SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Phakic Toric Intraocular Lens (IOL)
Device Trade Name:	Visian® TORIC ICL (Implantable Collamer® Lens)
Device Procode:	QCB
Applicant's Name and Address:	STAAR Surgical Company 1911 Walker Avenue Monrovia, CA 91016
Date(s) of Panel Recommendation:	March 14, 2014
Premarket Approval Application (PMA) Number:	P030016/S001
Date of FDA Notice of Approval:	September 13, 2018

The original PMA P030016 for the Visian® ICL was approved on December 22, 2005 and is indicated for patients 21-45 years of age:

- to correct myopia ranging from -3.0D to ≤ -15.0D with less than or equal to 2.5D of astigmatism at the spectacle plane;
- for the reduction of myopia in adults with myopia ranging from greater than -15.0D to - 20.0D with less than or equal to 2.5D of astigmatism at the spectacle plane;
- with an anterior chamber depth (ACD) of 3.00 mm or greater, and a stable refractive history (within 0.5D for 1 year prior to implantation).

The SSED to support the indication is available on the CDRH website at https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P030016 and is incorporated by reference here. The current supplement was submitted to expand the indication to include the STAAR Visian® TORIC ICL™ for the treatment of myopic astigmatism

II. INDICATIONS FOR USE

The Visian® Toric ICL is indicated for use in patients 21-45 years of age:

1. for the correction of myopic astigmatism with spherical equivalent ranging from -3.0D to ≤-15.0D (in the spectacle plane) with cylinder (spectacle plane) of 1.0D to 4.0D.
2. for the reduction of myopic astigmatism with spherical equivalent ranging from greater than -15.0D to -20.0D (in the spectacle plane) with cylinder (spectacle plane) 1.0D to 4.0D.
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 0.5D 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.

III. CONTRAINDICATIONS

The Visian® Toric ICL is contraindicated in patients

1. with a true ACD of <3.00mm*;
2. with anterior chamber angle less than Grade III as determined by gonioscopic examination;
3. who are pregnant or nursing;
4. less than 21 years of age;
5. who do not meet the minimum endothelial cell density (ECD).

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.

The table indicates the minimum ECD per age group at time of implantation for three different ACD ranges. This data was developed as part of the STAAR Visian® ICL™ for Myopia Clinical Study. This table was developed using rates of 2.47%, 2.44% and 2.15% (the upper 90% confidence interval of the average cell loss for eyes with the specified ACD) for the ≥ 3.0mm, ≥ 3.2mm, and ≥ 3.5mm groups, respectively. It sets minimum ECD criteria as functions of age that should result in at least 1000 cells/mm^2 at 75 years of age. Specular microscopy should be

performed preoperatively and ECD should be monitored postoperatively at intervals dictated by the physician's medical judgment.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the STAAR Visian® TORIC ICL™ (Implantable Collamer Lens™) labeling.

V. DEVICE DESCRIPTION

The Visian®® Toric Implantable Collamer® Lens (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 Visian® 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 lens capsule.

The Visian® TICL features an optic diameter that varies with the dioptric power; the smallest optic diameter being 4.9mm and the largest 5.8mm. 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 3.5mm 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.

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

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative treatments for the correction of myopia with astigmatism in phakic eyes include eye glasses, contact lenses or surgery. Surgical options include: 1) laser in situ keratomileusis (LASIK), 2) radial keratotomy (RK), and 3) photorefractive keratectomy (PRK). Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The Visian® Toric ICL™ has been commercially available since 2002, and marketed in over 50 countries in the EU and EFTA, Latin America, Asia Pacific, North America, and the Middle East. The Visian® TORIC ICL™ has not been withdrawn from any market for any reason relating to the safety and effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects associated with the use of the device. Specific risks of the Visian® Toric ICL™ include: Anterior subcapsular opacities/cataract, narrowing of the anterior chamber angle, pupillary block, increased intraocular pressure (IOP), glaucoma, chronic corneal endothelial cell loss, secondary surgical interventions, loss of best spectacle-corrected visual acuity, increase in refractive astigmatism, pigment dispersion and iris transillumination defects.

Potential adverse events for all cataract or implant surgery may include but are not limited to: infection (endophthalmitis), hypopyon, corneal endothelial damage, IOL dislocation out of the posterior chamber, cystoid macular edema, corneal edema, pupillary block, iritis, retinal detachment, transient or persistent glaucoma, vitritis, iris prolapse, rupture of the capsule, and secondary surgical intervention. Increased visual symptoms related to the optical characteristics of the IOL including: halos, glare and/or double vision.

Secondary surgical interventions include, but are not limited to: lens repositioning, lens replacement, lens removal, iridotomy or iridectomy for pupillary block, wound leak repair, retinal detachment repair and corneal transplantation.

For the specific adverse events that occurred in the clinical studies, please see Section X below.

IX. SUMMARY OF NONCLINICAL STUDIES

The Visian® TICL material is the same as the Collamer® material used for the parent Visian® ICL. The material testing was conducted in accordance with the applicable EN ISO 10993 series and the EN ISO 11979 series of standards and other standards as listed.

Since the Visian® TICL is made with the same Collamer® material as the parent lens, existing non-clinical testing performed for on the Visian® ICL remains applicable. These tests are provided in the SSED for PMA P030016. Non-clinical testing performed on the Visian® TICL are provided in tables below.

A. Laboratory Studies

Test	Purpose	Acceptance Criteria	Results
Optical Requirements	To determine if the ICL meets the optical requirements.	As described in EN ISO 11979-2	Pass
Mechanical Requirements	To characterize the mechanical properties of the ICL	As described in EN ISO 11979-3	Pass

B. Animal Studies (Biocompatibility)

The Biocompatibility studies were reported in the Summary of Safety and Effectiveness Data (SSED) for PMA P030016.

C. Additional Studies

Test	Purpose	Acceptance Criteria	Results
On-line Toric Calculator			
Software Validation	To verify the Toric Calculator will function as intended	As described in FDA Guidance "General Principles of Software Validation"	Passed

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of implantation in the ciliary sulcus of the eye with STAAR Surgical's Visian® TICL for the correction of moderate to high myopic astigmatism in patients in the US under IDE G010252. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study of the TICL is presented below.

A. Study Design

Patients were treated (implanted) between August 29, 2002 and January 19, 2006. The database for this Panel Track Supplement reflected data collected through February 16, 2007 and included 124 patients (210 eyes). There were 7 investigational sites.

The study was a prospective, multi-center, non-randomized, open label 12 month study of subjects with -3.0 to -20.0D of myopia and 1.0 to 4.0D of cylinder, with preoperative best spectacle corrected visual acuity (BCDVA) of 20/40 or better and

no pre-existing progressive sight-threatening ocular disorders other than pathological refractive error. The design of the Visian® TICL is nearly identical to that of the currently approved Visian® MICL. The only difference between the Visian® TICL and the Visian® MICL is the incorporation of a toric surface on the front (anterior) side of the optic. Therefore, the study was intended to evaluate the effectiveness of the ICL design to achieve toric correction and to provide supplemental safety data. The statistical plan was based upon frequentist statistical analysis.

