TITLE PAGE

A Multicenter Clinical Evaluation of the EVO/EVO+ Visian® Implantable Collamer® Lens

PROTOCOL

STUDY #CP19-01

SPONSOR:

STAAR Surgical Company

1911 Walker Avenue

Monrovia, California 91016

Telephone USA: 626-303-7902

This clinical investigation is being conducted in accordance with 21 CFR Parts 50, 54, 56 and 812, EN-ISO 14155: 2011 Clinical Investigation of Medical Devices for Human Subjects-Good Clinical Practice (with the exception of having Investigators sign the study report), 42 USC 282(j), and with the ethical principles laid down in the Declaration of Helsinki.

Revision Chronology:

Revision 2.0	-	2020.01.30

SPONSOR APPROVAL PAGE

A Multicenter Clinical Evaluation of the EVO/EVO+ Visian® Implantable Collamer® Lens

PROTOCOL

STUDY #CP19-01

[redacted]
Approved By:

[redacted]
Vice President, Global Clinical and Medical Affairs

31 JAN 2020
Date

[redacted]
Global Head Regulatory Affairs

January 31, 2020
Date

[redacted]
Chief Technology Officer

31st January 2020
Date

[redacted]
Vice President Global Quality

2020-01-31
Date

The final document associated with this signature approval is maintained in the STAAR Surgical eQMS system.

INVESTIGATOR STATEMENT OF APPROVAL

A Multicenter Clinical Evaluation of the EVO/EVO+ Visian® Implantable Collamer® Lens

PROTOCOL

STUDY #CP19-01

I have read the attached document, concur that it contains all information necessary to conduct the study, and agree to abide by all provisions set forth therein.

I agree to conduct this study in accordance with the relevant, current version of this protocol, 21 CFR Parts 50, 54, 56 and 812, EN-ISO 14155: 2011 Clinical Investigation of Medical Devices for Human Subjects-Good Clinical Practice (with the exception of having Investigators sign the study report), 42 USC 282(j), and with the ethical principles laid down in the Declaration of Helsinki. I will not initiate the study until I have obtained written approval by the appropriate IRB and have complied with all financial and administrative requirements of the governing body of the clinical institution and the Sponsor. I will obtain written informed consent from each study subject prior to performing any study specific procedures.

I understand that my signature on a case report form indicates that the data therein has been reviewed and accepted by me.

I understand that this document and related information is subject to confidentiality terms found in my signed Confidentiality or Clinical Services Agreement. I agree to protect the confidentiality of my patients when allowing the Sponsor of this clinical investigation, and/or relevant regulatory authorities and IRBs, direct access to my medical records for study subjects.

_____

Principal Investigator, Printed Name

_____ _____

Principal Investigator, Signature Date

Upon signing, provide a copy of this page to STAAR Surgical Company and retain a copy for your files.

PERSONNEL AND FACILITIES

NOTE: The information on this page is subject to change. All changes will be provided under separate cover.

Sponsor STAAR Surgical Company 1911 Walker Avenue Monrovia, California 91016 Telephone: 626-303-7902 **Study Manager (Primary Study Contact) and Contact for Reporting Serious Adverse Events and Product Complaints** [redacted] **Scientific & Clinical Affairs** [redacted] **Medical Monitor** [redacted]	**Clinical Investigator(s)** (Provided under separate cover.)

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LIST OF ABBREVIATIONS

Abbreviation /Acronym	Term
ACD	Anterior chamber depth
AC	Anterior Chamber
ADE	Adverse device effect
AE	Adverse event
AL	Axial length
ATA	Angle to angle
BSS	Balanced salt solution
CDVA	Corrected distance visual acuity
CECC	Corneal endothelial cell count
CFR	Code of Federal Regulations
CLR	Crystalline lens rise
CRF	Case Report Form
CME	Cystoid macular edema
D	Diopters
CV	Coefficient of variation
DFE	Dilated fundus exam
DIA	Device Investigator Agreement
DOA	Delegation of Authority
ECD	Endothelial cell density
eQMS	Electronic Quality Management System
EVO Visian ICL	Brand name for VICMO and VTICMO ICL models.
EVO+ Visian ICL	Brand name for VICM5 and VTICM5 lens models.
FDA	United States Food and Drug Administration
FTP	Foam tip plunger
GCPs	Good Clinical Practices
% hex	Percent hexagonality
HEMA	Hydroxyethyl methacrylate
HPMC	Hydroxypropyl methylcellulose
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICL	Implantable Collamer Lens
IOD	Implantation Orientation Diagram
IOL	Intraocular lens
IOP	Intraocular pressure
IRB	Institutional Review Board
ISO	International Organization for Standardization
LogMAR	Logarithm of Minimal Angle of Resolution
MICL	Visian ICL for Myopia
MRSE	Manifest refractive spherical equivalent

Abbreviation /Acronym	Term
NSAID	Non-steroidal, anti-inflammatory drug
OCOS	STAAR Visian ICL Online Calculation and Ordering Software
OCT	Optical coherence topography
PI	Principal Investigator/ Peripheral iridotomy
PMA	Premarket Approval Application
PTP	Pigment to pigment
QOL	Quality of life
QID	Four times per day
RD	Retinal detachment
SAE	Serious Adverse Event
SE	Spherical equivalent
SOP	Standard Operating Procedure
SPE	Safety and performance endpoint
STS	Sulcus to sulcus
SUN	Standardization of uveitis nomenclature
TASS	Toxic anterior segment syndrome
TMICL	Visian Toric ICL for Myopia with Astigmatism
[redacted]	
UDVA	Uncorrected Distance Visual Acuity
US	United States
UV	Ultraviolet
VA	Visual acuity
VICM5	Model number for EVO+ Visian ICL for Myopia
VTICM5	Model number for EVO+ Visian ICL for Myopia with Astigmatism
VICMO	Model number for EVO Visian ICL for Myopia
VTICMO	Model number for EVO Visian ICL for Myopia with Astigmatism
WTW	White to white
YAG	Yttrium Aluminum Garnet

NOTE: The first occurrence of some abbreviations is not spelled out in the document (e.g., units of measure).

SYNOPSIS

STAAR Surgical Company Study #CP19-01	
Revision chronology:	Rev 2, 2020.01.30
Title:	A Multicenter Clinical Evaluation of the EVO/EVO+ Visian® Implantable Collamer® Lens
Type of study:	Prospective, open-label, multicenter.
Objective(s):	The objective of this study is to evaluate the safety, and to collect supportive data concerning the effectiveness of the EVO/EVO+ Visian® Implantable Collamer® Lens (ICL).
Study design:	This study will enroll and implant approximately 333 subjects (up to 333 primary eyes and up to an additional 333 fellow eyes) at up to 20 clinical sites in the US. Potential subjects who meet all eligibility criteria will be offered consecutive enrollment in the study and have surgery to implant study lenses in either one or both eyes. Postoperatively, subjects will return for visits at regularly scheduled intervals through Postoperative Visit 8 (1050 – 1170 days after surgery; see Appendix A). The analysis of the primary endpoints will be conducted after a minimum of 300 primary eyes complete Postoperative Visit 5 (Day 147 – 182) to support Supplement 35 to PMA P030016.
Inclusion criteria:	1. Subjects 21 through 45 years old at time of surgery. 2. For EVO/EVO+ ICL for Myopia: • Moderate to high myopia ranging from -3.00 D to ≤ -20.00 D spherical equivalent (SE) in the spectacle plane, with less than or equal to 2.50 D of astigmatism (in the spectacle plane). For EVO/EVO+ Toric ICL for Myopia with Astigmatism: • Moderate to high myopic astigmatism with spherical equivalent ranging from -3.00 D to ≤ -20.00 D (in the spectacle plane) and cylinder in the range of 1.00 D to 4.00 D (in the spectacle plane). • Stable refractive history within 0.50 D cylinder for 1 year prior to implantation as determined by the Investigator. 3. Stable refractive history within 0.50 D for spherical equivalent 1 year prior to implantation as determined by the Investigator. 4. For a subject who is expected to have residual postoperative cylindrical refractive error of ≥ 1 D (as determined by STAAR Online Calculation and Ordering Software, OCOS), the subject should be given the opportunity to experience his/her vision with the anticipated correction. 5. Anterior chamber depth (ACD) 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens. 6. Meet minimum endothelial cell density (ECD) requirements for age and ACD (refer to the "Minimum ECD for Age and True ACD*" table below).

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	7. Correctable Distance Visual Acuity (CDVA) to at least 20/40 in the eye(s) to be treated; and absent of ocular pathology (except that myopic degeneration is allowed). 8. Difference between cycloplegic refraction spherical equivalent (CRSE) and manifest refraction spherical equivalent (MRSE) of < 0.75 D. 9. For current contact lens wearers, stable MRSE (within ±0.5 D) on two consecutive examination dates with stability of the refraction determined by the following criteria: – Discontinuation of contact lens use for at least 2 weeks (rigid contact lenses and all toric contact lenses) or 3 days (non-toric soft contact lenses) prior to the first refraction; – Two refractions performed at least 7 days apart. 10. Able and willing to return for scheduled follow-up examinations after surgery. 11. Subjects must be able to read, understand and provide written informed consent on the Institutional Review Board (IRB) approved Informed Consent Form (ICF) and provide authorization as appropriate for local privacy regulations.
Exclusion criteria:	1. Younger than 21 or older than 45 years of age. 2. With true ACD < 3.00 mm*. 3. Anterior chamber angle less than Grade III as determined by gonioscopic examination. 4. Do not meet the minimum ECD as defined in the "Minimum ECD for Age and True ACD*" table below. 5. Coefficient of variation (CV) of endothelial cell area of > 0.45. 6. Percent hexagonality (% hex) of endothelial cell shape ≤ 45 %. 7. Unstable or worsening nearsightedness. 8. Ocular hypertension or glaucoma. 9. Pseudoexfoliation. 10. Pigment dispersion. 11. History or clinical signs of iritis/uveitis. 12. Insulin-dependent diabetes or diabetic retinopathy. 13. History of previous ocular surgery. 14. Cataract of any grade. 15. Progressive sight threatening disease or other previous or current ocular conditions, other than myopia or myopic degeneration, which may predispose for future complication in either eye. 16. Serious, acute, chronic or systemic, non-ophthalmic disease or illness that would increase the operative risk, confound the outcome(s) of the study or which may preclude study completion (e.g., immunocompromised, connective tissue disease, clinically significant atopic disease, uncontrolled diabetes, etc.).

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17. Monocular subjects.
18. For EVO/EVO+ ICL for myopia: myopia less than -3.00 D or greater than -20.00 D SE (in the spectacle plane) and/or with greater than 2.50 D of astigmatism (in the spectacle plane).
19. For EVO/EVO+ Toric ICL for myopia with astigmatism: myopia less than -3.00 D or greater than -20.00 D SE (in the spectacle plane) and/or refractive cylinder (in the spectacle plane) less than 1.00 D and greater than 4.00 D.
20. Pregnant or nursing women, or those who plan to become pregnant over the course of this clinical study or has another condition with associated fluctuation of hormones that could lead to refractive changes.
21. Involved in another clinical study or who may have been involved in a different clinical study within 30 days prior to this clinical study or will be involved in a different clinical study while participating in this study.
22. Subjects who, in the judgment of the Investigator, present any emotional, physiologic, or anatomical condition which may preclude participation in this study or provide an inappropriate landscape for the intended study treatment.

Minimum Endothelial Cell Density for Age and True ACD*

Age	Minimum ECD ACD ≥ 3.0 mm	Minimum ECD ACD ≥ 3.2 mm	Minimum ECD ACD ≥ 3.5 mm
21-25	3875 cells/mm^2	3800 cells/mm^2	3250 cells/mm^2
26-30	3425 cells/mm^2	3375 cells/mm^2	2900 cells/mm^2
31-35	3025 cells/mm^2	2975 cells/mm^2	2625 cells/mm^2
36-40	2675 cells/mm^2	2625 cells/mm^2	2350 cells/mm^2
41-45	2350 cells/mm^2	2325 cells/mm^2	2100 cells/mm^2
>45	2075 cells/mm^2	2050 cells/mm^2	1900 cells/mm^2

*The true ACD is defined as the distance from the apex of the posterior corneal surface to the apex of the anterior crystalline lens surface. Many measuring devices provide an ACD measurement defined as the distance from the apex of the anterior corneal surface to the apex of the anterior crystalline lens surface. If the surgeon is using an instrument that measures from the anterior corneal surface, the thickness of the cornea must be subtracted to get the true ACD.

Duration of Treatment

Eligible subjects who are enrolled in the study will be seen for 8 postoperative study visits over the course of approximately 3 years (1050 – 1170 days) after surgery.

