

SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Intraocular Lens

Device Trade Name: RayOne EMV Toric

Model Number: RAO210T

Device Procode: HQL, MJP

Applicant's Name and Address: Rayner Intraocular Lenses Limited
The Ridley Innovation Centre
10 Dominion Way, Worthing, West Sussex
BN14 8AQ, United Kingdom

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P060011/S039

Date of FDA Notice of Approval: TBD

The C-flex™ intraocular lens (IOL; model 570C) is the parent device, approved in P060011 on May 3, 2007. RayOne EMV Toric is a modification to the approved parent device by introducing a toric surface to the lens to provide a reduction of residual refractive astigmatism in adult patients with greater than or equal to 1.00 diopters (D) of corneal astigmatism, compared to a monofocal IOL. The C-flex™ was approved with the following Indications for Use (IFU) statement: The Rayner C-flex™ intraocular lens is indicated for primary implantation for the visual correction of aphakia in adults in whom a cataractous lens has been removed by phacoemulsification. The lens is intended to be placed in the capsular bag. The SSED supporting the original indication is available on the CDRH website.

II. INDICATIONS FOR USE

The RayOne EMV Toric (Model RAO210T) consists of the EMV Toric IOL (210T) preloaded within the RayOne injection system (RAO). The EMV Toric IOL is intended for primary implantation in the capsular bag of the eye for the visual correction of aphakia, in adult patients in whom a cataractous

lens has been removed by phacoemulsification and providing reduction of residual refractive astigmatism in adult patients with greater than or equal to 1.00 diopter (D) of corneal astigmatism The RayOne injection system is used to fold and assist in inserting the IOL into the eye.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the RayOne EMV Toric labeling.

V. DEVICE DESCRIPTION

Rayner intraocular lenses (IOLs) are single piece optical devices, manufactured from Rayacryl (hydroxyethyl methacrylate/methyl methacrylate copolymer with UV blocker). These devices are designed to be surgically implanted in the human eye as a replacement for the crystalline lens and are intended for placement in the capsular bag following phacoemulsification.

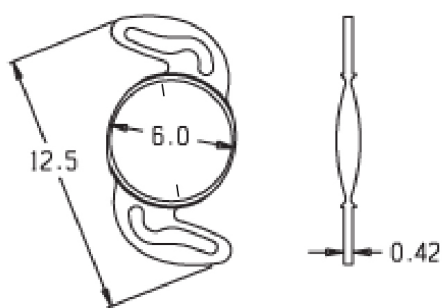
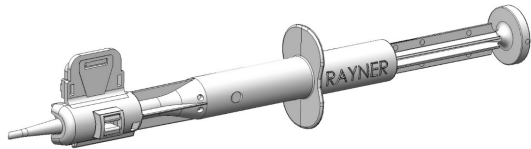
Rayner IOLs are intended to provide adjustment to the dioptric power of the eye. Toric models are intended to provide adjustment to the astigmatism of the eye.

The RayOne EMV Toric (RAO210T) has an aspheric posterior surface designed to control the spherical aberration of the IOL; this lens is designed to have positive spherical aberration and is intended to add to the positive spherical aberration of the cornea. This addition to positive spherical aberration is controlled with pupil size and smooth transitions to negative spherical aberration towards the edge of the optic to prevent excessive positive spherical aberration reducing image quality at larger pupil sizes. In addition, RayOne EMV Toric (Model RAO210T) is intended to provide adjustment to the astigmatism of the eye.

The RayOne injection system is a Fully Preloaded system that delivers a 6 mm optic diameter lens into the eye through a micro incision. The RayOne injector is designed to mechanically fold a lens and insert it into the eye during routine cataract surgery.

The physical characteristics of RayOne EMV Toric are shown in **TABLE 1**.