Up to 125 male or female phakic subjects from a maximum of 7 investigative sites who met all eligibility criteria were to be enrolled in the study and followed for approximately one year after surgery.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Visian® TICL study was limited to patients who met the following inclusion criteria:

- phakic with moderate to high myopia (-3.0D to -20.0D sphere) measured at the spectacle plane and astigmatism in the range of 1.0D to 4.0D measured as "plus" cylinder
- must have had a stable refraction for the previous 12 months as documented by previous clinical records (MRSE progressed at a rate of 0.5D or less during the year prior to the baseline examination)
- BCDVA to at least 20/40 or better in the eye to be treated
- absent of ocular pathology except myopia
- at least 21 years of age and at most 45 years of age at the time of surgery
- contact lens tolerant, willing to limit fellow eye treatment to approved refractive procedures and/or agreeable to waiting for approval from FDA for the use of the TICL in their fellow eye
- signed written informed consent form
- able and willing to return for scheduled follow-up examinations after surgery
- did not meet any of the protocol exclusion criteria

Potential patients were not permitted to enroll in the Visian® TICL study if they met any of the following exclusion criteria:

- history of/or clinical signs of, iritis, uveitis, synechiae, pigment dispersion syndrome, retinal disease (other than manifestations of myopic degeneration), chronic intraocular inflammation, macular degeneration, irregular astigmatism, keratoconus or cystoid macular edema in either eye
- had diabetes
- had glaucoma in either eye
- had a history of previous intraocular surgery (including refractive surgery) in the eye to be treated
- were amblyopic or blind in the fellow eye
- did not fall in the range of pre-treatment myopia and astigmatism outlined in the inclusion criteria
- had a serious (i.e., life-threatening) non-ophthalmic condition, which may have precluded study completion

- had a progressive sight-threatening disease (patients with retinal findings associated with pathological myopia were allowed)
- had a diagnosis of ocular hypertension
- were involved in another clinical study at the time of enrollment or were involved in another clinical study within 30 days prior to this study or planned to be involved in a different clinical study within 30 days after beginning this study
- had Fuchs dystrophy or other corneal pathology
- had keratoconus, cataract in either eye, or systemic collagen sensitivity
- had an unstable refraction in the prior 12 months (myopia and/or astigmatism)
- were pregnant or nursing

2. Follow-up Schedule

All patients were scheduled to return for follow-up examination at: 13 – 30 hours (Form 1), 7 – 14 days (Form 2), 3 – 6 weeks (Form 3), 10 – 14 weeks (Form 4), 5 – 7 months (Form 5), and 11 – 14 months (Form 6) postoperatively.

Preoperatively, manifest refraction, best corrected distance visual acuity (BCDVA), uncorrected distance visual acuity (UCDVA), tonometry, slit lamp evaluation, and patient satisfaction questionnaires were performed. Postopeeratively, the objective parameters measured during the study included manifest refraction spherical equivalent (MRSE), manifest cylinder, BCDVA, UCDVA, tonometry, slit lamp observations (including crystalline lens opacities), and patient satisfaction questionnaires. These were performed at every postoperative visit except that the manifest refraction and BCDVA were not performed at the 1 day postoperative visit, and the patient questionnaire was only performed at Form 4 and Form 6. Adverse events and complications were recorded at all visits.

The key timepoints are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety, the key study endpoints were preservation of Best Corrected Distance Visual Acuity (BCDVA) and incidence of adverse events.

With regard to effectiveness, the key study endpoints were:

a. The decrease in manifest cylinder and manifest refraction spherical equivalent (MRSE) from baseline (evaluated at 12 months postoperatively)
b. Predictability (accuracy of attempted vs. achieved correction) of MRSE and manifest cylindrical corrections (evaluated at 12 months postoperatively)
c. Uncorrected Distance Visual Acuity (evaluated at 12 months postoperatively)
d. Stability of the MRSE and manifest cylinder components of the manifest refraction, over time
e. Rotation of the ICL over time (stability)

With regard to success/failure criteria, the following show those endpoints for which there were specific criteria for study success, and what the criteria were:

- For Preservation of BCDVA – Performance targets were:
  - <5% of eyes should lose 2 lines or more BCDVA
  - ≤l% of eyes should have BCDVA worse than 20/40 (if 20/20 or better BCDVA preoperatively)

- For decrease in manifest cylinder – the mean paired difference between preoperative and 12 month postoperative manifest cylinder was to be analyzed using a paired t-test paired to demonstrate statistically significant reduction

- For Predictability of MRSE –
  Performance targets (evaluated at 12 months postoperatively) were:
  - 75% of eyes should achieve predictability (attempted versus achieved) of the MRSE of ± 1.00D
  - 50% of eyes should achieve predictability (attempted versus achieved) of the MRSE of ± 0.50D

- For Predictability of Absolute Manifest Cylinder –
  Performance targets (evaluated at 12 months postoperatively) were:
  - 65% of eyes should achieve predictability (attempted versus achieved) of the manifest cylinder to within 1.00D
  - 40% of eyes should achieve predictability (attempted versus achieved) of the manifest cylinder to within 0.50D

- For Uncorrected Distance Visual Acuity (UCDVA) –
  Performance target (evaluated at 12 months postoperatively) was:
  - 85% of eyes should achieve UCDVA of 20/40 or better (for those eyes with BCDVA of 20/20 or better preoperatively)

B. <u>Accountability of PMA Cohort</u>

At the time of the database lock, of 210 eyes (124 Primary eyes and 86 fellow eyes) of 124 patients enrolled in the PMA study, 92% (194/210) of eyes were available for analysis at the completion of the study, the 12 month postoperative visit (146 within the visit window and 48 outside the window). The clinical study protocol identified the following postoperative visit schedule; 1 day, 1 week, 1 month, 3 months, 6 months and 12 months. Refer to Table 1 for subject accountability by each scheduled visit.

Table 1: Accountability (by eye) —Visian® TICL Study Cohort

Total Enrollment N = 210	**1 D** n/N (%)	**1 W** n/N (%)	**1 M** n/N (%)	**3 M** n/N (%)	**6 M** n/N (%)	**12 M** n/N (%)
Available for Analysis (eyes)	210/210 (100%)	195/210 (92.9%)	184/210 (87.6%)	157/210 (74.8%)	167/210 (79.5%)	146/210 (69.5%)
Missing Eyes						
Discontinued[1]	0/210 (0%)	0/210 (0%)	2/210 (1.0%)	3/210 (1.4%)	3/210 (1.4%)	3/210 (1.4%)
Missing at scheduled visit but seen later	0/210 (0%)	10/210 (4.8%)	16/210 (7.6%)	34/210 (16.2%)	15/210 (7.1%)	48/210 (22.9%)
Not seen but accounted for	0/210 (0%)	3/210 (1.4%)	6/210 (2.9%)	13/210 (6.2%)	16/210 (7.6%)	0/210 (0%)
Lost to follow-up[2]	0/210 (0%)	2/210 (1.0%)	2/210 (1.0%)	3/210 (1.4%)	9/210 (4.3%)	13/210 (6.2%)
Active	0/210 (0%)	0/210 (0%)	0/210 (0%)	0/210 (0%)	0/210 (0%)	0/210 (0%)
Accountability	210/210 (100%)	195/210 (92.9%)	(184/208) 88.5%	(157/207) 75.8%	(167/207) 80.7%	(146/207) 70.5%
Accountability including out-of-window visits[3]	210/210 (100%)	(205/210) 97.6%	(200/208) 96.2%	(191/207) 92.3%	(182/207) 87.9%	(194/207) 93.7%

[1] Cumulative total number of eyes discontinued is 3.

[2] Cumulative total number of eyes lost to follow-up is 13.

[3] Calculated (available for analysis+missing at scheduled visit but seen later)/(enrolled-discontinued).

Overall accountability for this study consisted of follow-up for 194 eyes examined for the one-year postoperative visit, including 48 eyes seen outside the defined visit window of 11 to 14 months. There were 146 eyes seen timely at the 1 year visit. Analyses showed that it was reasonable to include the eyes available outside the 12 month visit window. Therefore, all 12 month analyses included those seen outside the window. Thirteen eyes from 12 study subjects were lost to follow-up over the course of the Visian® TICL clinical study. In 7 of the 13 cases lost to follow-up, the site was unable to locate or contact the subjects. In 4 of the cases, the subject moved and was not available for examination. In two cases, the subjects were deployed to Iraq and were unavailable for examination prior to study closure.

