PROTOCOL CSP-028

A SINGLE CENTER EXPLORATORY STUDY TO EVALUATE UNCORRECTED DISTANCE VISION AND QUALITY OF VISION AFTER LIGHT TREATMENTS OF AN IMPLANTED RXSIGHT LIGHT ADJUSTABLE LENS (RXLAL) WITH THE LIGHT DELIVERY DEVICE (LDD) IN SUBJECTS WITH PREOPERATIVE CORNEAL ASTIGMATISM

RxSight, Inc.
100 Columbia, Suite 120
Aliso Viejo, CA 92656
Version 04
April 27, 2018

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

_____ _____
Principal Investigator's Signature *Date*

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1 STUDY SYNOPSIS

STUDY OBJECTIVE

The objective of this study is to evaluate uncorrected distance vision and quality of vision as measured by the McAlinden QoV questionnaire 3 months following the final lock-in treatment of an implanted RxSight Light Adjustable Lens (RxLAL) with the Light Delivery Device (LDD) in subjects with preoperative keratometric astigmatism. This is an exploratory study. No primary effectiveness endpoints will be defined.

STUDY POPULATION

The study population will consist of up to 150 eyes in up to 75 subjects with 0.50 to 3.00 D of pre-operative keratometric astigmatism implanted with the RxLAL. Approximately 1/2 of the study population should have ≥0.50 D and ≤1.5 D of preoperative keratometric astigmatism and approximately 1/2 of the study population should have >1.5 D and ≤3.00 D of preoperative keratometric astigmatism. At least 10 eyes should have >2 D of preoperative keratometric astigmatism.

STUDY DESIGN

A prospective, single center, randomized, exploratory clinical study will be conducted. Subjects will be followed for a 6-month period.

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent. If both eyes of a patient meet study eligibility, a pre-determined randomization scheme will be utilized to designate each of the patient's eyes as the primary eye or the fellow eye. If only one eye of a patient meets study eligibility, that eye will automatically be designated as the primary eye.

At 3 weeks post-implantation, eyes will be refracted, undergo visual testing, and receive a power adjustment based on the manifest refraction. Subjects will return 3 to 7 days after their adjustment and the same measurements performed again. Depending on the adjustment(s) performed, subjects will receive one to three adjustments and one or two lock-in treatments.

Postoperatively, subjects will undergo complete ophthalmic examinations at regular intervals over a 6-month period.

Uncorrected distance visual acuity (UCDVA) and responses from the Quality of Vision (QoV) questionnaire will be summarized. All ocular adverse events (device related and unrelated) during the conduct of the study will be reported. All Secondary Surgical Interventions (SSIs) in study eyes during the conduct of the study will also be reported.

Both eyes of all subjects should be screened for eligibility.

INCLUSION CRITERIA

- Must sign a written Informed Consent form and be willing to undergo cataract surgery for unilateral or bilateral implantation of the RxLAL.
- Between the ages of 40 and 80 inclusive on the day the cataract surgery is performed.
- Study eye must have preoperative keratometric cylinder of ≥0.50 D and ≤3.00 D .
- Study eye must have cataract causing reduction in best corrected distance visual acuity (BCDVA) to a level of 20/32 or worse with or without a glare source.
- Study eye must have best corrected distance visual acuity projected (by clinical estimate based upon past ocular history or retinal exam) to be 20/20 or better after cataract removal and IOL implantation.
- If only one subject eye is enrolled in the study, the non-study eye must have potential for BCDVA of 20/40 or better after cataract removal and IOL implantation.
- Study eye has clear intraocular media other than cataract.
- Willing and able to comply with the requirements for study specific procedures and visits.
- Study eye has a dilated pupil diameter of ≥7.0 mm.
- Study eye requires an IOL power within the range available for the RxLAL.

EXCLUSION CRITERIA

- Study eye with zonular laxity or dehiscence.
- Study eye with pseudoexfoliation.
- Study eye with age-related macular degeneration involving the presence of geographic atrophy or soft drusen.
- Study eye with retinal degenerative disorder or macular disorder (other than mild macular degeneration) that is expected to cause future vision loss.
- Study eye with diabetes with any evidence of retinopathy.
- Study eye with evidence of glaucomatous optic neuropathy.
- Study eye with history of uveitis.

- Study eye with significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma.
- Study eye with corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20.
- Study eye with keratoconus or suspected of having keratoconus.
- Study eye with prior history of Intacs, Radial keratotomy (RK), Conductive keratoplasty (CK), Astigmatic keratotomy (AK), Phakic Implantable Collamer Lens (ICL), Corneal Inlay, or with previous pterygium excision unless the pterygium did not extend more than 2mm onto the cornea from the limbus.
- Study eye with clinically significant dry eye syndrome (DES).
- Study eye with clinically significant corneal haze.
- Study eye with clinically significant corneal opacity.
- 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.
- Study eye with irregular astigmatism.
- Study eye with history of ocular herpes simplex virus.
- Study eye with history of a congenital color vision defect.

OUTCOME PARAMETERS

Exploratory Effectiveness Parameter:

- Percent of eyes with UCDVA of 20/20 or better at 6 Months Postop (3 Months Post Lock-In)

Exploratory effectiveness analyses will be based on the 6-month UCDVA of eyes successfully implanted with the RxLAL.

Safety Parameters:

The following safety parameters will be evaluated at 6 Months Postop (3 Months Post Lock-In):

- Ocular adverse events (device related and unrelated) of the study eyes that occur during the conduct of the study.

- Secondary Surgical Interventions (SSIs) of the study eyes that occur during the conduct of the study.

