PROTOCOL CSP-033

A PROSPECTIVE RANDOMIZED CONTROLLED MULTI-CENTER CLINICAL STUDY TO EVALUATE THE SAFETY AND EFFECTIVENESS OF THE RXSIGHT LIGHT ADJUSTABLE LENS (LAL) IN SUBJECTS DESIRING AN EXTENDED DEPTH OF FOCUS

RxSight, Inc.
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Version 17
October 12, 2020

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*

TABLE OF CONTENTS

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1 STUDY SYNOPSIS

1.1 STUDY OBJECTIVE

The primary objective of this study is to evaluate, for the visual correction of aphakia and presbyopia, the safety and effectiveness of the RxSight Light Adjustable Lens (LAL) to provide an extended depth of focus (improve intermediate and near visual acuity without compromising distance visual acuity) in subjects who have undergone bilateral implantation with the LAL and subsequent light treatments for refractive and presbyopia correction (LAL group). To assess for effectiveness, a control group consisting of subjects bilaterally implanted with commercially available IOLs (SofPort LI61AO monofocal IOL, Bausch + Lomb) (Control group) will be used. Primary effectiveness will be demonstrated by comparing monocular measurements of depth of focus (DOF), photopic distance corrected intermediate visual acuity (67 cm), and photopic best corrected distance visual acuity (4 meters) between primary eyes in the LAL group and Control group at the Postop Month 6 visit. Secondary effectiveness will be demonstrated by comparing monocular measurements of primary eyes of photopic uncorrected distance visual acuity (UCDVA) (4 meters)/uncorrected intermediate visual acuity (UCIVA) (67 cm)/uncorrected near visual acuity (UCNVA) (40 cm) and monocular measurements of primary eyes of photopic uncorrected distance visual acuity (4 meters) and photopic distance corrected near visual acuity (40 cm) between the LAL group and Control group at the Postop Month 6 visit.

1.2 STUDY POPULATION

The study population will consist of up to 350 subjects enrolled (informed consent form signed) to allow for up to 230 subjects with implantation of either the LAL IOL or Control IOL attempted in the Full Analysis Set (FAS). An additional 17 subjects were previously implanted in the pre-COVID-19 population. Each subject will desire to improve their depth of focus (improve intermediate and near visual acuity without compromising distance visual acuity), will be good candidates for bilateral IOL implantation, and will agree to participate in a randomized clinical study. Study subjects will be randomized 1:1 to either undergo bilateral LAL implantation and light treatments for refractive and presbyopia correction (LAL group) or to undergo bilateral implantation with commercially available IOLs (SofPort LI61AO monofocal IOL, Bausch + Lomb) (Control group). All study subjects must have preoperative keratometric astigmatism of <0.75 D in both eyes. Subject's eyes must meet all other applicable inclusion criteria and none of the exclusion criteria.

1.3 STUDY DESIGN

A prospective, randomized, controlled, multi-center, clinical study will be conducted at a maximum of 11 sites located in the United States. Subjects will be followed for a 6 month period. A minimum of 20 subjects will undergo study implantation at each participating site, with less than 25% of the total study population implanted at one clinical site.

Patients who require bilateral cataract extraction and intraocular lens implantation and who wish to improve their depth of focus will be pre-screened for eligibility as part of pre-entry activity. If it is determined that the 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. Written informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research. The patient is enrolled upon signing the informed consent. Both eyes of all subjects must be screened for eligibility at the same preoperative visit. If at any time during the preoperative screening, either eye does not meet inclusion or exclusion criteria, screening for that subject should be discontinued and the subject will be exited from the study. Subjects that meet all inclusion/exclusion criteria will be randomly assigned in a 1:1 ratio to either the LAL group or Control group. In addition, each eye of the subject will be assigned as either the primary eye or fellow eye. Pre-determined randomization schemes will be utilized. The primary eye of each subject will be scheduled for surgery first with implantation of the fellow eye separated by 7 to 14 days.

All study eyes will be targeted for post cataract surgery emmetropia as measured on a 4 meter exam lane. If surgical complications (either prior to attempting to implant the study IOL or after study IOL implantation has been attempted) occur with the primary eye and no study IOL is implanted, the subject should be followed until any adverse event that may have occurred is stable or has resolved per the investigator's assessment; at which time the subject should be exited from the study. No study IOL should be implanted in the fellow eye. Subjects that have successful implantation of a study IOL in the primary eye but not the fellow eye will not be required to have monocular clinical measurements of their fellow eye performed throughout the study.

<u>Subjects randomized to the LAL group</u>
Commencing at the Postop Week 3 [redacted] visit (17-24 days post-Fellow eye operative visit), both eyes will receive an [redacted]

At the Adjustment #1 visit (3-7 days after the Postop Week 3 [redacted] visit), both eyes will receive an adjustment #1 light treatment based on the measured manifest refraction on a 4 meter lane at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

At the Adjustment #2 visit (3-7 days after the Adjustment #1 visit) both eyes will receive an adjustment #2 light treatment also based on the measured manifest refraction on a 4 meter

lane at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

Three to 7 days after the Adjustment #2 light treatment, both eyes will be eligible to receive an adjustment #3 light treatment. If the eye's |MRSE| is ≥0.25 D OR manifest cylinder is measured at ≥0.50 D, then the eye will receive an adjustment #3 light treatment; otherwise the eye will be eligible to proceed to lock-in #1.

The lock-in #1 light treatment will be performed in the primary eye 3 to 7 days after the subject's final adjustment light treatment followed 3 to 7 days later by the lock-in #2 treatment, if needed. The lock-in #1 treatment will be performed in the fellow eye 3 to 7 days after the final lock-in in the primary eye and after confirmation that there has been no ultraviolet (UV) retinal damage per Sections 7.3.2.1 and 7.3.2.2 followed 3 to 7 days later by lock-in #2, if needed. Subjects in the LAL group will receive [redacted], up to three sphero-cylindrical/non-astigmatic light treatments, and one or two lock-in treatments in each eye.

Examinations will occur at regular intervals over a 6 month period to evaluate the safety and effectiveness outcomes. For eyes in the LAL group, if an eye is diagnosed with ultraviolet (UV) retinal damage, an additional follow-up exam will be added at 12 months postoperatively to confirm resolution or document sequelae, if any. Masked examiners will be utilized at the Postop Month 6 visit.

Safety for all study eyes will be evaluated per ISO 11979-7.

1.4 INCLUSION CRITERIA

- Must sign a written Informed Consent Document and be willing to undergo cataract surgery for bilateral implantation of either the LAL or SofPort LI61AO IOL (Bausch + Lomb).
- Must be willing to be randomized to either the LAL group (bilaterally implanted with the LAL and receive light treatments for refractive and presbyopia correction) or the Control group (bilateral implantation with the SofPort LI61AO monofocal IOL).
- Between the ages of 40 and 80 inclusive on the day the first cataract surgery is performed.
- Preoperative keratometric cylinder <0.75 D in both eyes.
- Cataractous lens changes as demonstrated by best corrected distance visual acuity (BCDVA) of 20/40 or worse with or without a glare source in both eyes.
- Best corrected distance visual acuity projected to be 20/20 or better after cataract removal and intraocular lens (IOL) implantation in both eyes as estimated by potential acuity meter (PAM) or surgeon estimation.
- Clear intraocular media other than cataract in both eyes.
- Willing and able to comply with the requirements for study specific procedures and visits.

- [redacted]
- Able to complete a written questionnaire in English.
- Requires an IOL power within the range available for both the LAL and SofPort LI61AO IOLs.

1.5 EXCLUSION CRITERIA

- Pseudoexfoliation in either eye.
- Pre-existing macular disease in either eye.
- Patient with sufficiently dense cataract that precludes examination of the macula in either eye.
- Retinal degenerative disorder that is expected to cause future vision loss in either eye.
- Diabetes with any evidence of retinopathy in either eye.
- Evidence of glaucomatous optic neuropathy in either eye.
- History of uveitis in either eye.
- Significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma in either eye.
- Pupil that is deformed including ectopic pupil condition in either eye.
- Corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20 in either eye.
- Any corneal dystrophy including basement membrane dystrophy in either eye that in the opinion of the investigator may confound the outcome.
- Keratoconus or suspected of having keratoconus in either eye.
- Has undergone previous corneal or intraocular surgery in either eye, except 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 either eye.
- Irregular astigmatism in either eye.

- History of ocular herpes simplex virus in either eye.
- Previous trauma or developmental defects in which appropriate support of the intraocular lens (IOL) is not possible in either eye.
- Current vitreoretinal disease or a high risk for future vitreoretinal disease that may require silicone oil as part of therapy in either eye.
- [redacted]
- Subject who has participated within another ophthalmic clinical trial within the last 3 months.

1.6 OUTCOME PARAMETERS

Effectiveness Parameters:

Primary Endpoints

- Monocular Depth of Focus (DOF) measured at the logMAR 0.20 level at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates at least 0.5 D greater monocular photopic negative lens induced distance-corrected depth of focus compared to the Control group (primary eyes) at 0.20 logMAR visual acuity threshold.

- Monocular photopic Distance Corrected Intermediate Visual Acuity (DCIVA) at 67 cm at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean monocular photopic DCIVA at 67 cm. [one-sided test using level of significance of 0.025]

- Outcome of Monocular photopic DCIVA at 67 cm better than or equal to 0.20 logMAR for the LAL group at Postop Month 6

  At Postop Month 6, the proportion of the LAL primary eyes reaching this outcome is at least 50%. In other words, the median of photopic monocular DCIVA at 67 cm for the LAL group (primary eyes) is at least 0.20 logMAR.

- Monocular photopic Best Corrected Distance Visual Acuity (BCDVA) at Postop Month 6

  At Postop Month 6, the LAL group (primary eye) is statistically non-inferior to the Control group (primary eyes) on mean of monocular photopic BCDVA using a non-inferiority margin of 0.10 logMAR.

[redacted]

Secondary Endpoints

The secondary effectiveness endpoints listed below [redacted]

[redacted]

- Monocular photopic Distance Corrected Near Visual Acuity (DCNVA) at 40 cm at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean photopic monocular DCNVA at 40 cm [one-sided test using level of significance of 0.025]

- Outcome of Monocular photopic DCNVA at 40 cm better than or equal to 0.20 logMAR at Postop Month 6

  At Postop Month 6, the proportion of the LAL primary eyes reaching this outcome is at least 50%. In other words the median of monocular photopic DCNVA at 40 cm for the LAL group (primary eyes) is at least 0.20 logMAR.

- [redacted]

- Monocular photopic Uncorrected Distance Visual Acuity (UCDVA) using a +0.25 D lens at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean monocular photopic UCDVA using a +0.25 D [redacted]

[redacted]

The analyses of the secondary effectiveness endpoints will be [redacted]

Safety Parameters:

Primary Endpoint

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

The ISO-event rates for all subjects in the LAL group and Control group will be presented separately. Additionally the event rate of the LAL subjects will be compared to the "safety and performance endpoints (SPE)" rates specified in ISO.

[redacted]

The incidence of all other adverse events will also be presented separately for the LAL group and Control group. In addition, the incidence of secondary surgical intervention (SSI) related to the optical properties of the lens will be provided.

1.7 EXAMINATION SCHEDULE

LAL Group:

Evaluation	
Preoperative OU	Maximum of 60 days prior to Operative Visit for either Primary Eye or Fellow Eye
Operative Primary Eye	Day 0, day of surgery for Primary Eye
Postop Day 1 Primary Eye	Days 1 to 2 post-Operative Visit Primary Eye
Postop Week 1 Primary Eye	Days 7 to 14 post-Operative Visit Primary Eye
Operative Fellow Eye	7 to 14 days post-Operative Visit Primary Eye
Postop Day 1 Fellow Eye	Days 1 to 2 post-Operative Visit Fellow Eye
Postop Week 1 Fellow Eye	Days 7 to 14 post-Operative Visit Fellow Eye
Postop Week 3 [redacted] (bilateral)[1]	Days 17 to 24 post-Operative Visit Fellow Eye
Adjustment #1 (bilateral)[1]	3 to 7 days after the Postop Week 3 (EDF Light Treatment) visit
Adjustment #2 (bilateral)[1]	3 to 7 days post Adjustment #1 Visit
Adjustment #3 (bilateral, if needed)[2]	3 to 7 days post Adjustment #2 Visit
Lock-in #1 Primary Eye	3 to 7 days post subject's final Adjustment Visit
Lock-in #2 Primary Eye, if needed	3 to 7 days post lock-in #1 Visit for Primary Eye
Lock-In #1 Fellow Eye	3 to 7 days post final lock-in Visit for Primary Eye
Lock-In #2 Fellow Eye, if needed	3 to 7 days post lock-in #1 Visit for Fellow Eye
Postop Month 3 (bilateral)	Days 60 to 90 post-Operative Fellow Eye Visit
Postop Month 6 (bilateral)	Days 120 to 180 post-Operative Fellow Eye Visit
Postop Month 12, if needed	Days 330 to 420 post-Operative Fellow Eye Visit

1- Light treatments will be performed bilaterally at the same visit
2- Adjustment #3 will be peformed bilaterally (if needed) at the same visit if specific clinical criteria are measured as described in section 7.3.2 of the protocol

A Postop Month 12 visit will be conducted if a subject is diagnosed with UV retinal damage to confirm resolution or document sequelae, if any.