Investigational device:

The investigational devices, EVO/EVO+ lenses, include a refractive optic and features a single piece lens design with a convex/concave optic zone of 4.9 to 6.1 mm diameter (according to model and power) and a 0.36 mm

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	diameter central port. The lens is manufactured from Collamer, a proprietary hydroxyethyl methacrylate (HEMA)/porcine-collagen biocompatible polymer material with an ultraviolet (UV) absorber. The lens is manufactured in four overall diameters: 12.1, 12.6, 13.2, and 13.7 mm to accommodate different eye sizes and feature a plate-haptic design with a central convex/concave optical zone and incorporate a forward vault to minimize contact with the central anterior capsule. The lens is supplied with a delivery system for implantation through an incision of 3.5 mm or less. EVO/EVO+ lenses have orientation markings on the footplates to ensure they are implanted in the correct orientation. When correctly oriented the orientation markings will be on the leading right/trailing left footplates. The EVO/EVO+ Toric lenses are labeled using a plus cylinder axis format and have two engraved lines, one on each side of the optic to aid with the axis alignment of the lens. The following EVO/EVO+ Models will be included in this study: • EVO/EVO+ Visian Implantable Collamer Lens for Myopia: VICMO12.1, VICMO12.6, VICMO13.2, VICMO13.7, VICM5_12.1, VICM5_12.6, VICM5_13.2, VICM5_13.7 • EVO/EVO+ Visian Toric Implantable Collamer Lens for Myopia with Astigmatism: VTICMO12.1, VTICMO12.6, VTICMO13.2, VTICMO13.7, VTICM5_12.1, VTICM5_12.6, VTICM5_13.2, VTICM5_13.7 All study lenses will be available in -3.00 D to -16.00 D spherical equivalent dioptric powers. The EVO/EVO+ Visian Toric ICLs will also be available in cylinder dioptric power of 1.00 D to 4.00 D.
Study endpoints:	Primary Endpoints Primary endpoints will be evaluated in primary eyes only. • Incidence of peripheral iridotomy (PI) required to treat elevated intraocular pressure (IOP) caused by mechanical pupillary block through Postoperative Visit 5 (Day 147 – 182). The prespecified safety and performance endpoint (SPE rate) target for the first primary study endpoint is the rate of secondary PI required to treat elevated IOP caused by mechanical pupillary block with the approved and currently marketed MICL and TMICL devices in the United States, which is approximately 0.3%. The additional primary endpoints have no prespecified performance targets: • Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 5 (Day 147 – 182). • Incidence of adverse events (AEs) through Postoperative Visit 5 (Day 147 – 182). Secondary Endpoints Secondary endpoints will be evaluated in all eyes (primary and fellow eyes) using descriptive statistics with comparisons to PMA data for the approved and currently marketed MICL and TMICL devices, where

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	appropriate. The secondary endpoints have no prespecified performance targets. • Incidence of PI required to treat elevated IOP caused by mechanical pupillary block through Postoperative Visit 5 (Day 147 – 182). • Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 5 (Day 147 – 182). • Incidence of AEs through Postoperative Visit 5 (Day 147 – 182). Additional Study Parameters Additional Study Parameters will be evaluated in all eyes (primary and fellow eyes). There are no prespecified performance targets for the additional study parameters. • MRSE within ± 1.00 D of target at Postoperative Visit 5 • MRSE within ± 0.50 D of target at Postoperative Visit 5 • Uncorrected distance visual acuity (UDVA) of 20/40 or better at Postoperative Visit 5 (for those eyes with CDVA 20/20 or better at Preoperative Visit) • CDVA through Postoperative Visit 8 (Day 1050 – 1170) • Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 8
Statistical methods:	The first primary study endpoint is defined as the incidence of PI required to treat elevated IOP caused by mechanical pupillary block through Postoperative Visit 5. The primary analysis will be performed on a minimum of 300 primary eyes that have completed Postoperative Visit 5. Based on complaint data, the event rate for secondary PI required to treat elevated IOP caused by mechanical pupillary block for the approved and currently marketed MICL and TMICL devices pupillary block is approximately 0.3%. The other primary endpoints will be studied using the first treated (i.e., primary) eyes. Secondary endpoints and additional study parameters will be studied using all (primary and fellow) eyes. Data will be summarized with point estimates and exact binomial confidence intervals for binary outcomes such as MRSE within 0.50 D and 1.00 D of target and UDVA 20/40 or better. Continuous outcomes (e.g., %hex, CV) will be described with summary statistics to include N, mean, standard deviation, minimum and maximum, first and third quartiles, and median. Distributions, such as CDVA loss, trabecular pigmentation, peripheral anterior synechiae (PAS), anterior chamber (AC) cells and flare will be summarized by number and percentage for each visit. ECD loss over the 1050 – 1170 days of follow up will be modeled using a bi-exponential model with adjustment for correlation between paired eyes. ECD and change in ECD will be summarized at each visit. The number and percentage of eyes with ECD < 1000 and < 1500 will be summarized over time using descriptive statistics. [redacted]

1.0 INTRODUCTION

The Visian® ICL for myopia (model MICL) was approved by FDA (PMA P030016) in 2005. The Visian® Toric ICL for the correction/reduction of myopia with astigmatism (model TMICL) was approved by FDA (PMA Supplement P030016/S001) in 2018.

These lens models offer an intraocular alternative for the correction of refractive error in those who currently utilize spectacle and/or contact lens correction. Other alternative refractive surgical procedures include: excimer laser surgery (including photorefractive keratectomy (PRK), laser assisted in situ keratomileusis (LASIK) and small incision lenticular extraction (SMILE)), radial keratotomy (RK), automated lamellar keratectomy (ALK), epikeratoplasty, intracorneal implants (lenses or rings), anterior chamber and sulcus-placement phakic intraocular lenses (IOLs), or a combination of one or more of these procedures.

In 2011, alternate designs of the current FDA approved lenses were introduced outside of the US; the EVO Visian® Implantable Collamer® Lens for myopia (model VICMO), and EVO Visian® Toric Implantable Collamer® Lens for myopia with astigmatism (model VTICMO). These devices (EVO lenses) are largely the same as the parent devices available in the US (MICL and TMICL), with the main difference being the addition of a 0.36 mm central hole in the optic. In 2015, EVO+ lenses (models VICM5 and VTICM5 for myopia and myopia with astigmatism, respectively) were introduced outside of the US. These models include a slightly larger optic diameter than the EVO lens models to offer additional options for patients with larger pupil sizes.

The addition of the central hole to the EVO/EVO+ lens models facilitates the flow of aqueous humor through the lenses, eliminating the need for peripheral iridotomies (PIs) prior to implantation. Where these lens models are available, patients require fewer office visits and procedures prior to implant surgery, without introducing new adverse events (AEs) or increasing the occurrence of known AEs as compared to the parent devices.

The benefits of the STAAR ICL (all models) have been demonstrated by predictable, stable refractive correction[1] and a high efficacy index,[2] as well as improvements in quality of vision[3] and quality of life (QOL).[4] Long-term studies investigating the safety profile of the STAAR ICL have demonstrated low rates of AE.[5,6]

2.0 OBJECTIVE

The objective of this study is to evaluate the safety, and to collect supportive data concerning effectiveness of the EVO/EVO+ Visian® Implantable Collamer® Lens (ICL).

3.0 STUDY DESIGN

3.1 Description of Study Design

This study will enroll and implant approximately 333 primary eyes and up to an additional 333 fellow eyes from subjects who qualify for bilateral implantation, at up to 20 clinical sites in the US. Postoperatively, subjects will return for visits at regularly scheduled intervals through

Postoperative Visit 8 (Day 1050 – 1170) as described in Appendix A. The analysis of the primary endpoint will be conducted after a minimum of 300 primary eyes complete Postoperative Visit 5 (Day 147 – 182) to support the Premarket Application (PMA Supplement P0930016/S035) of the investigational devices.

3.2 Selection of Study Population

The study population will include approximately 333 primary eyes of up to 333 subjects who meet all eligibility criteria. Potential subjects who meet all eligibility criteria will be offered consecutive enrollment in the study. Enrolled subjects will have surgery to implant study lenses in either one or both eyes. For subjects who qualify to participate bilaterally, fellow eye implantation will occur between 7 days and 14 days after uneventful surgery in the first eye. If, in an Investigator's medical judgment, second eye surgery should be postponed to a date more than 14 days from primary eye implantation due to a safety concern, the Medical Monitor's approval for second eye surgery will be required.

3.2.1 Eligibility

3.2.1.1 Inclusion Criteria

This study will include subjects or eyes meeting the following criteria:

1. Subjects 21 through 45 years old at time of surgery.
2. For EVO/EVO+ ICL for Myopia:
   - Moderate to high myopia ranging from -3.00 D to ≤ -20.00 D spherical equivalent (SE) in the spectacle plane with less than or equal to 2.50 D of astigmatism (in the spectacle plane).

   For EVO/EVO+ Toric ICL for Myopia with Astigmatism:

   - Moderate to high myopic astigmatism with spherical equivalent ranging from -3.00 D to ≤ -20.00 D (in the spectacle plane) and cylinder in the range of 1.00 D to 4.00 D (in the spectacle plane).
   - Stable refractive history within 0.50 D cylinder for 1 year prior to implantation as determined by the Investigator.
3. Stable refractive history within 0.50 D for spherical equivalent 1 year prior to implantation as determined by the Investigator.
4. For a subject who is expected to have residual postoperative cylindrical refractive error of ≥ 1 D (as determined by STAAR Online Calculation and Ordering Software, OCOS), the subject should be given the opportunity to experience his/her vision with the anticipated correction.

5. Anterior chamber depth (ACD) 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens.
6. Meet minimum ECD requirements for age and ACD (refer to the "Minimum ECD for Age and True ACD*" table below).
7. CDVA to at least 20/40 in the eye(s) to be treated; and absent of ocular pathology (except that myopic degeneration is allowed).
8. Difference between cycloplegic refraction spherical equivalent (CRSE) and manifest refraction spherical equivalent (MRSE) of < 0.75 D.
9. For current contact lens wearers, stable MRSE (within ±0.5 D) on two consecutive examination dates with stability of the refraction determined by the following criteria:
   - Discontinuation of contact lens use for at least 2 weeks (rigid contact lenses and all toric contact lenses) or 3 days (non-toric soft contact lenses) prior to the first refraction;
   - Two refractions performed at least 7 days apart.
10. Able and willing to return for scheduled follow-up examinations after surgery.
11. Subjects must be able to read, understand and provide written informed consent on the IRB approved ICF and provide authorization as appropriate for local privacy regulations.

3.2.1.2 Exclusion Criteria

This study will exclude subjects or eyes meeting the following criteria:

1. Younger than 21 or older than 45 years of age.
2. With true ACD < 3.00 mm*.
3. Anterior chamber angle less than Grade III as determined by gonioscopic examination.
4. Do not meet the minimum ECD as defined in the "Minimum ECD for Age and True ACD*" table below.
5. Coefficient of variation (CV) of endothelial cell area of > 0.45.
6. Percent hexagonality (% hex) of endothelial cell shape ≤ 45 %.
7. Unstable or worsening nearsightedness.
8. Ocular hypertension or glaucoma.
9. Pseudoexfoliation.
10. Pigment dispersion.
11. History or clinical signs of iritis/uveitis.
12. Insulin-dependent diabetes or diabetic retinopathy.
13. History of previous ocular surgery.

14. Cataract of any grade.
15. Progressive sight threatening disease or other previous or current ocular conditions, other than myopia or myopic degeneration, which may predispose for future complication in either eye.
16. Serious acute, chronic or systemic, non-ophthalmic disease or illness that would increase the operative risk, confound the outcome(s) of the study or which may preclude study completion (e.g., immunocompromised, connective tissue disease, clinically significant atopic disease, uncontrolled diabetes, etc.).
17. Monocular subjects.
18. For EVO/EVO+ ICL for myopia: myopia less than -3.00 D SE (in the spectacle plane) or greater than -20.00 D SE (in the spectacle plane) and/or with greater than 2.50 D of astigmatism (in the spectacle plane).
19. For EVO/EVO+ Toric ICL for myopia with astigmatism: myopia less than -3.00 D or greater than -20.00 D SE (in the spectacle plane) and/or refractive cylinder (in the spectacle plane) less than 1.00 D and greater than 4.00 D.
20. Pregnant or nursing women, or those who plan to become pregnant over the course of this clinical study or has another condition with associated fluctuation of hormones that could lead to refractive changes.
21. Involved in another clinical study or who may have been involved in a different clinical study within 30 days prior to this clinical study or will be involved in a different clinical study while participating in this study.
22. Subjects who, in the judgment of the Investigator, present any emotional, physiologic, or anatomical condition which may preclude participation in this study or provide an inappropriate landscape for the intended study treatment.

Minimum Endothelial Cell Density for Age and True ACD*

Age	Minimum ECD ACD ≥ 3.0 mm	Minimum ECD ACD ≥ 3.2 mm	Minimum ECD ACD ≥ 3.5 mm
21-25	3875 cells/mm^2	3800 cells/mm^2	3250 cells/mm^2
26-30	3425 cells/mm^2	3375 cells/mm^2	2900 cells/mm^2
31-35	3025 cells/mm^2	2975 cells/mm^2	2625 cells/mm^2
36-40	2675 cells/mm^2	2625 cells/mm^2	2350 cells/mm^2
41-45	2350 cells/mm^2	2325 cells/mm^2	2100 cells/mm^2
>45	2075 cells/mm^2	2050 cells/mm^2	1900 cells/mm^2

*The true ACD is defined as the distance from the apex of the posterior corneal surface to the apex of the anterior crystalline lens surface. Many measuring devices provide an ACD measurement defined as the distance from the apex of the anterior corneal surface to the apex of the anterior crystalline lens surface. If the surgeon is using an

instrument that measures from the anterior corneal surface, the thickness of the cornea must be subtracted to get the true ACD.