Subjects who agree to participate in the study will return for the listed follow-up examinations for each study eye:

Examination Schedule:

Evaluation	
Preoperative	Day -60 to Day -1
Operative	Day 0, day of surgery
Postop Day 1	Days 1 to 2 postop
Postop Week 1	Days 7 to 14 postop
Postop Week 3	Days 17 to 24 postop: Adjustment #1
Adjustment #2, if needed	3 to 7 days post Adjustment #1
Adjustment #3, if needed	3 to 7 days post Adjustment #2
Lock-in #1	3 to 7 days post final adjustment
Lock-in #2, if needed	3 to 7 days post lock-in #1
Post Lock-In	3 to 7 days post final lock-in
1 Month Post Lock-In	30 to 60 days post final lock-in
3 Months Post Lock-In/6 Months Postop	Days 120 to 180 postop

Clinical Parameters:

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

1. Quality of Vision (QoV) questionnaire
2. Demographics
3. Ocular history including medications
4. Ocular Biometry: ACD and axial length (Optical biometry only)
5. Autorefraction
6. Corneal Keratometry
7. Vision Quality Measurement (HD Analyzer)
8. Subjective symptoms/complaints (subject reported)
9. Uncorrected distance visual acuity (UCDVA) Monocular
10. Manifest Refraction

[redacted]

13. City University Color Test
14. Intraocular pressure
15. Dilated pupil diameter
16. Slit Lamp Examination

17. Fundus Exam
18. Adverse Events

ABBREVIATIONS AND DEFINITION OF TERMS

AE	Adverse Event
AK	Astigmatic Keratotomy
ANSI	American National Standards Institute
BCDVA	Best Corrected Distance Visual Acuity
CI	Confidence Interval
CK	Conductive Keratoplasty
CRF	Case Report Form
D	Diopter
DES	Dry Eye Syndrome
ETDRS	Early Treatment Diabetic Retinopathy Study
GCP	Good Clinical Practice
ICH	International Conference on Harmonization
ICL	Phakic Implantable Collamer Lens
IOL	Intraocular Lens
IOP	Intraocular Pressure
LASIK	Laser Assisted In-Situ Keratomileusis
LDD	Light Delivery Device
MR	Manifest Refraction
MRCYL	Manifest Refraction Cylinder
MRSE	Manifest Refraction Spherical Equivalent
OD	Right eye
OS	Left eye
PCO	Posterior Capsular Opacity
PI	Principal Investigator
RxLAL	RxSight Light Adjustable Lens
SAE	Serious Adverse Event
SD	Standard Deviation
SE	Spherical Equivalent
UCDVA	Uncorrected Distance Visual Acuity

2 INTRODUCTION AND RATIONALE

In modern cataract surgery, spectacle freedom for the patient, either for distance vision, near vision, or both, is becoming more important. Globally, key cataract technology advancements (e.g.; monofocal, toric, and foldable IOLs; ultrasound, optical and intraoperative biometry; phacoemulsification and femtosecond laser assisted surgery), have resulted in important reductions in residual refractive error and improved uncorrected distance visual acuity (UCDVA), both of which are highly correlated with patient satisfaction following cataract surgery.[1,2]

However, while the potential for significant post-operative residual refractive error has been reduced, it remains the most frequent cataract surgery complication. Approximately 30-60% of patients undergoing monofocal IOL implantation and 15-30% of patients undergoing toric IOL procedures require spectacle correction for distance correction as a result of a non-emmetropic refraction.[3,4,5,6] The large majority of these patients have residual refractive errors that are less than 2 D of magnitude.[4,7,8]

The major causes for residual refractive error following cataract surgery include:

- Estimation errors for postoperative IOL position, preoperative axial length measurement and limitations of IOL calculation formulas that affect both spherical and toric IOLs.[9,10]
- Pre-existing corneal astigmatism (reported to exceed 1.00 D in approximately one-third of cataract patients) and imprecise preoperative measurement of corneal astigmatism.[11,12]

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1 Nordan, LT. The Surgical Rehabilitation of Vision. Gower Medical, New York, 1991.

2 Kirwan C, Nolan JM, Stack J, et al. Determinants of patient satisfaction and function related to vision following cataract surgery in eyes with no visually consequential ocular co-morbidity. Graefes Arch Clin Exp Ophthal 2015;253:1735-1744.

3 Agresta B, Knorz MC, Donatti C, Jackson D. Visual acuity improvements after implantiaton of toric intraocular lenses in cataract patients with astigmatism: a systematic review. Graefes Arch Clin Exp Ophthal 2012;12:41.

4 Brandser R, Haaskjold E, Drolsum L. Accuracy of IOL calculation in cataract surgery. Acta Ophthalmol Scan 1997;75:162-165.

5 Steinert RF, Aker BL, Trentacost DJ, Smith PJ, Tarantino N. A prospective comparative study of the AMO ARRAY zonal-progressive multifocal silicone intraocular lens and a monofocal intraocular lens. Ophthalmology 1999;106(7):1243-55.

6 Connors R 3rd, Boseman P 3rd, Olson RJ. Accuracy and reproducibility of biometry using partial coherence interferometry. J Cataract Refract Surg 2002;28(2):235-238.

7 Olsen T, Bargum R. Outcome monitoring in cataract surgery. Acta Ophthalmol Scand. 1995;73(5):433-7.

8 Wegener M, Alsbirk PH, Hojgaard-Olsen K. Outcome of 1000 consecutive clinic- and hospital-based cataract surgeries in a Danish county. J Cataract Refract Surg 1998;24(8):1152-60.

9 Norrby S. Sources of error in intraocular lens power calculation. J Cataract Refract Surg 2008; 34:368–376.

10 Hirnschall N, Hoffmann PC, Draschl P, et al. Evaluation of factors influencing the remaining astigmatism after toric intraocular lens implantation. J Refract Surg 2014;6:1–7.