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.

Control Group:

Evaluation	
Preoperative OU	Maximum of 60 days prior to Operative Visit for either Primary Eye or Fellow Eye
Operative Primary Eye	Day 0, day of surgery for Primary Eye
Postop Day 1 Primary Eye	Days 1 to 2 post-Operative Visit Primary Eye
Postop Week 1 Primary Eye	Days 7 to 14 post-Operative Visit Primary Eye
Operative Fellow Eye	7 to 14 days post-Operative Visit Primary Eye
Postop Day 1 Fellow Eye	Days 1 to 2 post-Operative Visit Fellow Eye
Postop Week 1 Fellow Eye	Days 7 to 14 post-Operative Visit Fellow Eye
Postop Week 3 (bilateral)	Days 17 to 24 post-Fellow Eye Operative Visit
Postop Month 3 (bilateral)	Days 60 to 90 post-Operative Fellow Eye Visit
Postop Month 6 (bilateral)	Days 120 to 180 post-Operative Fellow Eye Visit

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
[redacted]
5. Ocular history
6. History of Medications
7. Subjective symptoms/complaints (subject reported)
[redacted]
9. Corneal Topography
10. Wavefront aberrometry
11. Autorefraction
12. Undilated photopic pupil diameter [redacted]
13. Corneal Keratometry
14. Ocular Biometry: Axial length + Anterior Chamber Depth (Optical or immersion A-scan biometry)
15. Monocular photopic uncorrected distance visual acuity using a +0.25 D lens to compensate for 4 meter test distance
16. Binocular photopic uncorrected distance visual acuity using a +0.25 D trial lens over each eye to compensate for 4 meter test distance

17. Manifest Refraction
18. Monocular photopic best corrected visual acuity
19. Monocular photopic uncorrected distance visual acuity (no trial lens in front of eye)
20. Ocular Dominance
21. Undilated pupil diameter [redacted]
22. Depth of focus testing
23. Monocular mesopic distance corrected intermediate visual acuity
24. Monocular mesopic best corrected intermediate visual acuity
25. Monocular mesopic best corrected near visual acuity
26. Monocular mesopic distance corrected near visual acuity
27. Monocular photopic distance corrected near visual acuity
28. Monocular photopic uncorrected near visual acuity
29. Binocular photopic uncorrected near visual acuity
30. Binocular photopic uncorrected intermediate visual acuity
31. Monocular photopic uncorrected intermediate visual acuity
32. Monocular photopic distance corrected intermediate visual acuity

[redacted]

35. Mesopic undilated pupil diameter [redacted]
36. Distance corrected contrast sensitivity: Mesopic/Photopic with and w/o glare

[redacted]

38. Intraocular pressure
39. Slit Lamp Examination
40. Fundus Exam
41. Fundus Photos

[redacted]

43. IOL Stability (Tilt/Decentration)
44. Dilated pupil diameter [redacted]
45. Adverse Event

ABBREVIATIONS

ADE	Adverse Device Effect
AE	Adverse Event
ANCOVA	Analysis of Covariate
ANOVA	Analysis of Variance
ANSI	American National Standards Institute
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
D	Diopter
DCIVA	Distance corrected intermediate visual acuity
DCNVA	Distance corrected near visual acuity
DD	Device Deficiency
DES	Dry Eye Syndrome
DEQ	Defocus Equivalent
[redacted]	[redacted]
DOF	Depth of Focus
EC	Ethics Committee
EDC	Electronic Data Capture
EDF	Extended Depth of Focus
ETDRS	Early Treatment Diabetic Retinopathy Study
FA	Fluorescein Angiography
FAS	Full Analysis Set
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
ISO	International Organization for Standardization
ITT	Intent To Treat
KCYL	Keratometric Cylinder
LAL	RxSight Light Adjustable Lens

LDD	Light Delivery Device
MR	Manifest Refraction
MRCYL	Manifest Refraction Cylinder
MRSE	Manifest Refraction Spherical Equivalent
NEI	National Eye Institute
OCT	Optical Coherence Tomography
PCO	Posterior Capsular Opacity
PD	Protocol Deviation
PHI	Protected Health Information
PMA	Premarket Application
PP	Per Protocol Population
PPC	Precision Pulse Capsulotomy
[redacted]	[redacted]
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SD	Standard Deviation
SDT	Source Document Template
SE	Spherical Equivalent
SPE	Safety and Performance Endpoints
SPK	Superficial Punctate Keratitis
SSI	Secondary Surgical Intervention
[redacted]	[redacted]
UADE	Unanticipated Adverse Device Effect
UCDVA	Uncorrected Distance Visual Acuity
UCIVA	Uncorrected Intermediate Visual Acuity
UCNVA	Uncorrected Near Visual Acuity
UV	Ultraviolet
VA	Visual acuity

2 INTRODUCTION AND RATIONALE

Virtually all cataract surgery patients experience presbyopia post-operatively, resulting in difficulty performing intermediate and near tasks at a customary working distance. This represents a significant disability due to the increasing importance of intermediate vision for cell phones and computer monitors. While multifocal IOLs can improve near and intermediate vision, they are often associated with adverse effects, such as dysphotopsia, visual disturbances at night, halos, and glare.[1] These effects have been shown to be exacerbated by both relatively small amounts of IOL decentration and residual postoperative refractive error.[2,3,4,5,6]

[redacted]

[redacted]

To evaluate effectiveness, the study compares the 6 month post-operative results for subjects receiving bilateral LAL implantation and subsequent [redacted] light treatment with a control group bilaterally implanted with commercially available IOLs (SofPort LI61AO monofocal IOL).

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1 Labiris G, Giarmoukakis A, Patsiamanidi M, et al. Mini-monovision versus multifocal intraocular lens implantation. J Cataract Refract Surg 2015; 41:53-57.

2 De Vries NE, Webers CA, Touwslager WR, et al. Dissatisfaction after implantation of multifocal intraocular lenses. J Cataract Refract Surg 2011; 37:859-865.

3 Woodward MA, Randleman JB, Stulting RD. Dissatisfaction after multifocal intraocular lens implantation. J Cataract Refract Surg 2009; 35:992-997.

4 Hayashi K, Manabe S-I, Yoshida M, Hayashi H. Effect of astigmatism on visual acuity in eyes with a diffractive multifocal intraocular lens. J Cataract Refract Surg 2010; 36:1323-1329.

5 Braga-Mele R, Chang D, Dewey S, et al. Multifocal intraocular lenses: Relative indications and contraindications for implantation. J Cataract Refract Surg 2014; 40:313-322.

6 Karhanova M, Pluhacek F, Mlcak P, et al. The importance of angle kappa evaluation for implantation of diffractive multifocal intra-ocular lenses using pseudophakic eye model. Acta Ophthalmol. 2015:93 e123-e128.

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).

In November 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, for the visual correction of aphakia and presbyopia, the safety and effectiveness of the RxSight Light Adjustable Lens (LAL) to provide an extended depth of focus (improve intermediate and near visual acuity without compromising distance visual acuity) in subjects who have undergone bilateral implantation with the LAL and subsequent light treatments for refractive and presbyopia correction (LAL group). To assess for effectiveness, a control group consisting of subjects bilaterally implanted with commercially available IOLs (SofPort LI61AO monofocal IOL, Bausch + Lomb) (Control group) will be used. Primary effectiveness will be demonstrated by comparing monocular measurements of depth of focus (DOF), photopic distance corrected intermediate visual acuity (67 cm), and photopic best corrected distance visual acuity (4 meters) between primary eyes in the LAL group and Control group at the Postop Month 6 visit. Secondary effectiveness will be demonstrated by comparing monocular measurements of primary eyes of photopic uncorrected distance visual acuity (UCDVA) (4 meters)/uncorrected intermediate visual acuity (UCIVA) (67 cm)/uncorrected near visual acuity (UCNVA) (40 cm) and monocular measurements of primary eyes of photopic uncorrected distance visual acuity (4 meters) and photopic distance corrected near visual acuity (40 cm) between the LAL group and Control group at the Postop Month 6 visit.

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At the Adjustment #2 visit (3-7 days after the Adjustment #1 visit), both eyes will receive an adjustment #2 light treatment also based on the measured manifest refraction at 4 meters at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

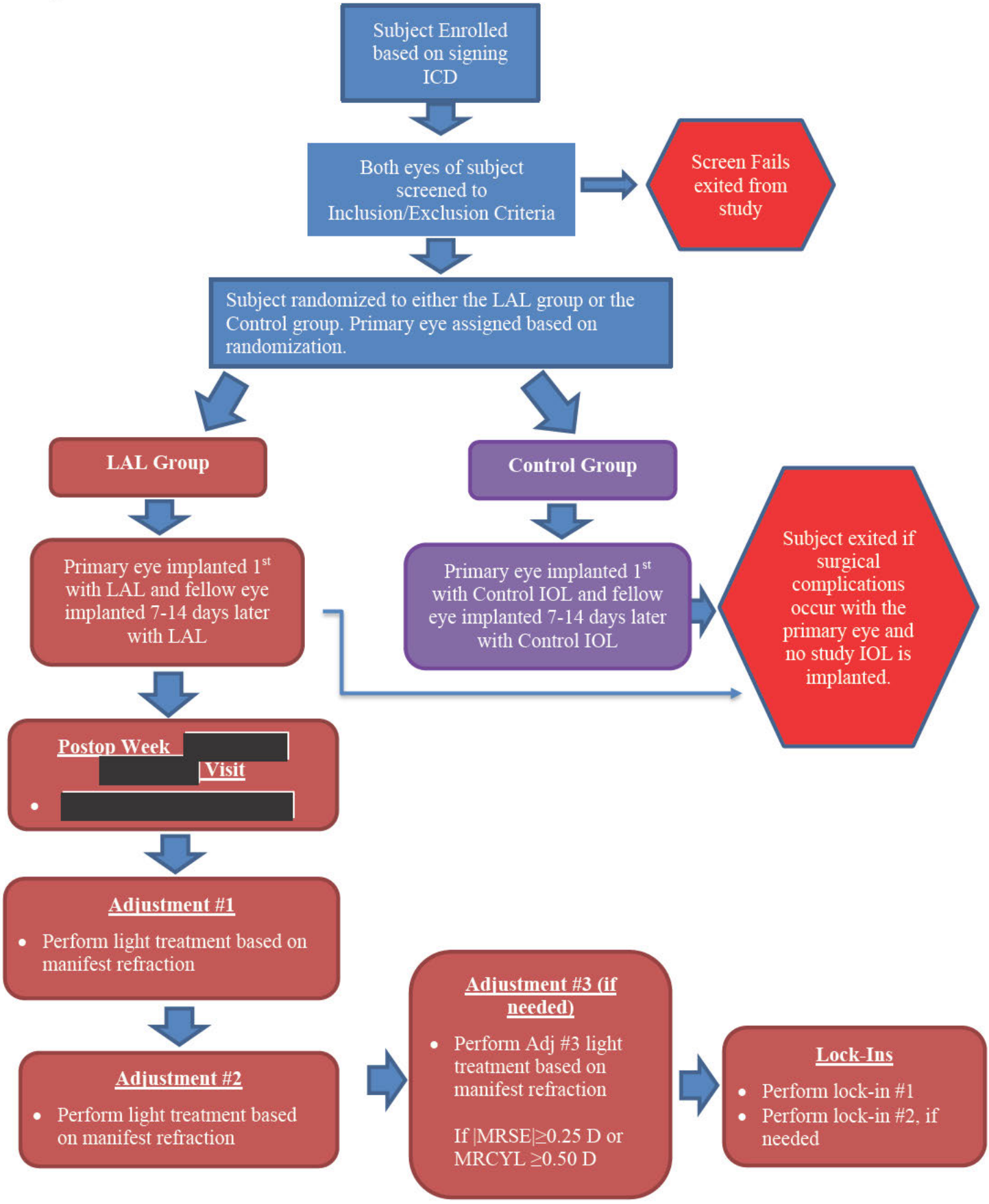
Three to 7 days after the Adjustment #2 light treatment, both eyes will be eligible to receive an adjustment #3 light treatment. If the eye's |MRSE| is ≥0.25 D OR manifest cylinder is measured at ≥0.50 D, then the eye will receive an adjustment #3 light treatment; otherwise the eye will be eligible to proceed to lock-in #1.

The lock-in #1 light treatment will be performed in the primary eye 3 to 7 days after the subject's final adjustment light treatment followed 3 to 7 days later by the lock-in #2 treatment, if needed. The lock-in #1 treatment will be performed in the fellow eye 3 to 7 days after the final lock-in in the primary eye and after confirmation that there has been no ultraviolet (UV) retinal damage per Sections 7.3.2.1 and 7.3.2.2 followed 3 to 7 days later by lock-in #2, if needed. Subjects in the LAL group will receive [redacted], up to three sphero-cylindrical/non-astigmatic light treatments, and one or two lock-in treatments in each eye.