There were 3 eyes of 3 subjects discontinued from the Visian® TICL Study Cohort. In all of these cases, the Visian® TICL was removed with no subsequent ICL implantation.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a study performed in the U.S. for this type of refractive surgery population.

Clinical study subject demographics for the 210 eyes from 124 subjects enrolled in the Visian® TICL Study Cohort are summarized in Table 2. The mean preoperative manifest refraction spherical equivalent (MRSE) for the Visian® TICL Study Cohort was highly myopic at –9.37D (range of−2.38D to −19.50D). The mean preoperative manifest refractive cylinder was 1.95D (range of 1.00D to 4.00D). See Table 3 for Baseline Characteristics.

Table 2: **Demographics**

N = 124 Subjects	
Age	
Mean (SD)	35.0 (6.8) yrs
Range	21 to 45 yrs
Race	**n/124, %**
Caucasian	102, 82.3%
Hispanic	10, 8.1%
Black	6, 4.8%
Other	6, 4.8%
Gender	
Female	69, 55.6%
Male	55, 44.4%

Table 3: Baseline Characteristics

	Mean	**Standard Deviation**	**Min**	**Max**
Preoperative Spherical Equivalent (n = 210 eyes)	−9.37D	2.67D	−19.50D	−2.38D
Preoperative Cylinder (n = 210 eyes)	1.95D	0.84D	1.00D	4.00D

Table 4 provides the distribution of preoperative cylinder stratified by preoperative manifest refraction spherical equivalent for the Visian® TICL population.

Table 4: Distribution of Preoperative Manifest Refraction by Preoperative Cylinder

Preoperative MRSE	Preoperative Cylinder (N = 210 eyes)						
	1.00 - 1.50D n/210 (%)	1.51 - 2.00D n/210 (%)	2.01 - 2.50D n/210 (%)	2.51 - 3.00D n/210 (%)	3.01 - 3.50D n/210 (%)	3.51 - 4.00D n/210 (%)	Total n/210 (%)
≤ −3.00 to −8.00D	31 (14.8%)	20 (9.5%)	7 (3.3%)	11 (5.2%)	0 (0.0%)	4 (1.9%)	73 (34.8%)
−8.01 to −12.00D	46 (21.9%)	15 (7.1%)	18 (8.6%)	5 (2.4%)	12 (5.7%)	7 (3.3%)	103 (49.1%)
−12.01 to −15.00D	10 (4.8%)	8 (3.8%)	6 (2.9%)	2 (1.0%)	2 (1.0%)	0 (0.0%)	28 (13.3%)
−15.01 to −20.00D	3 (1.4%)	1 (0.5%)	1 (0.5%)	1 (0.5%)	0 (0.0%)	0 (0.0%)	6 (2.9%)
Total	**90 (42.9%)**	**44 (21.0%)**	**32 (15.2%)**	**19 (9.0%)**	**14 (6.7%)**	**11 (5.2%)**	**210**

D. Safety and Effectiveness Results

The analysis of safety was based on the all-implanted cohort of 210 eyes available through the 12 month evaluation. The key safety outcomes for this study are presented below in Tables 5 to 6 and Figure 1. Adverse effects are reported in Tables 7 to 8.

The parent lens that underwent a pivotal clinical trial was the MICL approved under PMA P030016. FDA concluded that the safety data from this prior clinical study is applicable to the TICL. Please see the SSED for PMA P030016 for this clinical data.

1. Safety Results

Preservation of BCDVA

At 12 months postoperatively, 3/194 eyes (1.5%) lost ≥ 2 lines of BCDVA. Persistent loss of BCDVA > 2 lines occurred in one eye (0.5%); loss of 2 lines in 2 eyes (1.0%). No eyes (0%) had BCDVA worse than 20/40 (if preoperative BCDVA 20/20 or better) between 1 and 12 months postoperative. See Table 5 and Figure 1.

The protocol defines the following targets:

- < 5% of eyes should lose 2 lines or more BCDVA.
- ≤ l% of eyes should have BCDVA worse than 20/40 (if 20/20 or better BCDVA preoperatively).

Therefore, the study results were successful with regard to these 2 targets.

The applicant also provided last visit carried forward (LVCF) analyses for preservation of BCDVA and reported no change in the number of eyes with loss of ≥ 2 lines of BCDVA between the 12 month or later data and the LVCF.

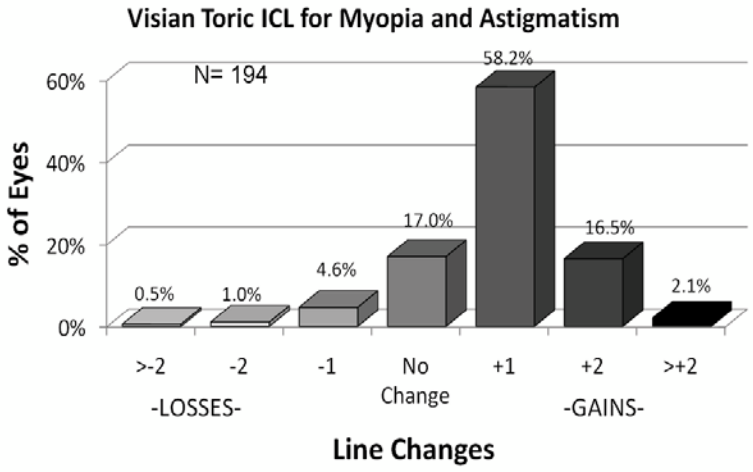
BCDVA for the cohort of those eyes with preoperative BCDVA of 20/20 or better and the change in BCDVA for the Visian® Study Cohort is provided in Table 5 and Figure 1 below.

Table 5: Best Corrected Distance Visual Acuity (BCDVA) - Eyes with Preoperative BCDVA 20/20 or better

BCDVA	**6 Months N=155 Eyes** n/155, %	**12 Months N=159 Eyes** n/159, %
20/12.5 or better	71, 45.8%	72, 45.3%
20/16 or better	141, 91.0%	143, 89.9%
20/20 or better	155, 100%	159, 100%
20/25 or better	155, 100%	159, 100%
20/40 or better	155, 100%	159, 100%

A total of 1.4% eyes (3/210) (reported a loss of > 2 lines of BCDVA between the preoperative and 12 month visit. A loss of > 2 lines of BCDVA (20/25 to 20/50) occurred at the 12 month visit in 0.5% of eyes (1/210) due to anterior subcapsular cataract. There was no information regarding treatment or resolution at the time of study closure. A loss of 2 lines of BCDVA was reported in 1.0% (2/210). In one eye, the preoperative BCDVA was 20/12.5 and at the 12 month visit the BCDVA was 20/20. There were no lens opacities noted at any visit and the patient consistently rated her satisfaction with the procedure as very satisfied. The other eye was amblyopic with preoperative BCDVA of 20/40 and postoperative BCDVA of 20/60 at both the 6 and 12 month visits. This patient was subsequently seen 5 months after the 12 month visit and BCDVA was within 1 line of preoperative BCDVA. No eyes (0%) had BCDVA worse than 20/40 (if preoperative BCDVA was 20/20 or better) between 1 and 12 months postoperative.

Figure 1: Change in BCDVA - Preoperative vs. 12-Month Visit



Adverse effects that occurred in the PMA clinical study:

Key Adverse Events (AEs) and Complications in the PMA Supplement Clinical Trial

Incidence of key AEs/complications are provided in Table 6. For a benchmark, they are compared with the ISO historical rate for posterior chamber IOLs for aphakia implanted in the capsular bag (from EN ISO 11979-7). (But note that because of differences in the study populations and the position of the TICL within the eye, results are not strictly comparable.) Details concerning the types of surgical reinterventions are presented in Table 7.

