Manifest Refraction Cylinder
MRSE	Manifest Refraction Spherical Equivalent
OCT	Optical Coherence Tomography
PCO	Posterior Capsular Opacity
PD	Protocol Deviation
PHI	Protected Health Information
PMA	Premarket Application

SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDT	Source Document Template
SE	Spherical Equivalent
SIRC	Surgical Induced Refractive Correction
SPE	Safety and Performance Endpoints
SPK	Superficial Punctate Keratitis
SSI	Secondary Surgical Intervention
UADE	Unanticipated Adverse Device Effect
UCDVA	Uncorrected Distance Visual Acuity
UV	Ultraviolet
VA	Visual acuity

2 INTRODUCTION AND RATIONALE

The commercially available RxSight LAL and LDD system that was approved in P160055 and modified in approved Supplements allows for correction of spherical (-2.0 D to +2.0 D) and astigmatic refractive errors (-0.75 D to -2.0 D) to improve uncorrected visual acuity. As seen in the results of the Phase III study conducted under G100240, eyes with <0.75 D of cylinder had lower rates of UCVA of 20/20 or better compared to eyes in the 0.75 D-1.25 D group. At 6 months postoperatively, eyes with <0.75 D of cylinder who did not undergo cylinder treatment had UCVA of 20/20 or better in 67.6% (71/105) while those eyes in the 0.75 D-1.25 D group who did undergo cylinder treatment had UCVA of 20/20 or better in 76.8% (156/203) of cases. RxSight would like to receive FDA approval to allow treatment of 0.50 D of cylinder during light treatments.

As the RxSight LAL and LDD are commercially approved, this clinical study protocol proposes allowing commercial implantation of the LAL with evaluation of the manifest refraction cylinder prior to Adjustment #1. If the patient has a cylinder of exactly 0.50 D as measured by two independent refractionists, they will be offered participation in the clinical study to have their 0.50 D of cylinder treated. Given that these are commercial patients who will already be undergoing light treatment for their remaining refractive error there are no additional risks based on participation in the clinical study and the only difference in treatment is that they will receive treatment for 0.50 D of cylinder rather than based on the MRSE.

Treatment results will be compared to eyes implanted during the clinical study conducted under IDE G100240 and reported in P160055. The patient population studied in this IDE is the same as the population of patients who will be eligible for implantation with the commercially available LAL. [redacted]

2.1 CLINICAL STUDIES PERFORMED WITH PRIOR VERSION OF THE LIGHT ADJUSTABLE LENS AND LIGHT DELIVERY DEVICE

Phase III Study Conducted Under IDE G100240

A 600 eye prospective, randomized, controlled, multi-center clinical trial of the LAL and LDD designed to evaluate safety and effectiveness over a 12-month period was conducted at 17 sites. In addition to the visual correction of aphakia, reduction in residual spherocylindrical refractive error and improvement in uncorrected visual acuity were evaluated following LAL implantation and subsequent refractive adjustment of the LAL by the LDD.

Eyes with ≥0.75 and ≤2.5 diopters (D) of keratometric cylinder were randomly assigned to receive either the LAL or a commercially available, posterior chamber, non-accommodating, control monofocal IOL. Six hundred eyes were implanted with 403 eyes randomized to the LAL group and 197 eyes to the Control group.

Co-primary effectiveness endpoints included percent reduction in manifest cylinder, percent mean absolute reduction in manifest refraction spherical equivalent (MRSE), and rotation of the LAL. All primary effectiveness endpoints compared pre-adjustment (LAL) or 17-21 days (Control) to 6 months postoperatively and the first two endpoints compared results between the LAL and Control groups. All three co-primary effectiveness endpoints were met with a p-value <0.0001. The difference in means for percent reduction in manifest cylinder was 54.7%, with a p-value <0.0001. The difference in means for percent reduction in absolute MRSE was 41.1% with a p-value <0.0001. Rotation of the LAL of ≤5 degrees was observed in 96.1% of LAL implanted eyes with both the upper and lower bound of the 95% confidence interval exceeding the requirement of 90%.

100% of eyes in both the LAL and Control groups had BSCVA of 20/40 or better, exceeding the historic grid rate of 92.5% (ISO 11979-7). The incidence of sight-threatening complications and adverse events for the LAL and Control groups were also below the threshold rates calculated from the 1-year historical grid for intraocular lenses (ISO 11979-7, Ophthalmic implants-Intraocular lenses- Part 7: Clinical investigations) except for the category of Secondary Surgical Interventions (SSI), which was significantly higher than the historical rate (p<.05).

On November 22, 2017, the Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) approved RxSight's premarket approval application (PMA) for the Light Adjustable Lens (LAL) and Light Delivery Device (LDD) system. This system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag; in adult patients:

- With pre-existing corneal astigmatism of ≥ 0.75 diopters
- Without pre-existing macular disease

The system also reduces the likelihood of clinically significant residual spherical refractive errors.

3 STUDY OBJECTIVE

The primary objective of this study is to evaluate the safety and effectiveness of performing 0.50 D cylinder correction on the RxSight Light Adjustable Lens (LAL) in patients who have undergone implantation with the FDA approved, commercially available LAL. In preparation for the first LDD light adjustment treatment, all patients undergo manifest refraction. Patients found to have an eye with 0.50 D of manifest cylinder will be invited to participate in the clinical study where they will receive a light adjustment treatment of their spherical refractive error combined with 0.50 D of manifest cylinder (LAL treatment group). Only one eye of a patient may undergo study light treatments. [redacted]

4 STUDY DESIGN

A prospective, controlled, multi-center, clinical study will be conducted at a maximum of 2 sites located in the United States. Subjects will be followed for a 3 month period as the underlying safety and effectiveness of the LAL and LDD was established in P160055. A minimum of 10 subjects will undergo study light treatment at each participating site.

The study population will consist of patients who have undergone implantation of a commercially available LAL after cataract extraction, who have 0.50 D of manifest cylinder measured in one eye prior to their first light adjustment treatment, who wish to have their 0.50 D of manifest cylinder treated, and who meet all study inclusion/exclusion criteria. If a subject's first eye receives the investigational light treatment, then this subject's fellow eye immediately becomes ineligible for future study enrollment and investigational light treatment. If a subject enrolls in this study and their first eye does not end up receiving the investigational light treatment, then (1) the subject is exited from this study, and (2) the subject may subsequently re-enroll in this study (and sign a new consent form) for evaluation and potential investigational treatment of the fellow eye.

If it is determined that an eye of a patient may be eligible to participate, delegated and trained study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant.

The patient is enrolled upon signing the informed consent and study specific visual testing at the Study Visit #1, including manifest refraction performed by two independent examiners on a 4 meter lane, will be performed.

[redacted]

[redacted]

If at any other time during the Study Visit #1, the subject's eye does not meet inclusion or exclusion criteria, the study exam for that subject should be discontinued and the subject will be exited from the study. Exited subjects will undergo light treatments per the PMA approved labeling. LAL subjects that meet all inclusion/exclusion criteria will receive a first light adjustment treatment (Adjustment #1) at Study Visit #1.

Depending on the adjustment(s) performed, subjects will return for two or three light adjustment treatments. The study eye will receive a minimum of one lock-in treatment and a lock-in #2 may be performed, if necessary. Examinations will occur at regular intervals over a 3 month period to evaluate the performance of 0.50 D cylinder treatments on the LAL. At the Postop Month 3 visit, two independent examiners will perform the same refraction process as performed at the Adjustment #2 and #3 visits to determine the final refraction.

DURATION OF STUDY

Each subject will participate in the study for approximately 4 months. [redacted]

STUDY SITE

The study will be performed in ophthalmology clinics. The investigators will be ophthalmic surgeons trained in cataract surgery with implantation of intraocular lenses. Study responsibilities will be registered in a delegation log that will be kept at the investigational site. The overall responsibility at the study clinic remains with the investigator.

5 OUTCOME PARAMETERS

5.1 EFFECTIVENESS PARAMETER

- Manifest refraction cylinder (MRCYL)

Mean MRCYL of the LAL treatment group at Postop Month 3 will be compared to Mean MRCYL of the LAL historical control group and Monofocal IOL historical control group at Postop Month 6.

- Change in manfiest refraction cylinder (MRCYL)
  Mean change in MRCYL between baseline (Visit #1/Adjustment #1) and Postop Month 3 for the LAL treatment group will be compared to Mean change in MRCYL between baseline (Adjustment #1 (LAL)/17-21 days postop (Control)) and Postop Month 6 of the LAL historical control group and Monofocal IOL historical control group. The comparison will be made by descriptive statistics only.

5.2 SAFETY PARAMETERS

- Incidence of ocular serious adverse events including persistent and cumulative events defined per ISO 11979-7

The incidence of all other adverse events will also be presented.

