TITLE PAGE

Post-Market Evaluation of the EVO ICL

PROTOCOL
STUDY #CP22-01

Sponsor:

STAAR Surgical Company

1911 Walker Avenue

Monrovia, California 91016

Telephone USA: 626-303-7902

This clinical study is being conducted in accordance with 21 CFR Parts 11, 50, 54, 56, 803, 814.82(a)(2), 820; 42 USC 282(j), FDA GCPs and the with the ethical principles laid down in the Declaration of Helsinki.

Revision Chronology:

Revision 2	-	25Apr2023

SPONSOR APPROVAL PAGE

Post-Market Evaluation of the EVO ICL

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Signature: Joanne Egamino

Electronically signed by: Joanne Egamino
Reason: I am the Signer.
Date: Apr 26, 2023 07:46 EDT

Email: jegamino@staar.com

Author: Joanne Egamino PhD,
Vice President, Global Clinical Affairs

Date

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Global Head Regulatory Affairs

2023-04-25
Date

Phil Tsung
Vice President Global Quality

2023-04-26
Date

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

INVESTIGATOR STATEMENT OF APPROVAL

Post-Market Evaluation of the EVO ICL

PROTOCOL
STUDY #CP22-01

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 11, 50, 54, 56, 803, 814.82(a)(2), 820; 42 USC 282(j), FDA GCPs 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** Jennifer Lynch MSc Director, Clinical Operations Email: jlynch@staar.com **Clinical Affairs** Joanne Egamino PhD Vice President, Global Clinical Affairs Email: jegamino@staar.com **Medical Monitor** Mark Packer MD Mark Packer MD Consulting, Inc. 1400 Bluebell Ave. Boulder, CO 80302 Tel: +1 541 915 0291 Email: mark@markpackerconsulting.com	**Clinical Investigator(s)** (Provided under separate cover.)

TABLE OF CONTENTS

PAGE

LIST OF ABBREVIATIONS

Abbreviation /Acronym	Term
AC	Anterior Chamber
ACD	Anterior Chamber Depth
ADE	Adverse Device Effect
AE	Adverse Event
AS-OCT	Anterior Segment Optical Coherence Tomography
BID	Twice a Day
CDVA	Corrected Distance Visual Acuity
CFR	Code of Federal Regulations
CME	Cystoid Macular Edema
CRF	Case Report Form
CRSE	Cycloplegic Refraction Spherical Equivalent
CV	Curriculum Vitae
D	Diopters
DFU/eDFU	Directions for Use/electronic Directions for Use
DIA	Device Investigator Agreement
DOA	Delegation of Authority
EC	Ethics Committee
ECD	Endothelial Cell Density
EVO ICL	Brand name for VICMO and VTICMO lens models
EVO+ ICL	Brand name for VICM5 and VTICM5 models
FDA	United States Food and Drug Administration
GCPs	Good Clinical Practices
HEMA	Hydroxyethyl Methacrylate
HIPAA	Health Insurance Portability and Accountability Act
HPMC	Hydroxypropylmethylcellulose
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICL	Implantable Collamer Lens
IOL	Intraocular Lens
IOP	Intraocular pressure
IRB	Institutional Review Board
MRSE	Manifest Refraction Spherical Equivalent
NSAID	Non-steroidal Topical Anti-inflammatory Drug

Abbreviation /Acronym	Term
OCT	Ocular Coherence Topography
OVD	Ophthalmic Viscoelastic Device
PAS	Post Approval Study/Peripheral Anterior Synechiae
PI	Principal Investigator
PIB	Patient Information Booklet
PMA	Premarket Approval Application
QD	Once a day
QID	Four times a day
RD	Retinal Detachment
SAE	Serious Adverse Event
SE	Spherical Equivalent
SOP	Standard Operating Procedure
SSI	Secondary Surgical Intervention
STAAR	STAAR Surgical Company
SUN	Standardization of Uveitis Nomenclature
TASS	Toxic Anterior Segment Syndrome
US	United States
UV	Ultraviolet
VA	Visual Acuity