TABLE 1 RAYONE EMV TORIC PHYSICAL CHARACTERISTICS

Characteristic	RayOne EMV Toric
Lens image	Front view of IOL and side view of IOL All dimensions in mm 
Injector image	
Lens material	Rayacryl

Characteristic	RayOne EMV Toric
Injector material	Polypropylene & TPE
Design features	Aspheric, Toric, Monofocal capsular bag fixated
Injection system	Fully preloaded
Overall diameter (mm)	12.5 ± 0.2
Optic diameter (mm)	6.0 ± 0.1
Limb width (mm)	0.38 ± 0.1
Limb thickness (mm)	0.41 ± 0.15
Haptic style	Closed C-loop
Square edge	360° posterior Enhanced Square Edge
Sphere power range (increments)	+7.75 to 23.875 D
Spherical equivalence (increments)	+10 to 25 D (0.5 D)
Cylinder power range (increments)	+1.5 to 4.5 D (0.75 D)
Index of refraction	1.46

The effective corneal powers for each of the test lens plane cylindrical powers of the test IOLs are shown in **TABLE 2**.

TABLE 2 CYLINDER POWER AND CORNEAL ASTIGMATISM CORRECTION RANGE

IOL Type	IOL Power at IOL Plane (D)	Cyl Power on Corneal Plane (D)	Specified Range (D) Lower	Specified Range (D) Upper
T3	1.5	1.03	1.03	1.53
T4	2.25	1.54	1.54	2.04
T5	3	2.05	2.05	2.56
T6	3.75	2.57	2.57	3.07
T7	4.5	3.08	3.08	3.59

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for restoring functional vision of the aphakic eye. Non-surgical options include special cataract glasses or contact lenses. Surgical options such as monofocal, multifocal, simultaneous vision or accommodative IOLs are also available. 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 RayOne EMV Toric has not been marketed in the United States. This product has been available in the European Union since receiving CE Mark in September 2022. Since launch, there have been no recalls of RayOne EMV Toric (Model RAO210T). Additionally, there are no countries where the device has been removed from the market for any reason(s) related to the safety or effectiveness of the device.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device:

- Secondary glaucoma
- IOL replacement or extraction
- Precipitates
- Reduced vision
- Vitreous herniation
- Excessive intraoperative vitreous loss
- IOL decentration
- Secondary membrane
- Expulsive hemorrhage
- IOL dislocation and subluxation
- Retrolenticular membrane
- Corneal edema
- Endophthalmitis and panophthalmitis
- Retinal detachment
- Corneal dystrophy
- Hemorrhage
- Iris atrophy
- Pupillary block
- Cystoid macular edema
- Severe ametropia and aniseikonia
- Iridocyclitis and hyalitis
- Deviation from target refraction
- Fibrin reaction.

Secondary surgical interventions include, but are not limited to, lens repositioning, lens replacement, vitreous aspiration or iridectomy for pupillary block, wound leak repair, and retinal detachment repair.

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

IX. SUMMARY OF NON-CLINICAL STUDIES

The RayOne EMV Toric (Model 210T) is composed of identical materials to the currently approved family of hydrophilic Rayacryl intraocular lenses (P060011). Non-clinical studies were performed on the material parent device (P060011) instead of the final proposed device. These tests are as follows: physicochemical and biocompatibility testing, sterilization, packaging, shelf-life, and transport stability testing.

Physicochemical Testing

The results of physicochemical testing are shown in **TABLE 3**.