6 STUDY POPULATION

The study population will consist of a minimum of 25 eyes in 25 subjects. Each subject will have been implantated with the commercially available LAL, have 0.50 D of manifest cylinder measured in one eye prior to their first light adjustment treatment, and agree to receive a light adjustment treatment of their spherical refractive error combined with 0.50 D of manifest cylinder (LAL treatment group). All study eyes must meet all the applicable inclusion criteria and none of the exclusion criteria. Only one eye of a patient may undergo study light treatments. [redacted]

6.1 INCLUSION CRITERIA

- A patient who has undergone uncomplicated implantation of the PMA approved LAL in a commercial setting in which all surgeons and IDE investigators:
  - Have received and read the FDA-approved physician labeling (Directions for Use and LDD Operator's Manual);
  - [redacted]
  - Have implanted the LAL in accordance with instructions in the labeling [redacted] and used the FDA-approved insertion device (Nichamin III Foldable Lens Inserter with Nichamin II Foldable Lens Insertion Forceps);
  - Have confirmed that the patient was within the intended population as specified in the Indications for Use statement.
- The patient received the FDA-approved patient information booklet prior to LAL implantation.

- The patient received and was trained in use of the UV spectacles that are in compliance with all FDA labeling.
- A study eye implanted with the PMA approved LAL that has not undergone any previous LDD treatments.
- A study eye that was implanted with the PMA approved LAL between 17-24 days prior to Study Visit #1/Adjustment #1.
- A study eye with manifest refraction cylinder of 0.50 D measured by two independent examiners at the Adjustment #1 visit prior to the first light adjustment treatment.
- Sign a written Informed Consent form and be willing to receive light treatment for their 0.50 D of cylinder.
- Between the ages of 40 and 80 inclusive on the day the informed consent form is signed.
- Study eye with best corrected distance visual acuity (BCDVA) of 20/20 or better measured at the Adjustment #1 visit prior to the first light adjustment treatment.
- Study eye with clear intraocular media.
- Good vision in the fellow eye with BCDVA 20/40 or better.
- Willing and able to comply with the requirements for study specific procedures and visits.
- Study eye with average dilated pupil diameter of ≥7.0 mm.

6.2 EXCLUSION CRITERIA

- Clinically significant dry eye syndrome (DES) in the study eye.
- Pre-existing macular disease in the study eye.
- Retinal degenerative disorder that is expected to cause future vision loss in the study eye.
- Diabetes with any evidence of retinopathy in the study eye.
- Evidence of glaucomatous optic neuropathy in the study eye.
- History of uveitis in the study eye.
- Significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma in the study eye.
- Corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20 in the study eye.
- Any corneal dystrophy including basement membrane dystrophy in the study eye.
- Keratoconus or suspected of having keratoconus in the study eye.
- Has undergone previous corneal or intraocular surgery in the study eye, except for the cataract surgery and eyes with previous pterygium excision are permitted as long as the pterygium did not extend more than 2mm onto the cornea from the limbus.
- Subjects with serious co-morbid conditions that in the judgment of the investigator makes inclusion in the study not in the best interest of the subject.

- Subjects taking systemic medication that may increase sensitivity to UV light such as tetracycline, doxycycline, psoralens, amiodarone, phenothiazines, chloroquine, hydrochlorothiazide, hypericin, ketoprofen, piroxicam, lomefloxacin, and methoxsalen. LDD treatment in patients taking such medications may lead to irreversible phototoxic damage to the eye. This is only a partial list of photosensitizing medications. Please evaluate all medications that the patient is taking for this effect prior to consideration for implantation.
- Subjects taking a systemic medication that is considered toxic to the retina such as tamoxifen.
- Subjects who the doctor believes will be unable to maintain steady fixation that is necessary for centration of the LDD light treatment in the study eye.
- Irregular astigmatism in the study eye.
- History of ocular herpes simplex virus in the study eye.
- Subject who has participated within another ophthalmic clinical trial within the last 3 months.
- Sutures used at the time of surgery to close the incision wound in the study eye
- A study eye at time of screening noted with an ocular adverse event that could be negatively impacted by light treatment or negatively impact the effectiveness or safety of a light treatment. This includes corneal edema and superficial punctate keratitis (SPK) (Grade 3 (moderate) or more severe)), retinal conditions including diabetic retinopathy and cystoid macular edema, epithelial defect, and endophthalmitis.
- A study eye with any ongoing adverse event.
- A study eye at time of screening noted with evidence of premature photopolymerization as evidenced as a zone on the lens surface.
- A study eye at time of screening noted with any evidence of posterior capsular opacity (PCO).

7 STUDY MATERIALS AND METHODS

7.1 DEVICE DESCRIPTION

RxSight's Light Adjustable Lens (LAL) is a silicone intraocular lens whose shape and focusing characteristics can be modified after implantation using an office-based UV light source, the RxSight Light Delivery Device (LDD), to improve uncorrected visual acuity.

7.1.1 RXSIGHT LIGHT ADJUSTABLE INTRAOCULAR LENS

The RxSight Light Adjustable Lens (LAL) is the identical device approved in P160055 and approved supplements. It will be implanted in a commercial environment.

The LAL is foldable posterior chamber, UV filtering, three-piece photoreactive silicone lens with blue PMMA (polymethylmethacrylate) modified-C haptics, a 6.0 mm biconvex optic with squared posterior edge, and an overall diameter of 13.0 mm. The LAL optic design (Figure 1) also features a UV filtering posterior surface layer, to further enhance the UV absorbing properties of the LAL lens and limit retinal exposure.

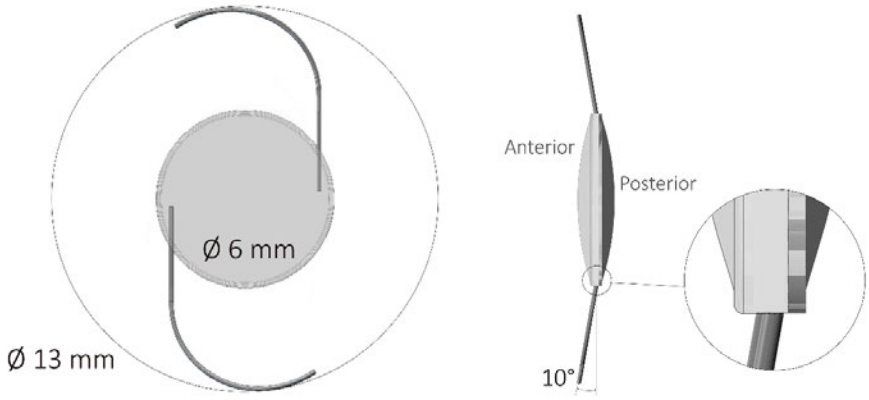

FIGURE 1: RXSIGHT LIGHT ADJUSTABLE LENS (LAL) (A) TOP VIEW AND (B) CROSS-SECTION VIEW OF THE OPTIC SHOWING LAL WITH A POSTERIOR LAYER

A summary of the LAL design characteristics is presented below:

Lens Optic

- Material: Photo-reactive, UV absorbing Silicone
- Light transmission: UV cut-off at 10% T ≥ 392 nm for all lens power
- Index of refraction: 1.43
- Diopter power: +10 to +15.0 diopters and +25.0 to +30.0 D in 1.0 diopter increments; +16.0 to +24.0 diopters in 0.5 diopter increments
- Optic type: Biconvex
- Optic edge: Square on posterior surface and round on anterior surface
- Overall diameter: 13.0 mm
- Optic diameter: 6.0 mm

Haptics

- Configuration: Modified C
- Material: Blue polymethylmethacrylate
- Haptic angle: 10°

The LAL silicone material is designed to respond to a narrowband UV light by incorporating photoreactive components in the cross-linked silicone lens matrix. Post implantation, the LAL shape may be altered non-invasively (refractive power may be increased or decreased) by photoinitiation of a select spatial intensity profile. The silicone material contains photoreactive additive, which is selectively photo-polymerized in targeted areas upon exposure to the near UV light to alter the lens shape thus modifying spherical and spherocylindrical power of the LAL. The change in the shape becomes permanent when the remaining photoreactive additive is consumed following application of a non-profiled beam of the same ultraviolet light.

The LAL will be introduced into the eye using the Nichamin III Foldable Lens Inserter (Rhein Medical 05-2349) with the Nichamin II Foldable Lens Insertion Forceps (Rhein Medical 05-2348).

7.1.2 LIGHT DELIVERY DEVICE (LDD)

The RxSight Light Delivery Device (LDD) is the device approved in P160055 and approved supplements. [redacted]

RxSight's Light Delivery Device (LDD) is a UV light projection system (Figure 2) used to induce a predictable change in LAL power after implantation. RxSight's LDD consists of an anterior segment biomicroscope with the addition of an optical projection system, electronic control circuitry, and a UV source. The LDD delivers light profiles with adequate intensity and duration to induce polymerization of photoreactive additive leading to a refractive power change of the LAL. Because this procedure is performed after implantation, residual refractive errors can be minimized, reducing the need for spectacles, corneal refractive procedures, or additional IOL procedures to optimize a patient's vision.