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

SYNOPSIS

STAAR Surgical Company Study #CP22-01: Post-Market Evaluation of the EVO ICL	
Revision chronology:	**Rev 1, 06May2022**
Title:	Post-Market Evaluation of the EVO ICL
Type of study:	Post-approval study (PAS)
Objective(s):	To assess the rate of early intraocular pressure (IOP) increases following implantation of EVO/EVO+ICL lenses (EVO ICL).
Study design:	This new enrollment, prospective, multi-center, single arm PAS will be conducted at up to 10 clinical sites in the United States (US). The study is designed to evaluate the success of the EVO Physician Certification Program in reducing the rate of early IOP increases at 1 – 6 hours after implantation of EVO ICL lenses by surgeons who have been trained and certified under the EVO Physician Certification Program. This PAS will enroll a minimum of 200 subjects (i.e., 200 primary eyes and 200 fellow eyes) who are eligible for EVO ICL surgery in both eyes. All subjects are intended to undergo bilateral implantation with the second-eye surgery occurring from 1 – 14 days (1≤14 days) following the day of first eye surgery. Surgeons will use 2% HPMC OVD for EVO ICL surgery as recommended in the EVO ICL Directions for Use (DFU). Subjects will be seen for 4 postoperative visits at the following timepoints: • 1 – 6 hours postoperatively • 1 day postoperatively • 5 – 9 days postoperatively • 10 – 18 days postoperatively
Study duration:	This study is expected to require approximately 28 months following initiation, including approximately 24 months for enrollment, approximately 2 – 3 weeks for follow-up of each eye and approximately 3 months for data analysis and reporting.
Eligibility criteria:	Subjects aged 21 to 45 years implanted with EVO ICLs in both eyes, in accordance with the product labeling and the following eligibility criteria: <u>Inclusion Criteria</u> 1. Subjects 21 through 45 years old at time of surgery. 2. For 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 Toric ICL for Myopia with Astigmatism:

STAAR Surgical Company Study #CP22-01: Post-Market Evaluation of the EVO ICL	
	• 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. Anterior chamber depth (ACD) 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens. 5. Meet minimum endothelial cell density (ECD) requirements for age and ACD (refer to the "Minimum ECD for Age and True ACD*" table below). 6. Correctable distance visual acuity (CDVA) of at least 20/40 in the eye(s) to be treated; and absence of ocular pathology (except that myopic degeneration is allowed). 7. Difference between cycloplegic refraction spherical equivalent (CRSE) and manifest refraction spherical equivalent (MRSE) of < 0.75 D. 8. Able and willing to return for scheduled follow-up examinations after surgery. 9. 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. <u>Exclusion Criteria</u> 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. Unstable or worsening nearsightedness. 6. Ocular hypertension or glaucoma. 7. Pseudoexfoliation. 8. Pigment dispersion. 9. History or clinical signs of iritis/uveitis. 10. Insulin-dependent diabetes or diabetic retinopathy. 11. History of previous ocular surgery.

STAAR Surgical Company Study #CP22-01: Post-Market Evaluation of the EVO ICL

12. 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.
13. 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.).
14. Monocular subjects.
15. For 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).
16. For 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.
17. 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.
18. 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.
19. 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

STAAR Surgical Company Study #CP22-01: Post-Market Evaluation of the EVO ICL	
	from the anterior corneal surface, the thickness of the cornea must be subtracted to get the true ACD.
Device description:	The EVO/EVO+ lenses approved under PMA P030016/S035 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 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: VICMO 12.1, VICMO 12.6, VICMO 13.2, VICMO 13.7, VICM5 12.1, VICM5 12.6, VICM5 13.2, VICM5 13.7 • EVO/EVO+ Visian Toric Implantable Collamer Lens for Myopia with Astigmatism: VTICMO 12.1, VTICMO 12.6, VTICMO 13.2, VTICMO 13.7, VTICM5 12.1, VTICM5 12.6, VTICM5 13.2, VTICM5 13.7 All lenses are available in -3.00 D to -16.00 D SE dioptric powers. The EVO/EVO+ Visian Toric ICLs are also available in cylinder dioptric power of 1.00 D to 4.00 D.
Indications for Use:	***(EVO/EVO+ Sphere Lenses)*** The EVO ICL lens is indicated for use in patients 21-45 years of age: 1. for the correction of myopia with spherical equivalent ranging from -3.0 D to ≤ -15.0 D with less than or equal to 2.5 D of astigmatism at the spectacle plane; 2. for the reduction of myopia with spherical equivalent ranging from greater than -15.0 D to -20.0 D with less than or equal to 2.5 D of astigmatism at 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 EVO ICL lens is intended for placement in the posterior chamber

STAAR Surgical Company Study #CP22-01: Post-Market Evaluation of the EVO ICL	
	(ciliary sulcus) of the phakic eye. ***(EVO/EVO+ Toric Lenses)*** The EVO TICL 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 EVO TICL lens is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.
Study endpoints:	**Primary:** The proportion of primary (i.e., first implanted) eyes that have IOP ≥ 30 mmHg and IOP ≥ 40 mmHg at 1 – 6 hours postoperatively. **Secondary:** The proportion of fellow eyes that have IOP ≥ 30 mmHg and IOP ≥ 40 mmHg at 1 – 6 hours postoperatively.
Statistical methods:	Analysis of the superiority of the proportion of primary eyes that have IOP ≥ 30 mmHg and IOP ≥ 40 mmHg at 1 – 6 hours postoperatively compared with the outcomes of Premarket Approval Application (PMA) Study CP19-01, i.e., 15.3% (50/327) primary eyes with IOP ≥ 30 mmHg, and 7.0% (23/327) primary eyes with IOP ≥ 40 mmHg. Analysis of fellow eye rates will be used to support the findings of the two primary eye analyses. Summaries for continuous variables will include the sample size, mean, standard deviation, median, minimum, and maximum. Summaries for discrete variables will include the tabulation of frequencies and percentages.