Table 6: Incidence of Key Adverse Events and/or Complications

Incidence of Key Adverse Events and/or Complications				
Adverse Event	**Cumulative N=210 Eyes**	**ISO[1] Historical Rate**	**Persistent (12 Months)**	**ISO Historical Rate**
	n/210, %	**%**	**n/194, %**	**%**
Endophthalmitis	0, 0%	0.1%	0, 0%	---
Hyphema[4]	0, 0%	---	0, 0%	---
Hypopyon	0, 0%	0.3%	0, 0%	---
IOL Dislocation	0, 0%	0.1%	0, 0%	---

Cystoid Macular Edema	0, 0%	3.0%	0, 0%	0.5%
Raised IOP Requiring Treatment[4]	1, 0.5%	---	0, 0%	0.4%
Pupillary Block	1, 0.5%	0.1%	0, 0%	---
Retinal Detachment[2]	1, 0.5%	0.3%	0, 0%	---
Surgical Reintervention[3]	8, 3.8%	0.8%	0, 0%	---
BCDVA loss ≥ 2 lines[4]	3, 1.5%	---	3, 1.5%	---
Corneal Edema[4] (after 1 week)	0, 0%	---	0, 0%	0.3%
Iritis[4] (after 1 week)	0, 0%	---	0, 0%	0.3%
Anisocoria[4]	1, 0.5%	---	0, 0%	---

[1] ISO-11979-7: Ophthalmic implants– Intraocular Lenses Part 7: Clinical Investigations

[2]Comparison should be made to literature for retinal detachment rates for high myopia. Retinal detachment rates increase with increasing myopia. The risk of retinal detachment within one year of implantation of this device is 0.5%. The risk of retinal detachment for high myopes following implantation with the Visian® MICL[†] is more than 10 times the risk without surgery, i.e., greater than 10 fold the background rate of retinal detachment for high myopes (>-3D) 5.0% in myopes >-6D and 0.8% to 7.5% in pseudophakic eyes with high axial myopia.

[†] Visian® MICL Clinical Trial

[3] Refer to table below for details on Surgical Reinterventions.

[4]There is no ISO historical rate for cumulative hyphema, raised IOP requiring treatment, iritis (after 1 week), BCDVA loss ≥ 2 lines, corneal edema (after 1 week) and anisocoria.

Surgical Reinterventions

Table 7: Visian® TICL Related Additional Surgery

Visian® TICL Related Additional Surgery	n/210*	(%)
TICL Repositioning	1	0.5%
Visian® TICL Replacement (too long)	1	0.5%
Visian® TICL Removal (no ICL or IOL replacement)	3	1.4%
Yag Iridotomy**	3	1.4%
Total *Total Eye Cohort (N = 210)	**8**	**3.8%**

**Three cases (1.4%) underwent an additional iridotomy. One of these was performed on the day of surgery because the surgeon felt the previous YAG procedure was inadequate. The IOP was 14 mmHg or less at all postoperative visits. The second case had an additional YAG iridotomy performed at 5 days postoperative to deepen the anterior chamber which was successful. This case was not associated with an increase in IOP. In the third case, the procedure was performed at 1 day postoperative to enlarge the preoperative iridotomy which was occluded by retained viscoelastic material, resulting in elevated IOP. Subsequent to the YAG procedure, the IOP returned to normal and stayed normal for the remainder of the follow-up.

The 8/210 cases (3.8%) of surgical intervention listed in Table 7 all had improvement/no change in BCDVA or no significant loss in BCDVA (1 line in 1 case) at the last follow-up visit.

Corneal edema and iritis were not reported after the 1 week visit. There was 1 case (0.5%)(1/210) of retinal detachment. No cases of endophthalmitis, corneal ulcer, ocular hypertension, corneal haze/edema (after 1 week), or corneal melting were reported during the study.

FDA concluded that key adverse events occurred at rates generally within the bounds of those seen in the clinical study of the parent MICL device, which is known to have higher rates of secondary surgical reintervention than historical rates for intraocular lenses for aphakia, implanted in the capsular bag (the source of the ISO historical rates).

Pigment, Flare and Cell Incidence

Routine clinical assessment of aqueous flare and cellular reaction was performed at every study visit across all investigative centers in the Visian® TICL clinical investigation following standard clinical diagnostic techniques.

No flare or cellular reaction > 1+ was seen in any patient at 1 week or later postoperatively. Furthermore, 1+ flare/cellular reaction was reported in only 1 eye at 1 month. This case demonstrated no flare or cellular reaction at the 3 month and 6 month postoperative visits. No flare or cell was reported at 3, 6 or 12 months after TICL implantation.

No fibrin in the anterior chamber was reported in any case. No patients required treatment with anti-inflammatory medication after the 1 month postoperative visit.

Pigmentary precipitates were observed at various time intervals but were not associated with any other inflammatory signs.

Slit Lamp Examination - Lens Opacities

The standardized Lens Opacities Classification System (LOCS III) photographic images were utilized across all clinical sites in the Visian® TICL clinical investigation for the assessment of the incidence, type, and severity of lens opacities. Anterior subcapsular appearance was assessed using photographs for posterior subcapsular appearance, and the slit lamp examination localized the opacity anteriorly.

There were no cases of trace or greater for nuclear color, nuclear opalescence, cortical, or posterior subcapsular changes preoperatively or at any postoperative visit.

Anterior subcapsular opacities, not all clinically significant, were observed postoperatively in 2.9% of eyes (6/210). Two of these six eyes (1.0%) had clinically significant cataracts. The remaining 4 subjects were asymptomatic with 20/16 or better BCDVA and 20/25 or better UCDVA at their last reported visit.

The parent MICL device is similarly known to be associated with increases in subcapsular opacities in the crystalline lens.

Increase in Intraocular Pressure (IOP)

One eye (0.5%)(1/210) had increased IOP at one day postoperative, which was related to pupillary block and resolved with an additional Nd:YAG iridotomy. IOP at the one day follow up visit after Nd:YAG iridotomy was 12 mmHg. At the final 12 month postoperative visit, BCDVA was 20/25 and IOP was 14mmHg. One eye

(0.5%)(1/210) experienced an IOP > 25mmHg at 6 months postoperative, which dropped to 17mmHg at 12 months. Two eyes (1.0%) (2/210) of two subjects experienced an increase of > 10 mmHg over preoperative IOP during the 12 month follow-up period. These eyes experienced IOP increases from 8 mmHg to 21 mmHg and from 10 mmHg to 22 mmHg. No treatment was reported in any of these cases.

Patient Subjective Symptoms

Optical Visual Symptoms

A standardized subjective patient questionnaire was administered across all investigative sites to all subjects in the Visian® TICL Study Cohort preoperatively and after ICL implantation. Study subjects' subjective assessments of ocular symptoms of glare, halos, double vision, night vision and night driving difficulties were evaluated for each eye at the preoperative and at the 3 and 12 month postoperative follow-up visits. Subjects were asked to grade the level of the specific ocular symptom in one of five categories: Absent, Mild, Moderate, Marked or Severe. See Table 8 for the results.

Table 8: Eyes with Symptoms Worse at 12 Months compared to Preoperative

Visual Symptom	Worse at 12 Months than Preoperative
	n/N, %
Glare	28/185, 15.1%
Halos	33/185, 17.8%
Double Vision	3/185, 1.6%
Night Vision	22/184, 11.9%
Night Driving Difficulties	24/182, 13.2%

Note: The questionnaire and methodology used to evaluate these subjective symptoms were not considered by the FDA to be validated.