11 Ferrer-Blasco T, Montes-Mico R, Peixoto-de-Matos SC, et al. Prevalence of corneal astigmatism before cataract surgery. J Cataract Refract Surg 2009;35:70–75.

12 Lekhanont K, Wuthisiri W, Chatchaipun P, Vongthongsri A. Prevalence of corneal astigmatism in cataract surgery candidates in Bangkok, Thailand. J Cataract Refract Surg 2011;37:613–615.

- Surgical variations in the size and central position of the capsulorhexis which may influence the final position of the IOL inside the bag and are surgeon-dependent, and surgically induced astigmatism (SIA).[13]
- Healing process, such as anterior movement of the IOL resulting from postoperative capsular bag fibrosis and contraction.[13]

When spectacle or contact lens correction is not adequate or desired, secondary surgical procedures currently available to address residual refractive error include excimer laser corneal surgery, astigmatic keratotomy, piggyback (second) IOL placement and IOL exchange. Incorrect lens power remains one of the major causes cited for the removal of intraocular lenses.[5,6,14]

RxSight addresses the problem of residual refractive error with an IOL for which spherical and cylindrical power can be adjusted post-implantation. Following surgical implantation and a period of post-operative stabilization, patients return for examination and refractive adjustment in the office using a profiled beam of light from the Light Delivery Device (LDD). By producing the desired change in lens curvature and spherocylindrical power of the implanted RxSight Light Adjustable Lens (RxLAL), this approach can obviate the need for secondary surgical procedures for the vast majority of patients with residual refractive error.

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

U.S. Phase III Study

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 the United States under an Investigational Device Exemption. In addition to the visual correction of aphakia, reduction in residual spherocylindrical refractive error and improvement in uncorrected distance 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

[13] McIntyre JS, Werner L, Fuller SR, et al. Assessment of a single-piece hydrophilic acrylic IOL for piggyback sulcus fixation in pseudophakic cadaver eyes. J Cataract Refract Surg 2012;38:155–162.

[14] Mamalis, N.; Spencer, T. S.; Complications of foldable intraocular lenses requiring explantation or secondary intervention – 2000 survey update. J Cataract Refract Surg 2001;27(8):1310-1317.

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 BCDVA of 20/40 or better, exceeding the historic grid rate of 92.5% (ISO 11979-7).

OUS Clinical Evaluations

Other clinical evaluations have been conducted outside the United States to study the effectiveness and safety of spherical and spherocylindrical light treatment profiles of the LAL in aphakic patients.

In a post-CE mark study published by Hengerer et al.[15] of 122 LAL eyes with eighteen months follow-up in Bochum, Germany, the authors reported 88% of eyes achieving a UCDVA of 20/20 or better and 98% of eyes within 0.50 diopters of their intended target refraction at 18 months after lock-in treatment. 100% of the eyes met the ≥20/40 BCDVA safety criteria.

In summary, clinical evaluations have demonstrated that the Light Adjustable Lens and Light Delivery Device provide a predictable, stable, and safe treatment of aphakia in patients in whom the cataractous natural lens has been removed by phacoemulsification and who wish to minimize their postoperative spherical/spherocylindercial refractive error and improve their uncorrected distance visual acuity.

[15] Hengerer F, Dick HB, Conrad-Hengerer I. Clinical Evaluation of an Ultraviolet Light Adjustable Intraocular Lens Implanted after Cataract Removal: Eighteen Months Follow-up. Ophthalmology 2011; 118:2382-2388.

3 STUDY OBJECTIVE

The objective of this study is to evaluate uncorrected distance vision and quality of vision as measured by the McAlinden QoV questionnaire 3 months following the final lock-in treatment of the implanted RxSight Light Adjustable Lens (RxLAL) with the Light Delivery Device (LDD) in subjects with preoperative keratometric astigmatism. This is an exploratory study. No primary effectiveness endpoints will be defined.

4 STUDY DESIGN

A prospective, single center, randomized, exploratory clinical study will be conducted. Subjects will be followed for a 6-month period.

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risks/benefits and subject responsibilities to the potential participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent. If both eyes of a patient meet study eligibility, a pre-determined randomization scheme will be utilized to designate each of the patient's eyes as the primary eye or the fellow eye. If only one eye of a patient meets study eligibility, that eye will automatically be designated as the primary eye.

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5 OUTCOME PARAMETERS

5.1 EXPLORATORY EFFECTIVENESS PARAMETERS

- Percent of eyes with UCDVA of 20/20 or better at 6 Months Postop (3 Months Post Lock-In)

Exploratory effectiveness analyses will be based on the 6-month UCDVA of eyes successfully implanted with the RxLAL.

5.2 SAFETY PARAMETERS

The following safety parameters will be evaluated at 6 Months Postop (3 Months Post Lock-In):

- Ocular adverse events (device related and unrelated) of the study eyes during the conduct of the study.
- Secondary Surgical Interventions (SSIs) of the study eyes during the conduct of the study.

6 STUDY POPULATION

The study population will consist of up to 150 eyes in up to 75 subjects with 0.50 to 3.00 D of pre-operative keratometric astigmatism implanted with the RxLAL. Approximately 1/2 of the study population should have ≥0.50 D and ≤1.5 D of preoperative keratometric astigmatism and approximately 1/2 of the study population should have >1.5 D and ≤3.00 D of preoperative keratometric astigmatism. At least 10 eyes should have >2 D of preoperative keratometric astigmatism.

Both eyes of all subjects should be screened for eligibility.