1.0 INTRODUCTION

The EVO Visian Implantable Collamer Lenses (ICLs) were approved by the US Food and Drug Administration (FDA) in March 2022[1] for the following indications:

(EVO/EVO+ Sphere Lenses)

The EVO ICL lens is indicated for use in patients 21-45 years of age:

1. for the correction of myopia with spherical equivalent ranging from -3.0 D to ≤ -15.0 D with less than or equal to 2.5 D of astigmatism at the spectacle plane;
2. for the reduction of myopia with spherical equivalent ranging from greater than -15.0 D to -20.0 D with less than or equal to 2.5 D of astigmatism at 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 EVO ICL lens is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

(EVO/EVO+ Toric Lenses)

The EVO TICL 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 EVO TICL lens is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

All surgeons are required to be certified by STAAR Surgical Company (STAAR) prior to being granted access to order STAAR ICLs for their patients. The EVO Physician Certification Program has been revised to align with the device labeling approved by the FDA.[2] STAAR is conducting a Post-Approval Study (PAS) designed to evaluate the

effectiveness of the EVO certification training program in reducing the risks of early postoperative Intraocular Pressure (IOP) increases due to incomplete removal of 2% hydroxypropylmethylcellulose (HPMC) ophthalmic viscoelastic device (OVD).

2.0 OBJECTIVE

The objective of this PAS is to assess the rate of early IOP increases following implantation of EVO ICL lenses.

3.0 STUDY DESIGN

3.1 Description of Study Design

This prospective, multi-center, single arm PAS will enroll subjects who are eligible for EVO ICL surgery at up to 10 clinical sites in the US. A minimum of 200 subjects (i.e., 200 primary eyes and 200 fellow eyes) will be enrolled in the study. All subjects are intended to undergo bilateral implantation with the second-eye surgery occurring from 1 – 14 days (1≤14 days) following the day of first eye surgery.

Enrolled subjects will have EVO ICL surgery performed by an Investigator surgeon who has been trained and certified under the STAAR EVO Certification Program. A total of four postoperative visits will be conducted after surgery for each eye (OP Visit); at 1– 6 hours after surgery (Day 0), at 1 day after surgery (Day 1), at approximately 1 week (Week 1, days 5 – 9) and at approximately 2 weeks after surgery (Week 2, Days 10 – 18).

3.2 Selection of Study Population

Subjects will be selected from each clinical site's patient population. Patients meeting all of the eligibility criteria will be considered suitable study subjects and will be offered consecutive enrollment into this study.

3.2.1 Eligibility

3.2.1.1 Inclusion Criteria

1. Subjects must be between the ages of 21 and 45 at the time of surgery.
2. For 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 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. ACD 3.00 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline lens.
5. Meet minimum endothelial cell density (ECD) requirements for age and ACD (refer to **Table 1: Minimum Endothelial Cell Density for Age and True ACD***).
6. Correctable distance visual acuity (CDVA) of at least 20/40 in the eye(s) to be treated; and absence of ocular pathology (except that myopic degeneration is allowed).
7. Difference between cycloplegic refraction spherical equivalent (CRSE) and manifest refraction spherical equivalent (MRSE) of <0.75 D.
8. Subjects must be able and willing to return for scheduled follow-up examinations after surgery.
9. 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.

3.2.1.2 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 **Table 1: Minimum ECD for Age and True ACD**.
5. Unstable or worsening nearsightedness.
6. Ocular hypertension or glaucoma.
7. Pseudoexfoliation.
8. Pigment dispersion.
9. History or clinical signs of iritis/uveitis.
10. Insulin-dependent diabetes or diabetic retinopathy.

11. History of previous ocular surgery.
12. 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.
13. 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.).
14. Monocular subjects
15. 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).
16. 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.
17. 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.
18. 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.
19. 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.

Table 1: Minimum Endothelial Cell Density for Age and True ACD*

Age	Minimum ECD ACD ≥ 3.0mm	Minimum ECD ACD ≥ 3.2mm	Minimum ECD ACD ≥ 3.5mm
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

Age	Minimum ECD ACD ≥ 3.0mm	Minimum ECD ACD ≥ 3.2mm	Minimum ECD ACD ≥ 3.5mm
>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 the study lenses have been implanted bilaterally and the Sponsor receives completed case report form (CRF) documentation for all visits. Subjects who require further follow-up for an adverse event (AE) will be followed according to **Section 6.3.4**.

A Study Exit CRF for each eye must be completed for all subjects who complete the study.

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(es)
- explantation of the study lenses

If the study lens is explanted, a minimum of one post-explant visit should be completed to record safety measures for the subject (e.g., CDVA, IOP, etc.).

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 6.3.4**. Subject withdrawals will be documented clearly on the source document and applicable CRF.

Only subjects who do not receive successful bilateral implantation 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 last 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 10 clinical site(s) located in the US.

The study will be conducted by Investigator surgeons who have been trained and certified under the STAAR EVO Certification Program and who have been determined 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)/ Delegation of Authority Log (DOA).