FDA concluded that evidence indicates that the safety profile of the TICL device should be similar to that of the approved parent MICL device, and that prior clinical safety data is applicable to the TICL as well.

2. **Effectiveness Results**

The analysis of effectiveness was based on the 194 eyes of evaluable patients at the 12-month time point. Key effectiveness outcomes are presented in Tables 9 to 22.

Decrease in Refractive Myopia and Cylinder

Reduction in refractive myopia and cylinder (manifest refraction spherical equivalent [MRSE] and cylinder) were the primary efficacy outcomes for the study. The tables below provide MRSE and cylinder over time, and a comparison between preoperative and 12 month MRSE and cylinder for the consistent cohort. The mean MRSE improved from -9.38D preoperative to 0.03D at the 12 month follow-up visit. There was a highly significant ($p < 0.001$) 1.43D mean decrease in cylinder from preoperative to 12 months postoperative (paired t-test).

Table 9: MRSE over Time (TICL PMA Study Cohort)

MRSE	Preop	1 Wk	1 Mo	3 Mo	6 Mo	12 Mo
N (eyes)	210	205	200	191	182	194
Mean (D)	-9.38	0.02	0.13	0.13	0.11	0.03
SD	2.67	0.45	0.43	0.39	0.49	0.46
Range (D)	-19.50 to -2.38	-1.50 to 1.38	-1.63 to 1.75	-1.25 to 1.25	-1.75 to 2.63	-2.25 to 1.00

Table 10: MRSE: Preoperative vs. 12 Months (consistent cohort)

	Preop	12 Months
N (eyes)	194	194
Mean (D)	-9.34	0.03
SD	2.63	0.46
Range (D)	-19.50 to -2.38	-2.25 to +1.00

Table 11: Manifest Refraction Cylinder over Time

	Preop	1 Week	1 Month	3 Months	6 Months	12 Months
N (eyes)	210	205	200	191	182	194
Mean (D)	1.95	0.50	0.50	0.52	0.45	0.52
SD	0.84	0.54	0.49	0.49	0.45	0.48
Range (D)	1.00 to 4.00	0.00 to 3.00	0.00 to 3.00	0.00 to 3.00	0.00 to 2.00	0.00 to 3.00

Table 12: Manifest Refraction Cylinder: Preoperative vs. 12 Months (consistent cohort)

	Preop	12 Months
N (eyes)	194	194
Mean (D)	1.95	0.52
SD	0.85	0.48
Range (D)	1.00 to 4.00	0.00 to 3.00

Predictability of Refraction

The MRSE of the refraction was predictable with 97.4% (189/194) of eyes achieving within ± 1.0D from target at the 12 month examination. See Table 13 below.

Table 13: Accuracy of MRSE to Target

	12 Months N=194 Eyes
	n/194, %
Within ± 0.50D	149, 76.8%
Within ± 1.0D	189, 97.4%

The manifest cylinder was predictable with 92.3 % (179/194) of eyes achieving within ± 1.0D from target at the 12 month examination. See Table 14 below.

Table 14: Accuracy of Manifest Cylinder to Target*

	12 Months N=194 Eyes
	n/194, %
Within ± 0.50D	134, 69.1%
Within ± 1.0D	179, 92.3%

*At the corneal plane

The effect of a temporal corneal incision on corneal toricity was analyzed. On average, implantation of the TICL contributed less than 0.5D of "with-the-rule" astigmatism to the net corneal toricity.

Table 15 provides the accuracy of the MRSE correction to the Intended Target over time.

Table 15: Accuracy of MRSE vs. Intended Target[1] by Preoperative MRSE

Lens Group	Exam Interval	N (eyes)	Within ± 0.50D n/N, %	Within ± 1.0D n/N, %	Within ± 2.0D n/N, %
Study Cohort	1 Week	201	149/201, 74.1%	194/201, 96.5%	201/201, 100%
	1 Month	198	155/198, 78.3%	189/198, 95.5%	198/198, 100%
	3 Months	190	142/190, 74.7%	185/190, 97.4%	190/190,100%
	6 Months	181	122/181, 67.4%	174/181, 96.1%	180/181, 99.4%
	12 Months	194	149/194, 76.8%	189/194, 97.4%	194/194, 100%
≤ −7D Sub-Cohort	12 Months	33	28/33, 84.8%	33/33, 100%	33/33, 100%
> −7 to −10D Sub-Cohort	12 Months	93	76/93, 81.7%	92/93, 98.9%	93/93, 100%
> −10D to −15D Sub-Cohort	12 Months	62	42/62, 67.7%	59/62, 95.2%	62/62, 100%
> −15D Sub-Cohort	12 Months	6	3/6, 50.0%	5/6, 83.3%	6/6, 100%

[1] All Study Cohort Eyes

Table 16 provides of the accuracy of the manifest cylinder correction to the intended target over time.

Table 16: Accuracy of Manifest Cylinder vs. Intended Target (Over Time)

Lens Group[1]	Exam Interval	N (Eyes)	Within 0.25 D n/N[2], %	Within 0.50 D n/N[2], %	Within 1.00 D n/N[2], %	Within 2.00 D n/N[2], %
	Preop	210	0/210, 0%	0/210, 0%	43/210, 20.5%	134/210, 63.8%
	1 Week	205	92/201, 45.8%	128/201, 63.7%	184/201, 91.5%	198/201, 98.5%
Study Cohort	1 Month	200	84/198, 42.4%	128/198, 64.6%	180/198, 90.9%	197/198, 99.5%
	3 Months	191	77/190, 40.5%	123/190, 64.7%	174/190, 91.6%	186/190, 97.9%
	6 Months	182	87/181, 48.1%	128/181, 70.7%	167/181, 92.3%	181/181, 100%
	12 Months	194	78/194, 40.2%	127/194, 65.5%	177/194, 91.2%	193/194, 99.5%

[1] All Study Cohort Eyes
[2] Eyes with non-missing data

Improvement in UCDVA

Table 17 presents the UCDVA over time in those cases with preoperative 20/20 or better BCDVA.

Table 17: Uncorrected Distance Visual Acuity (UCDVA) - Eyes with Preoperative BCDVA 20/20 or Better

	Preoperative n/173 (%)	6 M n/155 (%)	12 M n/159 (%)
20/12.5 or better	0 (0%)	41 (26.5%)	40 (25.2%)
20/16 or better	0 (0%)	117 (75.5%)	101 (63.5%)
20/20 or better	0 (0%)	140 (90.3%)	142 (89.3%)
20/40 or better	0 (0%)	155 (100%)	159 (100%)
20/50 or worse	173 (100%)	0 (0%)	0 (0%)
20/200 or worse	173 (100%)	0 (0%)	0 (0%)

Table 18 below provides the UCDVA over time and by preoperative MRSE group (for eyes that had BCDVA of 20/20 or better preoperatively).

Table 18: UCDVA* Over Time and by Preoperative MRSE

MRSE Group	Exam Interval	N (eyes)	20/20 or Better n/N, %	20/40 or Better n/N, %
	1 Week	171	131/171, 76.6%	170/171, 99.4%
	1 Month	166	139/166, 83.7%	164/166, 98.8%
Study Cohort	3 Months	161	140/161, 87.0%	161/161, 100%
	6 Months	155	140/155, 90.3%	155/155, 100%
	12 Months	159	142/159, 89.3%	155/155, 100%
≤ -7D	12 Months	33	31/33, 93.9%	32/33, 97.0%
> -7D to -10D	12 Months	93	78/93, 83.9%	91/93, 97.8%
> -10D to -15D	12Months	61	47/61, 77.0%	59/61, 96.7%
> -15D	12Months	6	2/6, 33.3%	2/6, 33.3%

*In eyes with preoperative BCDVA of 20/20 or better

Table 19 below provides a comparison of postoperative UCDVA at 12 months to preoperative BCDVA values.