FIGURE 2: RXSIGHT LIGHT DELIVERY DEVICE (LDD)

7.1.3 TREATMENT CONTACT LENS

The treatment contact lens is applied to the eye prior to the initiation of the light treatment. The primary purposes of the handheld contact lens during LDD treatments are to maintain optical quality and to prevent blinking. Also, similar to other routine procedures that utilize a handheld contact lens, the risk of corneal abrasion is mitigated by the use of the coupling agent, which lubricates the corneal surface to reduce the potential for epithelial injury.

7.1.4 UV PROTECTIVE EYEWEAR

- UV protective spectacles [redacted] are supplied to the patient as a two-pair set, with one having clear lenses for indoor use and the other pair with tinted lenses for outdoor use. Instruct the patient to wear the spectacles at all times indoors and outdoors, keeping the eyes closed when changing spectacles, until 24 hours post the final lock-in treatment.
- Alternatively, an optional patch can be used postoperatively. If used, the patient should be instructed not to remove the patch and keep it in place until the surgeon removes it at the one day post-operative visit. The UV protective eyewear will be provided once the patch is removed at the one day post-operative visit.
- For patients requiring spectacle correction for refractive errors in the fellow eye, "fitover" UV protective spectacles [redacted] are supplied to the patients as a two-pair

set, with one pair having clear lenses for indoor use and the other pair with tinted lenses for outdoor use. Instruct the patient to wear the "fitover" UV protective eyewear over their existing corrective spectacles at all times; keeping the eyes closed when changing spectacles.

7.1.5 DEVICE MANUFACTURER

The LAL and LDD are manufactured by RxSight, Inc. located in Aliso Viejo, California (FDA Establishment Registration No. 3012712027). RxSight, Inc. has an established Quality Management System that is in conformance with the following standards:

- 21 C.F.R. Part 820 (Quality System Regulation)
- EN ISO 13485:2016 (Quality Management System with scope: design, manufacture, distribution and service of therapeutic, surgical and diagnostic devices and instruments especially for ophthalmology), and the Medical Device Directive 93/42/EEC.

The Sponsor will keep records to document the physical location of all investigational devices from shipment to the investigational sites until use, return or disposal. Traceability for both the LAL and LDD will be achieved by use of device serial numbers.

The principal investigator or an authorized designee shall keep records documenting the receipt, use, return, and disposal of the investigational devices, which shall include:

- The date of receipt
- Identification of each investigational device (batch number/serial number or unique code),
- The expiry date, if applicable,
- The date or dates of use,
- Subject identification
- Date on which the investigational device was returned/explanted from subject, if applicable, and
- The date of return of unused, expired or malfunctioning investigational devices, if applicable.

7.1.6 INDICATIONS FOR USE (NO CHANGE COMPARED TO PMA APPROVAL)

The Light Adjustable Lens and Light Delivery Device system is indicated for the reduction of residual astigmatism to improve uncorrected visual acuity after removal of the cataractous natural lens by phacoemulsification and implantation of the intraocular lens in the capsular bag, in adult patients:

- With pre-existing corneal astigmatism of ≥ 0.75 diopters
- Without pre-existing macular disease.

The system also reduces the likelihood of clinically significant residual spherical refractive errors.

7.2 SUBJECT ENTRY

The study population will consist of patients who have undergone implantation of a commercially available LAL after cataract extraction, who have 0.50 D of manifest cylinder measured in one eye prior to their first light adjustment treatment, who wish to have their 0.50 D of manifest cylinder treated, and who meet all study inclusion/exclusion criteria. If a subject's first eye receives the investigational light treatment, then this subject's fellow eye immediately becomes ineligible for future study enrollment and investigational light treatment. If a subject enrolls in this study and their first eye does not end up receiving the investigational light treatment, then (1) the subject is exited from this study, and (2) the subject may subsequently re-enroll in this study (and sign a new consent form) for evaluation and potential investigational treatment of the fellow eye.

Screening for study eligibility will occur 17-24 days after implantation of the commercial LAL and prior to any adjustment light treatments.

If it is determined that an eye of a patient may be eligible to participate, delegated and trained study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant.

The patient is enrolled upon signing the informed consent and study specific visual testing at the Study Visit #1, including manifest refraction performed by two independent examiners on a 4 meter lane, will be performed.

[redacted]

[redacted]

If at any other time during the Study Visit #1, the subject's eye does not meet inclusion or exclusion criteria, the study exam for that subject should be discontinued and the subject will be exited from the study. Those subjects who do not meet the inclusion/exclusion requirements will be considered a screen failure. Exited subjects will undergo light treatments per the PMA approved labeling. LAL subjects that meet all inclusion/exclusion criteria will receive a first light

adjustment treatment (Adjustment #1) at Study Visit #1. Subjects will continue to be enrolled until 25 subjects have had LDD light treatments.

Examinations will occur at regular intervals over a 3 month period to evaluate the performance of 0.50 D cylinder treatments on the LAL. At the Postop Month 3 visit, two independent examiners will perform the same refraction process as performed at the Adjustment #2 and #3 visits to determine the final refraction.

7.3 LIGHT TREATMENT PROCEDURE

All light treatments will be separated by 3-7 days.

Adjustment #1
The study eye will receive an adjustment #1 light treatment based on the final refraction as determined above.

Adjustment #2 visit
A second adjustment treatment will also be based on the measured manifest refractions performed by two independent examiners. [redacted]

Adjustment #3 (if necessary)
The same refraction process followed by two independent examiners at the Adjustment #2 visit will be followed. [redacted]

Depending on the adjustment(s) performed, subjects will receive two or three adjustments.

Lock-in light treatments
The study eye will receive a minimum of one lock-in treatment and a lock-in #2 may be performed, if necessary.

7.4 POSTPONEMENT OF LIGHT TREATMENT PROCEDURE(S)

LDD treatments should be delayed in the study eye if any of the following new symptoms or changes in performance are noted;

[redacted]

- Best Corrected Distance Visual Acuity: With any loss of BCDVA (unless the cause is known to be non-retinal) of 10 letters or more on an ETDRS (logMAR) chart compared to the Pre-Adjustment #1 BCDVA, treatment should be delayed.

If LDD treatment is delayed secondary to observations above, then the subject should return weekly and the testing repeated, until resolution of the changes including any signs suggesting phototoxic damage on OCT, at which time the next LDD treatment may be delivered. If after three weeks, there is no resolution, continue routine monitoring of the subject, at the physician's discretion, to evaluate improvement until resolution, at which time the next LDD treatment may be delivered. If there is no resolution of symptoms, explantation should be considered.

In addition, light treatments after the Adjustment #1 visit should be postponed in the study eye if any of the following are noted:

- A study eye with an ocular adverse event that could be negatively impacted by light treatment or negatively impact the effectiveness or safety of a light treatment should have light treatments delayed until after the adverse event has subsided. This includes corneal edema and superficial punctate keratitis (SPK) (Grade 3 (moderate) or more severe)), retinal conditions including diabetic retinopathy and cystoid macular edema, epithelial defect, and endophthalmitis.
- A study eye that is discovered with evidence of premature photopolymerization as evidenced as a zone on the lens surface. The investigator should contact the Sponsor for further instructions. (see Appendix 1 for additional details regarding premature photopolymerization).
- A study eye possessing clinically significant posterior capsular (PC) haze should undergo a YAG capsulotomy procedure prior to the adjustment. A minimum of 48 hours should separate the YAG treatment from the corresponding refraction and LDD adjustment.

7.5 REQUIREMENTS FOR ADDITIONAL TESTING

Additional testing should be performed as soon as possible to evaluate whether UV-related retinal damage has occurred if any of the following is observed. When additional testing is required, all light treatments should be delayed until after OCT images are obtained and no phototoxic damage is seen.

Any visit <u>after</u> Adjustment #1:

- BCDVA is reduced by 10 letters or more when compared with BCDVA at Pre-Adjustment #1 unless the cause of the BCDVA loss is known to be non-retinal.

OR

[redacted]

All OCT results should be provided to the reading center and RxSight for review.

[redacted]

OCT should be repeated at an additional follow exam to confirm resolution or document sequelae, if any. Results from any subsequent visit should be provided to RxSight and reading centers for review.

7.6 PROCEDURE PREPARATION

Protocol-required measurements should be completed prior to adjustment or lock-in treatments.

The subject should be prepared for light treatments as follows:

Study eye undergoing a light treatment will be prepared for light treatment with pupil dilation.

