TITLE PAGE

Post-Approval Study of the Visian Toric Implantable Collamer Lens

PROTOCOL

STUDY #CP18-02

SPONSOR:

STAAR Surgical Company

1911 Walker Avenue

Monrovia, California 91016

Telephone USA: 626-303-7902

This clinical investigation is being conducted in accordance with 21CFR 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.

Revision Chronology:

Revision #1	-	2018.Dec.19
Revision #2		2019.June.10

SPONSOR APPROVAL PAGE

Post-Approval Study of the Visian Toric Implantable Collamer Lens

PROTOCOL

STUDY #CP18-02

[redacted]

Approved By:

[redacted] 2019/07/22

Vice President, Global Clinical and Medical Affairs Date

[redacted] 2019-07-22

Global Head Regulatory Affairs and Quality Assurance Date

[redacted] 2019-07-22

Vice President Global Quality Date

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

INVESTIGATOR STATEMENT OF APPROVAL

Post-Approval Study of the Visian Toric Implantable Collamer Lens

PROTOCOL

STUDY #CP18-02

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, 21CFR 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/EC 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 IRB, 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
ADE	Adverse Device Effect
AE	Adverse Event
AREDS	Age-Related Eye Disease Study
BSS	Balanced Salt Solution
CDVA	Corrected Distance Visual Acuity
CECC	Corneal Endothelial Cell Count
CFR	Code of Federal Regulations
CRF	Case Report Form
D	Diopters
DFU	Directions For Use
DIA	Device Investigator Agreement
DOA	Delegation of Authority
EC	Ethics Committee
ECD	Endothelial Cell Density
eQMS	Electronic Quality Management System
ETDRS	Early Treatment of Diabetic Retinopathy Study
FDA	United States Food and Drug Administration
FTP	Foam Tip Plunger
GCPs	Good Clinical Practices
HEMA	Hydroxyethyl Methacrylate
HIPAA	Health Insurance Portability and Accountability Act
ICF	Informed Consent Form
ICH	International Conference on Harmonisation
ICL	Implantable Collamer Lens
IOL	Intraocular Lens
IOP	Intraocular Pressure
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent to Treat
LogMAR	Logarithm of Minimal Angle of Resolution
PAS	Post-approval Study
PI	Principal Investigator
PP	Per Protocol
SAE	Serious Adverse Event
SE	Spherical Equivalent
SOP	Standard Operating Procedure
TICL	Visan Toric Implantable Collamer Lens for Myopia

Abbreviation /Acronym	Term
UCVA	Uncorrected Visual Acuity
US	United States
UV	Ultraviolet
VA	Visual Acuity
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 #CP18-02	
Revision chronology:	Rev #2, 2019.June.10
Title:	Post-Approval Study of the Visian Toric Implantable Collamer Lens
Type of study:	Post-approval study (PAS)
Number of study centers and subjects:	The study will enroll and implant at least 124 eligible subjects (up to 248 eyes, with 124 being primary) at 6-8 clinical sites in the US, to ensure that at least 100 subjects (assuming an overall attrition of 10% per year) will be available for evaluation at 24 months after implantation.
Objective(s):	The objective of this PAS is to evaluate the long term (i.e. 24 months) clinical performance of the Visian® Toric Implantable Collamer® Lens (ICL) for Myopia (TICL) with respect to rotational stability, refractive and visual outcomes, and ocular adverse event (AE) rates.
Study design	This is a prospective, multicenter, open-label, single arm, post approval study. Up to 124 subjects who meet all eligibility criteria will be offered consecutive enrollment in the study. It is intended that each enrolled subject will undergo bilateral implantation with the TICL. If only one eye of a given subject meets all of the inclusion and exclusion criteria, or the subject desires surgery in only one eye and that eye meets all of the inclusion and exclusion criteria, then that eye will be the primary eye. If both eyes of a given subject meet all of the inclusion and exclusion criteria, and the subject desires surgery in both eyes, then the eye with the greater magnitude of manifest refraction cylinder will be designated as the primary eye. If both eyes of a given subject meet all of the inclusion and exclusion criteria and the refractive cylinder of the eyes are equal, then the right eye will be designated as the primary eye. A minimum of 14 subjects requiring a Toric ICL cylinder power of 3.5 or 4.0 diopters will be enrolled. Postoperatively, subjects will return for visits at regularly scheduled intervals through 24 months after surgery (see App A).
Subject Population	Investigators will all have prior clinical experience with the STAAR Surgical Implantable Collamer Lens. Subjects will be selected from each clinical site's patient population. Patients meeting all of the following criteria will be considered suitable study subjects. All subjects enrolled in this clinical study will meet the requirements under the indications for use outlined in the package insert directions for use (DFU) for the FDA approved lenses and additional eligibility criteria. (refer below)