3.2.2 Subject Completion

The subject has completed the entire study when Postoperative Visit 8 (Day 1050 – 1170) is concluded. Subjects who require further follow-up for an AE will be followed according to Section 6.0.

3.2.3 Subject Discontinuation

A subject may be discontinued (at the discretion of the Investigator, the Sponsor and/or the IRB) prior to the final study visit for several reasons, including, but not limited to:

- voluntary withdrawal
- death
- surgical complication preventing implantation of the study lens in any eye
- explant of the study lenses

If both EVO/EVO+ study lenses are explanted, a minimum of one post-explant visit should be completed to record safety measures for the subject (e.g., CDVA, cataract/lens evaluation, endothelial cell count, etc.) prior to subject discontinuation.

Prior to discontinuing a subject, every effort should be made to contact the subject, schedule a final study visit, and obtain as much follow-up data as possible.

Adverse events will be followed as described in Section 6.0. Subject withdrawals will be documented clearly on the source document and applicable CRF.

Only subjects who do not receive any study lenses MAY be replaced. Subjects who are discontinued from the study following treatment will not be replaced.

Discontinued subjects should be followed outside of the study protocol according to the Investigator's normal postoperative standard of care.

3.2.4 Lost to Follow-up

Subjects who do not return for the final study visit, as defined by the visit window and cannot be contacted, will be considered lost to follow-up. All follow-up attempts will be documented in the subject's source documentation, and the applicable CRFs will be completed.

3.3 Investigators

- The study will be conducted at up to 20 clinical site(s) located in the US.
- The study will be conducted by Investigators who have prior clinical experience with the STAAR Surgical ICL and who are determined by STAAR Surgical to be suitably qualified by training and experience to conduct this study in compliance with all applicable Good Clinical

Practices (GCPs) and FDA Federal Regulations. Sub-Investigators will be identified on the Device Investigator Agreement (DIA)/DOA (Delegation of Authority Log).

- Each clinical site should enroll a minimum of 20 subjects and no one site can have more than 25% of the total enrollment.
- In the event that selected sites do not meet full enrollment, the Sponsor may decide to increase enrollment as needed at other currently active sites and additional site(s) may be added to satisfy the enrollment requirements of the study.

3.4 Study Duration

The duration of the study, including the time to recruit all subjects, will be approximately 46 months. Eligible subjects who are enrolled in the study will be seen for 10 scheduled study visits (per eye) over the course of approximately 3 years (1050 – 1170 days) after surgery.

4.0 STUDY MATERIALS

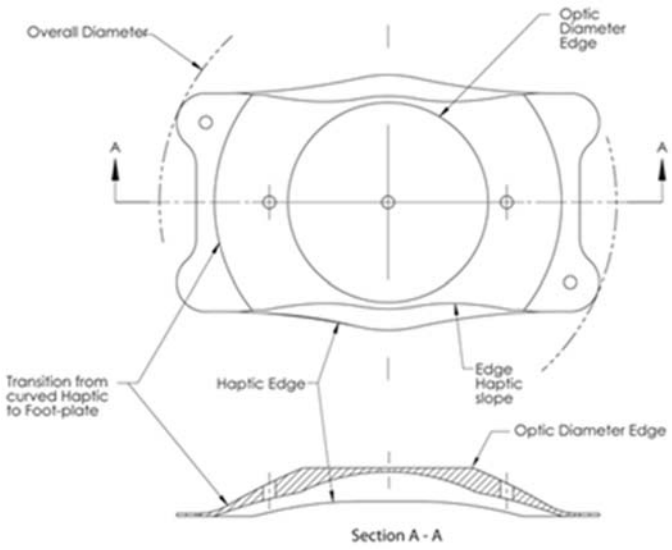
4.1 Description of Investigational Device

The EVO/EVO+ Visian® Implantable Collamer® Lens for Myopia, and EVO/EVO+ Visian® Toric Implantable Collamer® Lens for Myopia with Astigmatism investigational devices (EVO/EVO+ lenses), are sterile intraocular implants manufactured from Collamer, a proprietary hydroxyethyl methacrylate (HEMA)/porcine- collagen biocompatible polymer material. These lenses contain a UV absorber made from a UV absorbing material. The lenses feature a plate-haptic design with a central convex/concave optical zone and incorporate a forward vault to minimize contact with the central anterior capsule.

The EVO/EVO+ lenses feature a 0.36 mm central port, and an optic diameter that varies with the dioptric power; the smallest optic diameter being 4.9 mm and the largest 5.8 mm for EVO and 6.1 mm for EVO+. The implantable lenses are capable of being folded and inserted into the posterior chamber through an incision of 3.5 mm or less. The EVO/EVO+ lenses have orientation markings on the footplates to ensure the lenses are implanted in the correct orientation. When correctly oriented the orientation markings will be on the leading right/trailing left footplates.

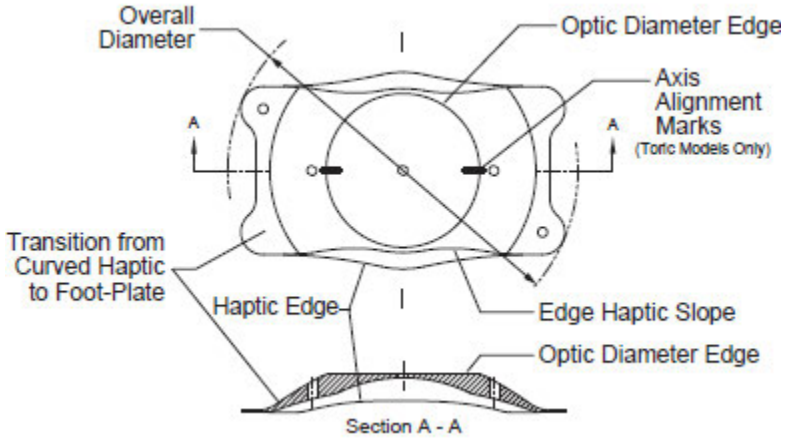
The EVO/EVO+ lenses are intended to be placed entirely within the posterior chamber (ciliary sulcus) directly behind the iris and in front of the anterior capsule of the human crystalline lens. When correctly positioned, the lenses function as a refractive element to optically reduce moderate to high myopia and myopic astigmatism (toric lens only).

Figure 1: EVO/EVO+ Lens Models for Myopia



The EVO/EVO+ Toric lenses are labeled using a plus cylinder axis format. The lens axis is labeled to the nearest degree and as such lenses of any axis between 1°to 180° may be held in inventory. The EVO/EVO+ Toric Lenses are designed to be rotated up to 22.5° clockwise or counterclockwise in order to align the lens axis at the preoperative plus cylinder axis. The lenses have two engraved lines, one on each side of the optic. These are to aid with the axis alignment of the lens. The markings indicate the meridian from which the cylinder axis is measured and do not indicate the cylinder axis of the lens.

Figure 2: EVO/EVO+ Toric Lens Models for Myopia with Astigmatism



The following EVO/EVO+ Models will be included in this study:

- EVO/EVO+ Visian Implantable Collamer Lens (ICL) for Myopia:

  VICMO12.1, VICMO12.6, VICMO13.2, VICMO13.7, VICM5_12.1, VICM5_12.6, VICM5_13.2, VICM5_13.7

- EVO/EVO+ Visian Toric ICL for Myopia with Astigmatism:

  VTICMO12.1, VTICMO12.6, VTICMO13.2, VTICMO13.7, VTICM5_12.1, VTICM5_12.6, VTICM5_13.2, VTICM5_13.7

Refer to Table 1 for a summary of design details for the investigational EVO/EVO+ lenses in addition to the MICL and TMICL lenses currently available in the US.

Table 1: Visian ICL Device Descriptions – Approved MICL/TMICL models and Investigational EVO/EVO+ Lenses

Lens Feature	Approved in the US	Investigational Study CP19-01 EVO/EVO+ lenses	
	MICL (P030016), TMICL (P030016/S001)	VICMO, VTICMO	VICM5, VTICM5
Haptic	Singe piece, plate haptic		
Material	Collamer		
Central Optic Feature	N/A	0.36 mm diameter center port (KS-AquaPORT®)	
Storage Solution	BSS		
Optic Diameters	4.9 - 5.8 mm	4.9 - 5.8 mm	5.0 - 6.1 mm
Optic Design	Spherical anterior and posterior surfaces		
Overall Lens Lengths	12.1, 12.6, 13.2, and 13.7 mm		
Optic Shape	Anterior: convex (toric convex as appropriate) Posterior: concave		
Haptics	Plate haptics with four foot plates and two (2) 0.36 mm diameter orientation partial depth ports	Plate haptics with four foot plates and two (2) 0.36 mm diameter orientation through ports	
Diopter Range	-3.00 D to -16.00 D (0.50 D steps)	-3.00 D to -16.00 D (0.50 D steps)	-3.00 D to -14.00 D (0.50 D steps)

Lens Feature	Approved in the US	Investigational Study CP19-01 EVO/EVO+ lenses	
	MICL (P030016), TMICL (P030016/S001)	VICMO, VTICMO	VICM5, VTICM5
Cylinder Diopter Range (Toric Only)	+1.0 D to +4.0 D (0.5 D steps)		

4.1.1 Instructions for Use and Administration

Surgery to implant the EVO/EVO+ lenses will be performed in accordance with instructions provided in Appendix B.

4.1.2 Storage Requirements

The study lenses are to be stored at room/ambient temperature. The storage location at the clinical site must have limited access, available to study site personnel only.

4.2 Treatment Replacement

A supplemental lens will be provided for each eye. Study lens accountability should be maintained as described in Section 4.5.

4.3 Other Materials

STAAR will provide the following materials:

- Supplemental lens for each study lens ordered,
- MICROSTAAR™ injector MSI-PF or MSI-TF reusable injector,
- SFC-45, single use cartridge for each study lens ordered,
- Foam tip plunger (FTP) for each study lens ordered, and
- 2% HPMC ophthalmic viscosurgical device (OVD)

4.4 Packaging and Labeling

Study lenses will be packaged in a glass vial, sealed in a polycarbonate tray with Tyvek lid placed in a white box, similar in shape and size to commercial product but without commercial artwork.

The visible information at the outer box level will include the following information:

- Sponsor name and address
- Study number
- Model number
- Serial number

- Dioptric power
- Expiration date
- Storage conditions
- Caution statement: e.g., "For clinical trial use only", "Investigational Device. Limited by Federal (or United States) Law to Investigational Use", etc.

The tray label will contain the following information:

- Sponsor name and address
- Study number
- Model number
- Serial number
- Dioptric power
- Storage conditions
- Caution statement: e.g., "For clinical trial use only", "Investigational Device. Limited by Federal (or United States) Law to Investigational Use", etc.

4.5 Accountability

The Investigator will be responsible for keeping current and accurate records of all study lenses received, dispensed, and returned to the Sponsor. The study lenses must be stored under the appropriate conditions in a secure, limited access area and are to be implanted only in subjects enrolled in the study, in accordance with the conditions specified in this protocol.

At time points throughout the study and/or upon completion of the study, the Sponsor/Sponsor's representative will review and verify the Investigator's accountability records. Following verification, and as directed by the Sponsor, all unused or explanted study lenses must be returned to the Sponsor.

4.6 Risk Assessment

Risk management is conducted in accordance with the principles described in ISO 14971:2012.

[redacted]

[redacted]

If new information regarding new risks to patients is made available during the course of the study, the IRB and applicable regulatory agencies will be notified, the informed consent will be updated, and the Investigator will be required to provide new information to patients and have them sign the revised ICF.

5.0 STUDY CONDUCT

5.1 Study Visits

All Subjects who meet the eligibility criteria will be seen according to the following schedule for each implanted eye:

VISIT	TIMING* (for each implanted eye)
• Preoperative Visit	Days -120 to -1
• Operative Visit	Day 0
• Postoperative Visit 1	1 day
• Postoperative Visit 2	5 – 9 days
• Postoperative Visit 3	21 – 35 days
• Postoperative Visit 4	70 – 98 days
• Postoperative Visit 5	147 – 182 days
• Postoperative Visit 6	330 – 420 days
• Postoperative Visit 7	690 – 810 days
• Postoperative Visit 8	1050 – 1170 days

* based upon days from surgery for each eye. Postoperative visits for both eyes may be scheduled on the same day only if visit window for each eye allows.