Examinations will occur at regular intervals over a 6 month period to evaluate the safety and effectiveness outcomes. For eyes in the LAL group, if an eye is diagnosed with ultraviolet (UV) retinal damage, an additional follow-up exam will be added at 12 months postoperatively to confirm resolution or document sequelae, if any. Masked examiners will be utilized at the Postop Month 6 visit.

Safety for all study eyes will be evaluated per ISO 11979-7.

The following flowchart illustrates the enrollment and the adjustment process for the proposed study.



DURATION OF STUDY

Each subject will participate in the study for approximately 6 months. The recruitment phase is expected to last approximately 14 months. The complete study period is expected to be approximately 20 months.

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 PARAMETERS

Primary Endpoints

- Monocular Depth of Focus (DOF) measured at the logMAR 0.20 level at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates at least 0.5 D greater monocular photopic negative lens induced distance-corrected depth of focus compared to the Control group (primary eyes) at 0.20 logMAR visual acuity threshold.

- Monocular Distance Corrected Intermediate Visual Acuity (DCIVA) at 67 cm at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean photopic monocular distance corrected intermediate visual acuity (DCIVA) at 67 cm. [one-sided test using level of significance of 0.025].

- Outcome of Monocular DCIVA at 67 cm better than or equal to 0.20 logMAR for the LAL group at Postop Month 6

  At Postop Month 6, the proportion of the LAL primary eyes reaching this outcome is at least 50%. In other words, the median of photopic monocular DCIVA at 67 cm for the LAL group (primary eyes) is at least 0.20 logMAR.

- Monocular Best Corrected Distance Visual Acuity (BCDVA) at Postop Month 6

  At Postop Month 6, the LAL group (primary eye) is statistically non-inferior to the Control group (primary eyes) on mean, monocular photopic BCDVA using a non-inferiority margin of 0.10 logMAR.

[redacted]

Secondary Endpoints

The secondary effectiveness endpoints listed below will be [redacted]

- Monocular photopic Distance Corrected Near Visual Acuity (DCNVA) at 40 cm at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean photopic monocular DCNVA at 40 cm [one-sided test using level of significance of 0.025]

- Outcome of Monocular photopic DCNVA at 40 cm better than or equal to 0.20 logMAR at Postop Month 6

  At Postop Month 6, the proportion of the LAL primary eyes reaching this outcome is at least 50%. In other words the median of monocular photopic DCNVA at 40 cm for the LAL group (primary eyes) is at least 0.20 logMAR.

- [redacted]

[redacted]

- Monocular photopic Uncorrected Distance Visual Acuity (UCDVA) using a +0.25 D lens at Postop Month 6

  At Postop Month 6, the LAL group (primary eyes) demonstrates statistical superiority over the Control group (primary eyes) on mean monocular photopic UCDVA using a +0.25 D lens [redacted]

The analyses of the secondary effectiveness endpoints [redacted]

5.2 SAFETY PARAMETERS

Primary Endpoint

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

The ISO-event rates for all subjects in the LAL group and Control group will be presented separately. Additionally, the event rate of the LAL subjects will be compared to the "safety and performance endpoints (SPE)" rates specified in ISO.

[redacted]

[redacted]

The incidence of all other adverse events will also be presented separately for the LAL group and Control group. In addition, the incidence of secondary surgical intervention (SSI) related to the optical properties of the lens will be provided.

6 STUDY POPULATION

The study population will consist of up to 350 subjects enrolled (informed consent form signed) to allow for up to 230 subjects with implantation of either the LAL IOL or Control IOL attempted in the Full Analysis Set (FAS). An additional 17 subjects were implanted in the pre-COVID-19 population. Each subject will desire to improve their depth of focus (improve intermediate and near visual acuity without compromising distance visual acuity), will be good candidates for bilateral IOL implantation, and will agree to participate in a randomized clinical study. Study subjects will be randomized 1:1 to either undergo bilateral LAL implantation and light treatments for refractive and presbyopia correction (LAL group) or to undergo bilateral implantation with commercially available IOLs (SofPort LI61AO monofocal IOL, Bausch + Lomb) (Control group). All study subjects must have preoperative keratometric astigmatism of <0.75 D in both eyes. Subject's eyes must meet all other applicable inclusion criteria and none of the exclusion criteria.

6.1 INCLUSION CRITERIA

- Must sign a written Informed Consent Document and be willing to undergo cataract surgery for bilateral implantation of either the LAL or SofPort LI61AO IOL (Bausch + Lomb).
- Must be willing to be randomized to either the LAL group (bilaterally implanted with the LAL and receive light treatments for refractive and presbyopia correction) or the Control group (bilateral implantation with the SofPort LI61AO monofocal IOL).
- Between the ages of 40 and 80 inclusive on the day the first cataract surgery is performed.
- Preoperative keratometric cylinder <0.75 D in both eyes.
- Cataractous lens changes as demonstrated by best corrected distance visual acuity (BCDVA) of 20/40 or worse with or without a glare source in both eyes.
- Best corrected distance visual acuity projected to be 20/20 or better after cataract removal and intraocular lens (IOL) implantation in both eyes as estimated by potential acuity meter (PAM) or surgeon estimation.
- Clear intraocular media other than cataract in both eyes.
- Willing and able to comply with the requirements for study specific procedures and visits.
- [redacted].
- Able to complete a written questionnaire in English.
- Requires an IOL power within the range available for both the LAL and SofPort LI61AO IOLs.

6.2 EXCLUSION CRITERIA

- Pseudoexfoliation in either eye.
- Pre-existing macular disease in either eye.
- Patient with sufficiently dense cataract that precludes examination of the macula in either eye.
- Retinal degenerative disorder that is expected to cause future vision loss in either eye.
- Diabetes with any evidence of retinopathy in either eye.
- Evidence of glaucomatous optic neuropathy in either eye.
- History of uveitis in either eye.
- Significant anterior segment pathology, such as rubeosis iridis, aniridia, or iris coloboma in either eye.
- Pupil that is deformed including ectopic pupil condition in either eye.
- Corneal pathology that is either progressive or sufficient to reduce BCDVA to worse than 20/20 in either eye.
- Any corneal dystrophy including basement membrane dystrophy in either eye that in the opinion of the investigator may confound the outcome.
- Keratoconus or suspected of having keratoconus in either eye.
- Has undergone previous corneal or intraocular surgery in either eye, except 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 either eye.
- Irregular astigmatism in either eye.
- History of ocular herpes simplex virus in either eye.

- Previous trauma or developmental defects in which appropriate support of the intraocular lens (IOL) is not possible in either eye.
- Current vitreoretinal disease or a high risk for future vitreoretinal disease that may require silicone oil as part of therapy in either eye.
- [redacted]
- Subject who has participated within another ophthalmic clinical trial within the last 3 months.

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 and depth of focus.

7.1.1 RXSIGHT LIGHT ADJUSTABLE LENS

The RxSight Light Adjustable Lens (LAL) 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 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.

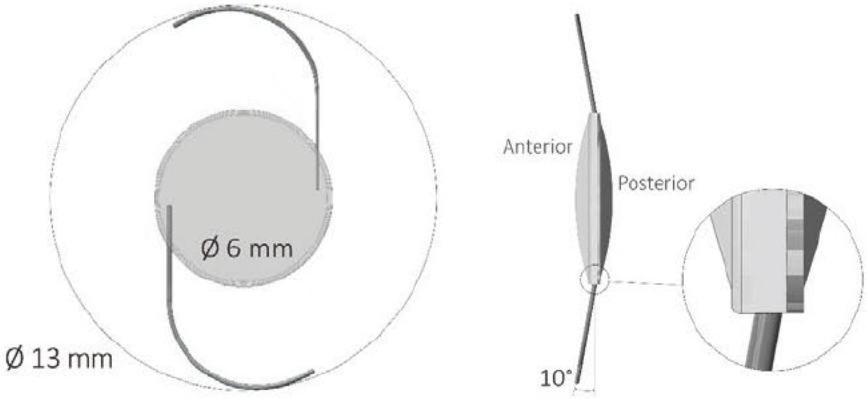


FIGURE 1: RXSIGHT LIGHT ADJUSTABLE LENS (LAL)
(A) TOP VIEW AND (B) CROSS-SECTION VIEW OF THE OPTIC SHOWING LAL WITH A POSTERIOR LAYER

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.

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 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 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.

7.1.4 INSERTION DEVICES

- The RxSight Insertion Device (K192926), which is comprised of a re-usable titanium injector and a single-use, non-preloaded polypropylene cartridge with lubricating coating, will be used as the primary device to insert the LAL and SofPort LI61AO IOL (Bausch + Lomb) into the eye.
- The Nichamin III Foldable Lens Inserter (Rhein Medical 05-2349) with the Nichamin II Foldable Lens Insertion Forceps (Rhein Medical 05-2348) can be used as back-up for the LAL only, if needed.

7.1.5 INDICATIONS FOR USE [redacted]

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.

[redacted]

[redacted]

7.2 SUBJECT ENTRY

If a COVID-related public health emergency declaration is in place at the time of the study, the study site should take appropriate measures in a clinic setting to minimize spread of the virus in conformance to professional society guidelines and applicable guidance from the states and counties in which the sites are located.

Patients who require bilateral cataract extraction and intraocular lens implantation and who wish to improve their depth of focus will be pre-screened for eligibility as part of pre-entry activity. If it is determined that the 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. Procedures that are performed as part of a routine cataract evaluation and which (1) would be done whether or not study entry was contemplated (2) are done in accordance with the protocol-specific clinical methods (3) are completed within the protocol Preop window and (4) are done by trained team members on the delegation log may be performed and the results subsequently used for determining study eligibility without first obtaining consent.

Written informed consent must be obtained prior to initiation of any clinical procedures that are performed solely for the purpose of determining eligibility for research. 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 patient is enrolled upon signing the informed consent and a study ID is assigned.

The preoperative examination will be performed no more than 60 days prior to surgery for either the Primary eye or the Fellow eye. Both eyes of all subjects must be screened for eligibility at the same preoperative visit. If the 60-day time period elapses, it is acceptable for patients to be re-screened by undergoing a complete preoperative examination. If at any time during the preoperative screening, either eye does not meet inclusion or exclusion criteria, screening for that subject should be discontinued and the subject will be exited from the study. All study subjects must have preoperative keratometric astigmatism of <0.75 D in both eyes. Subject's eyes must meet all other applicable inclusion criteria and none of the exclusion criteria.

The principal investigator or delegated MD Sub-Investigator will review the Inclusion/Exclusion checklist document provided for the study and, if the subject is eligible, sign and date the form. The documentation of eligibility must be completed prior to implantation. Subjects that meet all inclusion/exclusion criteria will be randomly assigned in a 1:1 ratio to either the LAL group or the Control group. In addition, each eye of the subject will be assigned as either the primary eye or the fellow eye based on randomization. Pre-determined randomization schemes will be utilized. A randomization schedule for the treatment assignments (LAL versus Control) with a block of 4 and a ratio of 1:1 will be generated using a random generator such as SAS. Randomization of subjects will occur immediately prior to commencing cataract surgery on the primary eye. Only subjects meeting all inclusion/exclusion criteria may be implanted. Those subjects who do not meet the inclusion/exclusion requirements will be considered screen failures. Exit forms will be completed for all screen fails. Up to 350 subjects may be enrolled to allow for up to 230 subjects who will have had implantation of the LAL IOL or Control IOL attempted in the FAS. An additional 17 subjects were implanted in the pre-COVID-19 population.

The implant lens powers for the LAL and Control IOLs will be calculated based upon ocular biometry data and a lens power formula of the investigator's choice. Optimized lens constants of the investigator's choice also may be utilized. These lens constants will not be changed during the clinical investigation. For all study eyes, a postoperative spherical equivalent (SE) outcome closest to emmetropia as measured on a 4 meter exam lane will be targeted. The lens power will not be altered based on intraoperative diagnostics.

<u>Subjects randomized to the LAL group</u>
Commencing at the Postop Week 3 [redacted] visit (17-24 days post-Fellow eye operative visit), both eyes will receive an [redacted]

At the Adjustment #1 visit (3-7 days after the Postop Week 3 [redacted] visit), both eyes will receive an adjustment #1 light treatment based on the measured manifest refraction at 4 meters at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

At the Adjustment #2 visit (3 to 7 days after the Adjustment #1 visit), both eyes will receive an adjustment #2 light treatment also based on the measured manifest refraction at 4 meters at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

Three to 7 days after the Adjustment #2 light treatment, both eyes will be eligible to receive an adjustment #3 light treatment. If the eye's |MRSE| is ≥0.25 D OR manifest cylinder is measured at ≥0.50 D, then the eye will receive an adjustment #3 light treatment; otherwise the eye will be eligible to proceed to lock-in #1.