1. The study eye will be dilated using pupil dilation drops [redacted] or pupil dilation gels [redacted] or pupil dilation agents of the investigator's choice. After waiting an appropriate amount of time for dilation to occur, the study eye will be examined to ensure that adequate dilation (enough of the edge of the LAL optic can be visualized to allow for centration during LDD light treatment) has been obtained. If adequate dilation has not been obtained, additional dilating drops with manual punctal occlusion or a sponge soaked in mydriatic medication and applied to the ocular surface can be utilized to try and gain further dilation. If adequate pupil dilation is still not achieved with the methods described above, the treatment will be rescheduled and the dilation attempted at another visit or another dilation method is used.
2. Once adequate pupil dilation is achieved, patch the subject's other eye and position the subject comfortably in front of the LDD with chin in the chinrest and forehead against the support bar. Ask the subject to grasp the handles on the LDD table for support. Inform the subject to concentrate on the green fixation light presented in front of them and to try and minimize eye movement.

7.7 ADJUSTMENT PROCEDURE(S)

Refer to the LDD Operator's manual for instructions on LDD start up and instructions for the daily alignment test to be performed prior to the first treatment of the day.

1. Within the Patient ID and Patient Data screens, follow the touchscreen prompts to enter requested information. Within the Patient ID screen, the subject's measured manifest refraction is entered into the manifest refraction input fields. Within the Patient Data screen, a refraction target will be entered as 0.00 sphere, 0.00 cylinder, and 0 axis.
2. Within the Confirmation screen, review all information and press the "Confirm" button.
3. Verify that the LDD ring lights and reticle target are activated.
4. Apply topical anesthetic.
5. Position the RxSight supplied contact lens ([redacted]) on the cornea using [redacted] the coupling medium.

   Note: The RxSight contact lens is similar to those used in other ophthalmic procedures in which customized magnification is required. To ensure correct magnification for treatment, use only the RxSight designated contact lens.
6. Instruct the subject to focus straight ahead on the LDD fixation light with the eye to be treated.
7. Using the microscope, focus on the cornea and verify that there are no trapped bubbles present. Confirm alignment of the contact lens by approximately aligning the Purkinje images to the inner circle of the reticle target.
8. Using the microscope, focus on the LAL haptics and align the reticle target with the periphery of the LAL. Press the "Ready" button. Initiate the UV exposure as prompted by the LDD display using the trigger. Use the joystick to keep the LAL centered in the alignment reticle. Perform micro adjustments to keep the reticle target centered to the LAL and to keep the LAL in focus. In the case of subject movement, loss of alignment, or loss of focus, pause the treatment, quickly refocus, realign the lens with respect to the reticle beam, and immediately resume treatment to limit the duration of any pauses once the light treatment has been initiated.

   Note: Always maintain the LAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.
9. In the case of an aborted Adjustment Treatment, do not initiate a new treatment sequence; instead; contact the Sponsor for further instructions.
10. Following the light adjustment, the subject will continue to wear their UV protective eyewear as instructed.

7.8 LOCK-IN PROCEDURE(S)

Refer to the LDD Operator's manual for instructions on LDD start up and instructions for the daily alignment test to be performed prior to the first treatment of the day.

1. Within the Patient ID screen, utilize the pop-out menu within the Patient ID field to select the appropriate subject identification with eye to be treated. Reconfirm information displayed on screen and follow the touch screen prompts to enter in newly requested information. Press the "Proceed" button.
2. Within the Confirmation screen, review all information and press the "Confirm" button.
3. Verify that the LDD ring lights and reticle target are activated.
4. Apply topical anesthetic.
5. Position the RxSight supplied contact lens ([redacted]) on the cornea using [redacted]he coupling medium.

   Note: The RxSight contact lens is similar to those used in other ophthalmic procedures in which customized magnification is required. To ensure correct magnification for treatment, use only the RxSight designated contact lens.
6. Instruct the subject to focus straight ahead on the LDD fixation light with the eye to be treated.
7. Using the microscope, focus on the cornea and verify that there are no trapped bubbles present. Confirm alignment of the contact lens by approximately aligning the Purkinje images to the inner circle of the reticle target.
8. Using the microscope, focus on the LAL haptics and align the reticle target with the periphery of the LAL.
9. Press the "Ready" button
10. Initiate the irradiation delivery as prompted by the LDD display using the joystick or foot pedal to keep the LAL centered in the alignment reticle.
11. Perform micro adjustments to keep the reticle target centered to the LAL and to keep the LAL in focus. In the case of subject movement, loss of alignment, or loss of focus, pause the treatment, quickly refocus, realign the lens with respect to the reticle beam, and immediately resume treatment to limit the duration of any pauses once the light treatment has been initiated.

    Note: Always maintain the LAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.
12. If the lock-in treatment is aborted before completion, do not initiate a new lock-in sequence; instead; contact the Sponsor for further instructions.
13. Upon completion of the lock-in #1 treatment, a notification may appear that informs the user that all required treatments are complete. If this notification appears, proceed to step #15. If no notification appears, then the subject will require a lock-in #2 treatment and proceed to step #14.
14. The subject will return for the second lock-in treatment 3 to 7 days after the first lock-in treatment.

15. The subject will be permitted to discontinue wear of the UV protective eyewear exactly 24 hours after the subject's final lock-in treatment for either eye (as appropriate) has been completed.

7.9 EXAMINATION SCHEDULE

Evaluation	
Study Visit #1/Adjustment #1	Day 0 (17 to 24 days post-implantation with the LAL)
Adjustment #2	3 to 7 days post Adjustment #1 Visit
Adjustment #3, if needed	3 to 7 days post Adjustment #2 Visit
Lock-in #1	3 to 7 days post final adjustment Visit
Lock-in #2, if needed	3 to 7 days post lock-in #1 Visit
Post Lock-In	7-14 days post final lock-in Visit
Postop Month 3	Days 75 to 120 post-implantation with the LAL

Unscheduled visits falling outside the designated ranges for scheduled visits will be considered "interim" visits for data recording purposes and a report form will be completed.

7.10 CLINICAL PARAMETERS

Clinical assessments when indicated will be performed in the following order:

1. Demographics
2. Ocular history including medications
3. Subjective symptoms/complaints (subject reported)
4. Compliance with UV spectacles
5. Autorefraction
6. Corneal Topography
7. Monocular UCDVA
8. Manifest Refraction
9. Monocular best corrected distance visual acuity (BCDVA)

[redacted]

12. Intraocular pressure
13. Slit Lamp Examination
14. Fundus Examination
15. Dilated pupil diameter
16. Spectral Domain OCT (if needed)
17. Adverse Event

Table 1. Schedule of Visits and Clinical Parameters

Visits	Study Visit #1/ Adjustment #1	Adjustment #2,	Adjustment #3, if needed	Lock-in #1	Lock-in #2, if needed	Postop Lock-in	Postop Month 3	Unscheduled Visit[1]
Demographics	X							
Ocular History	X							
History of Medications	X	X	X	X	X	X	X	X
Subjective Symptoms/Complaints (Subject reported)	X	X	X	X	X	X	X	X
Compliance with UV Spectacles	X	X	X	X	X			
Autorefraction	X	X	X	X	X	X	X	
Corneal Topography	X							
Monocular uncorrected distance visual acuity (UCDVA)	X	X	X	X	X	X	X	X
Manifest Refraction	X	X	X	X	X	X	X	
Monocular best corrected Visual Acuity Distance (BCDVA)	X	X	X	X	X	X	X	
[redacted]	[redacted]							
[redacted]								
Intraocular Pressure	X	X	X	X	X	X	X	
Slit Lamp Exam	X	X	X	X	X	X	X	X
Fundus Exam	X					X		
Dilated Pupil Diameter	X	X	X	X	X			
Spectral Domain OCT	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]	X[2]
Adverse Events	X	X	X	X	X	X	X	X

[1] Tests indicated with an "X" must be performed at each unscheduled visit. Other tests may be conducted based on the investigator's assessment of the subject.
[2] If needed

7.11 DATA REPORTING

Electronic data capture (EDC) will be utilized for this study. Case report forms (CRFs) will be developed by the sponsor. In order to facilitate data entry, the CRFs coincide with the data entry pages in the EDC system. Research sites will be provided with source document templates (SDTs) that correlate with the CRFs. The appropriate SDTs will be completed and initialed or signed where indicated at each examination. All SDTs will be completed in a legible manner in black/blue ink.

Any corrections to the SDTs will be made by drawing a single line through the incorrect entry, recording the correct information, and initialing and dating the change. The study SDTs and data entered in the EDC system will be reviewed by the Study Monitor.
All clinical data generated in the study will be submitted to the RxSight Clinical Affairs Department or designated CRO for quality assurance review and statistical analysis. All SDTs and data entered into the EDC system will be reviewed for completeness and evident recording errors will be rectified by contact with the appropriate clinical site. Computerized data checks will be used to identify unusual data entries for verification prior to statistical analysis.