Table 19: Comparison of Preoperative BCDVA to 12 Month Postoperative UCDVA

	Preoperative BCDVA N=193 Eyes **n/193 (%)**	**12 Month UCDVA** N=193 Eyes **n/193 (%)**
20/12.5 or better	7, 3.6%	40, 20.7%
20/16 or better	79, 40.9%	104, 53.9%
20/20 or better	159, 82.4%	158, 81.9%
20/25 or better	181, 93.8%	175, 90.7%
20/32 or better	190, 98.4%	180, 93.3%
20/40 or better	193, 100.0%	184, 95.3%
20/80 or better	193, 100.0%	191, 99.0%
20/200 or better	193, 100.0%	193, 100.0%
Worse than 20/200	0, 0%	0, 0%

Stability

Table 20 presents MRSE changes and between pairs of sequential postoperative follow-up visits within eyes present at both visits. Table 21 presents similar information for refractive cylinder changes between visits. It provides changes in both absolute cylinder and vector cylinder (taking into account changes in both magnitude and axis) for both analyses of eyes present at both of the adjacent visits, and for those eyes that were present at all relevant follow-up visits (consistent cohort).

Table 20: MRSE Change Between Visits

Change	1 Month to 3 Months N=184 Eyes n/184, %	3 Months to 6 Months N=172 Eyes n/172, %	6 Months to 12 Months N=177 Eyes n/177, %
Within ± 0.25D	136, 73.9%	129, 75.0%	139, 78.5%
Within ± 0.50D	169, 91.8%	159, 92.4%	167, 94.4%
Within ± 1.0D	184, 100%	170, 98.8%	176, 99.4%
> 1.0D	0, 0%	2, 1.2%	1, 0.6%
Mean Change	0.010	-0.009	0.081
SD	0.311	0.330	0.360
95% CI of the Mean	-0.04 to 0.05	-0.06 to 0.04	0.03 to 0.13

MRSE was stable with 99.4% (176/177) of eyes achieving less than or equal to ±1.0D of shift between 6 and 12 months after surgery.

Table 21: Manifest Cylinder Change Between Visits

Analysis Group	Exam Interval	N (Eyes)	Within ± 0.5D n/N, %	Within ± 1.0D n/N, %	Mean Change for Interval [95% Confidence Interval]
Vector Stability	1 to 3 Mo	184	143/184, 77.7%	179/184, 97.3%	0.26D [0.23 to 0.3]
	3 to 6 Mo	172	145/172, 84.3%	167, 97.1%	0.23D [0.19 to 0.26]
	6 to 12 Mo	177	141, 79.7%	172, 97.2%	0.26D [0.22 to 0.29]
Vector Stability Consistent cohort	1 to 3 Mo	167	130/167, 77.8%	162/167, 97.0%	0.26D [0.23 to 0.3]
	3 to 6 Mo		140/167, 83.8%	162/167, 97.0%	0.23D [0.19 to 0.27]
	6 to 12 Mo		134/167, 80.2%	163/167, 97.6%	0.24D [0.21 to 0.28]
Stability of	1 to 3 Mo	184	154/184, 83.7%	181/184, 98.4%	0.00D [-0.05 to 0.05]

Analysis Group	Exam Interval	N (Eyes)	Within ± 0.5D n/N, %	Within ± 1.0D n/N, %	Mean Change for Interval [95% Confidence Interval]
Absolute Cyl	3 to 6 Mo	172	153/172, 89.0%	170/172, 98.8%	-0.03D [-0.08 to 0.01]
	6 to 12 Mo	177	151/177, 85.3%	174/177, 98.3%	0.04D [0 to 0.09]
Stability of Absolute Cyl Consistent Cohort	1 to 3 Mo	167	140/167, 83.8%	164/167, 98.2%	0.00D [-0.05 to 0.05]
	3 to 6 Mo		148/167, 88.6%	165/167, 98.8%	-0.03D [-0.08 to 0.01]
	6 to 12 Mo		143/167, 85.6%	165/167, 98.8%	0.03D [-0.02 to 0.07]

Rotation of the Visian® TICL

Study investigators were asked to examine the patient at the slit lamp and estimate the orientation of the long axis of the Visian® TICL based upon the alignment markings or haptic edges if visible. The lens orientation was then recorded in clock hours. For instance, if the lens was oriented exactly horizontally it would be recorded as either the 3:00 or 9:00 o'clock position. Rotation was evaluated based upon the change in clock hour orientation of the Visian® TICL postoperatively. A change of a half clock hour would represent 15 degrees of rotation and a change of a quarter clock hour would represent 7.5 degrees of rotation. Table 22 provides the results.

Table 22: Rotation of the TICL Between Visits (from direct observation of TICL)

	1 Day – 1 Wk	1 Wk – 1 Mo	1 Mo – 3 Mo	3 Mo – 6 Mo	6 Mo – 12 Mo
N (Eyes)	121	155	148	136	140
Rotation	**n/121, %**	**n/155, %**	**n/148, %**	**n/136, %**	**n/140, %**
≤ 5°	118, 97.5%	148, 95.5%	141, 95.3%	133, 97.8%	132, 94.3%
≤ 10°	121, 100%	155, 100%	147, 99.3%	135, 99.3%	137, 97.9%

FDA concluded that the TICL study results provided reasonable assurance that the device is effective in reducing MRSE and manifest cylinder, in improving uncorrected distance visual acuity, and in achieving refractive and rotational stability.

Subjective Quality of Vision:
A standardized subjective patient questionnaire was administered across all investigative sites to all subjects in the Visian® TICL Study preoperatively and after ICL implantation. Study subject's subjective assessments of their quality of vision were evaluated for each eye at the preoperative and at the 3 and 12 month postoperative follow-up visits. Subjects were asked to rate their level of quality of vision in one of five categories: Excellent, Very Good, Good, Poor or Very Poor".

Table 23: Subjective Quality of Vision - All Eyes

Quality of Vision Grading	Preoperative N = 210	12 Months N=184
	n/210 %	n/184, %
Excellent/Very Good	135, 64.3%	174, 94.6%
Good	53/210, 25.2%	10/184, 5.4%
Poor/Very Poor	22/210, 105.5%	0/184, 0%

Note: The questionnaire and methodology used to evaluate these subjective symptoms were not considered by the FDA to be validated.

3. **Subgroup Analyses**

The following preoperative characteristics were evaluated for potential association with outcomes: preoperative refractive cylinder, ICL cylinder power and preoperative MRSE.

Stratification by preoperative refractive cylinder was done for the analysis of percent reduction of absolute (non-vector) cylinder. As the magnitude of preoperative cylinder increased, the percent reduction of absolute (non-vector) cylinder increased. Refer to Table 24, below.

Stratification by ICL cylinder power was done for the analyses for change in cylinder, residual cylinder and percent reduction of absolute (non-vector) cylinder. With regards to change in cylinder and residual cylinder, there was no degradation of the effectiveness of the ICL cylinder correction at the higher powers and essentially there was no correlation between residual cylinder power and the ICL power at 12 months. With regard to percent reduction of absolute (non-vector) cylinder, the greatest percent reduction occurred in those eyes with $\geq$ 1.8D to $\leq$ 3.0D of ICL cylinder power.