The lock-in #1 light treatment will be performed in the primary eye 3 to 7 days after the subject's final adjustment light treatment followed 3 to 7 days later by the lock-in #2 treatment, if needed. The lock-in #1 treatment will be performed in the fellow eye 3 to 7 days after the final lock-in in the primary eye and after confirmation that there has been no ultraviolet (UV) retinal damage per Sections 7.3.2.1 and 7.3.2.2 followed 3 to 7 days later by lock-in #2, if needed. Subjects in the LAL group will receive [redacted], up to three sphero-cylindrical/non-astigmatic light treatments, and one or two lock-in treatments in each eye.

Examinations will occur at regular intervals over a 6 month period to evaluate the safety and effectiveness outcomes. For eyes in the LAL group, if an eye is diagnosed with ultraviolet (UV) retinal damage, an additional follow-up exam will be added at 12 months postoperatively to confirm resolution or document sequelae, if any. Masked examiners will be utilized at the Postop Month 6 visit.

Safety for all study eyes will be evaluated per ISO 11979-7.

7.3 LAL IMPLANTATION AND REFRACTIVE ADJUSTMENT

Each investigative site will follow a standard regimen of pre-, intra-, and postoperative medications to be used in the study that has been reviewed and approved by the study medical monitor. This standard regimen will also specify the ophthalmic viscoelastic device to be used during surgery.

7.3.1 SURGICAL PROCEDURE

The LAL will be implanted using standard microsurgical techniques.

<u>No additional corneal refractive procedures are allowed until after the subject has been exited from the study.</u>

The surgical procedure for the LAL will be performed as follows:

1. Prepare and drape the eye for surgery in accordance with standard surgical procedures.
2. A clear corneal incision will be made using the surgeon's standard instrumentation and techniques.
3. Use viscoelastic as agreed upon within the standard regimen 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 LAL, 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 LAL.
7. As a primary means of insertion, the LAL will be introduced into the eye's capsular bag using the RxSight Insertion Device through a clear temporal corneal incision up to 3.2 mm. The Nichamin III Foldable Lens Inserter (Rhein Medical 05-2349) with the Nichamin II Foldable Lens Insertion Forceps (Rhein Medical 05-2348) can be used as back-up if needed to introduce the LAL through a temporal clear corneal incision of 3.5-3.8 mm and placed into the eye's capsular bag. If utilizing additional surgical instruments near the incision upon insertion, precaution should be taken not to contact the LAL optic with this additional instrument.
8. Verify proper orientation of the LAL
9. Aspirate any residual viscoelastic from the eye using a preferred technique.
10. The wound may close without suturing. If the unsutured wound is not watertight, close it with a either a suture using standard technique or an ocular sealant (ReSure Sealant).
11. After completion of the surgery, postoperative medications should be administered per the agreed upon investigative site standard regimen.
12. The subject will be provided with RxSight approved UV protective spectacles to protect the implanted LAL 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 a patch was used at the conclusion of surgery, the subject will wait for the surgeon to remove the patch. Once removed, the subject will begin wear of the UV protective eyewear as instructed.

7.3.2 LIGHT TREATMENT PROCEDURE

Subjects randomized to the LAL group
Commencing at the Postop Week 3 [redacted] visit (17-24 days post-Fellow eye operative visit), both eyes will receive an [redacted]

At the Adjustment #1 visit (3-7 days after the Postop Week 3 [redacted] visit), both eyes will receive an adjustment #1 light treatment based on the measured manifest refraction at 4 meters at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

At the Adjustment #2 visit (3 to 7 days after the Adjustment #1 visit), both eyes will receive an adjustment #2 light treatment also based on the measured manifest refraction at 4 meters at this visit. Eyes measured with a manifest cylinder of ≥0.50 D will receive a sphero-cylindrical light

treatment while eyes with <0.50 D of manifest cylinder will receive a non-astigmatic light treatment.

Three to 7 days after the Adjustment #2 light treatment, both eyes will be eligible to receive an adjustment #3 light treatment. If the eye's |MRSE| is ≥0.25 D OR manifest cylinder is measured at ≥0.50 D, then the eye will receive an adjustment #3 light treatment; otherwise the eye will be eligible to proceed to lock-in #1.

The lock-in #1 light treatment will be performed in the primary eye 3 to 7 days after the subject's final adjustment light treatment followed 3 to 7 days later by the lock-in #2 treatment, if needed. The lock-in #1 treatment will be performed in the fellow eye 3 to 7 days after the final lock-in in the primary eye and after confirmation that there has been no ultraviolet (UV) retinal damage per Sections 7.3.2.1 and 7.3.2.2 followed 3 to 7 days later by lock-in #2, if needed. Subjects in the LAL group will receive [redacted], up to three sphero-cylindrical/non-astigmatic light treatments, and one or two lock-in treatments in each eye.

7.3.2.1 Postponement of Light Treatment Procedure(s)

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

- Color Vision Testing: Treatment should be delayed if the subject scores worse on Part 2 of the City University Color Test than the Postop Week 3 visit for Tritan evaluation.
- Erythropsia Evaluation: With any score of 2 (red), the treatment should be delayed.
- 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 Postop Week 3 visit BCDVA, treatment should be delayed.

The subject should return for follow-up visits until the subject's visual assessment of erythropsia is a score of 0 or 1 (indicates the paper looks white or pink), the BCDVA is within 10 letters of the Postop Week 3 visit BCDVA and an equivalent or better score than the Postop Week 3 visit test is measured in the Tritan section of the City University Color Test, at which time the next LDD treatment may be delivered.

- If sutures were utilized at the time of surgery to close the incision wound, light treatments should not commence on the eye until a minimum of 4 weeks after suture removal.[7]
- An 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, endophthalmitis

[7] 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.

or any other safety concern that the investigator believes may be negatively impacted by light treatment.

- If an 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 Appendix 1 for additional details regarding premature photopolymerization).
- Any 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.

7.3.2.2 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 on either eye should be delayed until after OCT images are obtained and no phototoxic damage is seen. Testing should always include spectral domain OCT and if indicated [redacted].

Spectral Domain OCT Testing Only

Any visit after the Postop Week 3 visit:

- BCDVA is reduced by 10 letters or more when compared with BCDVA at the Postop Week 3 visit unless the cause of the BCDVA loss is known to be non-retinal.

OR

- An increase in score of more than 1 on Part 2 of the Tritan evaluation (City University Color Test) when compared to the Postop Week 3 visit score.

Spectral Domain OCT [redacted]

At the Postop Month 3 visit or later (includes all unscheduled visits after the Postop Month 3 visit):

- BCDVA is reduced by 10 letters or more when compared with the BCDVA at the Postop Week 3 visit unless the cause of BCDVA loss is known to be non-retinal.

OR

- An increase in score of 1 or greater on Part 2 of the Tritan evaluation (City University Color Test) when compared to the Postop Week 3 visit score except in cases where the Part 2 score changes to a 1 from a Postop Week 3 visit score of 0 as this change is considered normal.[8]

OR

- Any score of 1 (pink) or 2 (red) on the in-office erythropsia assessment.

OR

- Any report of moderate or severe amounts of added pink or reddish color [redacted]

[8] The City University Colour Vision Test, 3rd Edition, 1998, Keeler Ltd., Windsor.

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

A diagnosis of retinal phototoxicity will be made based on any of the following:

- OCT scans that demonstrate disruption of the inner/outer segment junction, the outer nuclear layer, or retinal pigment epithelial layer,
- Observed fundus changes consistent with retinal phototoxicity (such as focal pigment epithelial changes with varying degrees of pigment clumping),
- Confirmed perimetric observations on at least 2 post light treatment visual field tests that were unnoted at the Postop Week 3 visit. Perimetric observations with known associations to other retinal findings will not be diagnosed as retinal phototoxicity, or
- Unresolved Tritan color vision changes >1 at the Postop Month 6 visit, or
- Confirmed severe erythropsia (based upon in-office assessment or the [redacted] at the Postop Month 6 visit.

The eye should undergo [redacted] testing, if not already performed, to determine the correspondence between the imaging data and the location and severity of the sensitivity loss. The results of the visual field testing should be provided to an independent specialist/reading center and RxSight for review.

OCT and [redacted] testing should be repeated at an additional follow exam at 12 months postoperatively to confirm resolution or document sequelae, if any. Results from any subsequent visit should be provided to RxSight and reading centers for review.

7.3.2.3 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 [redacted] light treatment will be prepared for light treatment with pupil dilation. A study eye undergoing an [redacted] All lock-in light treatments will be performed through a dilated pupil.

If dilation is required ([redacted] light treatment + all lock-ins):

1. The study eye will be dilated using pupil dilation drops (examples: 0.5% Tropicamide, 1.0% Tropicamide, 2.5% or 10% Phenylephrine, 0.5%, 1%, 2% Cyclopentolate) or pupil dilation gels (example: 0.4% Ketorolac Tromethamine, 10% Phenylephrine, 2.5% Tropicamide) 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 opposite 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.

If no dilation is required [redacted]

1. The subject's opposite 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 and minimize eye movement.

* In the case the eye has been dilated for any reason at a visit requiring [redacted] light treatment, no light treatment should be performed. Based on the pharmacologic dilation agents utilized, the investigator should instruct the subject to return to the clinic at a time point in which it is thought the pupil dilation agents no longer affect the iris. At this next study visit, all clinical measurements should be re-performed prior to administration of the [redacted] light treatment.

7.3.2.4 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.

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. [redacted]
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 (M = 0.766x, black contact lens) on the cornea using hydroxypropyl methylcellulose as 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. For dilated pupil light treatments (all [redacted] light treatments), 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.

10. In the case of an aborted Adjustment Treatment, do not initiate a new treatment sequence; instead; contact the Sponsor for further instructions.
11. Following the light adjustment, the subject will continue to wear their UV protective eyewear as instructed.

7.3.2.5 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.

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 (M = 0.766x, black contact lens) on the cornea using hydroxypropyl methylcellulose or hypromellose as 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.
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 final lock-in treatment for the fellow eye has been completed.

7.4 CONTROL LENS IMPLANTATION

Each investigative site will follow a standard regimen of pre-, intra-, and postoperative medications to be used in the study that has been reviewed and approved by the study medical monitor. This standard regimen will also specify the ophthalmic viscoelastic device to be used during surgery.

Subjects randomized to the Control group will be implanted with the SofPort LI61AO monofocal IOL in both eyes. The commercially available SofPort LI61AO monofocal IOL (Bausch + Lomb) will be implanted with the RxSight Insertion Device (K192926). Up to a 3.2 mm, clear corneal incision of temporal orientation will be made using the surgeon's standard instrumentation and technique. All instruments and procedures used will be identical to those routinely used for phacoemulsification by each individual investigator. The implant lens power for the Control IOL (SofPort LI61AO monofocal IOL) will be calculated based upon ocular biometry data and a lens power formula of the investigator's choice. Optimized lens constants of the investigator's choice also may be utilized. These lens constants will not be changed during the clinical investigation. For all study eyes, a postoperative spherical equivalent (SE) outcome closest to emmetropia as measured on a 4 meter exam lane will be targeted. The lens power will not be altered based on intraoperative diagnostics.

7.5 EXAMINATION SCHEDULE

LAL Group:

Evaluation	
Preoperative OU	Maximum of 60 days prior to Operative Visit for either Primary Eye or Fellow Eye
Operative Primary Eye	Day 0, day of surgery for Primary Eye
Postop Day 1 Primary Eye	Days 1 to 2 post-Operative Visit Primary Eye
Postop Week 1 Primary Eye	Days 7 to 14 post-Operative Visit Primary Eye
Operative Fellow Eye	7 to 14 days post-Operative Visit Primary Eye
Postop Day 1 Fellow Eye	Days 1 to 2 post-Operative Visit Fellow Eye
Postop Week 1 Fellow Eye	Days 7 to 14 post-Operative Visit Fellow Eye
Postop Week 3 [redacted] (bilateral)[1]	Days 17 to 24 post-Operative Visit Fellow Eye
Adjustment #1 (bilateral)[1]	3 to 7 days after the Postop Week 3 [redacted] visit
Adjustment #2 (bilateral) [1]	3 to 7 days post Adjustment #1 Visit
Adjustment #3 (bilateral, if needed)[2]	3 to 7 days post Adjustment #2 Visit
Lock-in #1 Primary Eye	3 to 7 days post subject's final Adjustment Visit

Lock-in #2 Primary Eye, if needed	3 to 7 days post lock-in #1 Visit for Primary Eye
Lock-In #1 Fellow Eye	3 to 7 days post final lock-in Visit for Primary Eye
Lock-In #2 Fellow Eye, if needed	3 to 7 days post lock-in #1 Visit for Fellow Eye
Postop Month 3 (bilateral)	Days 60 to 90 post-Operative Fellow Eye Visit
Postop Month 6 (bilateral)	Days 120 to 180 post-Operative Fellow Eye Visit
Postop Month 12, if needed	Days 330 to 420 post-Operative Fellow Eye Visit

1- Light treatments will be performed bilaterally at the same visit
2- Adjustment #3 will be peformed bilaterally (if needed) at the same visit if specific clinical criteria are measured as described in section 7.3.2 of the protocol

A Postop Month 12 visit will be conducted if a subject is diagnosed with UV retinal damage to confirm resolution or document sequelae, if any.