Following identification of a potential subject, the Investigator (or designee) will explain the purpose of the study, procedures, risks/benefits, and subject responsibilities to the potential subject. The subject will be provided a copy of the IRB approved consent form and a copy of the Patient Information Booklet for the appropriate FDA approved parent model. The subject's willingness and ability to meet the follow-up requirements of the study will be determined. If the subject chooses to participate in the investigation, written informed consent will be obtained. The subject and the person obtaining written consent, will sign and date the IRB approved ICF. The original signed document will be retained in the subject records, and a copy will be provided to the subject. In addition, the applicable privacy regulation requirements must be met.

5.1.1 Preoperative Visit – Days -120 to Day -1

Prospective subjects who have provided informed consent will be screened to determine eligibility for implantation of study lenses in one or both eyes. Demographic information, relevant ocular medical history, and current ocular medication use will be collected. The preoperative clinical evaluation will consist of a complete ophthalmic examination conducted no more than 120 days prior to surgery. Determination of eligibility will include consideration of all inclusion and exclusion criteria, including preoperative ECD as measured by the central reading center, calculation of the appropriate spherical and cylindrical lens power and size as provided by the STAAR OCOS system, and the opportunity for prospective subjects to experience their correction in the event that postoperative cylindrical refractive error of ≥ 1 D is predicted.

Refer to Appendix A: Schedule of Visits and Parameters for assessments to be performed.

5.1.2 Operative Visit – Day 0

Subjects will be reassessed to confirm eligibility. In addition, any changes in concomitant medications or AEs will be recorded. If the subject no longer meets eligibility criteria, he/she will be considered a screen failure. If the subject is eligible, he/she will be enrolled in the study and undergo surgery according to the surgical procedure described in Appendix B. If the study lens is not implanted due to a surgical complication, the subject will be discontinued from the study.

At approximately 1-6 hours after surgery, an intraocular pressure (IOP) reading in the implanted eye will be conducted. Any complications, AEs, or associated treatment given will be appropriately documented and reported.

For subjects who qualify to participate bilaterally, fellow eye implantation will occur between 7 days and 14 days after uneventful surgery in the first eye. If, in an Investigator's medical judgment, second eye surgery should be postponed to a date more than 14 days from primary eye implantation due to a safety concern, the Medical Monitor's approval for second eye surgery will be required.

5.1.3 Postoperative Visits – Day 1 to Day 1170

Each treated eye will be seen for 8 postoperative visits according to the schedule in Appendix A. Postoperative visits for both eyes may be scheduled on the same day only if the study visit window for each eye allows.

5.1.4 Unscheduled Visits

Additional visits may be scheduled, as necessary, to ensure the safety and well-being of subjects. All additional exams should be fully documented in the source documents and on Unscheduled Visit case report forms (CRFs), as appropriate. Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit range, will also be captured on Unscheduled Visit CRFs. In these cases, the intended visit will be identified on the Unscheduled Visit CRF.

5.1.5 Missed Visits

Site personnel will make every effort to avoid missing data, for example, by scheduling visits early in each visit window, calling subjects to remind them of upcoming visits and promptly calling subjects who have missed a visit in order to reschedule their visit within the appropriate window. If, despite best efforts, a missed visit cannot be rescheduled, the visit will be documented as missed in the source documents and CRFs.

5.2 Study Completion

STAAR Surgical will notify the Investigator when to contact the IRB to inform them that the study is complete.

5.2.1 Early Study Termination

If during the study it becomes evident to the Sponsor that the study should be stopped prematurely, the study will be terminated and appropriate notification will be given to the Investigator(s), IRB, and FDA, as applicable. STAAR Surgical will instruct the Investigators to stop dispensing study materials/treatment, to assure appropriate follow-up for all enrolled subjects and arrange for study closeout at each site as appropriate.

In addition, should the study be discontinued prior to bilateral implantation, STAAR surgical will provide an appropriate commercially available ICL or suitable alternative refractive procedure for the subject’s fellow eye.

5.2.2 Post-study Follow-up

If a subject requires further follow-up of SAEs upon discontinuation or completion of the study, the Investigator should schedule post-study follow-up visits, as necessary. Refer to Section 6.3.4 for follow-up of SAEs following study exit.

5.3 Concomitant Medications/Therapy

5.3.1 Perioperative Medication Regimen

The following medication regimen will be followed by all sites:

- topical 4th generation fluoroquinolone QID starting 3 days prior to surgery for a total of 10 days,
- topical NSAID QID, BID or QD per NSAID labeled dosing instructions for postoperative inflammation starting 3 days prior to surgery for a total of 10 days and then tapered weekly through 28 days after surgery,
- topical steroid QID starting 3 days prior to surgery for a total of 10 days and then tapered weekly through 28 days after surgery.

Note: No prophylactic systemic or topical IOP lowering medications (e.g., acetazolamide) will be used.

During the study follow-up period, the Investigator may use any medical treatment that is judged appropriate and beneficial to the subject. All medications that are considered necessary for the subject's welfare may be used at the Investigator's discretion. Documentation of all medications used for ocular indications by the subject during this study will be recorded in the subject's source document and applicable CRFs.

5.4 Protocol Deviations

The date of and reason for deviations will be documented in all cases. Significant or major protocol deviations impacting the safety of the subject or the integrity of the study must be reported by the Investigator to the Sponsor and IRB immediately. Reporting of all other protocol deviations must adhere to the requirements of the governing IRB.

Protocol assessments will continue until the end of the study, unless the protocol deviations put the subject at risk or the subject's condition requires that he/she be discontinued from the study.

6.0 ADVERSE EVENT REPORTING

Throughout the course of this study, all efforts will be made to remain alert to possible AEs. If an AE occurs, the first concern will be the safety of the subject, and appropriate medical intervention will be made. All ocular AEs (only eyes implanted with study lenses) and all serious AEs (both ocular and non-ocular) will be reported in this study. Non-serious non-ocular AEs will not be reported. The collection of AEs begins at the time the subject completes the informed consent process to participate in the study.

Refer to Section 6.3.1 for instructions on events that require expedited reporting to the Sponsor.

6.1 Definitions

6.1.1 Adverse Event

An **Adverse Event** (AE) is any untoward medical occurrence in a subject that does not necessarily have a causal relationship to the study device and study protocol. Adverse events include **Adverse Device Effect**s (ADEs).

In this study, all untoward events (aside from the exceptions noted for the early postoperative period in the following sections) that occur during the study need to be reported as AEs. In addition, all secondary surgical interventions (SSIs) and events that cause these interventions, and all events that have sequelae should be reported as AEs, regardless of when they occur.

AEs Associated with IOLs

Complications during phakic IOL surgery must be reported as AEs on the AE CRF. A worsening of a pre-existing ocular condition during the study should be documented as an AE and evaluated according to the guidelines in Section 6.2. All events that have sequelae should be reported as AEs, regardless of when they occur.

Adverse events associated with implantation of all types of IOLs (i.e., aphakic and phakic), need to be reported in this study. These can include, but are not limited to the following:

- Chronic Anterior Uveitis: anterior segment inflammation characterized by grade 1+ cell or greater that is persistent for > 3 months after surgery, or relapses in < 3 months after discontinuation of therapy, or for which the subject is maintained on therapy for > 3 months to control inflammation should be reported as an AE. In addition, anterior chamber (AC) cells or flare of greater than grade 2 (using the Standardization of Uveitis Nomenclature, SUN criteria[10]) at Visit 2 (Day 5 – 9) or later should be reported as an AE.
- Clinically significant cystoid macular edema (CME): macular edema diagnosed by clinical examination and adjunct testing (e.g., optical coherence topography [OCT], fluorescein angiography) resulting in CDVA of 20/40 or worse at Visit 3 (Day 21 – 35) or later.
- Clinically significant corneal edema: corneal swelling (stromal or epithelial) at Visit 2 (Day 5 – 9) or later should be reported as an AE.
- Endophthalmitis: intraocular inflammation requiring diagnostic vitreous tap and intraocular antibiotics,
- Mechanical pupillary block: shallowing of anterior chamber due to obstruction of aqueous humor flow from the posterior to anterior chamber through the pupil by the crystalline lens, vitreous face, or implanted device.
- Rhegmatogenous retinal detachment (RD): partial or complete RD associated with retinal tear.

- Toxic anterior segment syndrome (TASS): acute, non-infectious inflammation of the anterior segment that starts within 24 to 48 hours after surgery, usually resulting in hypopyon and commonly presenting with corneal edema and improving with steroid treatment.
- All SSIs and events that cause these interventions should be reported as AEs, regardless of when they occur.
    - For SSIs of secondary IOL intervention*
        - Exchange – investigational device is replaced with the same lens model
        - Removal – investigational device is removed and replaced with a non-investigational lens or no lens is implanted
        - Reposition – existing IOL is surgically moved to another location or rotated

        *Exchanges, removals, and repositions should be further sub-categorized by the problem that caused the need for the intervention (e.g., pupil ovalization, subject-reported undesirable optical phenomena, damaged IOL, malpositioned IOL, lens optic abnormality, iris pigment epithelial loss, endothelial cell loss, incorrect IOL power, chronic anterior uveitis, cataract, etc.).

Experience with intraocular surgery and the implantation of IOLs has shown that some events can be considered normal or expected after these procedures. Early, low grade anterior chamber cell/flare, corneal edema, and increase in IOP can often be considered normal or expected after phakic IOL surgery. They do not need to be reported as AEs if they occur prior to 1 week postoperatively and if they meet the following criteria:

- AC cells or flare of grade 2 (using the Standardization of Uveitis Nomenclature, SUN criteria)[10] or less that require no change in standard postoperative medication regimen; if persisting to 1 week or more these **should** be reported as an AE.
- Corneal edema of ≤ grade 2 that does not reduce CDVA to 20/40 or worse and does not require any change in standard postoperative medication regimen; if corneal edema persists to 1 week or more it **should** be reported as an AE.
- Increased IOP that is <10 mmHg above baseline or is <25 mmHg and requires no change in standard postoperative medication regimen or any other special treatment; increased IOP ≥ 10 mmHg above baseline to a minimum of 25 mmHg at one week or later **should** be reported as an AE.
- Loss of CDVA ≥10 letters up to 1 week postoperatively; loss of CDVA ≥10 letters at any time point > 1 week postoperatively **should** be reported as an AE.
- All other untoward events that occur during the study, and all events that have sequelae **should** be reported as AEs, regardless of when they occur.

AEs Associated with the ICL Platform

Ocular AEs associated with the ICL platform will be reported in this study. These can include, but are not limited to the following:

- anterior subcapsular opacities or clinically significant anterior subcapsular cataracts
- narrowing of the anterior chamber angle
- glaucoma
- corneal endothelial cell loss
- loss of CDVA
- increase in refractive astigmatism
- pigment dispersion
- iris transillumination defects

In addition, ocular AEs associated with the ICL platform may require a secondary surgery in the implanted eye(s). The following surgeries have been associated with the ICL platform:

- secondary IOL intervention (see above*)
- vitreous aspiration
- iridotomy/iridectomy for pupillary block
- wound leak repair
- retinal detachment repair
- corneal transplantation

All ocular AEs that fall outside of the above definitions should still be reported as AEs. In addition all SSIs and events that cause these interventions, and, all events that have sequelae should be reported as AEs, regardless of when they occur.

6.1.2 Adverse Device Effects

Adverse Device Effects are any untoward or unintended responses to a medical device. This definition may include any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device or other device malfunctions. This definition includes any event that is a result of a user error.

6.1.3 Device Deficiency

A Device Deficiency is any inadequacy of the medical device with respect to its identity, quality, durability, reliability, safety or performance. This includes malfunctions, use errors and inadequate labeling. A malfunction is any failure of a medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or clinical study protocol. All device deficiencies are classified as product complaints and are to be reported to the Sponsor as described in Section 6.3.3.

6.2 Evaluation

Adverse events experienced in this study may be associated with the study device (i.e., ADE) or the study protocol.

When evaluating AEs, the Investigator must determine if the event is serious, assess the severity of symptoms, and evaluate the relationship of the event to the study device and study protocol, using the following guidelines:

A **Serious Adverse Event** (SAE) is any AE (ocular or non-ocular) that:

- results in death
- results in serious injury, defined as:
  - life-threatening
  - permanent impairment of a body structure or function (e.g., blindness)
  - necessitates medical or surgical intervention to prevent permanent impairment to a body structure or a body function, or
  - results in a potentially sight-threatening condition;
- is a malfunction that might cause or contribute to a serious injury or death if it were to recur
- requires in-patient hospitalization or prolongation of existing hospitalization[1]
- leads to fetal distress, fetal death, a congenital abnormality, or birth defect

[1]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 serious, or an AE:

- administrative admission (e.g., for yearly monitoring exam)
- optional admission not associated with a worsening of a pre-existing condition (e.g., scheduled repair of the rotator cuff)
- hospitalization for admission without a medical AE

Severity

- Mild: Subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with the 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

Relationship (Causality) to Study Device or Study Protocol

- Not Related: Adverse events which are clearly and incontrovertibly due to causes other than the study device or study protocol (e.g., concomitant disease, etc.)