Table 24: Percent Reduction of Absolute (non-vector) Cylinder* Attempted vs Achieved

Preoperative Cylinder	n (%)	Percent Reduction of Absolute (Non-Vector) Cylinder		
		Mean	Range	[% CI]
All	n/194 (%)	77.8	−62.7 to 151.9	[73.9 to 81.6]
> 0.5D to ≤ 1.0D	39 (20.1%)	75.1	−26.4 to 125.2	[65.4 to 84.8]
> 1.0D to ≤ 2.0D	86 (44.3%)	71.4	−62.7 to 137.3	[64.9 to 77.9]
> 2.0D to ≤ 3.0D	45 (23.2%)	87.1	44.8 to 151.9	[82.2 to 91.9]
> 3.0D to ≤ 4.0D	24 (12.4%)	87.6	29.0 to 125.6	[80.3 to 95]

*In spectacle plane

Stratification by MRSE included analyses for UCDVA and predictability of MRSE (attempted vs. achieved). With regard to UCDVA, all groups exceed the effectiveness endpoint of 85% of eyes with UCVA 20/40 or better (Refer to Table 18). With regard to predictability of MRSE (attempted vs. achieved), all groups met or exceeded the targets for accuracy within 0.50D and 1.00D of target (Refer to Table 13).

4. **Pediatric Extrapolation**

In this premarket application, existing clinical data was not leveraged to support approval of a pediatric patient population.

E. Financial Disclosure

DISCLOSABLE FINANCIAL ARRANGEMENTS: NO EFFECT ON RELIABILITY OF DATA

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 20 investigators of which none were full-time or part-time employees of the sponsor and 1 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 1

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. PANEL MEETING RECOMMENDATION AND FDA'S POST-PANEL ACTION

a. Panel Meeting Recommendation

At an advisory meeting held on March 14, 2014, the Ophthalmic Devices Advisory Panel voted 5-1-3 (yes, no, abstain) that there is reasonable assurance that the device is safe, 7-1-1 (yes, no, abstain) that there is reasonable assurance that the device is effective, and 6-0-3 (yes, no, abstain) that the benefits of the device outweigh the risks for use in patients who meet the criteria specified in the proposed indication.

The 24-hour meeting summary can be found at the following: https://wayback.archive-it.org/7993/20170114045350/http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OphthalmicDevicesPanel/UCM389566.pdf

The Panel also discussed potential topics they believed should be considered as a condition of approval. This included the evaluations of endothelial cell density (ECD) loss, device placement and stability, and a validated questionnaire to address issues related to visual distortion.

b. FDA's Post-Panel Action

Subsequent to the Advisory Panel, the applicant submitted the following items to the premarket application:

- Information that was not previously reviewed by FDA and was the basis for slides presented during the Advisory meeting, including several sensitivity analyses.
- Software validation data for the TICL power calculator software
- Revised professional labeling that incorporates the post approval study results from the parent MICL that evaluated long term safety data, including corneal endothelial loss data out to 5 years

- Master validation and verification documents to add a new manufacturing site

The new information as key to FDA's decision is incorporated into the discussion in Sections X and XI where relevant.

Regarding the conditions of approval recommended by Panel, it was determined that based on the similarities in design between the TICL and its parent MICL lens, the safety data collected during the pivotal trial and subsequent post approval studies (PAS) for the MICL were also applicable to the TICL lens. As a result, it was determined that the only PAS required as a condition of approval would be to evaluate rotational stability of the lens. See Section XIV for further details.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

a. Effectiveness Conclusions

The effectiveness outcomes reported during the Visian® TICL Clinical Investigation support the overall effectiveness of Visian® TICL implantation for the correction of moderate to high myopic astigmatism; the results are provided in Table 25.

Table 25: Summary of Effectiveness Variables

	12 Months Postoperative	Effectiveness Target
Decrease in Manifest Cylinder from Baseline		
Mean Decrease (paired anlaysis) n=194	1.43 D	NA
Decrease in MRSE from Baseline		
Mean Decrease (paired anlaysis) n=194	9.41 D	NA
UCDVA		
20/20 or better	158/193 (81.9%)	NA
20/40 or better	184/193 (95.3%)	NA
UCDVA (eyes with preoperative BCDVA 20/20 or better)		
20/20 or better	142/159 (89.3%)	NA
20/40 or better	159/159 (100%)	85%
Predictability of Manifest Cylinder; Accuracy of Attempted vs. Achieved		
± 0.50 D	135/194 (69.6%)	40%
± 1.00 D	179/194 (92.3%)	65%
Predictability of MRSE; Accuracy of Attempted vs. Achieved		
± 0.50D	149/194 (76.8%)	50%
± 1.00D	189/194 (97.4%)	75%

Reduction in manifest cylinder and manifest MRSE from pre-implantation status were clinically significant at 12 months. The reduction in manifest cylinder from baseline to 12 months was statistically significant ($p<0.001$) as per the protocol-defined hypothesis test (paired t-test). The reduction in MRSE exceeded 9 diopters and was clinically significant.

The 12 month results for UCDVA show high proportions of eyes achieving good levels of acuity. Similarly, the 12 month study results for predictability (accuracy)

of the manifest cylinder and MRSE show that most eyes achieved acceptable accuracy in the refractive correction.

The Visian® TICL study effectiveness results met all specific protocol-defined requirements, as noted above. In addition, stability of refractive outcomes and ICL rotational stability were found to be adequate based upon the data provided.

b. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies as well as data collected in clinical studies conducted to support PMA and PMA Supplement approvals as described above. Note that the toric ICL is only an optical modification of the parent myopia ICL device (approved December 22, 2005), and almost all risks should be similar for the two lenses. The U.S. premarket clinical trial data from the study of the myopia ICLs is the primary source of data supporting the safety of the Visian® TICL. As highlighted in Table 26, safety outcomes reported during the Visian® TICL clinical investigation provides additional support for the safety of the Visian® TICL for the correction of moderate to high myopic astigmatism.

Preservation of BCDVA was a key safety endpoint. The overall incidence of postoperative BCDVA worse than 20/40 in the subset of eyes in the Visian® TICL Study Cohort with preoperative best corrected vision of 20/20 or better was 0.0% (0/159). Additionally, at six months or later after Visian® TICL implantation, only 1.5% (3/194) of eyes had lost two or more lines of BCDVA (1.0% (2/194) lost 2 lines and 0.5% (1/194) lost > 2 lines), which is lower than the Protocol Target (< 5% of eyes with a $\geq$ 2 Line Loss).

The incidence of adverse events during the Visian® TICL clinical study included no cases of endophthalmitis, corneal ulcers, ocular hypertension, corneal haze/edema (after one week) or corneal melting. One case each (0.5%)(1/210) of retinal detachment, pupillary block and anisocoria were reported.

Table 26: Summary of Safety Variables

Variable Change	12 Month Result n/N (%)	Protocol Targets
Postoperative BCDVA worse than 20/40 if 20/20 or better preoperative	0/159 (0.0%)	≤ 1%
Loss of 2 Lines BCDVA	2/194 (1.0%)	< 5%
Loss of > 2 Lines BCDVA	1/194 (0.5%)	< 5%
ICL Repositioning	1/210 (0.5%)	NA
ICL Replacement, then Removal	0/210 (0%)	NA
ICL Replacement	1/210 (0.5%)	NA
ICL Removal no IOL or ICL replacement	3/210 (1.4%)	NA
ICL Removal/Cataract Extraction/IOL	0/210 (0%)	NA
Additional YAG Iridotomy	3/210 (1.4%)	NA
Total Surgical Reintervention	8/210 (3.8%)	NA
Anterior Subcapsular including clinically significant cataracts	6/210 (2.9%)	NA
Clinically Significant Anterior Subcapsular Cataracts	2/210 (1.0%)	NA
Pupillary Block	1/210 (0.5%)	NA
IOP > 10mm Hg Increase from Preoperative[1]	1/210 (0.5%)	NA
Endophthalmitis	0/210 (0%)	NA
Corneal Haze/Edema after 1 week postoperative	0/210 (0%)	NA
Retinal Detachment	1/210 (0.5%)	NA
Anisocoria	1/210 (0.5%)	NA

[1] Includes IOP from unscheduled visits 3 months or later postoperative.