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.

Control Group:

Evaluation	
Preoperative OU	Maximum of 60 days prior to Operative Visit for either Primary Eye or Fellow Eye
Operative Primary Eye	Day 0, day of surgery for Primary Eye
Postop Day 1 Primary Eye	Days 1 to 2 post-Operative Visit Primary Eye
Postop Week 1 Primary Eye	Days 7 to 14 post-Operative Visit Primary Eye
Operative Fellow Eye	7 to 14 days post-Operative Visit Primary Eye
Postop Day 1 Fellow Eye	Days 1 to 2 post-Operative Visit Fellow Eye
Postop Week 1 Fellow Eye	Days 7 to 14 post-Operative Visit Fellow Eye
Postop Week 3 (bilateral)	Days 17 to 24 post-Fellow Eye Operative Visit
Postop Month 3 (bilateral)	Days 60 to 90 post-Operative Fellow Eye Visit
Postop Month 6 (bilateral)	Days 120 to 180 post-Operative Fellow Eye Visit

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.

7.6 CLINICAL PARAMETERS

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

1. Demographics

[redacted]

[redacted]

5. Ocular history
6. History of Medications
7. Subjective symptoms/complaints (subject reported)

[redacted]

9. Corneal Topography
10. Wavefront aberrometry
11. Autorefraction
12. Undilated photopic pupil diameter [redacted]
13. Corneal Keratometry
14. Ocular Biometry: Axial length + Anterior Chamber Depth (Optical or immersion A-scan biometry)
15. Monocular photopic uncorrected distance visual acuity using a +0.25 D lens to compensate for 4 meter test distance
16. Binocular photopic uncorrected distance visual acuity using a +0.25 D trial lens over each eye to compensate for 4 meter test distance
17. Manifest Refraction
18. Monocular photopic best corrected distance visual acuity
19. Monocular photopic uncorrected distance visual acuity (no trial lens in front of eye)
20. Ocular Dominance
21. Undilated pupil diameter [redacted]
22. Depth of focus testing
23. Monocular mesopic distance corrected intermediate visual acuity
24. Monocular mesopic best corrected intermediate visual acuity
25. Monocular mesopic best corrected near visual acuity
26. Monocular mesopic distance corrected near visual acuity
27. Monocular photopic distance corrected near visual acuity
28. Monocular photopic uncorrected near visual acuity
29. Binocular photopic uncorrected near visual acuity
30. Binocular photopic uncorrected intermediate visual acuity
31. Monocular photopic uncorrected intermediate visual acuity
32. Monocular photopic distance corrected intermediate visual acuity

[redacted]

35. Mesopic undilated pupil diameter [redacted]

36. Distance corrected contrast sensitivity: Mesopic/Photopic with and w/o glare

[redacted]

38. Intraocular pressure
39. Slit Lamp Examination
40. Fundus Exam
41. Fundus Photos

[redacted]

43. IOL Stability (Tilt/Decentration)
44. Dilated pupil diameter [redacted]
45. Adverse Events

Table 1. Schedule of Visits and Clinical Parameters- LAL Group

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 [redacted] Treatment) (Bilateral)	Adjustment #1 (Bilateral)	Adjustment #2 (Bilateral)	Adjustment #3 (if needed) (Bilateral)	Lock-in #1 Primary Eye	Lock-in #2 Primary Eye, if needed	Lock-in #1 Fellow Eye	Lock-in #2 Fellow Eye, if needed	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Postop Month 12 (if needed)	Unscheduled Visit[3]
Demographics	X																		
[redacted]	X							X								X	X	X	
[redacted]	X							X								X	X	X	
[redacted]								X	X	X	X	X	X	X	X	X	X	X	X
Ocular History	X																		
History of Medications	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X
Subjective Symptoms/Complaints (Subject reported)			X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
[redacted]			X	X	X	X	X	X	X	X	X	X	X	X	X				X[4]
Corneal Topography	X							X									M		
Wavefront aberrometry								X									M		
Autorefraction				X			X	X	X	X	X	X	X	X	X	X	M	X	
Undilated photopic pupil diameter [redacted]	X							X									M		
Corneal Keratometry	X																		
Ocular Biometry (Axial length + Anterior Chamber Depth)	X																		

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 [redacted] Treatment) (Bilateral)	Adjustment #1 (Bilateral)	Adjustment #2 (Bilateral)	Adjustment #3 (if needed) (Bilateral)	Lock-in #1 Primary Eye	Lock-in #2 Primary Eye, if needed	Lock-in #1 Fellow Eye	Lock-in #2 Fellow Eye, if needed	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Postop Month 12 (if needed)	Unscheduled Visit[3]
Monocular photopic uncorrected distance visual acuity using a +0.25 D lens to compensate for 4 meter test distance	X		X	X		X	X	X	X	X	X	X	X	X	X	X	M	X	X
Binocular photopic uncorrected distance visual acuity using a +0.25 D lens over each eye to compensate for 4 meter test distance																	M		
Manifest Refraction	X			X			X	X	X	X	X	X	X	X[5]	X	X	M	X	X
Monocular photopic best corrected distance visual acuity	X			X			X	X	X	X	X	X	X	X[5]	X	X	M	X	X
Monocular photopic uncorrected distance visual acuity (no trial lens in front of eye)	X			X			X	X	X	X	X	X	X	X	X	X	M		X
Ocular Dominance	X							X									M		
Undilated pupil diameter [redacted]																	M		
Depth of focus testing																	M		
Monocular mesopic distance corrected intermediate visual acuity																	M		

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 [redacted] Treatment) (Bilateral)	Adjustment #1 (Bilateral)	Adjustment #2 (Bilateral)	Adjustment #3 (if needed) (Bilateral)	Lock-in #1 Primary Eye	Lock-in #2 Primary Eye, if needed	Lock-in #1 Fellow Eye	Lock-in #2 Fellow Eye, if needed	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Postop Month 12 (if needed)	Unscheduled Visit[3]
Monocular mesopic best corrected intermediate visual acuity																	M		
Monocular mesopic best corrected near visual acuity																	M		
Monocular mesopic distance corrected near visual acuity																	M		
Monocular photopic distance corrected near visual acuity																X	M		
Monocular photopic uncorrected near visual acuity																X	M		
Binocular photopic uncorrected near visual acuity																	M		
Binocular photopic uncorrected intermediate visual acuity																	M		
Monocular photopic uncorrected intermediate visual acuity																X	M		
Monocular photopic distance corrected intermediate visual acuity																X	M		
[redacted]								X	X	X	X	X	X	X[5]	X	X	M	X	X
[redacted]								X	X	X	X	X	X	X[5]	X	X	M	X	X
Mesopic undilated pupil diameter [redacted]																	M		

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 [redacted] Treatment) (Bilateral)	Adjustment #1 (Bilateral)	Adjustment #2 (Bilateral)	Adjustment #3 (if needed) (Bilateral)	Lock-in #1 Primary Eye	Lock-in #2 Primary Eye, if needed	Lock-in #1 Fellow Eye	Lock-in #2 Fellow Eye, if needed	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Postop Month 12 (if needed)	Unscheduled Visit[3]
[redacted]																			
Distance Corrected Contrast Sensitivity (Mesopic/Photopic w and w/o glare)																	M		
[redacted]								X								X[2]	X[2]	X[2]	
Intraocular Pressure	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Slit Lamp Exam	X		X	X		X	X	X	X	X	X	X	X	X	X	X	X	X	X
Fundus Exam	X								X								X	X	
Fundus Photos	X							X									X	X	
Spectral Domain Optical Coherence Tomography (SD-OCT)								X	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]	X[1]	
IOL Stability (Tilt/Decentration)									X							X	X		
Dilated Pupil Diameter [redacted]	X								X	X	X	X	X	X	X				
Adverse Events		X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X

[redacted]

[3] 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.

[4] Required at any unscheduled visit before the final lock-in light treatment

[5] Also performed on the primary eye to confirm that there has been no ultraviolet (UV) retinal damage per Section 7.3.2 before proceeding with lock-in #1 treatment on the fellow eye

[M] Measurements will be conducted by a masked observer who will not be aware of which lens has been implanted. The masked observer should not have access to the subject's medical and/or study records. The masked observer should not conduct any study examinations at follow-ups with masked examinations beyond the visual measurements indicated with the "M."

Table 2. Schedule of Visits and Clinical Parameters- Control Group

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 (Bilateral)	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Unscheduled Visit[1]
Demographics	X										
[redacted]	X							X	X	X	
[redacted]	X							X	X	X	
[redacted]								X	X	X	
Ocular History	X										
History of Medications	X	X	X	X	X	X	X	X	X	X	X
Subjective Symptoms/Complaints (Subject reported)			X	X		X	X	X	X	X	X
Corneal Topography	X							X		M	
Wavefront aberrometry								X		M	
Autorefraction				X			X	X	X	M	
Undilated photopic pupil diameter [redacted]	X							X		M	
Corneal Keratometry	X										
Ocular Biometry (Axial length + Anterior Chamber Depth)	X										

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 (Bilateral)	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Unscheduled Visit[1]
Monocular photopic uncorrected distance visual acuity using a +0.25 D lens to compensate for 4 meter test distance	X		X	X		X	X	X	X	M	X
Binocular photopic uncorrected distance visual acuity using a +0.25 D lens over each eye to compensate for 4 meter test distance										M	
Manifest Refraction	X			X			X	X	X	M	X
Monocular photopic distance corrected visual acuity (Distance)	X			X			X	X	X	M	X
Monocular photopic uncorrected distance visual acuity (no trial lens in front of eye)	X			X			X	X	X	M	X
Ocular Dominance	X							X		M	
Undilated pupil diameter [redacted]										M	
Depth of focus testing										M	
Monocular mesopic distance corrected intermediate visual acuity										M	
Monocular mesopic best corrected intermediate visual acuity										M	
Monocular mesopic best corrected near visual acuity										M	
Monocular mesopic distance corrected near visual acuity										M	
Monocular photopic distance corrected near visual acuity									X	M	
Monocular photopic uncorrected near visual acuity									X	M	
Binocular photopic uncorrected near visual acuity										M	

Visits	Preop (Bilateral)	Operative Primary Eye	Postop Day 1 Primary Eye	Postop Week 1 Primary Eye	Operative Fellow Eye	Postop Day 1 Fellow Eye	Postop Week 1 Fellow Eye	Postop Week 3 (Bilateral)	Postop Month 3 (Bilateral)	Postop Month 6 (Bilateral)	Unscheduled Visit[1]
Binocular photopic uncorrected intermediate visual acuity										M	
Monocular photopic uncorrected intermediate visual acuity									X	M	
Monocular photopic distance corrected intermediate visual acuity									X	M	
[redacted]								X	X	M	
[redacted]								X	X	M	
Mesopic undilated pupil diameter [redacted]										M	
Distance Corrected Contrast Sensitivity (Mesopic/Photopic w and w/o glare)										M	
[redacted]								X			
Intraocular Pressure	X		X	X		X	X	X	X	X	X
Slit Lamp Exam	X		X	X		X	X	X	X	X	X
Fundus Exam	X							X		X	
Fundus Photos	X							X		X	
[redacted]								X			
IOL Stability (Tilt/Decentration)								X	X	X	
Dilated Pupil Diameter [redacted]	X							X			
Adverse Events		X	X	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.

[M] Measurements will be conducted by a masked observer who will not be aware of which lens has been implanted. The masked observer should not have access to the subject's medical and/or study records. The masked observer should not conduct any study examinations at follow-ups with masked examinations beyond the visual measurements indicated with the "M".

7.7 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.

7.8 STUDY COMPLETION PROCEDURES

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

7.8.1 SUBJECT COMPLETION

For subjects with both eyes successfully implanted with a study IOL, study completion is when both the primary and fellow study eyes have completed the Postop Month 6 examination. For subjects with only the primary eye successfully implanted with a study IOL, study completion is when the primary study eye has completed the Postop Month 6 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.

7.8.2 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.

7.8.3 SUBJECT WITHDRAWAL DUE TO INTRAOPERATIVE COMPLICATIONS PRIOR TO OR DURING ATTEMPTED IMPLANTATION

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

7.8.4 SUBJECT DISCONTINUATION AFTER IMPLANTATION

After successful IOL implantation bilaterally or only in the primary eye, the subject will be withdrawn from the study if both IOLs are explanted or the IOL is explanted from the primary eye respectively 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.

7.8.5 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.

7.8.6 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

Subjects that meet all inclusion/exclusion criteria will be randomly assigned in a 1:1 ratio to either the LAL group or the Control group.