	Inclusion Criteria (each eye to be implanted) 1. Subjects 21 through 45 years old at time of surgery. 2. Moderate to high myopia with spherical equivalent ranging from -3.0 D to ≤ -15.0 D (in the spectacle plane) and cylinder in the range of 1.0 D to 4.0 D (in the spectacle plane). 3. Stable refractive history within 0.5 D for both spherical equivalent and cylinder for 1 year prior to implantation. 4. Anterior chamber depth (ACD) 3.0 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 Endothelial Cell Density for Age and True ACD*" table below). 6. Correctable (CDVA) to at least 20/40 in the eye to be treated; and absent of ocular pathology (except that myopic degeneration is allowed). 7. Subjects must be able to achieve a minimum dilated pupil size of 7 mm (via use of mydriatic and/or cycloplegic eye drops) in each eye to be treated. 8. Able to read, understand and provide written informed consent on the Institutional Review Board (IRB) approved Informed Consent Form (ICF). 9. Able and willing to return for scheduled follow-up examinations after surgery. **Exclusion Criteria (each eye to be implanted)** 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 Endothelial Cell Density for Age and True ACD*" table below. 5. Unstable or worsening nearsightedness. 6. History or clinical signs of iritis/uveitis. 7. Diabetic retinopathy. 8. Glaucoma. 9. History of previous eye surgery. 10. Serious (i.e., life threatening), 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.

	11. Progressive sight threatening disease or other previous or current ocular conditions, other than myopia, that may predispose for future complication. 12. Diagnosis of ocular hypertension (high eye pressure). 13. Insulin-dependent diabetes. 14. Pseudoexfoliation. 15. Pigment dispersion. 16. Spherical equivalent less than -3.0 D or greater than -15.0 D (in the spectacle plane) of nearsightedness; cylinder (spectacle plane) less than 1.0 D and greater than 4.0 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 within 30 days of beginning this study. **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 >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 11 study visits over the course of approximately 27 months.

Study parameters	**The study will evaluate:** • Rotational stability as determined through objective methods • Refractive and visual outcomes • Safety **Primary effectiveness endpoint:** • Rotation of less than or equal to five degrees between 18 and 24 months postoperative. **Primary effectiveness endpoint success criteria:** • At least 90% of the treated eyes rotate less than or equal to five degrees between 18 and 24 months postoperative (i.e., ≤10% of eyes exhibit >5° rotation). **Secondary effectiveness endpoints include:** • Absolute rotation between visits. • Absolute rotation <5 degrees, <10 degrees, <20 degrees, and <30 degrees from the intended orientation at each visit. • Absolute rotation from the intended orientation at each visit. • Postoperative manifest refraction spherical equivalent and cylinder at each visit. **Safety Endpoint:** • Ocular AE rates assessed in implanted eyes. There are no prespecified performance targets for the secondary endpoints or the safety endpoint.
Statistical methods	Based on clinical experience with stabilization of lens rotation over time, we assume that between 18 and 24 months no more than 2% of eyes will exhibit rotation >5°. Our null and alternate hypotheses are as follows: H_0 (null hypothesis): >10% of eyes with >5° rotation H_a (alternative hypothesis): ≤10% of eyes with >5° rotation [redacted] Rates of rotation of the TICL of <10, <20 and <30 degrees from the intended orientation will be reported. To allow for 10% attrition annually, a total of 124 subjects (up to 248 eyes, with 124 being primary) will be enrolled for assessment of the primary and secondary effectiveness/safety endpoints. [redacted]