Implantation of the TICL in the ciliary sulcus of phakic eyes of patients with moderate to high myopic astigmatism is associated with most of therisks that are associated with general posterior chamber IOL implantation in the capsular bag for patients with aphakia (e.g., intraocular infection, inflammation, corneal edema). However, because of the higher myopia of the TICL patients, the presence of the crystalline lens, and the different position of the TICL, there are additional increased risks of cataract, narrowing of the anterior chamber after implantation, pupillary block, raised intraocular pressure requiring treatment, retinal detachment (due to the greater rate of high myopia), and substantially increased rates of secondary surgical interventions to treat these problems and for lens removal or repositioning.

Note that the previously approved parent len(MICL) has been studied in pre-approval of a large number of eyes with 3 years of follow-up, and has been studied in a post-approval study through 60+ months of follow-up. Non-clinical and clinical data support the conclusion that the risks of the TICL and MICL should be similar. In the post-approval study for the MICL, rates of cataract, including those of anterior subcapsular cataract slowly increased in incidence throughout the follow-up of 60+months. The MICL study data also indicated an increased rate of chronic corneal endothelial cell loss. In the MICL post-approval study, at 60^{+} months post-opertatively 13/115 eyes (11.3%) had ≥30% loss of central endothelial cell density from the preoperative visit.

In conclusion, safety outcomes for the Visian® TICL are consistent with the approved parent Visian® MICL.

c. <u>Benefit-Risk Determination</u>

The probable benefits of the device are based on data collected in clinical studies conducted to support PMA approvals as described above. Over the course of the 12 month study, the cohort of all TICL-implanted eyes available at the final 12 month visit (194 eyes) went from a mean MRSE of -9.34 diopters to a mean MRSE of 0.03 diopters. The same cohort went from a mean manifest cylinder of 1.95 diopters to 0.52 diopters. Clinically speaking, these are large reductions. At 12 months, 76.8% (149/194) of these eyes were within 0.50 diopters of their target MRSE and 69.6% (135/194) were within 0.50 diopter of their target manifest cylinder, with >90% within 1.00 diopter of the target for each refractive outcome. For all implanted eyes with pre-operative BCDVA at least 20/20, 89.3% (142/159) at 12 months postoperatively had UCDVA of 20/20 or better. The duration of the benefit should be long term.

The TICL for correction of myopic astigmatism is only an optical modification (addition of a toric surface) of the Visian® MICL (parent lens for myopia correction). The clinical and preclinical data indicate that the risk profile of the TICL is similar to that of the approved MICL.

Additional factors to be considered in determining probable risks and benefits for the Visian® TICL device included:

- In pre-approval and long-term follow-up post-approval clinical studies, use of the parent MICL is associated with an increased rate of chronic corneal endothelial cell loss. However, these studies have had no reports of corneal decompensation or vision loss related to endothelial cell loss. The TICL should have the same concerns. The increased rate of chronic corneal endothelial cell loss is mitigated by a contraindication against implantation in patients with lower baseline densities, and by a Warning stating that patients' endothelial cell densities should be monitored periodically, for as long as they remain implanted with the TICL.
- The Visian® MICL (parent lens for myopia correction) has been commercially available in the U.S. market since December 22, 2005 and outside the U.S. in over 50 countries and has not been withdrawn from any market. Approximately 227,000 Myopic Implantable Collamer Lenses have been implanted outside the U.S.
- The Visian® TICL has been commercially available outside of the U.S. in over 50 countries and has not been withdrawn from any market. Approximately 104,000 Toric Myopic Implantable Collamer Lenses have been implanted outside the U.S.
- The results of the TICL pivotal clinical trial appear to be generalizable to the intended patient population.

1. **Patient Perspectives**

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for use in patients 21-45 years of age:

1. for the correction of myopic astigmatism with spherical equivalent ranging from -3.0D to ≤ -15.0D (in the spectacle plane) with cylinder (spectacle plane) of 1.0D to 4.0D.
2. for the reduction of myopic astigmatism with spherical equivalent ranging from greater than -15.0D to -20.0D (in the spectacle plane) with cylinder (spectacle plane)1.0D to 4.0D.
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 0.5D for both spherical equivalent and cylinder for 1 year prior to implantation).
4. for placement in the posterior chamber (ciliary sulcus) of the phakic eye.

the probable benefits outweigh the probable risks.

This conclusion is further supported by the deliberations and voting results of the Ophthalmic Devices Advisory Committee members. Although the clinical study included protocol deviations, missing data, and out of window visits, the panel members found the data supported the conclusion that the Visian® Toric ICL provides a reasonable assurance of safety and effectiveness, and the benefits outweigh the risks when used in accordance with the proposed indications.

d. Overall Conclusions

The data and information provided in PMA P030016-S001 supports the safety and effectiveness of the Visian® TICL when used in accordance with the indications for use. This builds upon the larger body of safety data from the parent Visian® MICL presented in PMA P030016 and is supported by the worldwide clinical experience with over 700,000 Visian® TICLs and Visian® MICLs implanted.

The U.S. FDA clinical trial data from the approved myopia study with spherical ICLs is the primary source of data supporting the safety of the Visian® TICL. The safety outcomes reported during the Visian® TICL Clinical Investigation provide additional support for the safety of the Visian® TICL for the correction of moderate to high myopic astigmatism. All primary safety outcomes with the Visian® TICL were better or comparable to those previously reported with the FDA-approved Spherical Visian® MICL.

The effectiveness outcomes reported during the Visian® TICL Clinical Investigation support the overall effectiveness of Visian® TICL implantation for the correction of moderate to high myopic astigmatism. The data show that the Visian® TICL exceeds the targets in the protocol.

The benefits outweigh the risks for the Visian® TICL for the treatment of moderate to high myopia with astigmatism. This conclusion is supported by 1) the results from this clinical study and 2) the results from the extensive clinical results for the Visian® TICL from around the world in over 50 countries since 2002, and 3) the deliberations and voting results of the Ophthalmic Devices Advisory Panel members.

XIII. CDRH DECISION

CDRH issued an approval order on September 13, 2018. The final conditions of approval cited in the approval order are described below.

This new enrollment study will be conducted as per the protocol agreed upon between FDA and STAAR Surgical. The study protocol outline is as follows:

STAAR Surgical will conduct a prospective, multicenter, open-label, single arm, new enrollment post-approval study, designed to evaluate the long-term safety and

effectiveness of the Visian® TICL A total of 124 subjects (up to 248 eyes, with 124 being primary), will be enrolled at 6-8 clinical sites in the USA. One hundred (100) subjects (assuming an overall attrition of 10% per year) will be available for evaluation at 24 months after implantation. A minimum of 14 subjects requiring a Toric ICL cylinder power of 3.5 or 4.0 diopters will be enrolled. Study subjects will be followed at Day 0, Day 1, Week 1, Month 1, 3, 6, 12, 18, and 24 postoperatively.

The primary study endpoint is to evaluate the long-term rotational stability as determined relative to objective landmarks on the eye. The performance goal is to detect if at least 90% of the treated eyes rotate less than or equal to five degrees between 18 and 24 months postoperative. The secondary study 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, and Postoperative manifest refraction spherical equivalent and cylinder at each visit. The 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. 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. Ocular adverse event (AE) rates assessed in implanted eyes will be estimated.

The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

Hazards to Health from Use of the Device: See Indications, Contraindications, Warnings, Precautions, and Adverse Events in the device labeling.

Post-approval Requirements and Restrictions: See approval order.