To minimize the amount of missing data, investigators will be trained on the deleterious effect that missing data have on trial integrity and credibility and that missing data could diminish the scientific value of all subjects' altruistic contributions.

7.12 STUDY COMPLETION PROCEDURES

An End of Study Form must be completed for all subjects enrolled in the study upon subject completion, withdrawal or discontinuation.

7.12.1 SUBJECT COMPLETION

Subjects are considered to have completed the study if the study eye has completed the Postop Month 3 examination.

Subjects with ocular serious adverse events or adverse device effects that are unresolved at study exit should continue to be followed until resolution of the event or until they are stable per the investigator's evaluation.

7.12.2 SUBJECT DISCONTINUATION AFTER LIGHT TREATMENTS

The subject will only be withdrawn from the study if the LAL is explanted in the study eye after Adjustment #1 or the subject has deceased.

The reason for discontinuation will be recorded on the appropriate study worksheet. Subjects who are discontinued from the study will still be a part of the study analyses up until the point they are exited. In the case of an explant, the investigator should continue follow-up for a period that ensures no adverse consequences have resulted. When possible, all necessary clinical assessments will be performed prior to the Subject exiting the study even if the assessment was not scheduled at that particular visit.

7.12.3 LOST TO FOLLOW-UP

Subjects for which the final post-operative case report form is overdue and who refuse to be followed, or have difficulty being followed, or cannot be contacted despite extensive written and telephone follow-ups to determine the final clinical outcome, will be considered lost to follow-up. Sites must make a minimum of three documented attempts via telephone, email, or regular mail to contact the subject. If the subject does not reply to any of these attempts, the site must send a letter by certified mail (with a request for notification of receipt of delivery) to the subject. If a subject is non-responsive to these follow-up attempts, the subject will be considered to be lost to follow-up.

7.12.4 STUDY TERMINATION

The study may be stopped at any time by the Sponsor for reasonable cause with appropriate notification. Conditions that may warrant study termination include, but are not limited to the following:

- Safety concerns. Clinical data from the study will be monitored to assure the safety of enrolled subjects.

If the clinical study is prematurely terminated, the Sponsor will inform the Investigator, the IRB, and other appropriate regulatory bodies. If the Sponsor terminates the study for safety reasons, it will immediately notify the Investigator, the IRB, and other appropriate regulatory bodies and provide an explanation of the reasons for termination. The Investigator will be provided with instructions for study termination and applicable subject follow-up. The Sponsor will continue to provide resources to fulfill the Clinical Study Plan obligations for follow-up of the subjects enrolled in the study.

8 STATISTICAL METHODS

8.1 SAMPLE SIZE CALCULATION

8.1.1 SAMPLE SIZE FOR THE EFFECTIVENESS ENDPOINTS

There is no formal sample size calculation for this study. The comparisons for the effectiveness parameters will be made by descriptive statistics only. In order to have at least 20 LAL subjects (i.e. 20 LAL eyes) at 3 Months, a sample size of 25 subjects is needed with study eyes undergoing treatment based on spherical error combined with 0.50 D cylindrical refractive error.

[redacted] The historical control groups will consist of all eyes that meet the requirements for inclusion in the respective group and each group will include a minimum of 25 eyes.

[redacted]

In refractive surgery, 20 eyes per one diopter bin is considered adequate for evaluation to demonstrate effectiveness of the refractive correction within that bin. As the LAL used in this study is an FDA approved, commercially available device, RxSight believes this approach to determining sample size is appropriate.

8.1.2 SAMPLE SIZE FOR THE SAFETY ENDPOINTS

As the LAL that is used in this study is an FDA approved, commercially available device, there are no safety endpoints. Additionally, the LDD is also the FDA approved, commercially available device with the exception of the the availability of correction of 0.50 D cylinder.

8.1.3 SAMPLE SIZE FOR THE STUDY

The planned study sample size of 25 enrolled subjects is sufficient.

8.2 GENERAL CONSIDERATION

The statistical analysis of the data will be performed using SAS version 9.3 or higher or another industry standard statistical software package. Continuous variables will be summarized using descriptive statistics, specifically the mean, median, standard deviation,

minimum and maximum. Categorical variables will be summarized by frequencies and percentages. The summaries will be provided for the LAL eyes that undergo 0.50 D cylinder correction (LAL treatment group) versus both the LAL historical control group and the Monofocal IOL historical control group. The 95% confidence interval for mean or for percentage may be provided.

8.3 BASELINE CHARACTERISTICS

Demographics (such as age, gender, and race) and baseline characteristics will be summarized for the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control groups separately.

8.4 POPULATIONS FOR ANALYSIS

8.4.1 SAFETY POPULATION

The safety population consists of any subject (or eye) who has signed the informed consent for participation in CSP-034 and has had the LDD light treatment attempted, which is defined as the point at which the light treatment is started. This population will be used for the safety analysis. No imputation will be performed.

8.4.2 EFFECTIVENESS POPULATION

The effectiveness population consists of study eyes of subjects who have signed the informed consent for participation in CSP-034, have had the LDD light treatments completed on the study eye, and who have completed a Postop Month 3 visit. This population will be used for the effectiveness analysis. No imputation will be performed.

[redacted]

8.5 EFFECTIVENESS ANALYSES

Effectiveness analyses will be based on the Effectiveness population described in Section 8.4.2. [redacted]

8.5.1 PRIMARY ANALYSES FOR THE EFFECTIVENESS PARAMETERS

The mean and standard deviation of MRCYL at Postop Month 3 and the corresponding 95% confidence interval will be calculated for the LAL treatment group. The mean and standard deviation of MRCYL at the Postop Month 6 visit and the corresponding 95% confidence interval will be calculated separately for the LAL historical control group and the Monofocal IOL historical control group. The Postop Month 3 outcomes of the LAL treatment group will be numerically compared and clinically assessed to the Postop Month 6 visits of the LAL historical control group and the Monofocal IOL historical control group. No formal statistical comparison will be performed.

In addition, the mean and standard deviation of the change in MRCYL from baseline (Visit #1/Adjustment #1) to Postop Month 3 and the corresponding 95% confidence interval will be calculated for the LAL treatment group. The mean and standard deviation of the change in MRCYL from baseline (Adjustment #1 (LAL)/17-21 days postop (Control)) to Postop Month 6 and the 95% confidence interval will be calculated separately for the LAL historical control group and the Monofocal IOL historical control group.

Clinical studies have shown that after standard phacoemulsification and IOL implantation, refractive stability of the eye has been observed as early as 2 months postoperatively[1]. Additionally, studies in which a suture was needed to close the incision after intracapsular cataract surgery, it has been noted that the refraction in these eyes had stabilized sufficiently enough to allow prescription of first glasses at a mean time of 10.2 weeks after surgery[2]. These documented time points of refractive stability provide evidence that the refractive results of the LAL at Postop Month 3 are stable enough to compare against the historical control groups at Postop Month 6.

8.5.2 ADDITIONAL EFFECTIVENESS ANALYSES

The following effectiveness outcomes will be summarized descriptively based on the observed data of the Effectiveness population, separately for the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control group. No imputation for missing values will be performed. The 95% confidence interval of the mean, if required, will be calculated based on the t-distribution; the 95% confidence interval of the proportion, if required, will be derived by the binomial distribution. It should also be noted that, for the MRCYL data analyses, the absolute MRCYL value will be used to present the summaries for simplicity.

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[1] Conrad-Hengerer I, Al Sheikh M, Hengerer FH, et al. Comparison of visual recovery and refractive stability between femtosecond laser-assisted cataract surgery and standard phacoemulsification: Six-month follow-up. J Cataract Refract Surg 2015; 41:1356-1364.

[2] Baranyovits P. Stabilisation of refraction following cataract surgery. British Journal of Ophthalmology, 1988, 72, 815-819.

8.5.2.1 Manifest Cylinder (MRCYL)

The MRCYL will be summarized beginning at Adjustment #1 using descriptive statistics for continuous outcomes stratified by the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control group. The number and percent of eyes with a MRCYL of ≤0.25 D, 0.50, 0.75 D, 1.0 D, and >1.0 D at each visit observed by either the LAL treatment group, the LAL historical control group, or the Monofocal IOL historical control group will be reported.

8.5.2.2 Vector Difference

Error vector (EV) for the LAL treatment group will be presented as the vector difference between intended refractive correction (IRC) vector at Adjustment #1 and surgically induced refractive correction (SIRC) vector at Postop Month 3.