- Related: Adverse events which are felt with a reasonable degree of certainty to be related to the study device or study protocol
- Unknown: Adverse events for which a connection with the study device or study protocol cannot be ruled-out with certainty, or not enough information is available to assess the relationship

6.3 Reporting

6.3.1 On-Site Expedited Reporting

The Investigator is obligated to report the following to the Sponsor within 24 hours of becoming aware of the event to ensure the safety of all participants in the study and to meet regulatory reporting requirements:

- all **SAEs**, regardless of relationship to study device or study protocol,
- all secondary surgical interventions (removal, replacement or repositioning) involving the study lens and events that cause these interventions,
- loss of CDVA ≥10 letters compared to the baseline (Preop Visit) at Postoperative Visit 5 (Day 147-182), or later
- all **non-serious AEs** determined to be related to the study device (ADEs)
- all device malfunctions that do not result in one of the above reportable events

When reporting these events to the Sponsor, the site should forward any supporting documents along with the appropriate reporting form and the corresponding CRF, if applicable. Refer to the Personnel and Facilities section for Sponsor contact information for reporting of SAEs/ADEs and device malfunctions. Sites must also report applicable events to the reviewing IRB per its established reporting procedures.

6.3.2 Off-Site SAE Reporting

When participating in multicenter clinical trials, Principal Investigators may receive “off-site” reports (e.g., SAE Report). These are Sponsor reports of SAEs which occurred at other sites for the same trial, or in different trials using the same test article, that met the criteria for reporting to a regulatory agency. These should be reported to the reviewing IRB per their established reporting procedures. The IRB may require a revision to the ICF and reconsenting of patients if the SAE provides new information regarding risk to the study subject.

6.3.3 Reporting of Complaints for Marketed STAAR Surgical Products

All information collected on a CRF could potentially be identified as a product complaint, as defined in Section 6.1.3. During clinical monitoring by the Sponsor/designee, the information collected on the CRFs will be evaluated to determine if any of the information should be forwarded to the Sponsor for consideration as a complaint according to STAAR standard operating

procedures (SOPs) for complaint handling. The Sponsor has the responsibility for evaluating and investigating potential complaints in accordance with STAAR's internal complaint handling procedures.

Any complaints, malfunctions or similar events related to ancillary STAAR Surgical marketed products used in this study should be reported by the Investigators in accordance with the reference information provided on the commercial packaging.

6.3.4 Adverse Events and SAEs at Subject Exit

Ongoing ocular AEs at study exit will be documented as such in the CRFs and followed per the Investigator's standard of care.

Ongoing SAEs and ADEs will be followed until resolution or no further change in the condition is expected. Non-serious AEs that are ongoing at the study exit visit or upon discontinuation from the study will be followed per the Investigator's standard of care. Documentation in the eCRF of this follow-up is not required although subject care should continue as appropriate.

7.0 STATISTICAL METHODS

7.1 Study Endpoint and Parameters

7.1.1 Primary Endpoints

Primary endpoints will be evaluated in primary eyes only.

- Incidence of PI required to treat elevated IOP caused by mechanical pupillary block through Postoperative Visit 5 (Day 147 – 182).

The prespecified safety and performance endpoint (SPE rate) for the first primary study endpoint is the rate of PI required to treat elevated IOP caused by mechanical pupillary block with the approved and currently marketed MICL and TMICL devices, which is approximately 0.3%.

The additional primary endpoints have no prespecified performance targets:

- Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 5 (Day 147 – 182).
- Incidence of AEs through Postoperative Visit 5 (Day 147 – 182).

7.1.2 Secondary Endpoints

Secondary endpoints will be evaluated in all eyes (primary and fellow eyes) using descriptive statistics with comparisons to PMA data for the approved and currently marketed MICL and TMICL devices, where appropriate. The secondary endpoints have no prespecified performance targets.

- Incidence of PI required to treat elevated IOP caused by mechanical pupillary block through Postoperative Visit 5 (Day 147 – 182).
- Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 5 (Day 147 – 182).
- Incidence of AEs through Postoperative Visit 5 (Day 147 – 182).

7.1.3 Additional Study Parameters

The following will also be assessed in this study:

- MRSE within ± 1.00 D of target at Postoperative Visit 5
- MRSE within ± 0.50 D of target at Postoperative Visit 5
- UDVA of 20/40 or better at Postoperative Visit 5 (for those eyes with CDVA 20/20 or better at Preoperative Visit)
- CDVA through Postoperative Visit 8 (Day 1050 – 1170)
- Distribution of percent ECD losses and the percent of eyes that have ECD <1500 and ECD <1000 through Postoperative Visit 8

There are no prespecified performance targets for the additional study parameters.

7.2 Sample Size

Based on complaint data, the event rate for secondary PI required to treat elevated IOP caused by mechanical pupillary block for the approved and currently marketed MICL and TMICL devices is approximately 0.3%. Following the recommended analysis in ISO 11979-7:2018, Annex E, for cumulative adverse events, the null hypothesis is that the true rate of PI required to treat elevated IOP caused by mechanical pupillary block is less than or equal to the SPE rate, and the alternative hypothesis is that the true rate of PI required to treat elevated IOP caused by mechanical pupillary block is greater than the SPE rate:

$$H_0 \text{ (null hypothesis): } \pi \leq 0.3\%$$
$$H_a \text{ (alternative hypothesis): } \pi > 0.3\%$$

where π is the observed rate of PI required to treat elevated IOP caused by mechanical pupillary block. Based on the analysis in ISO 11979-7:2018, Annex E, the maximum number of cases allowed before the SPE rate is exceeded for 300 primary eyes of 300 subjects is 3.

To allow for losses of 10% per year, a total of up to 333 primary eyes of up to 333 subjects will be enrolled.

In addition, in order to detect an AE with a true probability of occurrence among eyes of 1% with 95% probability, based on the binomial distribution, a sample of at least 300 eyes is required.

7.2.1 Sample Size Justification for a Bi-exponential Model of Endothelial Cell Loss

The fitting of a bi-exponential model involves estimating 4 parameters, named by SAS PROC NLIN, a, b, p, and q in the following model:

$$ECD = p*exp(-a*time) + q*exp(-b*time)$$

Prior modeling submitted by STAAR from the MICL PAS study[11] was based on data from 169 subjects. Based on that sample size, the standard errors for the four model parameters are provided in the following table:

Parameter	Estimate	Approx Std Error
a	13.2593	44.9425
b	0.0208	0.00278
p	66.2263	33.6633
q	2591.8	22.8947

The sample size was then doubled to slightly over 338, which is a number close to the proposed sample size in this study, i.e., 300, in order to demonstrate the resulting increased precision. That doubling of the sample size yielded a reduction of the standard errors, as would be expected:

Parameter	Estimate	Approx Std Error
a	13.2593	31.7562
b	0.0208	0.00197
p	66.2263	23.7864
q	2591.8	16.1773

The doubling of the sample has the effect of reducing the standard error for each parameter by about 30%, as would be expected given that the reduction in the standard error is a function of the square root of N. Thus, the planned sample size of 300 in this study will allow more precise estimation of the curve than previously presented to the FDA in P030016/S022. Given the diminishing return from increasing the sample size further, we believe that 300 eyes will provide sufficient accuracy to model endothelial cell loss.

7.3 Analysis Populations

The safety analysis population will include all eyes implanted with an investigational EVO/EVO+ lens. Imputation of missing data will not be performed.

7.4 Statistical Analysis

The first primary study endpoint is defined as the incidence of PI required to treat elevated IOP caused by mechanical pupillary block through Postoperative Visit 5. The primary analysis will be performed on a minimum of 300 primary eyes that have completed Postoperative Visit 5. Based on complaint data, the SPE rate for secondary PI required to treat elevated IOP caused by mechanical pupillary block is approximately 0.3% for MICL/TMICL. Based on the recommended analysis in ISO 11979-7:2018, Annex E, the maximum number of cases allowed before the SPE rate is exceeded for 300 primary eyes of 300 subjects is 3.

The other primary endpoints will be studied using the first treated (i.e., primary) eyes. Secondary endpoints and additional study parameters will be studied using all (primary and fellow) eyes. Data will be summarized with point estimates and exact binomial confidence intervals for binary outcomes such as MRSE within 0.50 D and 1.00 D of target and UDVA 20/40 or better. Continuous outcomes (e.g., %hex, CV) will be described with summary statistics to include N, mean, standard deviation, minimum and maximum, first and third quartiles, and median. Distributions, such as CDVA loss, trabecular pigmentation, PAS, AC cells and flare will be summarized by number and percentage for each visit.

ECD loss over the 1050 – 1170 days of follow up will be modeled using a bi-exponential model with adjustment for correlation between paired eyes. ECD and change in ECD will be summarized at each visit. The number and percentage of eyes with ECD < 1000 and < 1500 will be summarized over time using descriptive statistics.

[redacted]

8.0 DATA QUALITY ASSURANCE

8.1 Study Monitoring

STAAR Surgical (or its representatives/agents/designees) must be allowed to visit all study site locations to assess the data, quality, and study integrity in a manner consistent with applicable health authority regulations and internal SOPs.

Prior to the start of the study, member(s) of STAAR Clinical and Medical Affairs Department (or designees) will review the protocol, CRF, regulatory obligations, and other material or equipment relevant to the conduct of the study with the Investigator/Sub-Investigator and relevant site personnel.

Monitoring visits and telephone consultations will occur as necessary during the course of the investigation to verify the following:

- the rights and well-being of subjects are protected

- the conduct of the investigation is in compliance with the currently approved protocol/amendment, IRB requirements, 21 CFR Parts 50, 54, 56 and 812, EN-ISO 14155: 2011 Clinical Investigation of Medical Devices for Human Subjects-Good Clinical Practice (with the exception of having Investigators sign the study report), 42 USC 282(j), and with the ethical principles laid down in the Declaration of Helsinki
- the integrity of the data, including adequate study documentation
- the facilities remain acceptable
- the Investigator and site personnel remain qualified and able to conduct the study
- test article accountability

During the course of the study, if the Sponsor determines that an Investigator is non-compliant with the study plan and/or applicable regulatory requirements, the Sponsor will take action to secure compliance. In addition, the Sponsor may terminate the Investigator's participation in the study if appropriate, or if the Investigator remains non-compliant despite the Sponsor's actions.

8.2 Source Documentation

All medical information obtained at each study visit must be recorded in the subject's record (source documentation) in real time as it is collected. Source documentation consists of original subject documents, as well as data and records with information relevant to the subject and his/her participation in the study.

Examples of acceptable source documents include: hospital records, clinical and office charts, notes, or memoranda. The signed ICF, evaluation checklists, recorded data from automated instruments, and subject files. Source data also include information initially recorded in an electronic format (e.g., specular microscopy images, etc.).

Source documentation worksheets may be provided by the Sponsor to record pertinent information. The completed worksheets can then be incorporated into the subject's medical chart. If it is preferred to not use the worksheets in the subject's permanent record, then the worksheets should be used as a reference to determine the type of study data to record in the subject's permanent record.

8.3 Case Report Forms and Data Verification

Subject data required by this protocol are to be recorded onto electronic CRFs for each eye enrolled in the study. The Investigator and his/her study site personnel will be responsible for completing the CRFs. The Investigator is required to verify that all of the requested information is accurately recorded on the CRFs. All information requested on the CRFs needs to be supplied, including subject identification and initials, date(s), assessment values, etc., and any omission or discrepancy will require explanation. All information on CRFs must be traceable to source documents if not otherwise specified in the Monitoring Plan for the study.

A STAAR Surgical designee will be responsible for reviewing and verifying the data recorded on the CRFs, utilizing the original source documentation and issuing queries as necessary for clarifications or discrepancies. The Investigator and study site personnel will be responsible for answering all queries. The CRFs will be submitted to STAAR Surgical via an electronic data capture system for quality assurance review and statistical analysis.

A copy of the CRFs will be retained by the Investigator at the conclusion of the study, who must ensure that it is stored in a secure place.

8.4 Recording of Data and Retention of Documents

Subject data recorded on CRFs during the study will be documented in a coded fashion. The subject will only be identified by the subject number, and by their initials/year of birth if also required. Confidentiality of subject records must be maintained to ensure adherence to applicable local privacy regulations.

The Investigator must retain essential documents indefinitely after the completion of the study, unless otherwise notified by the Sponsor.

Essential documents include but are not limited to the following:

- study protocol/amendments
- Protocol Signature Page signed and dated by PI
- IRB approved blank as well as copies of all signed subject ICFs
- all IRB approvals, correspondence and reports (e.g., SAE reports, protocol deviations, and safety updates)
- curriculum vitae (CV) and medical licenses for the PI and all sub-investigators (if applicable)
- regulatory documents (e.g., financial disclosure and DOA forms)
- source documents
- archive of CRFs
- Device Investigator Agreement
- investigational device accountability records
- relevant correspondence from and to the Sponsor
- any other documents relevant to the conduct of the study

In the event that the Investigator withdraws from the study (e.g., retirement, relocation), study records will be transferred to a mutually agreed upon designee (e.g., another Investigator, site IRB). The Investigator will provide notice of such transfer in writing to STAAR Surgical.