	A sample of 100 eyes provides 94.9% power to reject the null hypothesis that >10% of eyes will exhibit >5° rotation. The two-sided 95.0% upper confidence limit of the proportion of eyes with >5° absolute rotation is ≤ 0.1. The null hypothesis will be rejected if the two-sided 95.0% upper confidence limit of the proportion of eyes with >5° absolute rotation between 18 and 24 months is ≤0.1. To allow for losses of 10% per year, a total of up to 124 primary eyes of 124 subjects will be enrolled.

1.0 INTRODUCTION

The STAAR Visian® Toric Implantable Collamer® Lens (ICL) for Myopia (TICL) received FDA approval on September 13, 2018. The STAAR 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 diopters (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 Visian TICL is intended for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

As a condition of FDA approval, STAAR is conducting a new enrollment post-approval study (PAS) in order to provide continued reasonable assurance of the safety and effectiveness of the TICL.

2.0 OBJECTIVE

The objective of this PAS is to evaluate the long term (i.e., 24 months) clinical performance of the TICL with respect to rotational stability, refractive and visual outcomes, and ocular adverse event (AE) rates.

3.0 STUDY DESIGN

3.1 Description of Study Design

This is a prospective, multicenter, open-label, single arm, post-approval study. A total of 124 subjects (up to 248 eyes, with 124 being primary) who meet all eligibility criteria will be enrolled at 6-8 clinical sites in the United States (US).

It is intended that each enrolled subject will undergo bilateral implantation with the TICL. If only one eye of a given subject meets all of the inclusion and exclusion criteria, or the subject desires surgery in only one eye and that eye meets all of the inclusion and exclusion criteria, then that eye will be the primary eye. If both eyes of a given subject meet all of the inclusion and exclusion criteria, and the subject desires surgery in both eyes, then the eye with the greater magnitude of manifest refraction cylinder will be designated as the primary eye. If both eyes of a given subject meet all of the inclusion and exclusion criteria and the refractive cylinder of the eyes are equal, then the right eye will be designated as the primary eye.

A minimum of 14 subjects requiring a Toric ICL cylinder power of 3.5 or 4.0 D will be enrolled.

Study subjects will be followed at Day 0, Day 1, Week 1, Month 1, 3, 6, 12, 18, and 24 postoperatively (Refer to Appendix A).

STAAR will submit periodic study reports to FDA every six (6) months during the first two (2) years of the study and annually thereafter, unless otherwise specified by FDA. The first report will be submitted 6 months after the initial approval of this study protocol.

3.2 Selection of Study Population

Investigators will all have prior clinical experience with the STAAR Surgical Implantable Collamer Lens. Subjects will be selected from each clinical site's patient population. Patients meeting all of the following criteria will be considered suitable study subjects. All subjects enrolled in this clinical study will meet the requirements under the indications for use outlined in the package insert directions for use (DFU) for the FDA approved lenses and the additional eligibility criteria described below.

3.2.1 Eligibility

3.2.1.1 Inclusion Criteria

1. 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.
2. Subjects must be of the ages of 21 through 45 at the time of surgery.
3. Moderate to high myopia with spherical equivalent ranging from -3.0 D to ≤ -15.0 D (in the spectacle plane) and cylinder in the range of 1.0 D to 4.0 D (in the spectacle plane).
4. Stable refractive history within ± 0.5 D for both spherical equivalent and cylinder for 1 year prior to implantation.
5. ACD 3.0 mm or greater, when measured from the corneal endothelium to the anterior surface of the crystalline.
6. Meet minimum endothelial cell density (ECD) requirements for age and ACD (refer to the "Minimum Endothelial Cell Density for Age and True ACD*" table below).
7. Subjects must be able to achieve a minimum dilated pupil size of 7 mm (via mydriatic and/or cycloplegic eye drops) in each eye to be treated.
8. Correctable (CDVA) to at least 20/40 in the eye to be treated; and absent of ocular pathology (except that myopic degeneration is allowed).
9. Able to read, understand and provide written informed consent on the IRB approved ICF.
10. Subjects must be able and willing to comply with all treatment and follow-up study procedures.