Each Investigator will enroll approximately 20 subjects (40 eyes) and no individual site may enroll 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 28 months following study initiation (see **Table 1**). Eligible subjects who are enrolled in the study will be seen for 4 scheduled study visits (per eye) over the course of approximately 2 weeks after surgery.

Table 1: Enrollment Milestones

Milestone	Date
First Subject Enrolled	Within 6 months of FDA approval of PAS protocol
20% of Subjects Enrolled (40 subjects)	Within 12 months of FDA approval of PAS protocol
50% of Subjects Enrolled (100 subjects)	Within 18 months of FDA approval of PAS protocol

Milestone	Date
100% of Subjects Enrolled (200 subjects)	Within 24 months of FDA approval of PAS protocol

In addition, STAAR will provide interim study reports every 6 months from FDA approval of the PAS supplement, then every 6 months thereafter until subject enrollment has been completed, and then annually thereafter until completion of the post-approval study according to the schedule provided in **Table 2**.

Table 2: Reporting Schedule Plan

Milestone	Date
FDA Approval of Study Protocol	TBD
6 Month Status Report	6 months after FDA approval of PAS protocol
12 Month Status Report	12 months after FDA approval of PAS protocol
18 Month Status Report	18 months after FDA approval of PAS protocol
24 Month Status Report	24 months after FDA approval of PAS Protocol
Final Report	Within 3 months of database lock following last subject exit from study.

4.0 STUDY MATERIALS

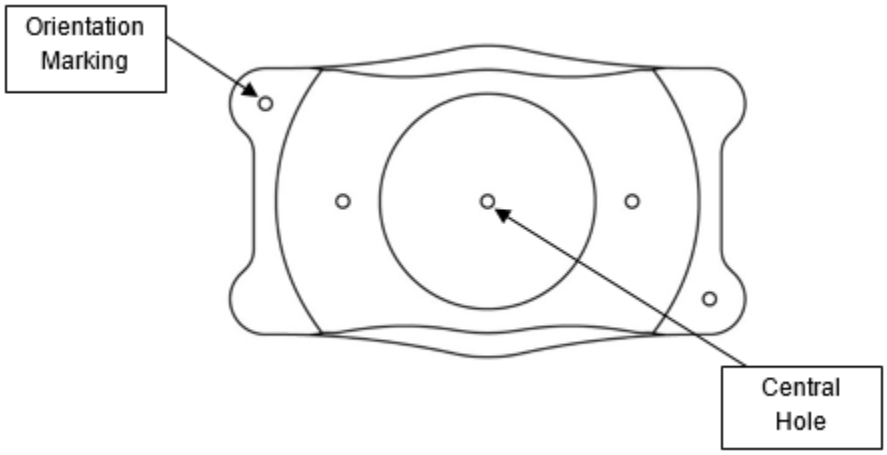
4.1 Description of Investigational Device

The EVO/EVO+ Visian Implantable Collamer Lens for Myopia (**Figure 1**), and EVO/EVO+ Visian Toric Implantable Collamer Lens for Myopia with Astigmatism (**Figure 2**) study lenses (EVO lenses), are sterile intraocular implants manufactured from Collamer, a proprietary hydroxyethyl methacrylate (HEMA)/porcine- collagen biocompatible polymer material. These lenses contain an Ultraviolet (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 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 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.

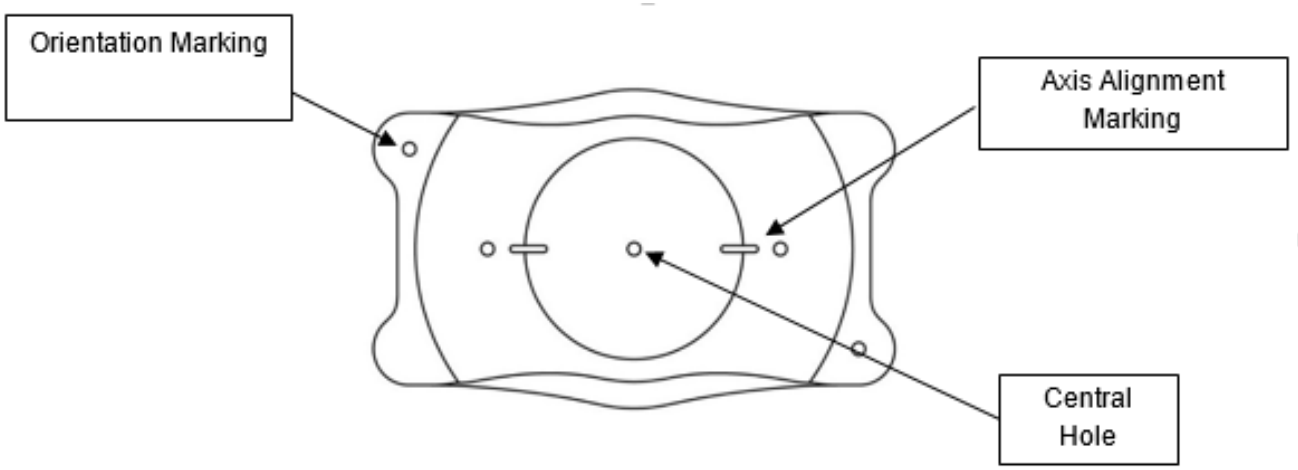
The EVO lenses are intended to be placed entirely within the posterior chamber (ciliary sulcus) directly behind the iris and in front of the anterior capsule of the human crystalline lens. When correctly positioned, the lenses function as a refractive element to optically reduce moderate to high myopia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