8.5 Auditing Procedures

Audits of clinical research activities in accordance with the Sponsor's internal SOPs to evaluate compliance with the principles of GCP may take place. A regulatory authority may also wish to

conduct an inspection (during the study or after its completion). If an inspection is requested by a regulatory authority and/or IRB, the Investigator must inform the Sponsor immediately that this request has been made.

8.6 Institutional Review Board/Ethics Committee Approval

The Investigator should ensure that participation in the study, in addition to the protocol, subject recruitment materials and the ICF to be used in this study are approved by their institution IRB, or if not using their institution's IRB, approved by the reviewing central IRB prior to entering any subjects in the study. Documentation of IRB approval of the study protocol and informed consent must be provided to the Sponsor prior to initiation of the study and maintained during the course of the study. In addition, the Investigator must ensure that the reviewing IRB, and Sponsor have provided approval for any protocol amendments prior to implementation. If the amendment necessitates a revision to the ICF, the Investigator should ensure the revised form is also submitted to and approved by the Sponsor and the IRB prior to re-consenting study subjects.

8.7 Publication of Results

All data generated as a result of this study will be regarded as confidential, until appropriate analysis and review by the Sponsor or its designee are completed. The results of the study may be published or presented by the Investigator(s) after the review by, and in consultation and agreement with the Sponsor, and such that confidential or proprietary information is not disclosed.

Prior to publication or presentation, a copy of the final text should be forwarded by the Investigator(s) to the Sponsor or its designee, for comment. Such comments shall aim to ensure the scientific integrity of the proposed publications and/or presentations and ensure that the data and material referring to STAAR Surgical products and activities receive fair, accurate, and reasonable presentation.

APPENDIX A: SCHEDULE OF VISITS AND PARAMETERS

All study tasks should be performed by qualified study site personnel as indicated on the DOA log under the supervision of the PI.

Table 2: Preoperative, Surgical Assessments, and Postoperative Assessments (for each implanted eye)
Note: Postoperative visits for both eyes may be scheduled on the same day only if the study visit window for each eye allows.

PROCEDURE/ ASSESSMENTS	**PreOp**[&] Day -120 to Day -1		**Op** Day 0	**V1** Day 1	**V2** Day 5-9	**V3** Day 21-35	**V4** Day 70-98	**V5** Day 147-182	**V6** Day 330-420	**V7** Day 690-810	**V8** Day 1050-1170
Demographics/ Medical and Ocular History	X										
UDVA	X	X[a]		X	X	X	X	X	X	X	X
CDVA	X	X[a]			X	X	X	X	X	X	X
Manifest Refraction	X	X[a]			X	X	X	X	X	X	X
Keratometry	X										
Gonioscopy	X							X	X	X	X
Slit Lamp Examination	X			X	X	X	X	X	X	X	X
Crystalline Lens Status	X*					X*	X*	X*	X*	X*	X*
Specular Microscopy (CECC[@])	X							X	X	X	X
[@]AL, ACD, WTW, pupil size, corneal topography	X										
IOP	X		X	X	X	X	X	X	X	X	X
Dilated Fundus Exam	X					X			X	X	X
Cycloplegic Refraction	X										
[redacted]	[redacted]										
[redacted]	[redacted]										
Lens Vault[$] (via OCT)						X	X	X	X	X	X
ConMeds/AEs	X		X	X	X	X	X	X	X	X	X

[a]Contact lens wearers only-see Appendix B of study protocol.

[&]Subject must provide informed consent to participate in study prior to undergoing any study specific procedures

* Assign LOCS III grade (see Appendix C). If lens opacity observed, obtain photograph at this visit and each subsequent visit

[@]CECC: corneal endothelial cell count; AL: axial length; WTW: white to white

[redacted]

$distance between the posterior surface of the phakic IOL and the anterior surface of the natural crystalline lens

APPENDIX B: INSTRUCTIONS FOR USE

STAAR Surgical EVO/EVO+ Visian® Implantable Collamer® Lens for Myopia, and EVO/EVO+ Visian® Toric Implantable Collamer® Lens for Myopia with Astigmatism Investigational Devices (EVO/EVO+ lenses)

Study CP19-01: INSTRUCTIONS FOR USE

Manufacturer:

STAAR Surgical Company
1911 Walker Avenue
Monrovia, CA 91016
USA

Tel: (800)352-7842
Fax: (800) 952-4923

CAUTION – Investigational Device. Limited by Federal (or United States) law to investigational use

INDICATIONS

The **EVO/EVO+ ICL for myopia** is indicated for use in patients 21-45 years of age:

1. for the correction of myopia ranging from -3.0 D to ≤ -15.0 D spherical equivalent (SE) in the spectacle plane, with less than or equal to 2.5 D of astigmatism (in the spectacle plane);
2. for the reduction of myopia ranging from greater than -15.0 D to -20.0 D SE (in the spectacle plane), with less than or equal to 2.5 D of astigmatism (in the spectacle plane);
3. with an anterior chamber depth (ACD) of 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens, and a stable refractive history (within 0.5 D for 1 year prior to implantation).
4. The ICL is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

The ICL functions as a refractive element to optically reduce moderate to high myopia.

The **EVO/EVO+ Toric ICL for myopia with astigmatism** is indicated for use in patients 21-45 years of age:

1. for the correction of myopic astigmatism with spherical equivalent ranging from -3.0 D to ≤-15.0 D (in the spectacle plane) with cylinder (spectacle plane) of 1.0 D to 4.0 D.

2. for the reduction of myopic astigmatism with spherical equivalent ranging from greater than -15.0 D to -20.0 D (in the spectacle plane) with cylinder (spectacle plane) 1.0 D to 4.0 D.
3. with an anterior chamber depth (ACD) of 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens and a stable refractive history (within 0.5 D for both spherical equivalent and cylinder for 1 year prior to implantation).
4. The Toric ICL is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

The Toric ICL functions as a refractive element to optically reduce moderate to high myopia with astigmatism.

CONTRAINDICATIONS AND EXCLUSION CRITERIA

- Younger than 21 or older than 45 years of age.
- With true ACD < 3.00 mm*.
- Anterior chamber angle less than Grade III as determined by gonioscopic examination.
- Do not meet the minimum ECD as defined in the "Minimum ECD for Age and True ACD*" table below.
- Unstable or worsening nearsightedness.
- Coefficient of variation of endothelial cell area of > 0.45.
- Percent hexagonality of endothelial cell shape ≤ 45 %.
- Difference between cycloplegic refraction spherical equivalent (CRSE) and manifest refraction spherical equivalent (MRSE) of > 0.75 D.
- Ocular hypertension or glaucoma.
- Pseudoexfoliation.
- Pigment dispersion.
- History or clinical signs of iritis/uveitis.
- Insulin-dependent diabetes or diabetic retinopathy.
- History of previous ocular surgery.
- Cataract of any grade.
- Progressive sight threatening disease or other previous or current ocular conditions, other than myopia or myopic degeneration, which may predispose for future complication in either eye.
- Serious, acute, chronic or systemic, non-ophthalmic disease or illness that would increase the operative risk, confound the outcome(s) of the study or which may

preclude study completion (e.g., immunocompromised, connective tissue disease, clinically significant atopic disease, uncontrolled diabetes, etc.).

- Monocular subjects.
- For EVO/EVO+ ICL for myopia: myopia less than -3.00 D SE (in the spectacle plane) or greater than -20.00 D SE (in the spectacle plane) and/or with greater than 2.50 D of astigmatism (in the spectacle plane).
- For EVO/EVO+ Toric ICL for myopia with astigmatism: myopia less than -3.00 D or greater than -20.00 D SE (in the spectacle plane) and/or refractive cylinder (in spectacle plane) less than 1.00 D and greater than 4.00 D.
- Pregnant or nursing women, or those who plan to become pregnant over the course of this clinical study or has another condition with associated fluctuation of hormones that could lead to refractive changes.
- Involved in another clinical study or who may have been involved in a different clinical study within 30 days prior to this clinical study or will be involved in a different clinical study while participating in this study.
- Subjects who, in the judgment of the Investigator, present any emotional, physiologic, or anatomical condition which may preclude participation in this study or provide an inappropriate landscape for the intended study treatment.

Minimum Endothelial Cell Density for Age and True ACD*

Age	Minimum ECD ACD ≥ 3.0 mm	Minimum ECD ACD ≥ 3.2 mm	Minimum ECD ACD ≥ 3.5 mm
21-25	3875 cells/mm^2	3800 cells/mm^2	3250 cells/mm^2
26-30	3425 cells/mm^2	3375 cells/mm^2	2900 cells/mm^2
31-35	3025 cells/mm^2	2975 cells/mm^2	2625 cells/mm^2
36-40	2675 cells/mm^2	2625 cells/mm^2	2350 cells/mm^2
41-45	2350 cells/mm^2	2325 cells/mm^2	2100 cells/mm^2
>45	2075 cells/mm^2	2050 cells/mm^2	1900 cells/mm^2

*The true ACD is defined as the distance from the apex of the posterior corneal surface to the apex of the anterior crystalline lens surface. Many measuring devices provide an ACD measurement defined as the distance from the apex of the anterior corneal surface to the apex of the anterior crystalline lens surface. If the surgeon is using an instrument that measures from the anterior corneal surface, the thickness of the cornea must be subtracted to get the true ACD.

WARNINGS

- Some subjects in the STAAR ICL for Myopia Clinical Study demonstrated endothelial cell loss >30% (range, 30.9% to 42.6%) at 5-7 years postoperatively. The longer-term effects (beyond 5 – 7 years) on the corneal endothelium have not been established. Subjects should be advised about the potential risk of corneal edema, possibly requiring corneal transplantation. ECD should be monitored periodically as long as the ICL remains implanted in the eye(s).

- Secondary to implantation of the ICL, subjects may have increased risk of development of cataract, including visually significant cataract that continues to increase with each year. Implanted eyes should be monitored for cataract periodically as part of normal standard of care for ICL subjects. The long-term risk of visually significant cataract and related secondary surgery may be higher in older subjects and those with higher myopia. The long-term rate (beyond 5-7 years) of cataract formation secondary to implantation, removal and/or replacement of the ICL is unknown.
- Implantation of the ICL is associated with an elevated risk of early postoperative increase in intraocular pressure (IOP; usually associated with pupillary block) that requires secondary surgical intervention. The long-term risks of glaucoma, peripheral anterior synechiae and pigment dispersion are not well established.
- Do not attempt to resterilize or repackage the ICL.
- Do not autoclave the ICL. Do not expose to temperature greater than 40°C. Do not freeze. If temperature requirements are not met, return the ICL to STAAR Surgical as instructed by the study monitor.
- The iridocorneal angle distance may decrease after implantation of the ICL. Iridocorneal angle should be assessed 1 week after implantation and monitored if the angle is extremely narrow.
- A subject with mesopic pupil size that is greater than the optic diameter of the ICL may experience symptoms of glare and/or halos. Subjects should be advised about this potential risk prior to ICL implantation.
- Complete removal of viscoelastic from the eye after completion of the surgical procedure is essential. STAAR Surgical will provide a low molecular weight 2% hydroxypropyl methylcellulose (HPMC) ophthalmic viscosurgical device (OVD) for use in the study.

  NOTE: The primary OVD used with the MICL/TMICL during the FDA clinical trials was a low molecular weight 2% HPMC preparation. Short chain sodium hyaluronate acids (viscoelastics) are not to be used in the study due to increased risk of cataract formation related to trapped viscoelastic.

PRECAUTIONS

Prior to surgery, the Investigator must provide prospective subjects with a copy of the study informed consent form and patient information booklet for the predicate product approved in the US and inform subjects of the possible benefits and complications associated with the use of this device.

- Subjects with higher degrees of myopia or myopic astigmatism may experience lower efficacy and higher rates of adverse events (AEs) and complications.
- Inadequate flushing of the viscoelastic from the eye may lead to IOP spikes. IOP will be checked at 1-6 hours after surgery at the Op Visit and at the 1 day postoperative visit.
- The effectiveness of ultraviolet (UV) absorbing intraocular lenses (IOLs) in reducing the incidence of retinal disorders has not been established.

- The relationship between the ICL and retinal detachment is undetermined.

ADVERSE EVENTS

All ocular AEs (only eyes implanted with study lenses) and all serious AEs (both ocular and non-ocular) will be reported in this study. The collection of AEs begins at the time the subject completes the informed consent process to participate in the study.

Adverse events that have been associated with the ICL platform include:

- anterior subcapsular opacities or clinically significant cataracts,
- narrowing of the anterior chamber angle,
- increased IOP,
- pupillary block,
- glaucoma,
- corneal endothelial cell loss,
- loss of CDVA,
- increase in refractive astigmatism,
- pigment dispersion,
- iris transillumination defects.

In addition, ocular AEs associated with the ICL platform may require a secondary surgery in the implanted eye(s). The following surgeries have been associated with the ICL platform:

- surgery to exchange, remove or reposition the lens,
- vitreous aspiration,
- iridotomy/iridectomy for pupillary block,
- wound leak repair,
- retinal detachment repair,
- corneal transplantation.