3.2.1.2 Exclusion Criteria

This study will include subjects who do not meet 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 Endothelial Cell Density for Age and True ACD*" table below.
5. Unstable or worsening nearsightedness.
6. History or clinical signs of iritis/uveitis.
7. Diabetic retinopathy.
8. Glaucoma.
9. History of previous eye surgery.
10. Serious (i.e., life threatening), 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.
11. Progressive sight threatening disease or other previous or current ocular conditions, other than myopia, that may predispose for future complication.
12. Diagnosis of ocular hypertension (high eye pressure).
13. Insulin-dependent diabetes.
14. Pseudoexfoliation.
15. Pigment dispersion.
16. Spherical equivalent less than -3.0 D or greater than -15.0 D (in the spectacle plane) of nearsightedness; cylinder (spectacle plane) less than 1.0 D and greater than 4.0 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 within 30 days of beginning this study.

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
>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 24 month follow-up visit is concluded. Subjects who require further follow-up for an AE will be followed according to Section 6.0.

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 in any eye
- explant of the study lenses

If both TICL 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 approximately 6-8 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 are determined by STAAR Surgical to be suitably qualified by training and experience to conduct this study in compliance with all applicable GCPs and FDA Federal Regulations. Sub-Investigators will be identified on the Device Investigator Agreement (DIA)/DOA (Delegation of Authority Log).

- Each clinical site will enroll approximately 20 subjects (40 eyes). 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 42 months. Eligible subjects who are enrolled in the study will be seen for 11 scheduled study visits (per eye) over the course of approximately 27 months.

4.0 STUDY MATERIALS

4.1 Description of Investigational Device

The Visian® Toric ICL (Implantable Collamer® Lens) for myopia and astigmatism (TICL), is an intraocular implant manufactured from Collamer®, a proprietary hydroxyethyl methacrylate (HEMA)/porcine-collagen based biocompatible polymer material. The Visian TICL contains a UV absorber made from a UV absorbing material. The TICL lens features a plate-haptic design with a central convex/concave optical zone and incorporates a forward vault to minimize contact of the Visian TICL with the central anterior capsule.

The Visian TICL features an optic diameter that varies with the dioptric power; the smallest optic diameter being 4.9 mm and the largest 5.8 mm. All descriptions of optic diameter, overall diameter or power refer to measurements in BSS unless otherwise noted. The Visian TICL is capable of being folded and inserted into the posterior chamber through an incision of 3.5 mm or less. The Visian TICL is intended to be placed entirely within the posterior chamber directly behind the iris and in front of the anterior capsule of the human crystalline lens. When correctly positioned, the Visian TICL functions as a refractive element to optically reduce moderate to high myopic astigmatism.

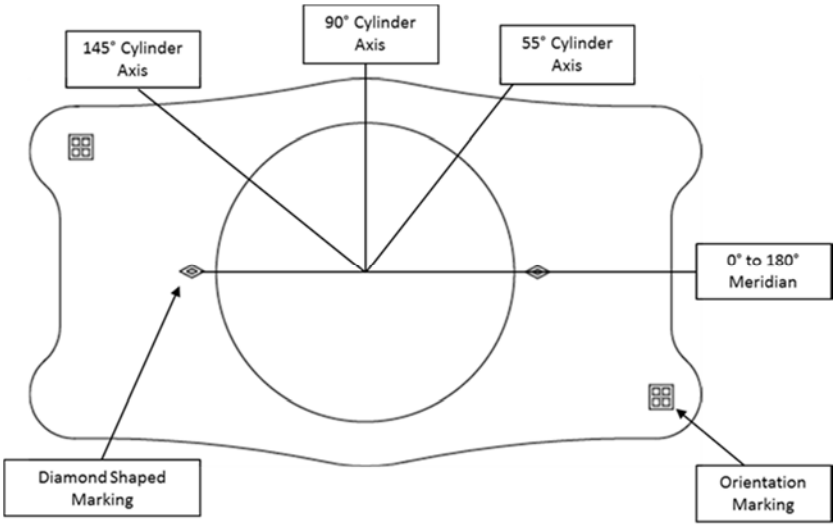
Study lenses will be available in the following powers and sizes:

Model Number	Spherical Equivalent Dioptric Power (D)	Cylinder Dioptric Power (D)	Overall Diameter (mm)	Optic Diameter (mm)	Haptic Design
TICL 12.1	-3.0 to -16.0 D	1.0 to 4.0	12.1	4.9 – 5.8	Flat, plate
TICL 12.6	-3.0 to -16.0 D	1.0 to 4.0	12.6	4.9 – 5.8	Flat, plate
TICL 13.2	-3.0 to -16.0 D	1.0 to 4.0	13.2	4.9 – 5.8	Flat, plate
TICL 13.7	-3.0 to -16.0 D	1.0 to 4.0	13.7	4.9 – 5.8	Flat, plate

The Visian TICL is labeled using a plus cylinder axis format. The lenses are labeled to the nearest degree and as such lenses of any axis between 1°to 180° may be held in inventory. The Visian TICL is 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 lens has two diamond shaped markings, one on each side of the optic, these are to aid with the 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.

The Visian TICL has orientation markings on the footplates to ensure the lens is implanted right side up. When correctly oriented the orientation markings will be on the leading right/trailing left footplates.

The sphere component of the Visian TICL label indicates the spherical power and not the spherical equivalent power.



4.2 Instructions for Use and Administration

Refer to current approved DFU for Visian Toric ICL for surgical instructions.[1]

4.2.1 Storage Requirements

As instructed on the package labeling, the following storage instructions should be followed:

- Store at room/ambient temperature.
- Do not autoclave.
- Do not expose to temperature greater than 40°C.
- Do not freeze.

4.3 Other Materials

STAAR will provide the following materials:

- a MICROSTAAR° injector MSI-PF or MSI-TF reusable injector,
- SFC-45, single use cartridge, and
- Foam tip plunger (FTP) for each study lens ordered.

4.4 Packaging and Labeling

All TICL lenses will be provided in commercial packaging, as approved by FDA on 13 Sep 2018.

4.5 Accountability

The Investigator will be responsible for keeping current and accurate records of all study lenses ordered, received, dispensed, and returned to the Sponsor. The study lenses must be stored at room/ambient temperature as described on the package labeling.

5.0 STUDY CONDUCT

5.1 Study Visits

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

- Preoperative Visit — Days -120 to 0
- Operative Visit — Day 0
- Postoperative Visit 1 — ~ 1-6 hours after surgery
- Postoperative Visit 2 — 1 to 2 days postoperatively
- Postoperative Visit 3 — 1 week (5 – 9 days)
- Postoperative Visit 4 — 1 month (3 – 5 weeks)
- Postoperative Visit 5 — 3 months (10 -14 weeks)
- Postoperative Visit 6 — 6 months (21 – 26 weeks)
- Postoperative Visit 7 — 12 months (11 – 14 months)
- Postoperative Visit 8 — 18 months (17 – 21 months)
- Postoperative Visit 9 — 24 months (23 – 27 months)

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'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 0

Prospective subjects who have provided informed consent will be screened to determine eligibility for treatment in the study. 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.

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 Investigator's standard practice for ICL surgery and in accordance with the surgical procedure described in the current DFU for the Visian Toric ICL[1].

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

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

5.1.4 Postoperative Visits – Day 1 to Month 24

Each treated subject will be seen for 8 postoperative visits according to the schedule in Appendix A.

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, will also be captured on Unscheduled Visit CRFs. In these cases, the intended visit will be identified on the Unscheduled Visit CRF.

5.1.6 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 serious adverse events (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

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 and all SAEs (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).

Complications during phakic IOL surgery of the study eye must be reported as AEs. 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.

Adverse events that have been associated with the ICL (TICL and MICL) 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.