Figure 1: EVO/EVO+ Lens Models for Myopia



The EVO 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 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 FDA-approved EVO Models are included in this study:

- EVO/EVO+ Visian ICL for Myopia:

  VICMO 12.1, VICMO 12.6, VICMO 13.2, VICMO 13.7, VICM5 12.1, VICM5 12.6, VICM5 13.2, VICM5 13.7

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

  VTICMO 12.1, VTICMO 12.6, VTICMO 13.2, VTICMO 13.7, VTICM5 12.1, VTICM5 12.6, VTICM5 13.2, VTICM5 13.7

4.2 Study Lens Supply

The lens power and size calculation will be performed by the surgeon using the STAAR EVO ICL Online Calculation and Ordering Software. (www.ocos.STAAR.com). Alternatively, the power and size of the lens may be determined utilizing the surgeon's standard of care method for ICL surgery. 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.

All EVO ICL lenses will be shipped to the site from STAAR Surgical. Lenses will be provided in commercial packaging, as approved by FDA in March 2022[1] and must be stored as specified on the package labeling.

4.2.1 Instructions for Use and Administration

Refer to current approved EVO ICL Directions for Use (DFU) for surgical instructions.[2]

Study surgeons will use 2% HPMC OVD for EVO ICL surgery as recommended in the DFU.[2]

The Investigator will be responsible for keeping current and accurate records of all study lenses received, dispensed, and returned to the Sponsor.

5.0 STUDY CONDUCT

5.1 Study Visits

All Subjects who meet the eligibility criteria will be seen according to the following schedule.

Table 3: Study Visit Schedule

Visit (per eye)	Time
Preoperative Visit	Days - 180 to 0
Operative Visit	Day 0
Postoperative Visit 1	1 to 6 hours postoperatively
Postoperative Visit 2	Day 1 postoperatively
Postoperative Visit 3	Day 5 - 9 postoperatively
Postoperative Visit 4	Day 10 - 18 postoperatively

Refer to Appendix A for a schedule of visits and parameters and **Appendix B** for methods of clinical evaluation.

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 also be provided with a copy of the FDA approved Patient Information Booklet (PIB) for the EVO ICL.[3] 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 -180 to Day -1

Prospective subjects who have provided informed consent will be screened to determine eligibility for treatment in the study. All preoperative testing for the study must be completed within 180 days prior to the first surgery. Data from routine (non-study specific) preoperative ophthalmic assessments for ICL surgery performed prior to the

informed consent process may be included. In such cases, the date of the test will be documented in the subjects' source document. 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 180 days prior to surgery.

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 and changes in concomitant medications or AEs will be recorded. Subjects who no longer meet eligibility criteria, or if they qualify but decide not to participate further in the study, or if they decide not to proceed with surgery, will be considered screen failures and exited from the study.

If the subject is eligible, he/she will be enrolled in the study and undergo surgery in accordance with the surgical procedure described in the current DFU for the EVO ICL.[2] If the study lens in not implanted due to a surgical complication, the subject will be discontinued from the study. For subjects who qualify to participate bilaterally, fellow eye implantation should occur from 1 – 14 days after uneventful surgery in the first eye. Any complications, AEs, or associated treatment given will be appropriately documented and reported in the CRFs.

5.1.3 Postoperative Visits

Each treated eye will be seen for 4 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.

5.1.3.1 Postoperative Visit 1 – Operative Day (1 – 6 hours after surgery)

At approximately 1 – 6 hours after surgery, an IOP reading and slit lamp examination in the implanted eye(s) will be conducted. Any complications, AEs, or associated treatment given will be appropriately documented and reported in the CRFs.

5.1.4 Postoperative Visits Day 1 – 18

An IOP reading will be performed at these visits in addition to other standard postoperative assessments as part of the normal postoperative standard of care. Any AEs of increased IOP compared to baseline will be documented. Evaluation of the anterior chamber angle is to be performed by gonioscopy or AS-OCT in cases where gonioscopy is contraindicated as presented in Appendix B. Associated treatments will be appropriately documented and reported in the CRFs.

5.1.5 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 CRFs, as appropriate. Visits intended to fulfill scheduled visit requirements that fall outside the designated scheduled visit range, are not Unscheduled Visits. In these cases, the visit data will be collected and transcribed to the appropriate scheduled visit CRF.