Experience with intraocular surgery and the implantation of IOLs has shown that some events can be considered normal or expected events after these procedures. Early, low grade anterior chamber cell/flare, corneal edema, and increase in IOP can often be considered normal or expected after phakic IOL surgery. They do not need to be reported as AEs if they occur prior to 1 week postoperatively and if they meet the following criteria:

- AC cells or flare of grade 2 (using the Standardization of Uveitis Nomenclature, SUN criteria[10]) or less that require no change in standard postoperative medication regimen; if persisting to 1 week or more these **should** be reported as an AE.
- Corneal edema of ≤ grade 2 that does not reduce CDVA to 20/40 or worse and does not require any change in standard postoperative medication regimen; if corneal edema persists to 1 week or more it **should** be reported as an AE.
- Increased IOP that is <10 mmHg above baseline or is <25 mmHg and requires no change in standard postoperative medication regimen or any other special treatment;

increased IOP ≥ 10 mmHg above baseline to a minimum of 25 mmHg at one week or later **should** be reported as an AE.

- Loss of CDVA ≥10 letters up to 1 week postoperatively; loss of CDVA ≥10 letters at any time point > 1 week postoperatively **should** be reported as an AE.
- All other untoward events that occur during the study, and all events that have sequelae **should** be reported as AEs, regardless of when they occur.

All ocular AEs that fall outside of the above definitions should still be reported as AEs.

SURGICAL INFORMATION

Implantation of the study lenses should only be attempted by a surgeon who has completed the STAAR Surgical Visian ICL Physician Certification Program. Only subjects who have provided written informed consent and meet all eligibility criteria listed in the study protocol can receive investigational lenses in Study CP19-01.

Calculation of Lens Power and Size

The lens power and size calculation for all eyes to receive EVO/EVO+ lenses will be performed by the surgeon using the STAAR Visian ICL Online Calculation and Ordering Software (www.ocos.STAAR.com). Postoperative target for all enrolled eyes will be emmetropia with an acceptable variation of ±0.50 D spherical equivalent (SE), at the Investigator's discretion. Investigators must use the lens diameter recommended by OCOS.

In the case of an EVO/EVO+ Toric ICL, OCOS will provide the surgeon a cylinder power and a range of spherical powers along with their expected postoperative values (i.e., residual sphere, cylinder, axis and spherical equivalent). An Implantation Orientation Diagram (IOD) will be generated for each study lens identifying the amount and direction of rotation required of the lens after insertion in the eye to provide optimal alignment.

IMPORTANT

Preoperative YAG iridotomies are NOT to be performed with the lenses to be implanted in this study.

Perioperative Medications

The following medication regimen will be followed by all sites:

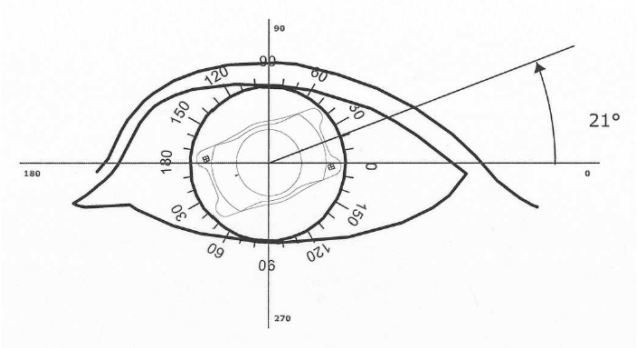
- Topical 4th generation fluoroquinolone QID starting 3 days prior to surgery for a total of 10 days.
- Topical NSAID QID, BID or QD per NSAID labeled dosing instructions for postoperative inflammation starting 3 days prior to surgery for a total of 10 days and then tapered weekly through 28 days after surgery.

- Topical steroid QID starting 3 days prior to surgery for a total of 10 days and then tapered weekly through 28 days after surgery.

Note: No prophylactic systemic or topical IOP lowering medications (e.g., acetazolamide) will be used.

Preoperative Procedures

- The subject will be prepared for surgery according to the surgeon's standard of care for STAAR Visian MICL/TMICL surgery.
- Examine the package for correct lens model, dioptric and cylinder power and overall diameter.
- ***EVO/EVO+ Toric ICLs Only***: As part of the implantation procedure, the lens may need to be rotated up to 22.5 degrees clockwise or counterclockwise from the 0°-180° meridian in order to align the lens axis at the preoperative plus cylinder axis. The surgeon should mark the horizontal axis (0°-180°) of the eye at the slit lamp prior to surgery. These horizontal axis marks will be used as reference points to mark the desired orientation of the lens under the operating microscope, using a suitable corneal axis marking device. For example, if the preoperative plus cylinder axis is at 136° and the lens selected has the cylinder axis at 115°, the lens will need to be rotated 21° counterclockwise from the temporal meridian in eye. In this case the desired axis marked on the cornea would be 21°counterclockwise from the 0°-180° meridian. The online ordering software for the toric ICL is designed to generate an IOD to guide the surgeon in determining the amount and direction of rotation for the specific lens selected. See example below:



Intraoperative Procedures

Preparation of the lenses for use

Perform the following steps in a sterile field.

- Inspect the lens vial. Ensure that it is not damaged or opened. Do not use if the vial is opened or damaged.
- Peel the Tyvek lid stock from the tray, then transfer the vial into the operating field.
- While keeping the vial in a vertical position, remove the aluminum seal and remove the cap.
- Carefully remove the lens from the vial. Handle the lens by the haptic portion. Do not grasp the optic with forceps as this could potentially lead to damage to the smooth anterior and posterior optical surfaces.
- Examine the lens carefully under the microscope for damage or particulate matter.
- Do not allow the ICL to dry after removal from the glass vial. It is recommended that the ICL be held in sterile BSS solution prior to implantation. It should not be exposed to any solutions other than the normally used intraocular irrigating solutions (e.g., isotonic saline, BSS, viscoelastic, etc.)

Delivery System

The lenses will be delivered using the provided MICROSTAAR® Injectors, Model MSI-TF (twist) or MSI-PF (push) with SFC-45 or SFC-45 FP Cartridge. Lenses will be loaded and delivered according to the surgeon's standard of care for STAAR Visian MICL/TMICL surgery.

CAUTION

The ICL should be injected within 1-2 minutes after loading. Viscoelastic materials tend to lose their lubricity if exposed to air too long.

Viscoelastic Usage

STAAR Surgical will provide 2% HPMC OVD for use in this study. Complete removal of OVD from the eye after completion of the surgical procedure is essential.

Do not use short chain OVDs due to increased risk of cataract formation related to trapped viscoelastic.

Surgical Procedures

1) Loading the cartridge
    a. Insert the foam-tipped plunger and holder into the injector, base first.
    b. The vertical tab of the holder is not intended to be snap locked into the notch of the injector.
    c. Keeping the plunger and holder in place, advance the injector cap until the ball end of the plunger interlocks with the injector.
    d. A click can be felt and heard when the plunger is properly secured.
    e. Retract the plunger fully. The foam-tipped plunger will remain locked in place.

f. Remove the holder by sliding it back out of the front of the injector.

g. Place the assembled foam-tipped plunger and injector into BSS, making sure that the tip of the injector and foam-tipped plunger are completely submerged.

h. Hydrate the foam tip plunger. Ensure adequate hydration of the foam tip plunger. If not properly hydrated, the foam tip plunger becomes dehydrated and compressed. In this case, the lens may become trapped between the cartridge and the foam.

i. Remove the cartridge from the package.

j. Add BSS to the cartridge.

k. Add low molecular weight 2% HPMC viscoelastic after BSS.

l. Grasp the lens haptic with forceps and place in cartridge loading area. Do not touch the optic of the lens.

m. Tuck one long edge and then the other long edge of the lens under the rails, ensuring proper orientation of the lens in the cartridge.

n. Close the jaws of the loading forceps and insert them into the barrel, from the front of the cartridge.

o. Advance the forceps through the cartridge until the jaws are about to contact the leading edge of the lens.

p. Open the jaws of the forceps and grasp the footplate of the lens so that the positioning mark is aligned with the jaws.

q. Slowly pull the lens into the barrel while moving the cartridge in the opposite direction.

r. Continue this process until the leading edge of the lens is adjacent to the end of the cartridge.

s. Release the lens from the forceps.

t. Insert the cartridge into the injector and lock into place.

u. Observe the lens for proper orientation in the cartridge.

v. The lens should be injected within 1 to 2 minutes after loading.

2) Marking the axis (toric lens only)

a. Using the horizontal axis marks placed preoperatively, mark the desired orientation of the lens under the operating microscope, using a suitable corneal axis marking device.

3) Constructing the incisions
    a. Construct one or two paracentesis incisions, 60 – 120 degrees away from the intended location of the temporal clear corneal main incision.
    b. Inject 2% HPMC viscoelastic into the anterior chamber; do not overfill.
    c. Construct a temporal clear corneal incision of approximately 3.5 mm or less in width, parallel to the iris plane, with a tunnel length of approximately 1.5 to 1.75 mm.
4) Inserting the lens
    a. Place the tip of the cartridge just inside the clear corneal incision.
    b. Inject slowly until the “leading right” orientation marking is visible.
    c. Continue to inject slowly, maintaining the proper orientation of the lens by rotating the cartridge as necessary, until the lens is released from the cartridge.
    d. Withdraw the cartridge from the incision.
5) Positioning the lens
    a. Inject additional viscoelastic, if needed, anterior to the lens.
    b. Use a manipulator to sequentially position the footplates posterior to the iris.
    c. Avoid crossing the manipulator over the central optical zone of the lens.
    d. For a toric lens, orient the lens in the position described on the IOD using the manipulator to rotate the lens by the edge, haptic body or footplates.
6) Removing the viscoelastic
    a. Thoroughly remove all viscoelastic by irrigating with BSS through a cannula or using bimanual irrigation and aspiration. Note that inadequate flushing of the viscoelastic from the eye may lead to elevated postoperative IOP.
    b. Do not irrigate or aspirate directly through the central port of the lens.
    c. Use slight incisional pressure while irrigating to allow egress of viscoelastic.
7) Constricting the pupil
    a. Ensure that all footplates are posterior to the iris by direct inspection.
    b. Ensure that lens axis alignment is at the intended position.
    c. Instill a miotic agent to constrict the pupil.

8) Sealing the incisions

    a. Ensure that the clear corneal incisions and the paracentesis are watertight.

Postoperative Procedures

- An IOP check will be conducted at approximately 1-6 hours after surgery, prior to release of subject.
- Perioperative concomitant medication regimen to be followed is described in the section "**Perioperative Medications**".
- Ensure all concomitant medications are documented on the subject case report form.

APPENDIX C: METHODS OF CLINICAL EVALUATION

Any changes to the procedures described in this appendix will be provided under separate cover.

1. Manifest Refraction

The refraction should be obtained by a qualified ophthalmologist, optometrist, or trained ophthalmic technician, in 0.25 D steps, in a calibrated refraction lane. If the subject has a current pair of glasses for distance vision, they can be measured with a lensometer and these measurements used as the beginning approximate refraction. If the subject does not have glasses for distance vision, retinoscopy should be performed by an examiner proficient in this procedure. If the subject is a contact lens wearer, they should be advised to arrive for preoperative testing wearing their spectacles. If the subject is a contact lens wearer, they will need to discontinue contact lens use for at least 2 weeks (rigid contact lenses and all toric contact lenses) or 3 days (non-toric soft contact lenses) prior to the first refraction.

AUTOREFRACTION ALONE IS NOT ALLOWED AT ANY POINT IN THIS STUDY. RESULTS MUST BE REFINED USING SUBJECTIVE TECHNIQUES.

The manifest refraction (adjusted for optical infinity as necessary) will be carried out using a standard "push plus" procedure, in 0.25 D increments and utilizing Jackson Cross-cylinder to assess toricity. The end result of the refraction must ensure the manifest refraction outcome reflects the very minimum "minus" power required to read the smallest line possible. If adding -0.25 D does not result in an additional letter read, it must not be added. Further, if adding +0.25 D does not result in a loss of letters read, it must be added.

The manifest subjective refraction result, adjusted for optical infinity, MUST be transferred to the trial frame for CDVA testing. The power of the lens used for the distance adjustment is subtracted from the sphere power before recording the refraction. For example, for testing at 4 meters, the power of the lens used for the distance adjustment is +0.25 D. The manifest refraction spherical power is +0.25 D less than the total sphere power measured at 4 meters. Both the adjusted and unadjusted manifest refractions should be recorded, if applicable.

2. Visual Acuity Testing

a) Equipment

Corrected (CDVA) and uncorrected visual acuity (UDVA) at all scheduled visits will be measured using the Early Treatment of Diabetic Retinopathy Study (ETDRS) charts at 4 meters or an equivalent optotype-adjusted distance (i.e., a projected or digital ETDRS chart may be placed at a distance other than 4 meters to accommodate the size of the examination room; however, the size of the optotype should be calibrated accordingly). UDVA should be performed using a trial lens with power of +1.00 D/(distance of chart in meters) to place the chart at optical infinity. CDVA (corrected distance visual acuity)

should be performed using a trial lens power reflecting the corresponding CDVA refraction.