As with implantation of other types of IOLs, potential AEs can also include, but are not limited to infection (endophthalmitis), hypopyon, corneal endothelial damage, IOL dislocation, cystoid macular edema, corneal edema, iritis, retinal detachment, transient or persistent glaucoma, vitritis, iris prolapse, and increased visual symptoms related to the optical characteristics of the IOL including halos, glare and/or double vision.

Ocular AEs associated with phakic IOLs may require a secondary surgery in the implanted eye(s). The following surgeries have been associated with the ICL (TICL and MICL):

- surgery to remove, replace 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 AEs can be considered normal or expected events after these procedures. The following

may be considered normal or expected events after phakic IOL surgery and only need to be reported as AEs at the time frames specified below:

- iritis/cells/flare (if at postoperative Visit 3 or later)
- corneal edema (if at postoperative Visit 3 or later)
- increased IOP if ≥ 30 mmHg or >10 mmHg above the preoperative measurement
- any expected postoperative ocular event requiring a change in standard postoperative medication regimen

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 **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

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 re-consenting of subjects if the SAE provides new information regarding risk to the study subject.

6.3.3 Reporting of Complaints for 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 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 Hypothesis

Based on clinical experience with stabilization of lens rotation over time, it is assumed that between 18 and 24 months postoperative, no more than 2% of eyes will exhibit rotation >5°. Our null and alternate hypotheses are as follows:

H_0 (null hypothesis): >10% of eyes with >5° rotation

H_a (alternative hypothesis): ≤10% of eyes with >5° rotation

7.2 Study Endpoints

7.2.1 Primary Effectiveness Endpoint

The primary endpoint for this study is rotation of less than or equal to five degrees between 18 and 24 months postoperative. The endpoint will be met if at least 90% of the treated

eyes rotate less than or equal to five degrees between 18 and 24 months postoperative (i.e., ≤10% of eyes exhibit >5° rotation).

7.2.2 Secondary Endpoints

The following additional endpoints will be evaluated:

- Absolute rotation between visits.
- Absolute rotation <5 degrees, <10 degrees, <20 degrees, and <30 degrees from the intended orientation at each visit.
- Absolute rotation from the intended orientation at each visit.
- Postoperative manifest refraction spherical equivalent and cylinder at each visit.
- Ocular AE rates assessed in implanted eyes.

There are no pre-specified performance targets for the secondary endpoints.

7.3 Analysis Populations

All subjects in whom surgery is attempted will be included in both the Intent to Treat (ITT) and in the Safety analysis populations. Effectiveness will also be evaluated using a Per Protocol (PP) analysis set. This set will include subjects with successful implantation, no major protocol deviations, and a non-missing primary effectiveness endpoint. The PP analysis set will be supportive of the ITT findings.

7.4 Sample Size

A sample of 100 eyes provides 94.9% power to reject the null hypothesis that >10% of eyes will exhibit >5° rotation. We assume that the rotational failure rate will be 2% or less. To allow for losses of 10% per year, a total of up to 124 primary eyes of 124 subjects will be enrolled. If a primary eye of an enrolled subject is explanted during the study, the enrolled fellow eye of that subject may be used in its place for the primary analysis. If the fellow eye was not enrolled or implanted, it may not be used in the primary analysis.

7.5 Statistical Analysis

The two-sided 95.0% upper confidence limit of the proportion of eyes with >5° absolute rotation will be calculated. The null hypothesis will be rejected if the two-sided 95.0% upper confidence limit of the proportion of eyes with >5° absolute rotation between 18 and 24 months is ≤0.1. An exact binomial confidence interval will be used.

Secondary endpoints, degrees of rotation between visits and misalignment from the intended orientation will be analyzed using descriptive statistics. Rates of rotation of the TICL of <10, <20 and <30 degrees from the intended orientation will be reported.

Evaluation of study endpoints will be conducted separately for study visits conducted within the protocol defined visit windows and separately for those outside of the visit windows. Out of window visits will be identified during analysis of study accountability. If separate evaluations of in-window and out-of-window data, including the distribution of times outside of the window that data were collected, justify poolability, then the endpoints will be analyzed using the pooled data.