TABLE 3 PHYSICOCHEMICAL TESTING

Test	Purpose	Acceptance Criteria	Results
ISO 11979-5 Exhaustive Extraction	Soxhlet extraction to recover polymerization residuals, impurities, and additives, quantitative analysis of extracts	No prespecified acceptance criteria. The results shall be evaluated to assess the risk for potentially harmful effects due to extractable components.	Performed
ISO 11979-5 Leachable study	The IOL material was extracted at 35°C for 72 h with water and hexane, respectively. The extracts were analysed for potential leachables.	No prespecified acceptable criteria The results shall be evaluated to assess the risk for potentially harmful effects due to leachable components.	Performed
ISO 11979-5 Test for Hydrolytic Stability	Test to verify material does not degrade by hydrolysis	Hydrolytic stability of IOLs by investigation of dioptric power, recording of transmission spectra, light microscopic inspection and scanning electron microscopic (SEM) inspection. The exposure medium shall be qualitatively and quantitatively analysed for any chemical entities at the end of the exposure period.	Pass
ISO 11979-5 Photostability test	Exposure to UV radiation in a saline solution using a radiation source (Xenon arc lamp) in order to simulate an in vivo exposure time of 20 years to evaluate the photostability.	The investigated lens material stable against ultraviolet/visible light exposure. No significant change shall be detected between the physical appearance, UV/Vis spectra, dioptric power and image quality of the test	Pass

Test	Purpose	Acceptance Criteria	Results
		material exposed to UV radiation and controls receiving no radiation. The exposure medium shall be qualitatively and quantitatively analysed for any chemical entities after irradiation and compared to non-irradiated controls.	
ISO 11979-5 Nd-YAG laser exposure test	To confirm IOL sample's stability when exposed to Nd:YAG lasers, and leakage of cytotoxic compounds.	No significant difference in physical appearance, spectral transmittance, or dioptric power after the exposure. No cytotoxic substances after laser exposure were detected. The exposure medium shall be qualitatively and quantitatively analysed for any chemical entities after laser exposure.	Pass
ISO 11979-5 Evaluation of insoluble inorganics	To assess the IOL material for the presence of residual insoluble inorganics on and in the lens arising from manufacturing materials and process aids.	No prespecified acceptance criteria. Quantitative determination of the inorganic ions presents in the test material.	Performed

Biocompatibility Testing

The RayOne EMV Toric (Model RAO210T) is made of the same material that was used with previously approved hydrophilic Rayacryl intraocular lenses (P060011).

Biocompatibility testing (**TABLE 4 BIOCOMPATIBILITY TESTING**) was performed to support P060011 in accordance with all relevant ISO Standards (ISO 11979-5 and ISO 10993-1), as well as the United States Food and Drug Administration. Use of International Standards ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process".

All tests to evaluate the biocompatibility were conducted in accordance with provisions of 21 CFR 58, Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies.

TABLE 4 BIOCOMPATIBILITY TESTING OF THE EMV TORIC (MODEL RAO210T)

Test	Purpose	Acceptance Criteria	Result
Intraocular Lens*			
Cytotoxicity - MEM elution (ISO 10993-5, ISO 11979-5)	To evaluate the potential for cellular toxicity.	Non-cytotoxic	Pass

Test	Purpose	Acceptance Criteria	Result
Cytotoxicity - Inhibition of Cell Growth Test (ISO 10993-5)	To evaluate the potential for cellular toxicity.	Non-cytotoxic	Pass
Cytotoxicity – Agarose Overlay (ISO 10993-5, ISO 11979-5)	To evaluate the potential for cellular toxicity.	Non-cytotoxic	Pass
Sensitization - Guinea Pig Maximization (ISO 10993-10, ISO 11979-5)	To assess dermal contact sensitization in guinea pig at 24 and 48 hours after patch removal.	Non-sensitizer	Pass
Sensitization - Magnusson-Kligman Maximization Test (ISO 10993-11)	To investigate delayed contact hypersensitivity of the IOL in guinea pigs.	Non-sensitizer	Pass
Ocular Irritation Study in Rabbits (ISO 10993-10)	To evaluate the potential for ocular reactions at 1, 24, 48 and 72 hours after the single exposure in rabbits.	Non-irritant	Pass
Acute Toxicity (Limit-Test) (ISO 10993-11)	To evaluate the potential for acute toxicity in rats.	Non-toxic	Pass
Genotoxicity - Mouse Peripheral Blood Micronucleus Study (ISO 10993-3, ISO 11979-5)	To evaluate the potential to produce cytogenetic damage, resulting in micronuclei formation.	No micronuclei formation	Pass
Genotoxicity - In vitro chromosome aberration test (ISO 10993-3, ISO 11979-5)	To determine genotoxic potential in Chinese hamster ovary.	Non-genotoxic	Pass
Genotoxicity - Mouse Lymphoma Assay (ISO 10993-3, ISO 11979-5)	To detect potential gene mutations or chromosomal damage.	Non-genotoxic	Pass
Genotoxicity – Mutagenic activity (ISO 10993-3, ISO 11979-5)	To evaluate mutagenic activity.	Non-mutagenic	Pass