6.1 INCLUSION CRITERIA

- Must sign a written Informed Consent form and be willing to undergo cataract surgery for unilateral or bilateral implantation of the RxLAL.
- Between the ages of 40 and 80 inclusive on the day the cataract surgery is performed.
- Study eye must have preoperative keratometric cylinder of ≥0.50 D and ≤3.00 D.
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- Willing and able to comply with the requirements for study specific procedures and visits.
- Study eye has a dilated pupil diameter of ≥7.0 mm.
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6.2 EXCLUSION CRITERIA

- Study eye with zonular laxity or dehiscence.
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- Study eye with age-related macular degeneration involving the presence of geographic atrophy or soft drusen.

- Study eye with retinal degenerative disorder or macular disorder (other than mild macular degeneration) that is expected to cause future vision loss.
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- Study eye with evidence of glaucomatous optic neuropathy.
- Study eye with history of uveitis.
- Study eye with significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma.
- Study eye with corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20.
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- Study eye with clinically significant dry eye syndrome (DES).
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- Study eye with clinically significant corneal opacity.
- 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.
- Study eye with irregular astigmatism.
- Study eye with a history of ocular herpes simplex virus.
- Study eye with a history of a congenital color vision defect.

7 STUDY MATERIALS AND METHODS

7.1 DEVICE DESCRIPTION

RxSight's Light Adjustable Lens (RxLAL) 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 distance visual acuity.

7.1.1 RXSIGHT LIGHT ADJUSTABLE INTRAOCULAR LENS

The RxSight Light Adjustable Lens (RxLAL) is a 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 RxLAL optic design (Figure 1) features a posterior surface layer, 0.05 mm thick, to further enhance the UV absorbing properties of the RxLAL lens and limit retinal exposure.

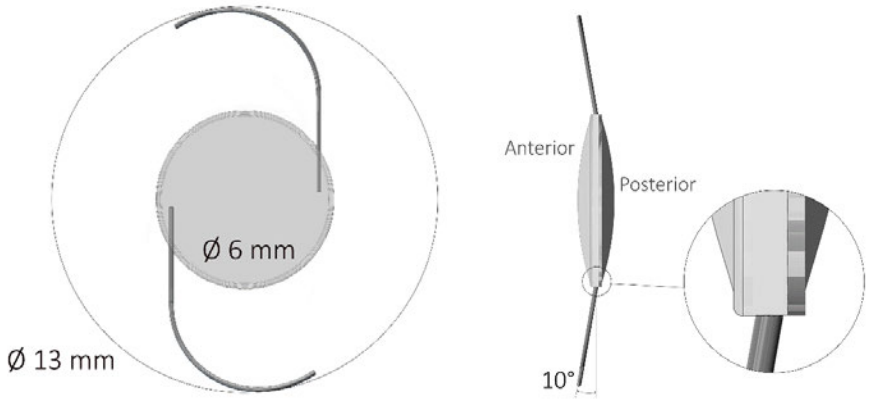

FIGURE 1: RXSIGHT LIGHT ADJUSTABLE LENS (RXLAL) (A) TOP VIEW AND (B) CROSS-SECTION VIEW OF THE OPTIC SHOWING RXLAL WITH A POSTERIOR LAYER

A summary of the RxLAL design characteristics is presented below:

Lens Optic

- Material: Photo-reactive, UV absorbing Silicone
- Light transmission: UV cut-off at 10% T = 394 ± 2 nm
- 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 RxLAL silicone material is designed to respond to a narrowband UV light 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 sphero-cylindrical power of the RxLAL. 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.

7.1.2 LIGHT DELIVERY DEVICE (LDD)

RxSight's Light Delivery Device (LDD) is a UV light projection system (Figure 2) used to induce a predictable change in RxLAL 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 spatially light profiles with adequate intensity and duration to induce polymerization of photoreactive additive leading to a refractive power change of the RxLAL. Because this procedure is performed after implantation, residual refractive errors can be corrected, reducing the need for spectacles, corneal refractive procedures, or additional IOL procedures to optimize a patient's vision.

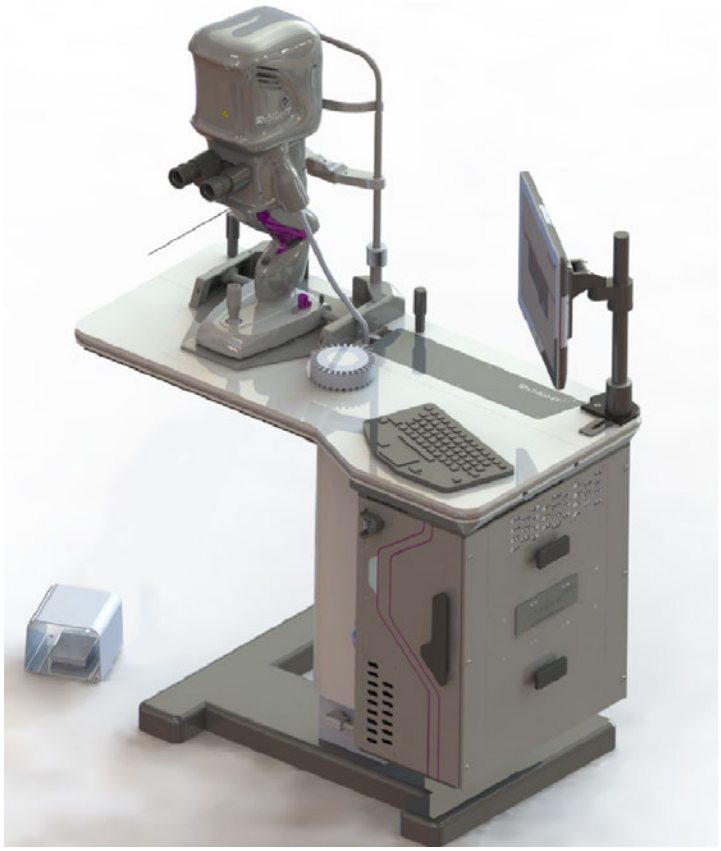

FIGURE 2: RXSIGHT LIGHT DELIVERY DEVICE (LDD)

7.1.3 RXSIGHT INSERTION DEVICE

The RxLAL can be inserted in to the eye using the RxSight Insertion Device, which is comprised of a re-usable titanium injector and a single-use, non-preloaded polypropylene cartridge with lubricating coating.