5.1.6 Missed Visits

If a subject misses any scheduled follow-up visit and cannot be seen prior to the start of the visit range for the next scheduled follow-up visit, 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.

5.2.2 Post-study Follow-up

If a subject requires further follow-up of an Adverse Event/Serious Adverse Event (SAE) 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

The following medication regimen will be followed by all sites:

- topical 4th generation fluoroquinolone four times a day (QID) starting 3 days prior to surgery for a total of 10 days,
- topical non-steroidal anti-inflammatory drugs (NSAIDs) QID, twice a day (BID) or once a day (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,

- topical steroid QID starting 3 days prior to surgery for a total of 10 days and then tapered weekly.

Note: No prophylactic systemic or topical IOP lowering medications (e.g., acetazolamide) will be used. Ocular hypotensive agents may not be used for prophylaxis of increased IOP because doing so will confound the results of the study.

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 and "other" non-medication therapy 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 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 and all serious AEs (both ocular and non-ocular) and all interventions to treat these AEs (i.e., concomitant medications, release of aqueous from a pre-existing corneal incision or needle paracentesis, etc.) will be documented on source documents and reported to the Sponsor/designee in the CRFs. 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** 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, see **Section 6.1.2**).

AEs Associated with IOLs

Adverse events associated with implantation of all types of Intraocular Lenses (IOLs) (i.e., aphakic and phakic), need to be reported as AEs on the AE CRF. These can include, but are not limited to the following:

- Complications during phakic IOL surgery
- Worsening of a pre-existing ocular condition during the study
- Chronic Anterior Uveitis: anterior chamber (AC) cells or flare of greater than grade 2 (using the Standardization of Uveitis Nomenclature, SUN criteria[4]) at postoperative Visit 3 (Day 5 – 9) or later
- 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 5-9) or later.
- Clinically significant corneal edema: corneal swelling (stromal or epithelial) at postoperative Visit 3 (Day 5 – 9) or later
- 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 Secondary Surgical Interventions (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 AEs 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 SUN criteria[3]) 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. Any increased IOP ≥ 10 mmHg above baseline to a minimum of 25 mmHg or any increase in IOP that is treated in any way, should be reported as an AE regardless of whether it is observed before or after 1 week postoperatively.
- 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 cataracts,
- narrowing of the anterior chamber angle,
- increased IOP,

- pupillary block,
- glaucoma,
- lens malposition,
- corneal endothelial cell loss (which may result in corneal edema),
- 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

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.

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** 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

All AEs, regardless of severity (Mild, Moderate or Severe) or causality (Not Related, Related, Unknown), will be reported to FDA.

6.3 Reporting

All untoward events (aside from the exceptions noted for the early postoperative period in **Section 6.1.1**) that occur during the study need to be reported as AEs.

All interventions used to treat AEs (i.e., concomitant medications, aqueous release from a pre-existing corneal incision or needle paracentesis to treat increased IOP) will be recorded in the subject's source document and applicable CRFs.

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 **non-serious AEs** determined to be related to the study device (ADE)
- all device malfunctions that do not result in one of the above reportable events
- all secondary surgical interventions (removal, replacement or repositioning) involving the study lens

In addition, the following events are to be reported to the Sponsor as SAEs in this study:

- endophthalmitis
- pupillary block
- retinal detachment
- stromal thinning/corneal melting
- ≥2 lines CDVA loss not secondary to any underlying condition

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.

Note: All device-related ADEs (SAEs or AEs related to the EVO ICL) must also be reported by the clinical site to STAAR Complaint Handling department according to STAAR Standard Operating Procedures (SOPs) for Complaint Handling.

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 Ancillary Marketed STAAR Surgical Products

All information collected on a CRF could potentially be identified as a product complaint, as defined in **Sections 6.1.2** and **6.3.1**. 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 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

Analysis of the superiority of the proportion of primary eyes that have IOP ≥ 30 mmHg and IOP ≥ 40 mmHg at 1 – 6 hours postoperatively compared with the outcomes of Study CP19-01, i.e., 15.3% (50/327) primary eyes with IOP ≥ 30 mmHg, and 7.0% (23/327) primary eyes with IOP ≥ 40 mmHg (**Table 3**, below). Analysis of fellow eye rates will be used to support the findings of the two primary eye analyses.

Any deviations from the analysis plan will be documented in the final report.

Table 3: Maximum IOP Among Incidences of Elevated IOP with Onset at Postoperative Visit 0 (Safety Population)

Adverse Event - Elevated IOP	**Primary Eyes (N=327)**	**All Treated Eyes (N=629)**
Number of elevated IOP events (n)	67	125
Maximum IOP (mmHg)	n (%)	n (%)
< 30	17 (5.2)	40 (6.4)
≥ 30	50 (15.3)	85 (13.5)
≥ 40	23 (7.0)	38 (6.0)
≥ 50	13 (4.0)	24 (3.8)
≥ 60	6 (1.8)	11 (1.7)
≥ 70	0 (0.0)	1 (0.2)

Source: Table 13, EVO/EVO+ DFU[2]
Percentage calculated as (n/N)*100.