Note: In vivo ‘Test for Local Effects’ (non-ocular) and ‘Ocular Implantation’ test is deemed unnecessary for RayOne Family of hydrophilic IOL devices, considering that they are manufactured from a raw material with extensive historical clinical use. (Based on the recommendations of ISO 10993-1; and as per ISO 11979-5:2020, the risks arising from the use of the material are deemed acceptable based on the information from previous clinical use and other relevant literature.)

Biocompatibility testing (**TABLE 5**) was performed on the patient-contacting components of the RayOne injection system.

TABLE 5 BIOCOMPATIBILITY TESTING OF RAYONE INJECTION SYSTEM

Test	Purpose	Acceptance Criteria	Result
Cytotoxicity - Growth Inhibition Test in L929 Mouse Fibroblasts (Elution Test) (ISO 10993-5)	To evaluate the potential for cytotoxic effects using an in vitro mammalian cell culture test.	Non-cytotoxic	Pass
Systemic Toxicity – Acute Systemic Toxicity (in Swiss Albino Mice) (ISO 10993-11)	To evaluate toxic characteristics.	Non-toxic	Pass
Sensitization - Guinea Pig Maximization Sensitization Test (ISO 10993-10)	To evaluate the potential for sensitization.	Non-sensitizer	Pass
Sensitization - Test for delayed-type hypersensitivity (Guinea Pig Maximisation Test) (ISO 10993-10)	To evaluate the potential for sensitization.	Non-sensitizer	Pass
Intracutaneous Reactivity Testing in Rabbits (ISO 10993-10)	To evaluate the potential for irritation.	Non-irritant	Pass
Intraocular Irritation Study in Rabbits (ISO 10993-10)	To evaluate the potential for irritation.	Non-irritant	Pass

Optical and Mechanical Testing

The optical properties of the Model 210T were tested per “ISO 11979-2: Ophthalmic implants – Intraocular lenses: Optical properties and test methods and ANSI Z80.30: Toric intraocular lenses.” The mechanical properties were tested per “ISO 11979-3: Ophthalmic implants – Intraocular lenses: mechanical properties and test methods.” In cases where the mechanical properties were related to the Rayacryl® material and overall IOL design (e.g. haptic design, optic body diameter), the testing is being leveraged from the parent device the Model 600C for the Model 210T, since both IOL models are manufactured from the same Rayacryl® material and are identical in non-optical design features (i.e. only differ by anterior and posterior optical surface design).

Testing was performed on lenses representing the low, the medium and the high diopter ranges: (spherical equivalent power (SE) = +10.0 D with cylinder = 0.75 D; SE = +20.0 D with cylinder = 0.75 D; SE = +25.0 D with cylinder = 0.75; SE = + 10.0 with cylinder 4.50; SE = + 20.0 with cylinder 4.50 D and SE = + 25.0 D with cylinder = 4.50 D.). The results of the testing demonstrate that the Model 210T meets the ISO and ANSI standards for optical and mechanical properties. The results of the testing demonstrate that the Model 210T meets all of the ISO and ANSI standards for optical and mechanical properties, as summarized in **TABLE 6** and **TABLE 7**.