7.1.4 INDICATIONS FOR USE

The RxSight Light Adjustable Lens (RxLAL) is an intraocular lens intended for primary implantation in the capsular bag for the visual correction of aphakia in adult patients with or without presbyopia in whom a cataractous lens has been removed. The Light Delivery Device (LDD) is used to improve uncorrected visual acuity by adjusting the RxLAL power to correct residual postoperative refractive error including -2.0 to +2.0 diopters of sphere and 0.50 to 3 diopters of cylinder and by changing lens curvature to introduce controlled amounts of spherical aberration (+/- 1 micron) and center near add (up to 2 diopters).

7.2 SUBJECT ENTRY

Patients who require cataract extraction and intraocular lens implantation will be screened for eligibility. If it is determined that the patient may be eligible to participate, study staff will explain the study purpose, procedures, risk/benefits and subject responsibilities to the potential participant. Written informed consent will be obtained prior to any study specific testing. The patient is enrolled upon signing the informed consent. The subject will sign and date the informed consent form in the presence of the person conducting the consent process. The investigator and/or the person conducting the consent process will also sign and date the consent form. The preoperative examination will be performed no more than 90 days prior to surgery. If the 90-day time period elapses, it is acceptable for patients to be re-screened by undergoing a complete preoperative examination. If both eyes of a patient meet study eligibility, a pre-determined randomization scheme will be utilized to designate each of the patient's eyes as the primary eye or the fellow eye. If only one eye of a patient meets study eligibility, that eye will automatically be designated as the primary eye.

Only subjects meeting all inclusion/exclusion criteria will be implanted. Those subjects who do not meet the inclusion/exclusion requirements will be considered screen failures. Subjects will continue to be enrolled until approximately 150 eyes in about 75 subjects have undergone implantation. Unique identification numbers will be assigned to each subject.

Study enrollment will be tracked to ensure that approximately 1/2 of the study population will have ≥0.50 D to ≤1.5 D of preoperative keratometric astigmatism and approximately 1/2 of the study population will have >1.5 D to ≤3.00 D of preoperative keratometric astigmatism. At least 10 eyes should have >2 D of preoperative keratometric astigmatism. Implantations in one bin may be suspended to ensure enrollment in all bins meets these requirements.

The implant lens power for the RxLAL will be calculated based upon the ocular biometry data and a lens power formula of the surgeon's choice with a postoperative spherical

equivalent (SE) outcome closest to emmetropia. If both eyes of a patient are enrolled, the primary eye will be scheduled for implantation prior to the fellow eye.

7.3 RXLAL IMPLANTATION AND REFRACTIVE ADJUSTMENT

7.3.1 SURGICAL PROCEDURE

The RxLAL will be implanted on Day 0 of the study using standard microsurgical techniques.

No additional refractive procedures are allowed until after the 3 Month Post Lock-In/6 months postop visit.

In subjects with both eyes enrolled, if surgical complications occur with the primary eye and no RxLAL is implanted, the subject should be Exited from the study and no RxLAL should be implanted in the fellow eye.

The surgical procedure will be performed as follows:

1. Prepare and drape the eye for surgery in accordance with standard surgical procedures.
2. A temporal clear corneal incision will be made at a location of the surgeon's discretion using the surgeon's standard instrumentation and techniques.
3. Use viscoelastic to fill the anterior chamber through the incision opening.
4. Perform an anterior circular capsulorhexis of a maximum of 5.2 mm in diameter using standard technique. The capsulorhexis should be well-centered with a 360° overlapping capsular edge to minimize IOL tilt and decentration and longitudinal IOL shift. The capsulorhexis and/or nuclear fragmentation can be performed with a femtosecond laser. Precision pulse capsulotomy (PPC) can also be used to perform the capsulorhexis.
5. The surgeon will extract the cataract by phacoemulsification.
6. In the event of an intraoperative complication prior to implantation of the RxLAL, including posterior capsule rupture, zonular rupture, radial capsulorhexis tear, vitreous loss, iris trauma, corneal complications or any intraoperative abnormality that may affect the postoperative pupillary dilation, or the centration or tilt of the intraocular lens, do not implant the RxLAL.
7. The RxLAL can be introduced into the eye using any of the following insertion systems:
    a. The RxSight Insertion Device through a clear temporal corneal incision up to 3.2 mm
    b. Nichamin III Foldable Lens Inserter (Rhein Medical 05-2349) with the Nichamin II Foldable Lens Insertion Forceps (Rhein Medical 05-2348) through a temporal clear corneal incision of 3.5-3.8 mm.
    c. An insertion system of the investigator's choice.

The RxLAL is placed into the capsular bag. If utilizing additional surgical instruments near the incision upon insertion, precaution should be taken not to contact the RxLAL optic with this additional instrument.

8. Verify proper orientation of the RxLAL
9. Aspirate any residual viscoelastic from the eye using a preferred technique.
10. Immediately after completion of the surgery, medications will be used as deemed necessary at the surgeon's discretion.
11. The subject will be provided with two pairs of RxSight approved UV protective spectacles (one clear and one tinted) to protect the implanted RxLAL from extraneous sources of UV light. It is important to direct the subject to follow all instructions that are provided with the UV protective spectacles.