7.1 Hypothesis

The observed rates of increased IOP seen in the absence of planned training in primary eyes in PMA Study CP19-01 were 15.3% (50/327) for IOP ≥ 30 mmHg and 7.0% (23/327) for IOP ≥ 40 mmHg. Based on Study CP19-01 data from investigators who followed the instructions in the proposed EVO Physician Certification Program regarding removal of OVD (Table 6), it is assumed that the proportion of primary eyes that will reach or exceed an IOP of 30 mmHg is 6% and the proportion of primary eyes that will reach or exceed an IOP of 40 mmHg is 1%.

Table 4: Incidence of elevated IOP in primary eyes for investigators who followed proposed EVO Physician Certification Program instructions for removal of OVD.[5]

Site #	Reported Irrigation Volume	Primary Eyes with elevated IOP in specified range (n)		Primary Eyes implanted	All Eyes with elevated IOP in specified range (n)		All Implanted Eyes
	cc	>/= 30	>/= 40	N	>/= 30	>/= 40	N
09	10-20 cc	5	0	39	9	0	74
13	20-30 cc	3	0	19	7	0	37
07	10-20 cc	1	0	10	1	0	20
02	> 30 cc	1	0	11	2	0	20
10	10-20 cc	0	0	29	0	0	36
11	20-30 cc	1	0	76	1	0	148
04	> 30 cc	0	0	12	0	0	22
06	10-20 cc	0	0	8	0	0	12
03	10-20 cc	4	0	31	11	0	60
05	20-30 cc	0	0	5	0	0	9
	Total	15	0	240	31	0	438
Proportion, n/N		**6.25%**	**0.00%**		**7.08%**	**0.00%**	

7.2 Study Endpoints and Statistical Analysis

Primary endpoints of this study are:

- the proportion of primary eyes that have IOP ≥ 30 mmHg at 1 – 6 hours postoperatively
- the proportion of primary eyes that have IOP ≥ 40 mmHg at 1 – 6 hours postoperatively

Secondary endpoints of this study are:

- the proportion of fellow eyes that have IOP ≥ 30 mmHg at 1 – 6 hours postoperatively
- the proportion of fellow eyes that have IOP ≥ 40 mmHg at 1 – 6 hours postoperatively

The following other endpoints of this study will be analyzed for the entire postoperative follow-up period (including the 1 – 6 hr postop Visit through Visit 4, postop Day 10 – 18):

- Rates of increased IOP in primary and all (primary + fellow) eyes attributed to retained OVD
- Rates of increased IOP in primary and all eyes attributed to other causes (e.g., pupillary block, steroid response, etc.)
- Rates of all categories of AEs (in primary and in all eyes)

The following will also be assessed in this study through postoperative Visit 4 using descriptive statistics:

- Device deficiencies,
- Distribution of lens vault measured by OCT,
- Slit lamp findings and distributions of gradings (e.g., anterior chamber cell and flare)
- Notable ophthalmoscopy findings;
- UDVA and CDVA
- Instances of loss of ≥10 letters of CDVA from baseline, along with analyses of the causes.

Statistical Analysis

Summaries for continuous variables will include the number of non-missing values, mean, standard deviation, median, minimum, and maximum. Summaries for discrete variables will include the tabulation of frequencies and percentages. Analyses of increases in IOP attributed to other causes will include distribution of maximum IOP measured and summaries of causes and treatments used. A presentation of all relevant clinical observations and symptoms, severity, diagnoses, treatments, duration, resolution, and sequelae will be provided for all significant AEs. In addition, classification of whether each event was a "serious adverse event" or "device or procedure-related" will be provided. Rates and descriptions of all device deficiencies and SAEs observed during the course of the study will be provided.

7.3 Sample Size

For a single sample exact binomial test with a two-tailed alpha of 0.05 to demonstrate that a hypothesized rate of 6% is significantly lower than 15.3% for IOP spikes ≥ 30 mmHg with 98% power, a sample of 181 eyes would be required. Demonstrating that the rate of IOP spikes ≥ 40 mmHg is significantly lower, given a hypothesized rate of 1% vs the Study CP19-01 rate of 7%, a sample size of 181 primary eyes of 181 subjects will achieve 96% power. Power to achieve both endpoints can be conservatively estimated by

the product of the two powers, .98 times .96, or 94%. Analysis of fellow eye rates will also be conducted, and results will be used to support the findings of the two primary eye analyses. We assume no more than 10% loss to follow up in this 2-week study, so plan to enroll a minimum of 200 subjects (i.e., 200 primary eyes and 200 fellow eyes).

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 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, 21 CFR Parts 11, 50, 54, 56, 803, 814.82(a)(2), 820; 42 USC 282(j), FDA GCPs, IRB requirements, and applicable local regulations
- 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., OCT 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. 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/designee 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/date of birth. 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 Principal Investigator (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 delegation of authority 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 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 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 has 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 reconsenting 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.