TABLE 6 SUMMARY OF OPTICAL TESTING FOR RAYONE EMV TORIC – ISO 11979-2 & ANSI Z80.30

Test	Purpose	Acceptance Criteria	Results
BS EN ISO 11979-2 Clauses 4.2.2 - Dioptric power for toric IOL (TIOL) – Average Power (SE) 4.2.2 - Dioptric power for toric IOL (TIOL) – Cylinder Power	To assess conformance to optical power tolerances (post injection*)	$+10.0 \leq SE \leq +15.0$ D: ± 0.3 D $+15.0 < SE \leq +25.0$ D: ± 0.4 D $SE < 25$ D and $0 < C \leq 2.5$: ± 0.3 D $SE < 25$ D and $2.5 < C \leq 4.5$: ± 0.4 D	Passed
BS EN ISO 11979-2 Clause 4.3.3 - Determination of imaging quality - Toric IOL (TIOL)	To assess conformance to image quality tolerances (post injection*)	MTF (modulation transfer function) measurement >0.43 100% Pass	Passed
BS EN ISO 11979-2 Clause 4.2.2 – Axis marks for toric IOL (TIOL)	To determine axis marks align with the meridian of lowest dioptric power.	$\leq 5^\circ$	Passed
BS EN ISO 11979-2 Spectral transmittance	To characterize the spectral transmission in the range 300 nm to 1100 nm, and the 10% cutoff wavelength	≥ 380 nm	Passed

TABLE 7 SUMMARY OF MECHANICAL TESTING FOR RAYONE EMV TORIC - ISO 11979-3

Mechanical Test	Purpose	Acceptance Criteria	Results
BS EN ISO 11979-3:2012 Clause 4.4 Compression force	To characterize the mechanical force exerted by the IOL haptics under compression initially	BS EN ISO 11979-3:2012: Measure and Report	Passed
BS EN ISO 11979-3:2012 Clause 4.5 Axial displacement in compression	To characterize the axial displacement of the IOL under compression	BS EN ISO 11979-3:2012: Measure and Report	Passed

Mechanical Test	Purpose	Acceptance Criteria	Results
BS EN ISO 11979-3:2012 Clause 4.6 Optic Decentration	To assess optic decentration under compression	$(\bar{X} + 2\sigma) < 10\%$ Clear Optic Diameter	Passed
BS EN ISO 11979-3:2012 Clause 4.7 Optic Tilt	To assess optic tilt under compression	$(\bar{X} + 2\sigma) < 5^\circ$	Passed
BS EN ISO 11979-3:2012 Clause 4.8 Angle of Contact	To characterise angle of contact of haptics under compression	Measure and Report	Passed
BS EN ISO 11979-3:2012 Clause 4.9 Compression Force Decay	To characterize the mechanical force exerted by the IOL haptics under compression after 24 hours	Measure and Report	Passed
BS EN ISO 11979-3:2012 Clause 4.10 Dynamic Fatigue Durability	To assess the capability of the haptics to cyclic compressive displacement	Withstand 250,000 cycles without damage	Passed
BS EN ISO 11979-3:2012 Clause 4.11 Surgical Manipulation	To assess the force required to separate the haptic from the IOL body	Force $> 0.25\text{N}$	Passed
BS EN ISO 11979-3:2012 Clauses 4.12 and 5(a) Surface and Bulk Homogeneity * IOL injections of the pre-loaded IOL through RayOne injector performed with OphteisBio 3.0%, a sodium hyaluronate OVD.	To ensure the IOL is free of surface and bulk defects	The IOL shall be essentially free from defects	Passed
BS EN ISO 11979-3:2012 Clause 5 (b) Overall Diameter and Sagitta	To assess conformance to dimensional tolerances	Overall Diameter $\pm 0.20\text{ mm}$ Sagitta $\pm 0.35\text{ mm}$	Passed

*Each 210T is optically tested and inspected for Surface and Bulk Homogeneity prior to packaging and loading into the delivery system as part of standard manufacturing quality control. These measurements confirm compliance with ISO 11979-2 requirements for Dioptric Power and Imaging Quality, and compliance with ISO 11979-3 requirements for Surface and bulk Homogeneity Pre-Injection. Post-injection testing was performed to confirm compliance with ISO 11979-2 and ISO 11979-3 requirements, to verify the integrity of the delivery system and ensure clinical performance.