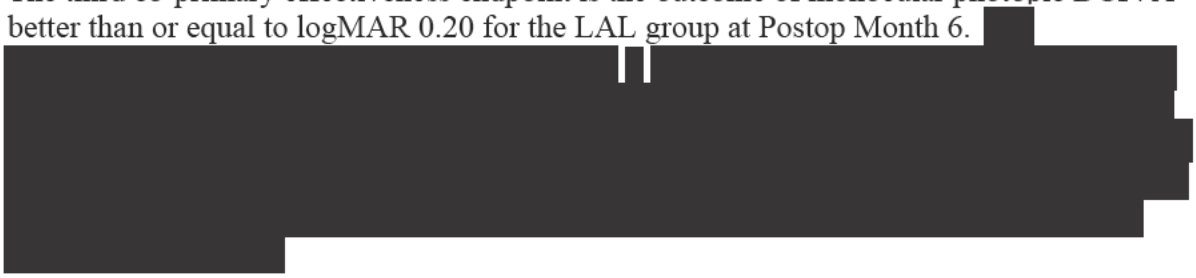
8.1.1 SAMPLE SIZE FOR THE EFFECTIVENESS ENDPOINTS

Primary Effectiveness Endpoints

The first co-primary effectiveness endpoint is the change in DOF measured at the 0.20 logMAR at Postop Month 6. It is to show that the DOF of the primary eyes in the LAL group at Postop Month 6 is at least 0.5 D greater than that of the primary eyes in the Control group. The DOF will be determined based on the defocus curve of visual acuity (plot of mean logMAR visual acuity versus corresponding lens diopter) measured during the depth of focus test at Postop Month 6 for the LAL and Control groups, separately. No formal statistical test will be performed for this endpoint.

The second co-primary effectiveness endpoint is the monocular photopic DCIVA at 67 cm at Postop Month 6.

The third co-primary effectiveness endpoint is the outcome of monocular photopic DCIVA better than or equal to logMAR 0.20 for the LAL group at Postop Month 6.



The fourth co-primary effectiveness endpoint is the monocular photopic BCDVA at Postop Month 6. The clinical objective is to demonstrate that the mean monocular photopic BCDVA at Postop Month 6 for the LAL primary eyes is not inferior to that of the Control primary eyes

[redacted]

[redacted]

Secondary Effectiveness Endpoints

[redacted]

The first secondary effectiveness endpoint is the monocular photopic DCNVA at Postop Month 6.

[redacted]

The second secondary effectiveness endpoint is the outcome of monocular photopic DCNVA better than or equal to 0.20 logMAR for the LAL group at Postop Month 6.

[redacted]

[redacted]

[redacted]

[redacted]

The fifth secondary effectiveness endpoint is the monocular photopic UCDVA using a +0.25 D lens at Postop Month 6.

[redacted]

[redacted]

Sample Size for the Effectiveness Endpoints

Based on the sample sizes discussed above for the primary and secondary effectiveness endpoints, a sample size of at least **180** (90 × 2) enrolled, randomized, and bilaterally treated subjects are needed for the effectiveness evaluation.

8.1.2 SAMPLE SIZE FOR THE SAFETY ENDPOINTS

Primary Safety Endpoint

The sample size for the incidence of ocular serious adverse events, including persistent and cumulative events defined per ISO 11979-7, is based on the recommendation from American Academy of Ophthalmology Task Force Consensus Statement for Extended Depth of Focus Intraocular Lenses, "*The EDF IOL group should consist of a minimum of **100** patients.*" With 100 LAL subjects, the study has 95% confidence to observe at least one incidence of safety events with a rate of at least 2.7%. With a drop-out rate of 10%, at least **112** LAL subjects with implantation attempted are needed. For comparison, at least 112 Control subjects with implantation attempted are needed.

8.1.3 SAMPLE SIZE FOR THE STUDY

Based on Sections 8.1.1 and 8.1.2, the planned study sample size of up to 230 (~ 112 × 2) enrolled and randomized subjects who have had LAL implantation (LAL group) or Control IOL implantation (Control group) attempted 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. For monocular measurements such as refraction or monocular visual acuity, the summaries will be provided for the primary eyes and fellow eyes of the LAL subjects and those of the Control subjects separately. For binocular measurements such as binocular visual acuity or the patient reported outcomes, the summaries will be provided for the LAL subjects and Control subjects separately. The 95% confidence interval for mean or for percentage may be provided.

Unless otherwise specified, all p-values will be two-sided for a two-sided significance level of 0.05 or one-sided for a one-sided significance level of 0.025. In general, the confidence intervals will be two-sided at 95% confidence level. For the ISO-specified cumulative or persistent adverse event rate, one-sided lower 95% confidence limit will be provided.

8.3 POPULATIONS FOR ANALYSIS

8.3.1 PRE-COVID-19 POPULATION

The Pre-COVID-19 population consists of any subject (or eye) who has signed the informed consent and has had the LAL or Control lens implantation attempted, which is defined as the point at which the lens makes contact with the eye, prior to the March, 2020 suspension of cataract surgeries. Safety and effectiveness analyses for subjects in this population will be

performed separately. Seventeen subjects (10 LAL and 7 Control) met this definition. Due to the COVID-19 pandemic, study visits for these 17 subjects may have been delayed outside protocol specified windows or missed completely. Therefore these subjects will be excluded from the modified safety and Full Analysis Set populations.

8.3.2 MODIFIED SAFETY POPULATION

The modified safety population consists of any subject (or eye) who has signed the informed consent and has had the LAL or Control lens implantation attempted, which is defined as the point at which the lens makes contact with the eye. The Pre-COVID-19 study subjects will be excluded from this population. This population will be used for the safety summaries. The lens groups of this population will be based on the actual received lens. No imputation will be performed.

For subjects encountering intraoperative complications before study lens implantation, their intraoperative complications will be listed separately.

8.3.3 INTENT-TO-TREAT (ITT) POPULATION AND FULL ANALYSIS SET (FAS)

The intent-to-treat (ITT) population contains all of the randomized subjects regardless of having the study lens implantation attempted. Since randomized subjects may not have implantation attempted due to intraoperative complications during cataract extraction or for other reasons such as delays due to the COVID-19 pandemic, the ITT population will not be used for the primary effectiveness analyses. Instead, the Full Analysis Set (FAS) which is defined as the ITT subjects with study lens implantation attempted (regardless of successful implantation) after cataract extraction will be used for the primary effectiveness analyses. The Pre-COVID-19 study subjects will be excluded from this population. The primary analyses of the primary effectiveness endpoints and the monocular outcomes of the secondary effectiveness endpoints will be based on the primary eyes of the FAS; the primary analyses of the binocular outcomes of the secondary effectiveness endpoints will be based on the subjects in the FAS. The analysis group will be based on the randomized group (LAL versus Control), not based on the actual lens received.

For the subjects that do not have the available data of the primary or secondary effectiveness endpoints or have lens exchange or explants before Postop Month-6, the imputation described in Section 8.5.1 will be used for the primary analysis of the primary and secondary effectiveness endpoints. Different imputations will be included in the sensitivity analyses described in Section 8.5.2 below.

8.3.4 PER-PROTOCOL (PP) POPULATION

The per-protocol population is a subset of the FAS and is comprised of the FAS subjects that do not have any major protocol deviations. Major protocol deviations will include those deviations that may impact subject safety, affect the integrity of study data and/or affect subject willingness to participate in the study, such as implantation, adjustment and lock-in procedures that are not performed as specified in the protocol and/or Operator's manual. The PP population will be used for supportive effectiveness analyses.

8.4 BASELINE CHARACTERISTICS

Demographics (such as age, gender, and race) and baseline characteristics will be summarized for the safety population and FAS subjects by the lens group (LAL versus Control lens). For the monocular measurements, the summary will be prepared for the primary eyes and the fellow eyes separately. The data of the fellow eyes that do not have the LAL or the control lens implanted will be excluded from the fellow-eye summaries and, if needed, may be listed separately.

The analyses will also be stratified by the study site in order to assess the similarity of these baseline characteristics among the study sites.

8.5 EFFECTIVENESS ANALYSES

The primary analyses for the primary effectiveness endpoints will be based on the FAS population described in Section 8.3.3. For each type of visual acuity for eyes with study lens exchange or explants before Postop Month-6, the worst observed Month-6 visual acuity of the corresponding lens group will be used to impute the Month-6 visual acuity whether or not the Month-6 data is available.

8.5.1 PRIMARY ANALYSES FOR THE EFFECTIVENESS ENDPOINTS

For the primary analyses of the primary and secondary effectiveness endpoints, the missing Postop Month-6 visual acuity will be imputed by the worst observed Month-6 visual acuity of the corresponding lens group.

First Co-Primary Effectiveness Endpoint

From the depth of focus test, the mean logMAR visual acuity of the primary eyes will be calculated and plotted against the corresponding lens diopter of the defocusing lens (defocus curve) at Postop Month 6 for the LAL and Control groups, separately. In case of missing visual acuity values from the depth of focus test, the worst observed visual acuity value of the corresponding defocusing lens diopter at Postop Month 6 of the same lens group will be used to impute the missing visual acuity values at Postop Month 6. A horizontal line at a Y-axis value of logMAR 0.20 will be included in the defocus curves. The lens diopter values corresponding to the intercepted point of the 0.20 logMAR horizontal line and the defocus curve for the negative diopter value will be estimated. The DOF at Postop Month 6 is the absolute difference between the negative lens diopter values corresponding to the 0.20 logMAR visual acuity and 0 diopter. The DOF at Postop Month 6 will be calculated for the two lens groups separately and numerically compared to the target difference value of 0.5 D. No formal statistical comparison will be performed.

Second Co-Primary Effectiveness Endpoint

The analysis will be based on the primary eyes of the FAS. The mean, standard deviation (SD), 95% confidence interval of the mean based on one-sample t-distribution, median, minimum, and maximum will be derived for logMAR monocular photopic DCIVA at Postop Month 6. [redacted]

[redacted]

Third Co-Primary Effectiveness Endpoint

The count and percent of the primary eyes of the LAL subjects in the FAS that have a monocular photopic DCIVA of 0.20 logMAR or better at Postop Month 6 will be calculated.

[redacted]

Fourth Co-Primary Effectiveness Endpoint

The analysis will be based on the FAS primary eyes. The mean, standard deviation (SD), 95% confidence interval of the mean based on one-sample t-distribution, median, minimum, and maximum will be derived for logMAR monocular photopic BCDVA by the lens group.

[redacted]

First Secondary Effectiveness Endpoint

The analysis will be based on the primary eyes of the FAS. The mean, standard deviation (SD), 95% confidence interval of the mean based on one-sample t-distribution, median, minimum, and maximum will be derived for logMAR monocular photopic DCNVA at Postop Month 6.

[redacted]

Second Secondary Effectiveness Endpoint

The count and percent of the primary eyes that have a monocular photopic DCNVA of 0.20 logMAR or better at Postop Month 6 will be calculated for the LAL subjects in the FAS.

[redacted]

[redacted]

Third Secondary Effectiveness Endpoint

[redacted]

Fourth Secondary Effectiveness Endpoint

[redacted]

Fifth Secondary Effectiveness Endpoint

The analysis will be based on the primary eyes of the FAS. The mean, standard deviation (SD), 95% confidence interval of the mean based on one-sample t-distribution, median, minimum, and maximum will be derived for logMAR monocular photopic UCDVA using a +0.25 D lens at Postop Month 6.

[redacted]

[redacted]

8.5.2 SECONDARY/SENSITIVITY ANALYSES FOR THE PRIMARY EFFECTIVENESS ENDPOINTS

The analyses described in Section 8.5.1 will be performed based on the PP population. Additionally, for the primary and secondary effectiveness endpoints, the analyses described in Section 8.5.1 will be performed based on the fellow eyes with lens implantation.

If there are FAS primary eyes with missing primary or secondary effectiveness endpoints but without lens reposition or explants before Postop Month 6, the analyses described in Section 8.5.1 will be performed using the following imputations for missing distance corrected visual acuity or uncorrected visual acuity (based on logMAR value) for eyes/subjects without secondary surgical interventions (SSI):

- Mean of observed logMAR value for the corresponding effectiveness endpoint in the corresponding lens group.
- Mean of observed logMAR value for the corresponding effectiveness endpoint in the other lens group.
- Worst observed logMAR value of the corresponding effectiveness endpoint in the other lens group. (note: use of the worst observed logMAR value in the corresponding lens group has been described in Section 8.5.1)
- Best observed logMAR value for the corresponding effectiveness endpoint in the corresponding lens group.
- Best observed logMAR value for the corresponding effectiveness endpoint in the other lens group.

Additionally, a tipping point analysis will be performed with imputations for eyes/subjects with missing values and without SSI as follows:

Continuous Outcomes: 2nd and 4th primary effectiveness endpoints and 1st and 5th secondary effectiveness endpoints

For each endpoint, each missing value of the LAL group will be imputed by the observed mean logMAR value of the LAL group added by an increment of 0.01 (i.e. 0.01 logMAR worse) sequentially; the missing value of the Control group will be imputed by the observed mean logMAR value of the Control group subtracted by an increment of 0.01 (i.e. 0.01 logMAR better) sequentially. Except for the 5th secondary effectiveness endpoints, the one-sided p-value of the two-sample t-test will be calculated based on the combinations of imputations until the p-value becomes > 0.025 (i.e. insignificant) or until the imputed value is the observed worst logMAR of the two lens group for the LAL group and the observed best logMAR value of the two lens group for the Control group, which comes first. The F-test of the ANCOVA will be performed for the 5th secondary effectiveness endpoint.