To verify poolability of data across sites, outcomes for the primary endpoint by site will be compared using a 0.15 alpha to test for differences in the primary endpoint among sites. If differences are found, data will be summarized separately by site and possible reasons for the finding will be investigated.

To allow for 10% attrition annually, a total of 124 subjects (up to 248 eyes, with 124 being primary) will be enrolled for assessment of the primary and secondary effectiveness/safety endpoints.

[redacted]

7.6 Missing Data Imputation

Missing primary effectiveness endpoint data will be imputed for the primary effectiveness analysis when using the ITT analysis population. The primary method used will be by multiple imputation using SAS PROC MI and MIANALIZE. The method, seed number, number of datasets generated, and predictors to be used will be specified in advance of data lock. Sensitivity analyses will be performed using an imputation of failure (worst case) for all missing and again with an imputation of success for all missing (best case). If the results of the two extreme imputation methods differ in the conclusion drawn, a tipping point analysis will be performed to determine the point at which significance tips.

7.7 Multiplicity Adjustment

No adjustment will be made for the testing of secondary endpoints. No claims will be made for these endpoints.

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 Standard Operating Procedures (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, as applicable:

- 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, and applicable local standards and 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., digital photographs, 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 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 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 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 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 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 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 delegation of authority log under the supervision of the Principal Investigator.

Table 1: Preoperative, Surgical Assessments, and Postoperative Assessments

PROCEDURE/ ASSESSMENTS	**PreOp** Day -120 to Day 0	**Op** Day 0	**V1** 1-6 hrs postop	**V2** Day 1-2	**V3** Day 5 - 9	**V4** Wk 3 – 5	**V5** Wk 10 – 14	**V6** Wk 21 – 26	**V7** Mo 11- 14	**V8** Mo 17- 21	**V9** Mo 23- 27
Informed Consent /HIPAA Authorization	X										
Demographics/Relevant Ocular Med Hx	X										
Uncorrected Visual Acuity (UCVA)	X			X	X	X	X	X	X	X	X
CDVA	X				X	X	X	X	X	X	X
Manifest Refraction	X				X	X	X	X	X	X	X
Keratometry	X										X
Slit Lamp Exam	X			X	X	X	X	X	X	X	X
Specular Microscopy (corneal endothelial cell count-CECC)	X										
Axial length, White to White (W2W), corneal topography and ACD	X										
Gonioscopy	X										
IOP	X		X	X	X	X	X	X	X	X	X
Cycloplegic refraction	X										
Rotational stability assessment[1]		X		X	X	X	X	X	X	X	X
Con meds/AEs	X	X	X	X	X	X	X	X	X	X	X

[1] 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.

Calculation of Lens Power and Size

The lens power and size calculation will be performed by the surgeon using the STAAR Visian Toric ICL Calculation Software. Alternatively, the power and size of the lens may be determined utilizing the surgeon's standard of care method.

Postoperative target will be emmetropia with an acceptable variation of ±0.50 D spherical equivalent (SE), at the Investigator's discretion.

It is recommended that preoperative and postoperative testing be completed in the same examination room by the *same* examiner. This will help to eliminate variability in testing equipment, methodology and environment.

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.

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 does not result in an additional letter read, it must not be added. Further, if adding +0.25 does not result in a loss of letters read, it must be added.

Visual Acuity

Corrected and uncorrected visual acuity 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.

The charts were designed according to the following principles described by Bailey and Lovie[2] and the National Academy of Science-National Research Council (NAS-NRC) Committee on Vision 1980[3]: 1) letters of equal legibility; 2) combine the letters so that each line is of approximately equal difficulty as described by Ferris et al[4]; 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.[4]

The subject should attempt to read each letter, line-by-line, left to right, beginning with line 1 at the top of the chart. The subjects should be told 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. 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.

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

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.

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 1 meter, 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 4.00 meters (13 feet and 1.5 inches, or 157.5 inches) from cornea to chart surface, when using a 4-meter chart. For testing at 1 meter, the distance must be 1.00 (39 and 3/8 inches). 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.