The charts are designed according to the following principles described by Bailey and Lovie[12] and the National Academy of Science-National Research Council (NAS-NRC) Committee on Vision 1980[13]: 1) letters of equal legibility; 2) combine the letters so that each line is of approximately equal difficulty as described by Ferris et al[14]; 3) present five letters at each acuity level; 4) space rows by the height of the smaller letter; 5) space letters by the width of same-sized letters; and 6) use a logarithmic progression of letter size from LogMAR (Logarithm of Minimal Angle of Resolution) -0.3 (20/10) to 1.68 (20/957). This standard describes a single method for the measurement of VA (which is strongly influenced by the methods used in the ETDRS and AREDS protocols) so that measurements obtained using the procedures listed below can be compared within and between sites.[14]

b) **Testing Methods**

In order to provide standardized and well-controlled assessment of VA, all VA assessments for a subject should be performed consistently (e.g., the same lighting conditions, viewing distance, etc.) at each visit.

During acuity testing, vision testers should:

- observe subjects carefully for squinting (or head turning, etc.) and frequently remind patients not to squint or turn their heads,
- inform subjects that the chart has letters only, no numbers. If the subject reads a number, he or she should be reminded that the chart contains no numbers, and the examiner should then request a letter in lieu of the number.
- The subject should be asked to read slowly, about one letter per second, so as to achieve the best identification of each letter. He/she is not to proceed to the next letter until he/she has given a definite response.
- A maximum effort should be made to identify each letter on the chart (without squinting or head turning, etc.).
- When the subject says he/she cannot read a letter, the subject should be encouraged to guess.
- If the subject identified two (2) letters (e.g., A or B), the subject should be asked to choose one letter and, if necessary, to guess.
- When it becomes evident that no further meaningful readings can be made despite encouragement to read or guess, the examiner should stop the testing for that eye. However, all letters on the last line should be attempted as letter difficulties vary and the last letter may be the only one read correctly. The number of letters missed or read incorrectly should be noted.

c) **Illumination of the ETDRS Chart and Examination Room**

The ETDRS chart background luminance should be 85 cd/m^2 (80 – 160 cd/m^2 acceptable range) for photopic testing. Luminance should be identical for all study sites. The internal illumination of the ETDRS chart should be turned on. This will provide the nominal contrast for each of the charts. Room illumination should be turned off to ensure that the illumination is consistent for each measurement. Ambient sources of light in the room should be kept at a minimum. The room lighting and any ambient sources should be consistent in their use and placement at each subject visit throughout the course of this study.

d) **Scoring Visual Acuity logMAR Tests**

The examiner records each letter identified correctly by circling the corresponding letter on the Visual Acuity Worksheet. Letters read incorrectly or not read at all are not marked on the form. Each letter read correctly is recorded as one. The total letters read is recorded on the source documents. The logMAR score will be calculated by the sponsor.

During the course of the study, if the subject is unable to read any letters at 4 meters, they will be asked to count fingers at 0.5 meters (1 foot and 7 ⅝ inches). If fingers cannot be counted at 0.5 meters, the vision will be considered hand motion. Hand motion will be determined at 0.5 meters. Light perception will be determined using an indirect ophthalmoscope.

The ETDRS chart must be placed at a distance of 4 meters (13 feet and 1.5 inches, or 157.5 inches) or an equivalent optotype-adjusted distance from cornea to chart surface. A measuring tape or meter stick should always be available to verify the chart distance, even if the examining chair is supposed to be immovable or if reference marks are placed on the floor or walls.

3. Keratometry/Corneal Topography

Keratometry/Corneal topography measurements will be collected using the Investigator's standard of care method for ICL surgery. The site is to ensure a consistent and healthy tear film is present on the corneal surface for these measurements. It is permissible to add a drop of artificial tears to the subject's eye if necessary, allowing them to blink several times to evenly distribute the drop, in order to obtain the highest quality and reproducible measurement possible.

4. Gonioscopy

Gonioscopy will be used to assess the anterior chamber angle, pigmentation in the posterior trabecular meshwork and peripheral anterior synechiae (PAS).

a) **Anterior Chamber Angle**

Gonioscopic examination of the anterior chamber angle will be utilized to determine the grade of the angle. The Shaffer system will be used for angle grading. The subject must have a Shaffer grade ≥ III in all four quadrants of an eye to be implanted.

The scale is:

0	Closed
I	10 – 15°
II	15 – 25°
III	25 – 35°
IV	> 40°

b) **Pigmentation of the Trabecular Meshwork**

Pigmentation will be graded on a 0 to 4 scale noting the amount of pigmentation in the posterior trabecular meshwork.

If a transillumination iris defect is identified at the Preoperative Visit, a photograph should be taken, and then at each subsequent visit, a photograph should be taken and compared with the preoperative photograph via a standardized photographic method.

c) **Peripheral Anterior Synechiae (PAS)**

PAS is defined as abnormal adhesions of the iris to the angle that are at least half a clock hour in width and present to the level of the anterior trabecular meshwork or higher.

It is important to distinguish PAS from iris processes (the uveal meshwork), which are open and lacy and follow the normal curve of the angle. The angle structures are visible in the open spaces between the processes. Synechiae are more solid or sheetlike. They are composed of iris stroma and obliterate the angle recess.

If present, PAS will be graded as number of clock hours (0.5 to 12.0 in 0.5 steps).

5. Slit Lamp Examination

This examination will be performed using a slit lamp biomicroscope. It is recommended to use a slit beam 1.0 mm wide by 1.0 mm high. The following information will be captured for this study:

a) **External and Cornea**

Lids	Normal/Abnormal
Conjunctiva	Normal/Abnormal
Cornea Superficial Punctate Keratitis (SPK)	0 - None 1 - Mild 2 - Moderate 3 - Severe 4 - Very Severe

Corneal Wound Edema	0 - None 1 - Mild 2 - Moderate 3 - Severe
Corneal Edema	0 - No evidence of corneal swelling with normal transparency 1 - Mild corneal swelling 2 - Moderate corneal swelling 3 - Severe and definite widespread cloudiness or haziness giving dull ground glass appearance to cornea, or numerous coalescent bullae

b) **Anterior Chamber**

Anterior chamber cells and flare will be graded using the Standardization of Uveitis Nomenclature (SUN) grading schemes.

For the cell and flare evaluation, use a slit lamp beam 1.0 mm wide and 1.0 mm high.

AC Cells		AC Flare	
Grade	Cells in field	Grade	Description
0	<1	0	None
0.5+	1-5	1+	Faint
1+	6-15	2+	Moderate (iris and lens details clear
2+	16-25	3+	Marked (iris and lens details hazy)
3+	26-50	4+	Intense (fibrin or plastic aqueous)
4+	> 50		
Iris/Pupil	Normal/Abnormal		

6. Crystalline Lens Status

The crystalline lens will be evaluated utilizing the LOCS III grading system[15]. If a lens opacity is observed, a photograph will be taken when the lens opacity is first observed and at each subsequent visit to document any progression of the opacity.

7. Biometry

a) Axial Length (AL), Corneal Thickness (CT) and Pupil Size

AL, pupil size and CT measurements will be performed using partial coherence laser interferometry and documented in the CRF in XX.XX mm, X.X mm and XXX μm, respectively.

b) Anterior Chamber Depth (ACD)

Preoperative ACD, defined as the distance from the apex of the posterior corneal surface to the apex of the anterior crystalline lens surface, will be measured using Investigator's standard method for ICL surgery and documented in X.XX mm. **Note:** Many measuring devices provide an ACD measurement defined as the distance from the apex of the anterior corneal surface to the apex of the anterior crystalline lens surface. If the surgeon is using an instrument that measures from the anterior corneal surface, the thickness of the cornea must be subtracted to get the true ACD.

c) White-to-White (WTW)

Preoperative WTW (white to white) as defined as horizontal distance from limbus to limbus, will be measured using the Investigator's standard method for ICL surgery and documented in XX.XX mm.

[redacted]

8. IOP

Goldmann applanation tonometry will be used except for Operative Visit day where a non-contact method may be used. On surgery day, IOP will be measured approximately 1-6 hours postoperatively.

9. Cycloplegic Refraction

Topical medication will be applied to dilate the pupil and paralyze the ciliary muscle for measurement of the cycloplegic refraction.

10. Dilated Fundus Examination (DFE)

A DFE will be performed according to Investigator's standard of care for ICL surgery. The retina will be examined for presence or absence of posterior segment pathology or ocular infection. The examiner will classify the fundus as "normal" or "abnormal." Any abnormal findings will be either documented in ocular history at time of enrollment or documented and graded as an AE as appropriate.

11. Lens Vault

The distance between the posterior surface of the phakic IOL and the anterior surface of the natural crystalline lens will be measured using OCT and documented in μm.

12. Assessment of Pupil Ovalization

If an oval or irregularly shaped pupil (dyscoria) is observed at any postoperative visit, photographs[16] should be taken at that visit and each subsequent visit to determine if the ovalization is progressive. The photographs may be taken with any camera, including but not limited to slit-lamp cameras, topographers, and Scheimpflug devices, but the eye images must be captured under photopic conditions (>200 foot-candles or 2153 lux) so the pupil is maximally constricted. The pupil constriction provides the setting for pupil ovalization. The major and minor diameters of the pupil, which may not be orthogonal, are measured on the photograph. For the measurement, the diameters must pass through the center of the least squares, best-fit ellipse or centroid of the pupil perimeter. The ratio of the major to minor diameter will be calculated and reported.

13. Specular Microscopy

Specular microscopy images will be captured using the Konan CellChek® [CECC] non-contact specular microscopy device[1] and submitted to an independent central reading center for analysis. Up to 333 subjects (333 primary eyes and up to 333 fellow eyes) will have eyes imaged for analysis.

In order to satisfy study eligibility requirements, each prospective eye must meet the following preoperative criteria:

- Minimum ECD requirements for age and true ACD identified in the table below
- CV ≤ 0.45
- Hex > 45%

[1] Konan CellCheck® SL and XL models are completely interchangeable

Minimum Endothelial Cell Density for Age and True ACD

Age	Minimum ECD ACD ≥ 3.0 mm	Minimum ECD ACD ≥ 3.2 mm	Minimum ECD ACD ≥ 3.5 mm
21-25	3875 cells/mm^2	3800 cells/mm^2	3250 cells/mm^2
26-30	3425 cells/mm^2	3375 cells/mm^2	2900 cells/mm^2
31-35	3025 cells/mm^2	2975 cells/mm^2	2625 cells/mm^2
36-40	2675 cells/mm^2	2625 cells/mm^2	2350 cells/mm^2
41-45	2350 cells/mm^2	2325 cells/mm^2	2100 cells/mm^2
>45	2075 cells/mm^2	2050 cells/mm^2	1900 cells/mm^2

Site Training

Prior to enrollment start, the reading center will establish an SOP for the study and conduct pre-study training and certification of site personnel delegated to capture images for the study. The reading center will provide image examples that represent the quality required for the clinical study.

Instructions to the sites will include the following:

- select cell areas to count with fewest distortions- no shadow, blur or wash out
- the quality of cells selected is critical; be aware of cells with polymegathism and pleomorphism post contact lens wear
- all images obtained in the study will be required to be clear with cells plainly visible and without an extreme amount of guttata
- three images will be obtained at a central corneal location for each eye
- the same trained imaging technician(s) should be used for all study subjects at each site

Microscopes at each site will be calibrated before study to ensure the same calibration throughout the study. Site readers will capture and submit sample images prior to start of enrollment as part of the certification process.

Grading of Images

Grading will be performed using the center dot method (manual process of identifying each endothelial cell in the image). In brief, the grader will identify a region in the image where cells are grouped together and will use the mouse or other input device to mark the center of each cell, until all the cells or a minimum of 100 cells in the region can be identified. Cell counting software will calculate the following parameters:

- endothelial cell density (ECD)
- coefficient of variation (CV)
- hexagonality (Hex)
- number of cells counted (n, maximum, minimum)

- average cell size

In addition, the grader will document the Confidence Score (CS) of the image as defined:

- CS1, at least 100 contiguous cells identified
- CS2, 25-99 contiguous cells identified (due to image quality or pathology)
- CS3, image ungradable (< 25 contiguous cells identified)

The reading center will report ECD, CV, % Hex, number of cells counted (n, max, min), average cell size, and mean of the cell counts across the 3 images to STAAR no later than 90 days of date specular microscopy is performed. The Sponsor will be notified if a reading indicates a cell density loss of 20% or more from the preoperative value or the ECD falls below 1500 cells/mm^2.

The Sponsor will notify the Investigator if a cell density loss of 20% or more from the preoperative value has occurred or the ECD falls below 1500 cells/mm^2. The Investigator will recall the subject to retest to confirm the cell loss. If confirmed, specular microscopy will be performed on eyes of concern every 4 to 6 months to evaluate the cell density stability. If there appears to be an accelerated annual cell loss rate above 1%/year, then the Investigator, in consultation with the Medical Monitor, will consider if implant removal may be warranted.

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