Dichotomous Outcomes: 3rd primary effectiveness endpoint and 2nd, 3rd, and 4th secondary effectiveness endpoint

For each endpoint, the analysis will assume all missing responses for the LAL group are non-responders, then one is responder and all other are non-responders, and gradually proceed to all missing responses for the LAL group are responders; similarly, the assumptions will be made for the missing response for the Control group. For the third secondary effectiveness endpoint, the p-value based on an approximate z-test will be calculated for each combination. For the third primary effectiveness endpoint and the second and fourth secondary effectiveness endpoint, the 95% confidence interval of the proportion will be calculated for each of the LAL-group assumption and these confidence intervals will be plotted.

8.5.3 COVARIATES AND SUBGROUP ANALYSES

The purpose of performing the covariates and subgroup analyses are to evaluate the possible effects of these covariates on the primary effectiveness endpoints. The intention of these analyses is not for claiming treatment effect on any subgroups. The following covariates will be evaluated based on the imputation for the missing data used for the primary analyses:

- Age group (based on observed quartiles)
- Gender (male and female)
- Race (White and non-White)
- Ethnicity (Hispanic-Latino and not Hispanic-Latino)
- Study site
- MRSE at Postop Week 3 (≤-3.00 D, >-3.00 D to -2.00D, >-2.00 D to -1.00 D, >-1.00 D to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 to <3.00 D, and ≥3.00D)
- MRCYL at Postop Week 3 (< 0.50 D, ≥0.50 D to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 to <3.00 D, and ≥3.00 D)
- DEQ at Postop Week 3 (0.00 D to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 to <3.00 D, and ≥3.00 D)

For the first co-primary effectiveness endpoint, the difference in monocular DOF at Postop Month 6 between the two lens groups will be derived for each level of each covariate. Additionally, DOF and the difference in DOF between the two lens groups will be stratified by the photopic pupil size (<3.0 mm, ≥3.0 to ≤4.0 mm, and >4.0 mm) measured at Postop Month 6. Meanwhile, the analysis will be performed by the axial length measured preoperatively (<21.0 mm, 21.0 mm to ≤26.0 mm, and >26.0 mm).

For the continuous effectiveness endpoints (the second and fourth co-primary effectiveness endpoints and the first and fifth secondary effectiveness endpoints), the mean, SD, 95% confidence interval of the mean, median, maximum, and maximum will be calculated by lens group for each level of each covariate. For each covariate, the mean differences among different levels of the covariate will be compared based on two-way analysis of variance (ANOVA) with lens group, covariate, and interaction of lens group and covariate as the

factors. A p-value of 0.15 will be used for evaluating the possible covariate and interaction effects.

For the third secondary effectiveness endpoints, the responder rate along with the exact 95% confidence intervals based on binomial distribution will be provided for each level of each covariate by the lens group. For each covariate, the difference in the responder rate between the two lens groups among the different levels of the covariate will be compared based on the Gail-Simon test. A p-value of 0.15 will be used for evaluating the possible covariate effects.

For the third co-primary effectiveness endpoint and the second and four secondary effectiveness endpoint, the responder rate along with the exact 95% confidence intervals based on binomial distribution will be provided for each level of each covariate based on the primary eyes of the FAS LAL subjects. For each covariate, the responder rate differences among different levels of the covariate will be compared based on Fisher's exact test. A p-value of 0.15 will be used for evaluating the possible covariate effects.

It should be noted that the subgroups of these covariates will be re-examined and may be re-categorized or eliminated due to small sample size (if there are < 10 subjects within each subgroup).

8.5.4 ADDITIONAL EFFECTIVENESS ANALYSES

The following effectiveness outcomes will be summarized descriptively based on the observed data of the implanted eyes or subjects in the FAS. 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.

8.5.4.1 Manifest Cylinder (MRCYL)

The MRCYL will be summarized by implanted eyes (primary versus fellow eyes) and lens group (LAL versus Control) beginning at the Postop Week 3 visit using descriptive statistics for continuous outcomes (such as mean and standard deviation). The number and percent of eyes with a MRCYL of ≤0.25 D, 0.50, 0.75 D, 1.0 D, 1.25 D, 1.5 D, 1.75, and ≥2.0 D at each visit will be reported. The descriptive statistics and percent of eyes with different MRCYL outcomes described previously will be stratified by MRCYL of < 0.50 D, ≥ 0.50 to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 D to <3.00 D, and ≥3.00 D at Postop Week 3 in order to compare the findings between the two lens groups.

In addition, the mean manifest cylinder at Postop Month 6 for each lens group and the number and percent of eyes by lens group with increases in cylinder ≥1.00 D between Postop Week 3 and Postop Month 6 will be reported.

8.5.4.2 Cylinder Correction Accuracy

For eyes measured with MRCYL < 0.50 D at the Postop Week 3 visit, two analyses will be performed. In the primary analysis, the intended cylinder correction will be assumed to be 0 and in a supportive analysis, the intended cylinder correction will be the highest MRCYL at any of the adjustment visits. For other eyes, the intended cylinder correction will be the MRCYL measured at the Postop Week 3 visit. The count and percent of eyes with accuracy of cylinder correction to intended target within 0.50 D and 1.00 D will be reported at Postop Month 3 and Postop Month 6 by eye (primary versus fellow) and lens group (LAL versus Control) for the implanted eyes/subjects in the FAS. Additionally, the deviation of the achieved adjustment from the attempted adjustment will be summarized by the descriptive statistics for continuous outcomes. In addition, the descriptive statistics for the LAL eyes with ≥0.50 D of cylinder at the Postop Week 3 visit will be further stratified into bins approximately 1.0 D in width.

8.5.4.3 Vector Difference

Vector differences between the intended cylinder change and the achieved cylinder change will be calculated and summarized descriptively by eye (primary versus fellow) and lens group (LAL versus Control). In eyes for which no cylinder adjustment is attempted, the intended change will be considered zero and the entire change from Postop Week 3 will be treated as an error.

The analyses will be performed based on the MRCYL and the cylinder of the aberrometry readings separately.

8.5.4.4 Refractive Cylinder Stability

Refractive cylinder stability will be presented for consistent cohort and eyes with two consecutive visits. The following statistics will be calculated by eye and lens group.

- Percentage of eyes that achieve change of ≤1.00 D of refractive cylinder;
- Percentage of eyes that achieve change of ≤0.50 D of refractive cylinder;
- Mean MRCYL change between two visits and the corresponding 95% confidence interval, mean change per month, and mean change per year

8.5.4.5 MRSE

The measured MRSE, adjusted MRSE (to account for the measured distance of 4 meters) and change in MRSE from Postop Week 3 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 for implanted primary eyes and implanted fellow eyes of the LAL group and of the Control group. The descriptive statistics will also be stratified by the MRSE at Postop Week 3 with bins of ≤-3.00 D, >-3.00 D to -2.00D, >-2.00 D to -1.00 D, >-1.00 D to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 to <3.00 D, and ≥3.00D for the two lens groups separately.

8.5.4.6 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 at each visit will be reported by eyes and lens group, at Postop Month 3 and Postop Month 6. For LAL eyes, the targeted post-adjustment MRSE is 0.00 D in all cases. The attempted MRSE adjustment is the Postop Week 3 MRSE in the primary analysis and will be the highest absolute MRSE at any of the adjustment visits in a supportive analysis. For Control eyes, the targeted post-adjustment MRSE is the Postop Week 3 MRSE and the attempted MRSE adjustment is 0. Additionally, the deviation of the achieved adjustment from the attempted adjustment will be summarized by the descriptive statistics for continuous outcomes. For the LAL group, the descriptive statistics will also be stratified by the MRSE at Postop Week 3 with bins of approximately 1.00 D wide.

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.

To evaluate any potential bias introduced by poor IOL power selection in the control arm, descriptive statistics of the difference in magnitude of MRSE measured at the Postop Week 3 visit will be calculated. 95% confidence intervals on the mean difference will be calculated.

8.5.4.7 Absolute MRSE

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

8.5.4.8 Refractive MRSE stability

The refractive stable point will be determined based on the criteria described in Section F.3 of ANSI Z80.11-2012 document as follows:

- At least 95% of the treated eyes have a change ≤1.00 D of MRSE between the two refractions;
- The mean rate of change in MRSE, as determined by a paired analysis, is ≤0.5 D per year (0.04 D/month) over the same time period;
- The mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging;
- The 95% confidence interval for mean rate of change includes zero or a rate of change attributable to normal aging.

The MRSE change between Postop Month 3 and Postop Month 6 will also be presented by eye and lens group.

8.5.4.9 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 by eye and lens group at Postop

Week 3, Postop Month 3, and Postop Month 6 visits. The number and percent of eyes with DEQ ≤0.5 D and 1.0 D will also be summarized at the corresponding visit.

8.5.4.10 Autorefraction

Autorefraction sphere, cylinder, and spherical equivalent will be summarized descriptively at each visit by eye and lens group. Additionally, the vector analysis based on an IRC of MRCYL at Postop Week 3 and SIRC based on autorefraction cylinder (ARCYL) at Postop Month 6 will be performed by eye and lens group.

8.5.4.11 Monocular Visual Acuity

The study includes the following monocular visual acuities:

- Distance Visual Acuity
    - Monocular photopic uncorrected distance visual acuity (no trial lens in front of eye)
    - Monocular photopic uncorrected distance visual acuity (monocular photopic UCDVA) using a +0.25 D lens to compensate for 4 meter test distance
    - Monocular photopic best distance corrected visual acuity (monocular photopic BCVDA)
- Intermediate Visual Acuity
    - Monocular photopic uncorrected intermediate visual acuity (monocular photopic UCIVA)
    - Monocular mesopic distance corrected intermediate visual acuity (monocular mesopic DCIVA)
    - Monocular photopic distance corrected intermediate visual acuity (monocular photopic DCIVA)
    - Monocular mesopic best corrected intermediate visual acuity (monocular mesopic BCIVA)
- Near Visual Acuity
    - Monocular photopic uncorrected near visual acuity (monocular photopic UCNVA)
    - Monocular mesopic distance corrected near visual acuity (monocular mesopic DCNVA)
    - Monocular photopic distance corrected near visual acuity (monocular photopic DCNVA)
    - Monocular mesopic best corrected near visual acuity (monocular mesopic BCNVA)

For each of the above monocular visual acuities, the outcomes will be presented with the number and percent of eyes that fall into each VA category at each visit (e.g. 0.00 logMAR or better, 0.10 logMAR or better, 0.20 logMAR or better, etc.) by eye (primary eyes and fellow eyes) and lens group (LAL versus Control). The logMAR values will be summarized by descriptive statistics for continuous outcomes for each visit by eye and lens group. Odd ratios, comparing LAL versus Control primary eyes and their confidence intervals will be presented for the odds of UCDVA with a +0.25 D lens being worse than logMAR 0.00, 0.10,

0.20, and 0.30. Change in visual acuity from the Postop Week 3 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" by eye and lens group. The change in logMAR values from the Postop Week 3 visit will also be presented by eye and lens group. A subgroup analysis will be performed based on the amount of refractive error present at the Postop Week 3 visit. A comparison of the mean difference between the LAL and Control for these subgroups will be presented.

For the postoperative 6-Month DCIVA (both mesopic and photopic) and DCNVA (both mesopic and photopic), the mean logMAR values will be stratified by the MRSE at Postop Week 3 with bins of ≤-3.00 D, >-3.00 D to -2.00D, >-2.00 D to -1.00 D, >-1.00 D to <1.00 D, ≥1.00 to <2.00 D, ≥2.00 to <3.00 D, and ≥3.00D for the LAL eyes.

In order to address the effect of pupil size, the analyses for the mesopic visual acuity described above will be stratified by the mesopic pupil size (<3.0 mm, ≥3.0 to ≤4.0 mm, and >4.0 mm). In order to assess the effect of the distance refractive error on the uncorrected acuity, a scatter plot with Postop Month 6 logMAR UCDVA using a +0.25 D lens as the Y-axis and Postop Month 6 MRSE as the X-axis will be prepared. The Regression Analysis with a regression model using logMAR UCDVA using a +0.25 D lens at Postoperative Month 6 as the dependent variable and the corresponding MRSE as the independent variable will be performed. The effect of the MRCYL and that of DEQ on the logMAR UCDVA using a +0.25 D lens will also be analyzed based on the same regression analysis. The scatter plot and the regression analysis will also be performed for the Postop Month 6 logMAR UCIVA and UCNVA.

It should be noted that the change in monocular photopic BCDVA are treated as key safety outcomes and the associated analyses are described in Section 8.6.2 below.