Error vector (EV) for the LAL historical control group will be presented as the vector difference between intended refractive correction (IRC) vector at Adjustment #1 and surgically induced refractive correction (SIRC) vector at Postop Month 6. For eyes in the LAL historical control group, the IRC will be the manifest refractive cylinder (0.5 D and MRaxis).

Error vector (EV) for the Monofocal IOL historical control group will be presented as the vector difference between intended refractive correction (IRC) vector at 17-21 days postop and surgically induced refractive correction (SIRC) vector at Postop Month 6. For eyes in the Monofocal IOL historical control group, the IRC will be the manifest refractive cylinder (0.5 D and MRaxis).

The mean magnitude of EV will be compared between the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control group.

The EV will be calculated for each eye based on Eydelman[3] as follows:

IRC = For all subjects, the magnitude of the IRC is 0.5 D. The IRC axis is the manifest refractive cylinder axis as measured at the Adjustment #1/17-21 day visit.

SIRC = the vector difference between astigmatic correction vector at Adjustment #1 and 3 Months (LAL treatment group) or 17-21 day/Adjustment #1 visit and Postop Month 6 (LAL historical control group and Monofocal IOL historical control group)

EV = the vector difference between IRC at Adjustment #1 and SIRC at 3 Months (LAL treatment group) or 17-21 day/Adjustment #1 visit and Postop Month 6 (LAL historical control group and Monofocal IOL historical control group) (IRC – SIRC).

The mean and standard deviation of the magnitude of EV will be calculated along with the 95% confidence interval of the mean for the LAL treatment group at Postop Month 3 and for the LAL historical control group and Monofocal IOL historical control group at Postop

[3] Malvina B. Eydelman, et al. "Standardized Analyses of Correction of Astigmatism by Laser Systems That Reshape the Cornea", Journal of Refractive Surgery Volume 22 January/February 2006, pp 81-95

Month 6, separately. The outcomes will be numerically compared and clinically assessed. No formal statistical comparison will be performed.

8.5.2.3 MRSE

The measured MRSE, adjusted MRSE (to account for the measured distance of 4 meters) and change in MRSE from Adjustment #1 will be summarized by the descriptive statistics for continuous outcomes (such as mean and standard deviation) and the 95% confidence interval of the mean at each visit observed by subjects within the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control group respectively.

8.5.2.4 Accuracy of MRSE

The number and percent of eyes with a MRSE correction compared to the intended target within 0.25 D, 0.50 D, 0.75 D, 1.0 D, 1.25 D, 1.5 D, 1.75 D, and ≥2.0 D will be reported for the LAL treatment group at Postop Month 3 and for the LAL historical control group and Monofocal IOL historical control group at Postop Month 6. Additionally, the deviation of the achieved adjustment from the attempted adjustment will be summarized by the descriptive statistics for continuous outcomes by LAL treatment group, LAL historical control group, and Monofocal IOL historical control group.

The 95% confidence interval of the mean deviation and the 95% confidence interval of the proportion of eyes within 0.50 D and 1.00 D will be provided.

8.5.2.5 Absolute MRSE

The analyses methods described for the MRSE will be used for analyzing the absolute MRSE.

8.5.2.6 Defocus Equivalent (DEQ)

The DEQ, as defined as the absolute value of the MRSE error to target plus half the absolute value of the MRCYL, will be summarized descriptively at the Adjustment #1 visit and Postop Month 3 for the LAL treatment group and at the Adjustment #1/17-21 day visit and Postop Month 6 visit for the LAL historical control group and Monofocal IOL historical control group. The number and percent of eyes with DEQ ≤0.5 D and 1.0 D will also be summarized at the corresponding visit.

8.5.2.7 Autorefraction

Autorefraction sphere, cylinder, and spherical equivalent will be summarized descriptively at each visit observed by subjects within the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control groups respectively.

8.5.2.8 Monocular Uncorrected Visual Acuity

Monocular UCDVA will be presented with the number and percent of eyes that fall into each category of UCDVA at each visit observed by subjects within the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control groups respectively

(e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.). The logMAR UCDVA will be summarized by descriptive statistics for continuous outcomes for each visit. Change in UCDVA from the 17-21 day/Adjustment #1 visit will be presented at each visit as categorical outcomes of "increase of 15 letters or more", "Increase of 10-14 letters", "Increase of 5-9 letters", "No change", "Decrease of 5-9 letters", "Decrease of 10-14 letters", and "Decrease of 15 letters or more". The change in logMAR UCDVA from the 17-21 day/Adjustment #1 visit will also be presented.

8.6 SAFETY PARAMETERS

The following safety outcomes will be summarized descriptively based on the observed data of the Safety population. The 95% confidence intervals for means or percentage may be presented, as appropriate.

8.6.1 ADVERSE EVENTS (AE)

For each adverse event, the number of reports, number and percent of subjects with the AE, and number and percent of eyes with the AE will be summarized at each postoperative visit. Serious ocular AEs and the non-ocular serious will be summarized in the same manner. Additionally, for each device-related AE reported during the study will be presented in the same manner.

8.6.2 MANIFEST CYLINDER (MRCYL)

For all eyes in the Safety population, MRCYL will be summarized at the final scheduled visit using descriptive statistics for continuous outcomes stratified by the LAL treatment group, the LAL historical control group, and the Monofocal IOL historical control group. The number and percent of eyes with a MRCYL of ≥1.00 D and ≥2.00 D observed by either the LAL treatment group, the LAL historical control group, or the Monofocal IOL historical control group will be reported.

8.6.3 BCDVA

For all eyes in the Safety population, the percentage of eyes that fall into each category of BCDVA at each visit (e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.) will be presented. In addition, the change in monocular BCDVA from the Adjustment #1 visit will be presented at each visit as categorical outcomes of "Increase of 15 letters or more", "Increase of 10-14 letters", " Increase of 5-9 letters", "No change", "Decrease of 5-9 letters", "Decrease of 10-14 letters", and "Decrease of 15 letters or more" for all eyes in the Safety Population. The mean change from the prior visit to the next visit will also be summarized in the same manner.

The listing of BCDVA and the possible reason for BCDVA loss of 10 letters or more will be provided for the eyes reported with a 10-letter or more loss in BCDVA from (1) pre-light treatment visit (Study Visit #1/Adjustment #1) to the final study visit (Postop Month 3) and (2) pre-light treatment visit (Study Visit #1/Adjustment #1) to any subsequent visit.

[redacted]

8.6.6 UV PROTECTIVE EYEWEAR COMPLIANCE

Periods of non-compliance with UV protective eyewear will be reported based on the number of periods and time of non-compliance.

8.6.7 SUBJECTIVE SYMPTOMS AND COMPLAINTS

Number and percent of subjects will be summarized at each reported subjective symptom for the Safety population.

8.6.8 OTHER OCULAR EXAMINATIONS

Slit lamp findings, fundus exam findings, and IOP including changes will be summarized descriptively for all eyes in the Safety population.

9 ADVERSE EVENTS

If an adverse event (AE) occurs, the first concern will be the safety and welfare of the subject; treatment should be provided as appropriate for the event. During the study, the Investigator should appropriately treat and follow each AE until it resolves, stabilizes, or it is determined that further improvement is not expected.

9.1 ADVERSE EVENT DEFINITIONS

An adverse event (AE) is 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.

Note 1 to entry: This definition includes events related to the investigational medical device or the comparator.

Note 2 to entry: This definition includes events related to the procedures involved.

Note 3 to entry: For users or other persons, this definition is restricted to events related to investigational medical devices.

Unanticipated Adverse Device Effects (UADE) are 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.

An investigator will submit to the Sponsor and to the reviewing IRB a report of any UADE occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect. The Sponsor will immediately conduct an evaluation of any unanticipated adverse device effect. The results of the evaluation will be reported to FDA and to all reviewing IRB's and participating investigators within 10 working days of the Sponsor becoming aware of the event. Thereafter the Sponsor shall submit additional reports concerning the effect as FDA requests. If a UADE is determined by the Sponsor to present an unreasonable risk to study subjects, all investigations or parts of the investigation presenting that risk will be terminated as soon as possible. Termination will occur not later than 5 working days after this determination is made, and not later than 15 working days after first receiving notice of the event. The investigation will not be resumed without IRB and FDA approval.

All events that the investigator regards as clinically significant should be reported to ensure full reporting of all significant adverse events. The list below provides additional guidance on specific events that will need to be reported as AEs as specified.