9.0 REFERENCES

1. https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P030016S035

2. Directions for Use, EVO Visian® ICL (Implantable Collamer® Lens). https://edfu.staar.com/edfu/

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4. Jabs DA, Nussenblatt RB, Rosenbaum JT. Standardization of uveitis nomenclature for reporting clinical data. Results of the First International Workshop. Am J *Ophthalmol.* 2005 Sep;140(3):509-16.

5. P030016_S035 Interactive Review 2-16-2022 Quest response, Attachment K - STAAR Surgical P030016 PAS#2 Protocol Synopsis 2-17-2022.

6. Isotani H, Fukumoto Y, Kitaoka H, et al. Oval pupil in patients with diabetes mellitus: examination by measurement of the dark-adapted pupillary area and pupillary light reflex. *Diabetes Res Clin Pract.* 1995; 29:43-48.

APPENDIX A: SCHEDULE OF VISITS AND PARAMETERS

All study tasks should be performed by qualified study site personnel as indicated on the delegation of authority log under the supervision of the Principal Investigator.

Table A1: Schedule of Visits and Parameters

PROCEDURE/ASSESSMENTS	**Preop**[1] Day -180 to -1	**Op** Day 0	**V1** 1-6 hrs. postop	**V2** Day 1	**V3** Day 5 - 9	**V4** Day 10 - 18
Informed Consent/HIPAA Authorization	X					
Demographics/ Ocular Hx	X					
Eligibility	X	X				
Surgical Procedure		X				
Pupil Diameter	X					
UDVA	X			X	X	X
CDVA	X				X	X
Manifest Refraction	X				X	X
Keratometry	X					
Gonioscopy[2]	X					X
Specular Microscopy (corneal endothelial cell count-CECC)	X					
Biometry[3]	X					
Slit Lamp Exam	X		X	X	X	X
IOP[2, 4]	X		X	X	X	X
Cycloplegic refraction	X					
Lens Vault (via OCT)			X	X	X	X
Dilated Fundus Exam	X					
[5]Adverse Events	X	X	X	X	X	X
Concomitant Medications	X	X	X	X	X	X

PROCEDURE/ASSESSMENTS	**Preop**[1] Day -180 to -1	**Op** Day 0	**V1** 1-6 hrs. postop	**V2** Day 1	**V3** Day 5 - 9	**V4** Day 10 - 18
Exit Subject						X

[1] Subjects must provide informed consent to participate in the study prior to undergoing any study specific procedures

[2] Gonioscopy will also be performed when an AE of increased IOP occurs. If gonioscopy is contraindicated, the reason will be documented and AS-OCT will be performed. Refer to Appendix B.

[3]Includes: axial length (AL), corneal thickness (CT), pupil size, anterior chamber depth (ACD), white-to-white (WTW) distance

[4]Goldmann applanation tonometry will be used at all study visits. Refer to Appendix B for instructions if Goldmann applanation is contraindicated at 1 – 6 hr or 1 day postop assessment.

[5]AEs will be collected from the time the subject signs the ICF to study exit.

NOTE: If an oval or irregularly shaped pupil (dyscoria) is observed at any postoperative visit, photographs should be taken at that visit and each subsequent visit to determine if the ovalization is progressive. Refer to **Appendix B.**

APPENDIX B: METHODS OF CLINICAL EVALUATION

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

The methods described in this section are to be used for the applicable assessments. All other assessments for this study will be conducted using the Investigator's standard of care methods for ICL surgery.

1. Gonioscopy

Gonioscopy will be used to assess the anterior chamber angle, pigmentation in the posterior trabecular meshwork and peripheral anterior synechiae. Gonioscopy will be performed at the Preoperative Visit and the Day 10 – 18 postoperative visit. Gonioscopy will also be performed when an AE of increased IOP occurs, unless contraindicated by the condition of the eye. If gonioscopy is not performed, the reason that gonioscopy is contraindicated will be recorded and the angle will be assessed by AS-OCT.

If AS-OCT is performed, the images obtained should provide a clear view of the anterior chamber angle. Copies of images should be preserved with the subject's source documents.

a) Anterior Chamber Angle

Gonioscopic examination of the anterior chamber angle will be utilized to determine the grade of the angle. If gonioscopy is not performed, the reason that gonioscopy is contraindicated will be recorded and the angle will be assessed by AS-OCT. 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°

a) 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.

b) **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).

2. 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
Crystalline Lens Status	Clear/Abnormal

3. IOP

Goldmann applanation tonometry will be used to measure IOP at all postoperative timepoints.* On surgery day, IOP will be measured approximately 1-6 hours postoperatively.

* If the Investigator determines Goldmann tonometry is contraindicated at the 1 – 6 hour or 1 day postoperative IOP assessment, the reason and an alternative method must be specified in the CRF.

4. 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.

5. Assessment of Pupil Ovalization

If an oval or irregularly shaped pupil (dyscoria) is observed at any postoperative visit, photographs[6] 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.