The 1-meter distance is measured from the eye of the participant, seated comfortably in a chair with his/her back firmly placed against the chair, to the center of the 2nd or 4th letter of the 3rd line of the chart. The measuring device can be home-made (e.g., a dowel rod accurately cut to a length of 1.00 m) or 1-meter ruler may be purchased.

If it is necessary to refract at the 1-meter distance, remember to add +0.75 sphere to the trial frame. Subtract the +0.75 sphere from the final refraction obtained at the 1-meter distance before recording the refraction.

Slit Lamp Examination

This examination will be performed using a slit lamp biomicroscope. It is recommended to use a slit beam 1 mm wide by 1 mm high. The following information will be captured for this study:

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

Anterior Chamber

For the cell and flare evaluation, use a slit lamp beam 0.3 mm wide and 1 mm high.

Cells	0 - No cells seen 1 - Mild 1-5 cells seen 2 - Moderate 6-15 cells seen 3 - Severe 16-30 cells seen 4 - Very severe >30 cells seen
Flare	0 - No Tyndall effect 1 - Mild Tyndall effect barely discernible 2 - Moderate Tyndall beam in anterior chamber is moderately intense 3 - Severe Tyndall beam in anterior chamber is severely intense 4 - Very severe Tyndall beam. The aqueous has a white and milky appearance
Iris/Pupil	Normal/Abnormal

Rotational stability of the implanted TICL will be performed as described in this section.

All other assessments for this study will be conducted using the Investigator's standard of care methods for ICL surgery.

Photographic Method for Rotational Stability

The aim of imaging the subject's eye is to establish the rotational stability of the TICL[5]. In order to achieve this on all images, both toric markings on the TICL need to be identifiable. Also, the iris architecture and scleral/conjunctival blood vessels should be identifiable.

A digital slit lamp, capable of 10x magnification and retroillumination photography will be used to capture images of the eye that visualize conjunctival vessels or iris features.

Procedures

1. Intraoperatively

   Surgical video will be recorded for each subject. Images should be acquired before any miotic agent is used to ensure that the axis markings on the TICL are visible in the image.

2. Postoperative Imaging

   At follow-up visits the subject should be dilated (e.g., using phenylephrine 2.5% and tropicamide 1.0%) to ensure that the axis markings on the TICL are visible.

   The eye will be placed and imaged with the photo slit lamp as follows:

   - 10x magnification
   - Retroilluminate the TICL with the illumination arm perpendicular to cornea
   - Use appropriate slit beam width and height to achieve optimal retroillumination and image quality

     Ensure that:

     - TICL markings visible
     - TICL edge visible
     - Eye centered in image
     - Scleral/conjunctival blood vessels / iris architecture clearly defined
   - A secondary light source should be used to optimize visibility of iris and scleral/conjunctival blood vessels. This secondary illumination system needs to be set high enough to provide general illumination of the entire eye in addition to where the slit beam is present. The secondary illumination system can be controlled by twisting the top of the slit lamp where the illumination system is.

3. Images will be downloaded and submitted to an independent reading center for analysis of the rotation of the TICL for degrees of rotation between each visit and from intended axis placement.

4. Image Analysis

   a) *Determination of the intended TICL axis placement.*

      On the intraoperative images, the axis markings on the TICL will be identified and a lens-marking-line will be drawn. Landmarks in the iris, sclera, or conjunctiva, such as blood vessels and iris features, will be

identified. A landmark-line connecting these landmarks will be drawn. The difference in degrees between the lens-marking-line and landmark-line will be the intended TICL axis placement.

b) Postoperative TICL Orientation Assessment

On all images obtained at follow-up visits, a lens-marking-line will be drawn. The same landmarks used to determine the TICL axis placement on the intraoperative images will be marked and the landmark-line will be drawn.

The TICL axis orientation will be calculated as the difference in degrees between the lens-marking-line and the landmark-line.

Refer to section 7.2 Study Endpoints for the planned analyses.

REFERENCES

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