    If an optional patch is used post-operatively according to the surgeon's preference, the subject will be instructed not to remove the patch and keep it in place until the surgeon removes it at the Postop Day 1 visit. The UV protective eyewear will be provided once the patch is removed.

7.3.2 LIGHT TREATMENT PROCEDURE

Seventeen (17) to 24 days after surgery, the subject will return for the Postop Week 3 evaluation and a 1st adjustment treatment of the RxLAL. Subsequent second and third adjustment treatments, if necessary, will all be separated by 3-7 days. The necessity of the second adjustment treatment is guided by the LDD. [redacted] Otherwise proceed to lock-in #1 treatment. The subject will receive the 1st lock-in treatment 3-7 days after the final adjustment treatment. If necessary, lock-in #2 may be performed 3-7 days after lock-in #1. Depending on the adjustment(s) performed, subjects will receive one to three adjustments and one or two lock-in treatments.

7.3.2.1 Postponement of Light Treatment Procedure(s)

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

- [redacted]
- [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, treatment should be delayed.

[redacted]

- If sutures were utilized at the time of surgery to close the incision wound, light treatments should not commence on the study eye until a minimum of 4 weeks after suture removal.[16]
- 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.
- If a study eye 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 [redacted] for additional details regarding premature photopolymerization).
- Any 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.

[16] Azar D, Stark W, Dodick J, et al. Prospective, randomized vector analysis of astigmatism after three-, one-, and no-suture phacoemulsification. J Cataract Refract Surg 1997; 23:1164-1173.

7.3.2.2 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:

1. The study eye will be dilated using any of the following pupil dilation drops [redacted] or pupil dilation gel [redacted]. 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 RxLAL 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.
2. Once adequate pupil dilation is achieved, the subject's fellow eye will be patched and the subject will be comfortably positioned in front of the LDD with chin in the chinrest and forehead against the support bar. The subject is asked to grasp the handles on the LDD for support and is asked to look straight ahead and concentrate on the green fixation light presented in front of them and to try to minimize eye movement.

7.3.2.3 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 to ensure the UV beam is aligned to the reticle. If the UV beam is not aligned to the reticle within the specifications detailed in the LDD Operator's manual, do not perform treatments and call RxSight customer service immediately.

1. All adjustment procedure(s) will be recorded.
2. Within the Patient ID and Patient Data screens, follow the touchscreen prompts to enter requested information. Press the "Proceed" button once information has been entered respectively for each screen.
3. With the Confirmation screen, review all information and press the "Confirm" button.
4. Verify that the LDD ring lights and reticle target are activated.
5. Apply topical anesthetic.
6. Position the RxSight supplied contact lens [redacted] on the cornea using [redacted] as the coupling medium. The contact lens supplied is similar to those used in other ophthalmic procedures. Only the RxSight designated contact lens shall be used.

7. Instruct the subject to focus straight ahead on the LDD fixation light with the study eye.
8. 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.
9. Using the microscope, focus on the RxLAL haptics and align the reticle target with the periphery of the RxLAL.
10. Press the "Ready" button
11. Initiate the irradiation delivery as prompted by the LDD display using the joystick or foot pedal to keep the RxLAL centered in the alignment reticle.
12. Perform micro adjustments to keep the reticle target centered to the RxLAL and to keep the RxLAL 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 RxLAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.
13. If the event of an aborted Adjustment Treatment, do not initiate a new treatment sequence; instead; instruct the subject to return 3-7 days later for refractive evaluation to assess whether an adjustment treatment is required or to proceed directly to a lock-in treatment.
14. Following the light adjustment, the subject will be instructed to continue to wear their UV protective eyewear as instructed until exactly 24 hours after all the lock-in treatments are completed.
15. The subject will return 3 to 7 days following the power adjustment treatment for another light treatment. Depending on the manifest refraction, the subject may receive up to 3 adjustment treatments before receiving the 1st lock-in treatment. The necessity of the second adjustment treatment is guided by the LDD. [redacted]
    Otherwise proceed to lock-in #1 treatment.

7.3.2.4 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 to ensure the UV beam is aligned to the reticle. If the UV beam is not aligned to the reticle within the

specifications detailed in the LDD Operator's manual, do not perform treatments and call RxSight customer service immediately.

1. All lock-in procedure(s) will be recorded.
2. 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.
3. Within the Confirmation screen, review all information and press the "Confirm" button.
4. Verify that the LDD ring lights and reticle target are activated.
5. Apply topical anesthetic.
6. Position the RxSight supplied contact lens [redacted] on the cornea using [redacted] as the coupling medium. The contact lens supplied is similar to those used in other ophthalmic procedures. Only the RxSight designated contact lens shall be used.
7. Instruct the subject to focus straight ahead on the LDD fixation light with the study eye.
8. 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.
9. Using the microscope, focus on the RxLAL haptics and align the reticle target with the periphery of the RxLAL.
10. Press the "Ready" button
11. Initiate the irradiation delivery as prompted by the LDD display using the joystick or foot pedal to keep the RxLAL centered in the alignment reticle.
12. Perform micro adjustments to keep the reticle target centered to the RxLAL and to keep the RxLAL 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 RxLAL in focus by focusing at the haptics. Never focus onto the CCC (capsulotomy) or Purkinje images.
13. If the lock-in treatment is aborted before completion, contact the Sponsor for technical assistance.
14. Upon completion of the lock-in #1 treatment, a notification may appear that informs the user that a lock-in #2 treatment is not required for the subject. If this notification appears, proceed to step #16. If no notification appears, then the subject will require a lock-in #2 treatment and proceed to step #15.
15. The subject will return for the second lock-in treatment 3 to 7 days after the first lock-in treatment.

16. The subject will be permitted to discontinue wear of the UV protective eyewear 24 hours after all lock-in treatments are completed.