8.5.4.12 Binocular Visual Acuity

The study includes the following binocular visual acuities:

- Binocular photopic uncorrected distance visual acuity (binocular photopic UCDVA) using a +0.25 D lens over each eye to compensate for 4 meter test distance
- Binocular photopic uncorrected intermediate visual acuity (binocular photopic UCIVA)
- Binocular photopic uncorrected near visual acuity (binocular photopic UCNVA)

The analyses methods described for the monocular uncorrected visual acuity will be performed for binocular visual acuity based on implanted subjects by lens group.

8.5.4.13 Depth of Focus

Descriptive statistics of the logMAR visual acuity measured at each lens diopter will be calculated for the depth of focus test performed at Postop Month 6 by eye and lens group.

The defocus curve and the estimated DOF will also be stratified by the photopic pupil size (<3.0 mm, ≥3.0 to ≤4.0 mm, and >4.0 mm) and by the axial length measured preoperatively (<21.0 mm, 21.0 mm to ≤26.0 mm, and >26.0 mm).

8.6 SAFETY PARAMETERS

The following safety outcomes will be summarized descriptively based on the observed data of the modified Safety population. The 95% confidence intervals for means or percentage may be presented, as appropriate. Key safety outcomes will also be provided for the Pre-COVID-19 population.

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 the operative visit and each postoperative visit by lens group. Serious ocular AEs and the non-ocular serious AEs will be summarized in the same manner. Additionally, for each device-related AE reported during the study will be presented in the same manner.

Each ISO-defined cumulative and persistent adverse event at Postop Month 6 will be summarized using the count and percent of the subjects reported with such event along with the one-sided lower 95% confidence limit of the percent based on the binomial distribution. If the lower limit is below the ISO specified SPE rate for the respective AE, then it will be concluded that the LAL does not have a rate higher than the corresponding SPE rate specified by the ISO.

8.6.2 CHANGE IN MONOCULAR PHOTOPIC BCDVA

The change in the monocular photopic BCDVA from Preoperative or from Postop Week 3 will be calculated for each study eye in the modified Safety Population:

The BCDVA change will be presented by lens group 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 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 (including losses related to LDD treatment) will be provided for the eyes reported with a 10-letter or more loss in BCDVA during the study (i.e. from preoperative visit or previous visit).

[redacted]

[redacted]

8.6.6 SUBJECTIVE SYMPTOMS AND COMPLAINTS

For each reported subjective symptom and complaint, number and percent of subjects will be summarized for each severity level of the symptom for the modified Safety population by lens group.

8.6.7 OTHER OCULAR EXAMINATIONS

Slit lamp findings, fundus exam findings, and IOP changes will be summarized descriptively for all eyes in the modified Safety population by lens group. Number of LAL eyes with fundus exam changes from the pre-op and from the Postop Week 3 visit including fundus changes associated with UV exposure will be summarized. In addition, number of LAL eyes with confirmed perimetric observations on at least 2 post light treatment visual field tests that were unnoted at the Postop Week 3 visit will be summarized descriptively.

[redacted]

[9] 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.

[redacted]

8.6.9 DISTANCE CORRECTED CONTRAST SENSITIVITY (MESOPIC/PHOTOPIC W AND W/O GLARE)

The contrast sensitivity (in log units) at each spatial frequency level under each of the four test conditions (photopic with and without glare and mesopic with and without glare) at Postop Month 6 will be summarized by mean, standard deviation, median, minimum, maximum and percentile (0^{th}, 25^{th}, 50^{th}, 75^{th}, and 100^{th}) by eye (primary eyes versus fellow eyes) and lens group (LAL group versus control group) in the modified Safety population. The mean difference in log contrast sensitivity between the two lens groups with a 90% non-parametric confidence interval will also be performed for each spatial frequency. The number and frequency of eyes that can and cannot see the target at 100% contrast for each spatial frequency will be presented. Mesopic contrast sensitivity testing results without glare and with glare will be stratified by measured mesopic undilated pupil size (<3.0 mm, ≥ 3.0 to ≤ 4.0 mm, and >4.0 mm).

8.6.10 IOL STABILITY (TILT/DECENTRATION)

The number of eyes reported with IOL tilt and/or IOL decentration at Postop Week 3 (Control)/Adjustment #1 (LAL), Postop Month 3, and Postop Month 6 will be provided. For eyes reported with IOL tilt and/or IOL decentration , the amount of IOL tilt and/or IOL decentration will be summarized descriptively in the modified Safety population.

8.6.11 WAVEFRONT ABERROMETRY

The sum of all higher order, non-spherical aberrations (S3+S5+S7) will be used as a clinically important Wavefront Aberrometer outcome. The outcomes at Postop Week 3 and at Postop Month 6 visits will be described by mean, standard deviation, median, minimum, and maximum by eye (primary eyes versus fellow eyes) and lens group (LAL versus Control) in the modified Safety population. In addition, for the LAL primary eye, two separate regression analyses will be performed for both the Postop Month 6 DCIVA logMAR and BCDVA logMAR (Y-axis) on the change in this Wavefront Aberrometer outcome from Postop Week 3 to Postop Month 6 (X-axis) to determine the effect of this Wavefront Aberrometer outcome on the Postop Month 6 DCIVA and BCDVA. The regression analysis will also be performed for the LAL fellow eyes

8.6.12 SECONDARY SURGICAL INTERVENTION (SSI)

Rates of secondary surgical intervention (IOL exchange, removal, and repositioning) related to the optical properties of the IOL will be reported by lens group (LAL versus Control) in the modified Safety population. The two-sided 95% confidence intervals of these rates will be calculated as well as on the difference in rates. SSIs related to the optical properties of the IOL are defined as an SSI due to subject intolerance of visual symptoms not adequately improved by spectacle correction. All SSIs should include investigator assessment

determining if it is “related” or “not related” to the IOL optical properties.

8.7 SEQUENCE OF PLANNED ANALYSES

8.7.1 FINAL ANALYSIS

When all enrolled subjects have completed or exited the study, the final statistical analyses based on the SAP will be performed.

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. [redacted]

[redacted]

[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 7.8.1 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)

9.6.1 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 UNANTICIPATED 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. 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. 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.

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. 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 which may be worse after implantation of an EDF type lens. Additionally reduced contrast sensitivity is also possible after implantation of an EDF type lens. These and other complications may result in permanent poor vision.

Additional specific risks of the LAL include:
The LAL 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 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 COVID-19 RISKS

If a COVID-related public health emergency declaration is in place at the time of the study, the study site should take appropriate measures in a clinic setting to minimize spread of the virus in conformance to professional society guidelines and applicable guidance from the states and counties in which the sites are located.

In addition, the study informed consent has been updated to outline additional subject risks that are related to trial participation during an ongoing COVID-19 pandemic. They are as follows:

- The subject will be exposing themselves to added risks due to the COVID-19 pandemic (including possible transmission of Coronavirus infection, and possible further complications including but not limited to hospitalization and/or death) beyond the risk of adverse events due to the investigational device and/or procedure(s).

- The subject will be at higher risk in an ophthalmic clinical study because of the close contact they will have with health care professionals during their procedure and assessment (since the examiner must make measurements close to their face), in addition to the need for multiple follow-up visits/exams which will expose them to other patients and/or healthcare professionals who could be transmitting the virus even if they do not have symptoms.
- Subjects may still be at risk even if appropriate measures are taken to minimize risks in conformance to FDA guidance, American Academy of Ophthalmology guidelines, and guidance from the states and counties in which the study clinics are located.
- Subjects should be aware that potential disruptions to the IDE study may be necessary due to current or future pandemic-related emergency restrictions, such as possible disruption of the study as a result of COVID-19 control measures that may lead to delays in scheduled follow-up visits.
- Subjects who experience an adverse safety event (i.e. a safety complication) may experience a delay in seeing their doctor either due to COVID restrictions and/or due to their own concerns or fears about COVID risk, that could potentially lead to a dangerous situation with serious permanent visual side effects including loss of vision. Adverse outcomes typically require subjects to return for additional and possibly frequent follow-up office visits and examinations; thus increasing their COVID-related risks.
- Subjects who have contracted COVID-19 or feel ill with flu-like symptoms during their participation in the study will not likely be permitted to continue routine scheduled study follow-up, thereby increasing the risk that diagnosis and treatment of potential adverse safety outcomes could be missed or delayed.

RxSight will interact with study sites based on geographic location to determine which sites may be more impacted by COVID-19 during a particular period of enrollment and potentially subject to study disruptions. Sites may be restricted from enrolling in the study for a period of time based on local disease conditions. RxSight will work with sites to ensure that light treatments are continued when possible during any period of study disruptions, while maintaining subject safety.

9.14 POTENTIAL BENEFITS

The subject's benefit from taking part in this study is the correction of residual postoperative spherical and/or astigmatic refractive error and extended depth of focus resulting in potential improvements in uncorrected distance, intermediate and near vision.

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:

[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 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.

Protocol deviations from the Pre-COVID-19 population will be reported separately with a description of those protocol deviations specifically related to COVID-19.

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

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4. Hayashi K, Manabe S-I, Yoshida M, Hayashi H. Effect of astigmatism on visual acuity in eyes with a diffractive multifocal intraocular lens. J Cataract Refract Surg 2010; 36:1323-1329.
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6. Karhanova M, Pluhacek F, Mlcak P, et al. The importance of angle kappa evaluation for implantation of diffractive multifocal intra-ocular lenses using pseudophakic eye model. Acta Ophthalmol. 2015:93 e123-e128.

7. 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.

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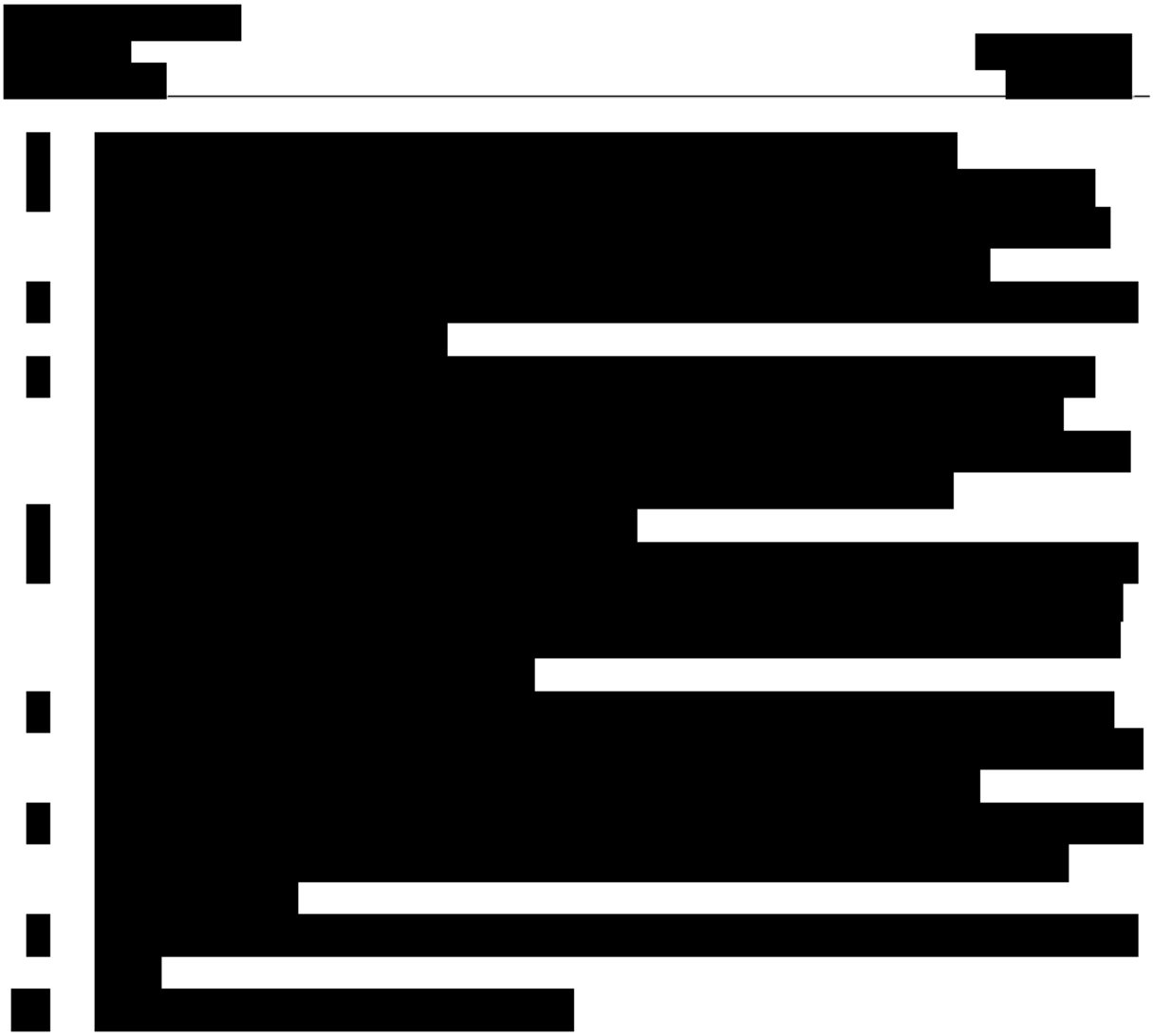

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