1. Anterior Chamber Inflammation
    - Iritis/cells/flare (if present after the Screening/Adjustment #1 visit and greater than grade 1 (trace)) or (any iritis/cells/flare present at Postop Month 3 of any grade) OR
    - Chronic anterior uveitis (Persistent anterior segment inflammation characterized by grade 1+ cell or greater using Standardization of Uveitis Nomenclature criteria; present at the Postop Month 3 visit, or relapses in less than 3 months after discontinuation of therapy, or the subject is maintained on therapy for more than 3 months to control inflammation).
2. Corneal edema:
    - If present after the Screening/Adjustment #1 visit and greater than grade 1 (trace)) or (if present at Postop Month 3 of any grade) OR
    - Corneal swelling (stromal or epithelial) resulting in BCDVA ≤20/40 after Screening/Adjustment #1 visit)
3. Conjunctival hyperemia and/or edema:
    - If present after Screening/Adjustment #1 visit and greater than grade 2 (mild)
4. Posterior capsular opacity (PCO) that requires YAG Capsulotomy treatment
5. Raised intraocular pressure (IOP) ≥10 mmHg above preoperative and greater than 25 mmHg (if present after Screening/Adjustment #1 visit) AND unrelated to mechanical pupillary block
6. Loss of BCDVA of ≥ 10 letters (when compared to Adjustment #1 BCDVA).

[redacted]

Per the Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses, the following types of adverse events will be reviewed by the Sponsor to determine if they meet the following definitions for reporting purposes:

Adverse Event	Definition
Clinically significant cystoid macular edema	Macular edema diagnosed by clinical examination and adjunct testing (e.g., OCT, FA, or other method) resulting in reduced BCDVA to20/40 or worse after Adjustment #1
Endophthalmitis	Postoperative intraocular inflammation requiring vitreous tap and use of intraocular antibiotics
Mechanical pupillary block	A shallowing of the peripheral and/or central anterior chamber with or without elevation of IOP by obstruction of the flow of aqueous humor from the posterior chamber through the pupil to the anterior chamber. This may be induced by the crystalline lens, vitreous face, or implanted devices
Rhegmatogenous Retinal Detachment	Partial or complete retinal detachment associated with retinal tear
Toxic anterior segment syndrome	An acute, noninfectious inflammation of the anterior segment of the eye that develops within 24 to 48 hours after surgery and is characterized by corneal edema and accumulation of white cells in the anterior chamber of the eye
Secondary IOL intervention	Exchange: The investigational device is replaced with the same lens model. Removal: The investigational device is removed and replaced with a noninvestigational lens or no lens is implanted. Reposition: The existing IOL is surgically moved to another location or rotated.

[redacted]

9.2 ADVERSE DEVICE EFFECT (ADE) DEFINITION

Adverse event related to the use of an investigational medical device.

Note 1: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

Note 2: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

9.3 DEVICE DEFICIENCY (DD) DEFINITION

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Note: Device deficiencies include malfunctions, use errors, and inadequate labeling.

9.4 SERIOUS ADVERSE EVENT DEFINITION

Serious Adverse Events (SAEs) are AEs that lead to:

- death
- a serious deterioration in the health of the subject that:
  - results in a life-threatening illness or injury
  - results in a permanent impairment of a body structure or function (e.g., blindness)
  - requires in-subject hospitalization or prolongation of existing hospitalization
  - results in medical or surgical intervention to prevent permanent impairment to a body structure or a body function
- fetal distress, fetal death, or a congenital abnormality or birth defect
- a potentially sight-threatening condition
- or is another important medical event.

9.5 UNANTICIPATED PROBLEM DEFINITION

An unanticipated problem is defined as any incident, experience, or outcome that meets all of the following criteria:

- Unexpected/unanticipated – (in terms of nature, severity, or frequency) given (a) the research procedures that are described in the protocol-related documents (protocol, ICD, product labeling, IB); and (b) the characteristics of the subject population being studied; and
- Related or possibly related to the participation in the research (possibly related means there is a reasonable possibility that the incident, experience, or outcome may have been caused by the drugs, devices, or procedures involved in the research); and
- Suggests that the research places participants or others at a greater risk of harm [new or increased risk (including physical, psychological, economic, or social)] than was previously known or recognized.

9.6 IDENTIFICATION AND COLLECTION

Identification and collection of an AE begins after informed consent has been obtained and documented. Standard sources of identifying AEs include:

- direct observation by the Investigator or study team member
- asking the study participant a specific question (e.g., "Since your last visit, have you experienced any problems with your eyes or vision?")
- unsolicited volunteering of information by the study participant (e.g., "Doctor, I have had numerous headaches since I started using this lens.")

Ocular AEs, ocular SAEs, and systemic SAEs observed or elicited by the Investigator, reported by the subject, or resulting from a test result, etc., occurring during the clinical investigation must be documented. During the study, the Investigator should treat the study subject as appropriate to ensure his/her safety and welfare. Refer to Section 7.12.1 for additional information pertaining to ongoing AEs at subject exit.

Pre-existing conditions will not be considered AE/SAEs but will be collected at the Screening/Adjustment #1 Visit as medical history. A worsening of a pre-existing condition during the study should be documented as an AE and evaluated accordingly.

Hospitalization is a criterion for assessment of seriousness. Hospitalization in the absence of a medical AE is not in itself an AE. For example, the following reports of hospitalization without a medical AE should not be considered either an SAE or an AE:

- Planned hospitalization for a pre-existing condition without serious deterioration in health (e.g., planned knee replacement surgery)
- Social admission (e.g., subject has no place to sleep)
- Administrative admission (e.g., for yearly physical exam or elective procedures not related to the study)
- Optional admission not associated with a precipitation medical AE (e.g., for elective cosmetic surgery)

9.6.1 EVALUATIONS

When evaluating AEs, the Principal Investigator or delegated MD sub-Investigator must determine if the event is serious, assess the severity of symptoms, the relationship of the event to the device or study protocol, using the following guidelines:

1. **Severity**

   Mild: subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with subject's daily activities

   Moderate: subject awareness of a sign or symptom which may be a low level of concern to the subject and may interfere with daily activities, but can be relieved by simple therapeutic care

Severe: a sign or symptom that interrupts the subject's daily activity and requires systemic therapy or other treatment

2. **Relationship (Causality) to Study Device or Study Protocol**

Related: There is at least a reasonable possibility that the AE/SAE is related to the study device or study protocol. Reasonable possibility means that there is evidence to suggest a causal relationship between the study device or study protocol and the AE.

Unrelated: There is little or no reasonable possibility that the AE/SAE is related to the study device or study protocol. This assessment implies that the AE/SAE has little or no temporal relationship to the study device and/or a more likely or certain alternative etiology exists.

9.7 SAE REPORTING

The site should report any event to the Sponsor and its representative in an expedited manner if it meets the criteria for an ocular or non-ocular SAE and/or is an IOL explant from a study eye. Expedited reporting is calling or e-mailing the Sponsor and its representative within 48 hours of becoming aware of the event. Contact details are as follows:

[redacted]

When reporting an SAE to the Sponsor and/or its representative, the site should forward any supporting documents along with the SAE Report Form to the Sponsor and its designee within 5 days of the initial communication. All supporting information must have all protected health information (PHI) removed and the subject ID added. Sites must also report these events to the reviewing IRB/IEC per its established reporting procedures.

9.8 UANTICIPATED ADVERSE DEVICE EFFECT (UADE) REPORTING

An investigator shall submit to the Sponsor and to the reviewing IRB/EC a report of any Unanticipated Adverse Device Effect (UADE) occurring during an investigation as soon as possible, but in no event later than 10 working days after the investigator first learns of the effect or in accordance with National Regulations. As soon as notification of a potential UADE is received by the Sponsor, an investigation will be initiated to determine if the event is a UADE. If the event is confirmed to be a UADE, the regulatory authorities, all other participating Investigators and each reviewing IRB/EC must be notified within 10 working days of the initial report from the site, as applicable or in accordance with National Regulations. If it is determined that the UADE represents an unreasonable risk to study subjects, the study must be terminated within 5 working days following the decision, and no later than 15 working days after first learning of the UADE or in accordance with National Regulations.

9.9 DEVICE DEFICIENCY (DD) REPORTING

All device deficiencies (DDs) should be reported to the Sponsor without unjustified delay. The Sponsor will assess the DD to determine whether it led to an adverse event (AE). AEs

resulting from DDs will be documented, assessed, and reported in accordance with adverse event guidelines. DDs that did not lead to an adverse event but could have led to a Serious Adverse Device Effect (SADE) will be reported in the future PMA as required in ISO 14155.

9.10 UNANTICIPATED PROBLEM (UP) REPORTING

If an incident, experience, or outcome meets all 3 criteria of the unanticipated problem definition described in section 9.5, then a UP should be reported to the Sponsor without unjustified delay. Furthermore, reporting of an unanticipated problem to the IRB should occur within 10 business days of discovery by the Investigator or Sponsor Representative reporting the event. The IRB will report unanticipated problems to the appropriate regulatory agencies and to the institutional official/sponsor, as appropriate.