7.4 EXAMINATION SCHEDULE

Subjects who agree to participate in the study will return for the listed follow-up examinations for each study eye:

Evaluation	
Preoperative	Day -90 to Day -1
Operative	Day 0, day of surgery
Postop Day 1	Days 1 to 2 postop
Postop Week 1	Days 7 to 14 postop
Postop Week 3	Days 17 to 24 postop: Adjustment #1
Adjustment #2, if needed	3 to 7 days post Adjustment #1
Adjustment #3, if needed	3 to 7 days post Adjustment #2
Lock-in #1	3 to 7 days post final adjustment
Lock-in #2, if needed	3 to 7 days post lock-in #1
Post Lock-In	3 to 7 days post final lock-in
1 Month Post Lock-In	30 to 60 days post final lock-in
3 Months Post Lock-In/6 Months Postop	Days 120 to 180 postop

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.

7.5 CLINICAL PARAMETERS

The following study parameters will be assessed as specified in Table 2. Assessments will be performed using the techniques described in [redacted] and in the order presented here and in Table 2.

1. Quality of Vision (QoV) questionnaire
2. Demographics
3. Ocular history including medications
4. Ocular Biometry: ACD and axial length (Optical biometry only)
5. Autorefraction
6. Corneal Keratometry
7. Vision Quality Measurement (HD Analyzer)
8. Subjective symptoms/complaints (subject reported)
9. Uncorrected distance visual acuity (UCDVA) Monocular

10. Manifest Refraction
11. Best corrected distance visual acuity (BCDVA) Monocular
[redacted]
14. Intraocular pressure
15. Dilated pupil diameter
16. Slit Lamp Examination
17. Fundus Exam
18. Adverse Events

Table 2. Schedule of Visits and Clinical Parameters for Eyes Implanted with the RxLAL

Visits	Preop	Operative	Postop Day 1	Postop Week 1	Postop Week 3	Adjustment #2 (if needed)	Adjustment #3 (if needed)	Lock-in #1	Lock-in #2 (if needed)	Post Lock-In	1 Month Post Lock-In	6 Months Postop (3 Months Post Lock-In)	Unscheduled Visit
Quality of Vision (QoV) Questionnaire	X				X						X	X	
Demographics	X												
Ocular History	X												
Medications	X	X	X	X	X	X	X	X	X	X	X	X	
Ocular Biometry	X												
Autorefraction				X	X	X	X	X	X	X	X	X	
Corneal Keratometry	X				X						X	X	
Vision Quality Measurement (HD Analyzer)	X				X						X	X	
Subjective Symptoms/Complaints (Subject reported)			X	X	X	X	X	X	X	X	X	X	X
Monocular uncorrected distance visual acuity (UCDVA)	X		X	X	X	X	X	X	X	X	X	X	X
Manifest Refraction	X			X	X	X	X	X	X	X	X	X	X
Monocular Best corrected Visual Acuity Distance (BCDVA)	X			X	X	X	X	X	X	X	X	X	X
Intraocular Pressure	X		X	X	X	X	X	X	X	X	X	X	
Dilated Pupil Diameter	X				X	X	X	X	X				
Slit Lamp Exam	X		X	X	X	X	X	X	X	X	X	X	X
Fundus Exam	X				X							X	

Visits	Preop	Operative	Postop Day 1	Postop Week 1	Postop Week 3	Adjustment #2 (if needed)	Adjustment #3 (if needed)	Lock-in #1	Lock-in #2 (if needed)	Post Lock-In	1 Month Post Lock-In	6 Months Postop (3 Months Post Lock-In)	Unscheduled Visit
Adverse Events		X	X	X	X	X	X	X	X	X	X	X	X

7.6 DATA REPORTING

All study data will be recorded onto case report forms (electronic or paper) designed for the study. CRFs can be signed by the investigator either by paper signature or by electronic signature. The CRF may be the source document for some data and each site will document this with a note to file describing in which cases source data will be recorded directly onto the CRF. If paper CRFs are used, all CRFs will be completed in a legible manner in black/blue ink.

Any corrections to the CRFs will be made by drawing a single line through the incorrect entry, recording the correct information, and initialing and dating the change. The CRFs and/or data entered in the EDC system will be reviewed by the Study Monitor.

All clinical data generated in the study will be submitted to RxSight or designated CRO for quality assurance review and statistical analysis. All CRFs 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.

7.7 STUDY COMPLETION PROCEDURES

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

7.7.1 SUBJECT COMPLETION

Subjects are considered to have completed the study if they have completed the 6 Months Postop (3 Months Post Lock-In) 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.

7.7.2 SUBJECT WITHDRAWAL PRIOR TO IMPLANTATION

Subjects may be withdrawn from the study prior to implantation if they do not meet all inclusion/exclusion criteria (screen failures) or decide not to participate in the study.

7.7.3 SUBJECT WITHDRAWAL DUE TO INTRAOPERATIVE COMPLICATIONS PRIOR TO IMPLANTATION

Subjects that meet all inclusion/exclusion criteria but do not undergo implantation of the RxLAL due to intraoperative complications prior to introduction of the RxLAL will be followed to resolution of any adverse events and then exited from the study.

7.7.4 SUBJECT DISCONTINUATION AFTER IMPLANTATION

After implantation, subjects may not be withdrawn from the study unless the study lens has been explanted. 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.

Subjects may be discontinued from the study only when the study lens has been explanted or 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.

7.7.5 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.

8 STATISTICAL METHODS

8.1 POPULATIONS FOR ANALYSIS

Exploratory effectiveness analyses will be performed on observed data for all primary eyes, fellow eyes, and all eyes successfully implanted with the RxLAL.

Safety analyses will be performed on observed data for all eyes of subjects who sign the informed consent and the procedure was attempted which is defined as the point at which the RxLAL makes contact with the eye. No imputation will be performed.

8.1.1 EXPLORATORY EFFECTIVENESS PARAMETERS

The following exploratory effectiveness outcomes will be summarized descriptively based on the observed data. Except for the Quality of Vision Questionnaire (QoV), all the observed data will be summarized for the primary eyes and fellow eyes successfully implanted with RxLAL separately. The summaries will also be performed for all eyes.

UCDVA

Number and percent of primary eyes, fellow eyes, and all eyes (i.e. primary and fellow eyes) successfully implanted with the RxLAL with a UCDVA of 20/20 or better at 6 Months Postop (3 Months Post Lock-In) will be presented and the corresponding 95% confidence interval for the percent based on the binomial distribution will be calculated.

UCDVA will be presented with the number and percent of eyes that fall into each category of UCDVA (e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.) at each visit. The mean UCDVA letter score will be calculated for each visit. Change in UCDVA from Postop Week 3 will be presented at each visit as categorical outcomes of "increase in 15 letters or more", "Increase in 10-14 letters", "Increase in 5-9 letters", "No change", "Decrease in 5-9 letters", "Decrease in 10-14 letters", and "Decrease in 15 letters or more". The mean change from Postop Week 3 will also be presented.

UCDVA will also be presented with the number and percent of eyes that fall into each category of UCDVA (e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.) stratified into two bins based on preoperative keratometric cylinder ($\geq$0.50 D and $\leq$1.50 D) and (>1.50 D and $\leq$3.00 D). The mean UCDVA letter score will be calculated for each of the two defined preoperative keratometric cylinder bins.

Quality of Vision[17] Questionnaire

Results of the Quality of Vision Questionnaire will be summarized descriptively for subjects bilaterally implanted with the RxLAL and for subjects with the RxLAL implanted only in the

[17] McAlinden C, Pesudovs K, Moore JE. The Development of an Instrument to Measure Quality of Vision: The Quality of Vision (QoV) Questionnaire. Invest Ophthalmol Vis Sci. 2010;51:5537-5545.

primary eye preoperatively, at Postop Week 3, 1 Month Post Lock-In, and at 6 Months Postop (3 Months Post Lock-In).

8.2 SAFETY PARAMETERS

All ocular adverse events (device related and unrelated) and all Secondary Surgical Interventions (SSIs) of the study eyes during the conduct of the study will be presented.

8.2.1 ADDITIONAL SAFETY ANALYSES

The safety outcomes will be summarized descriptively for all eyes that have the procedure attempted.

BCDVA

BCDVA will be presented with the number and percent of eyes who fall into each category of BCDVA at each visit (e.g. 20/20 or better, 20/25 or better, 20/32 or better, etc.). The mean BCDVA letter score will be calculated for each visit. Change in BCDVA from Postop Week 3 or from Preoperative will be presented at each visit as categorical outcomes of "Increase in 15 letters or more", "Increase in 10-14 letters", " Increase in 5-9 letters", "No change", "Decrease in 5-9 letters", "Decrease in 10-14 letters", and "Decrease in 15 letters or more".

[redacted]

[redacted]

Intraocular Pressure (IOP)

The IOP and change in IOP from preoperative will be summarized by mean, standard deviation, median, minimum and maximum. The number and percent of eyes reported with IOP $\geq$ 25 mmHg or an IOP increase of $\geq$ 10 mmHg from baseline will be provided at each visit.

Slit Lamp Examination and Fundus Examination Findings

The outcomes will be summarized descriptively by count and percent of eyes with each possible finding category.

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.

The following may be considered normal events after cataract surgery and only need to be reported as AEs as specified:

- Iritis/cells/flare (if present after Postop Week 1 and greater than grade 1 (trace)) or (any iritis/cells/flare present at 6 Months Postop (3 Months Post Lock-In) of any grade)
- Corneal edema (if present after Postop Week 1 and greater than grade 1 (trace)) or (if present at 6 Months Postop (3 Months Post Lock-In) of any grade)
- Raised intraocular pressure (IOP) >10 mmHg above preoperative and greater than 25 mmHg (if present after Postop Week 1)

In addition, the specific following events should be reported as an AE:

- A [redacted] at any time after Postop Week 3.
- An [redacted] at any time after Postop Week 3.
- An [redacted] at the 6 Months Postop (3 Months Post Lock-In) visit.

9.2 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.

9.2.1 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 and 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 7.7.1 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 Preoperative 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)

9.2.2 EVALUATIONS

When evaluating AEs, the 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.

9.2.3 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 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. 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. Sites must also report the SAE to the reviewing Ethics Committee per its reporting procedures.

9.2.4 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.

9.2.5 POTENTIAL ADVERSE EVENTS

The following have been identified as potential adverse events for all cataract surgeries including the RxLAL. 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, 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. 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 RxLAL include:

The RxLAL must be implanted following specific surgical procedures. If these procedures are not followed by the surgeon, the lens may become scratched or improperly placed in the eye and may need to be explanted prior to light treatments. 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 RxLAL 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 RxLAL 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 RxLAL. Vision loss may be permanent and may not be improved by replacing the RxLAL. 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.

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. 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 CRFs and/or 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.
- RxSight clinical personnel may visit the site at any time during the course of the study to observe implantation of the RxLAL and 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 [redacted].

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 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.

It is the responsibility of the Principal Investigator to obtain Ethics Committee approval of the Study Protocol and to keep the Ethics Committee informed of serious side effects or adverse events and any amendments to the protocol.

11.3 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 Ethics Committee; obtaining prospective informed consent; monitoring of the conduct of the study, the completeness of the study CRFs, and/or 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 Good Clinical Practice.

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