9.11 PREGNANCY

During the study, all female subjects of childbearing potential should be instructed to contact the investigator immediately if they suspect they might be pregnant (e.g., missed or late menstrual period). Female subjects who become pregnant during the study will be followed until completion of pregnancy. Every effort will be made to obtain the health status of the mother and infant or fetus (in cases of miscarriage or therapeutic abortion) at term. Pregnancy itself is not considered an AE.

All confirmed pregnancies must be immediately reported to the Sponsor within 48 hours of the investigator's awareness of the pregnancy.

9.12 POTENTIAL ADVERSE EVENTS

The following have been identified as potential adverse events for all cataract surgeries including the LAL. Please notify the Sponsor regarding any events that may be occurring more frequently than your customary rates, or more frequently than expected at your site.

Infection, inflammation, hypopyon, endophthalmitis, infectious keratitis, hyphema, retinal detachment or other retinal problems including cystoid macular edema and epiretinal membranes, toxic anterior segment syndrome, glaucoma, corneal endothelial damage, vitritis, corneal edema which may require correction with a corneal transplant, lens dislocation out of the posterior chamber, pupillary block, striation on the lens with or without visual sequelae, iritis, synechiae, ptosis, wound leak, flat anterior chamber, increased astigmatism, rupture of the capsule, iris prolapse, vitreous in the anterior chamber, and retained pieces of the lens in the eye. These adverse events may result in total loss of vision or the loss of an eye. In cases of monovision, induced strabismus may occur. Secondary surgery may be required after the cataract surgery to treat surgical complications. Additionally, a posterior capsulotomy may be required to treat posterior capsular haze after the cataract surgery. Visual problems after cataract surgery may include halos, glare, ghost images, and/or double vision. These and other complications may result in permanent poor vision.

Additional specific risks of the LAL include:

In order to perform the lens adjustment or the lens lock-in procedures, the subject's pupil needs to be adequately dilated. If this cannot be accomplished for any reason, additional eye drops, injections into the eye, or surgery may need to be utilized to adequately dilate the pupil. If the pupil cannot be adequately dilated after these types of treatments, the LAL may need to be explanted. An unpredicted change in vision can occur resulting from ocular exposure to daylight or any other UV source before the LAL is locked-in. The light treatments may not improve vision and/or manifest refraction, and the adjustment/lock-in procedure may make vision worse, such that it may be necessary to remove and replace the LAL. Vision loss may be permanent and may not be improved by replacing the LAL. There is a potential risk for UV-induced damage to the eye, including the cornea and retina, which may be permanent. UV light can sometimes cause a reactivation of previous herpes virus infection in the eye. A reactivation of herpes virus can cause scarring of the cornea, blurred vision, eye pain, extreme light sensitivity, permanent loss of vision, and possible need for corneal transplant. Temporary or persistent erythropsia and/or temporary or persistent color vision deficiency may occur. Corneal dryness and corneal abrasions from the lens used for adjustment and lock-in can occur. After the lens adjustment(s) or after the lens lock-in procedures, discomfort, itching and light sensitivity may occur. In cases where a spherocylinder adjustment is performed, it is possible that visual disturbances may occur if the IOL rotates or if the correction is not performed on the correct axis of astigmatism.

9.13 POTENTIAL BENEFITS

The benefit to subjects is the potential correction of their 0.50 D residual astigmatism. However, these results cannot be guaranteed..

10 STUDY MONITORING

RxSight clinical personnel or designated CRO will monitor all clinical studies in a manner consistent with any applicable health authority regulations and the clinical research standards adopted by RxSight's Clinical Affairs Department. Study monitoring will involve the following elements:

- Member(s) of RxSight's Clinical Affairs Department or designated CRO may meet with investigators prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol.
- A member of RxSight's Clinical Affairs Department or designated CRO may meet with the investigator(s) at the time study subjects begin to be enrolled in order to ensure that subjects are being properly selected and that study data are being correctly recorded.
- A member of RxSight or designated CRO may visit the clinical site at any time during the study to review study worksheets and data entered in the EDC system.
- Interim monitoring visits and telephone consultations will occur as necessary during the course of the study to ensure the proper progress and documentation of the study findings. Centralized and/or remote monitoring may be performed during the conduct of the study.
- RxSight clinical personnel may visit the site at any time during the course of the study to observe the adjustment and lock-in treatments to ensure that the procedures described in the protocol are being followed.
- RxSight clinical personnel may also observe examination techniques used by study personnel to ensure that the procedures being utilized are the procedures described in Appendix 1 of the protocol.

11 ETHICAL AND REGULATORY CONSIDERATIONS

11.1 SUBJECT INFORMATION AND CONSENT

It is the responsibility of the Principal Investigator or authorized designee to give each subject prior to inclusion in the study full and adequate verbal and written information regarding the objective and procedures of the study and the possible risks involved. The subjects will be informed about their right to refuse to participate in the study. The written consent form will be given to each subject before enrollment. It is the responsibility of the Principal Investigator to obtain a signed informed consent form and a HIPAA consent form (if required) and to ensure the subject is given a copy of each.

The Principal Investigator or authorized designee needs to file the informed consent forms for review by RxSight study monitors. The Investigator or authorized designee will acknowledge the receipt of the informed consent form from each subject by signing the appropriate pages of these documents.

11.2 DECLARATION OF HELSINKI

The study will be performed in accordance with the relevant recommendations guiding physicians in biomedical research involving human subjects adopted by the 18th World Medical Assembly, Helsinki, Finland, 1964 and later revisions, as well as applicable U.S. Food and Drug Administration regulations (21 CFR Parts 50, 56, and 812).

It is the responsibility of the Principal Investigator to obtain Institutional Review Board approval of the Study Protocol and related study documents and to keep the IRB informed of any unanticipated problems and any amendments to the protocol.

11.3 ISO 14155:2011 CLINICAL INVESTIGATION OF MEDICAL DEVICES FOR HUMAN SUBJECTS- GOOD CLINICAL PRACTICE

This study should be performed in compliance with ISO 14155:2011.

11.4 ADDITIONAL REGULATORY CONSIDERATIONS

The proposed study is subject to all applicable governmental rules and regulations concerning the conduct of clinical trials on human subjects. This includes, but is not necessarily limited to, the approval of an Institutional Review Board (where applicable); obtaining prospective informed consent; monitoring of the conduct of the study, the completeness of the study worksheets, and accuracy of data entered into the EDC system, as may be employed, by the Sponsor or its designee(s); and record retention by the Sponsor in accordance with 21 CFR Subpart G-Records and Reports.

11.5 STUDY INITIATION/CONDUCT

The study will not commence until (1) approval is obtained from the IRB and appropriate regulatory authorities and (2) written permission is given by the Sponsor. Any additional requirements imposed by the IRB or other appropriate regulatory authorities shall be followed.

11.6 COMPLIANCE WITH THE CLINICAL STUDY PROTOCOL

The Investigator shall conduct this clinical investigation in accordance with the signed agreement with the Sponsor, the investigational plan, and the applicable regulations. The Investigator shall avoid improper influence on or inducement of the subject, Sponsor, Monitor, other Investigator(s) or other parties participating in or contributing to the clinical investigation.

11.7 PROTOCOL DEVIATIONS (PDS)

Protocol deviations should be avoided. Any deviation from the protocol will be recorded on a Case Report Form together with an explanation for the deviation. Deviations should be reported to the Sponsor, who is responsible for analyzing them and assessing their significance.

Deviations should be reviewed to determine the need to amend the protocol or to terminate the investigation.

NOTE: The IRB and Competent Authorities or the appropriate regulatory bodies will be informed of protocol deviations per applicable reporting requirements.

11.8 PROTOCOL AMENDMENTS

Modification of the protocol is prohibited without prior written agreement in the form of a protocol amendment. All amendments will be created by the Sponsor and must be approved by the IRB or other regulatory bodies as needed prior to implementation except when required to mitigate immediate safety risks or when the changes involve only logistical or administrative revisions. All protocol amendments must be clearly summarized to outline the changes that were made.

11.9 PUBLICATION POLICY

The final report of the study will be available to the IRB and appropriate regulatory authorities.

11.10 INSURANCE AND INDEMNITY

The Sponsor shall ensure that acceptable insurance and indemnification is in place prior to enrollment of the first study subject.

12 REFERENCES

1. Conrad-Hengerer I, Al Sheikh M, Hengerer FH, et. al. Comparison of visual recovery and refractive stability between femtosecond laser-assisted cataract surgery and standard phacoemulsification: Six-month follow-up. J Cataract Refract Surg 2015; 41:1356-1364.

2. Baranyovits P. Stabilisation of refraction following cataract surgery. British Journal of Ophthalmology, 1988, 72, 815-819.

3. Malvina B. Eydelman, et al. "Standarized Analyses of Correction of Astigmatism by Laser Systems that Reshape the Cornea", Journal of Refractive Surgery Volume 22 January/February 2006, pp 81-95.