Injector Validation

Injector validation was conducted as part of the mechanical and optical testing of the EMV Toric, including the visual inspection of the IOL and injector pre-and post-injection. The test results summarized above reflect the compatibility of the RayOne injector and EMV Toric IOL.

The testing demonstrated that the EMV Toric IOL can be successfully delivered across the entire range of IOLs using OphteisBio 3.0% viscoelastics.

Sterilization and Shelf-Life Evaluation

The RayOne EMV Toric is moist heat sterilized. Sterilisation evaluation, shelf-life and transport stability testing, and bacterial endotoxin testing were performed to support the RayOne EMV Toric. The results are summarized in **TABLE 8**.

TABLE 8 SHELF-LIFE TESTING

Test	Purpose	Acceptance Criteria	Results
Moist heat sterilisation validation (Overkill method) (ISO 17665-1, ISO 17665-2 & ISO 17665-3)	Determination of process parameters for routine sterilisation of product, and demonstration that these process parameters can adequately achieve a Sterility Assurance Level (SAL) of 1.0E-6, based upon inactivation of control biological indicators (BIs, <i>G. stearothermophilus</i>) in process challenge devices (PCDs). Validated process parameters will be used for parametric release upon confirmation that Independent Recorder and controller meet batch release requirements.	Successful performance of Installation Qualification (IQ), Operational Qualification (OQ) and both Microbiological and Physical Performance Qualification (PQ) studies. The Microbiological PQ study requires total inactivation of BIs upon exposure to a half-cycle (e.g., half of the routine full-cycle exposure time) that meets the designated parameters. The Physical PQ study requires that routine full-cycle parameters can be achieved with minimum and maximum sterilisation loads. Together these PQ results will demonstrate the routine sterilisation process can achieve an SAL $\leq$ 1.0E-6.	Passed

Test	Purpose	Acceptance Criteria	Results
Transport stability (ISO 11979-6, ISO 11607-1, ASTM F1886, ASTM D4991, ASTM F1929, ASTM F88, & ASTM F1140)	Confirm that both the inner tray and outer pouch sterile barrier packaging can maintain device sterility throughout anticipated transport conditions. Testing includes visual inspection, whole package integrity (dye immersion – weight change, validated alternative method) and seal integrity assessments (seal peel and dye penetration testing for inner tray; burst test and dye penetration for outer pouch) after transport conditioning.	Meets sterile barrier packaging visual inspection, whole package integrity & seal integrity requirements. For visual inspection, no channels, voids, punctures, or breaches observed, and labels are legible. For dye immersion, - weight change, there is no reduction in weight of the inner tray after it is held under vacuum for 30 minutes in vacuum chamber. For seal peel strength, average peel strength exceeds minimum force. For burst test, internal pressure exceeds minimum burst pressure before package failure. For dye penetration, no penetration of dye into seal area is observed.	Passed
Shelf-life (ISO 11979-6, ISO 11607-1, ASTM F1886, ASTM D4991, ASTM F1929, ASTM F88, & ASTM F1140)	Confirm that both the inner tray and outer pouch sterile barrier packaging can maintain device sterility throughout claimed shelf life. Testing includes visual inspection, whole package integrity (dye immersion– weight change, validated alternative method) and seal integrity assessments (seal peel and dye penetration testing for inner tray; burst test and dye penetration for outer pouch) after aging (both accelerated aging and real-time aging conditions).	Meets sterile barrier packaging visual inspection, whole package integrity & seal integrity requirements. For visual inspection, no channels, voids, punctures, or breaches observed, and labels are legible. For dye immersion, - weight change, there is no reduction in weight of the inner tray after it is held under vacuum for 30 minutes in vacuum chamber. For seal peel strength, average peel strength exceeds minimum force. For burst test, internal pressure exceeds minimum burst pressure before package failure. For dye penetration, no penetration of dye into seal area is observed.	Passed
Bacterial Endotoxin Testing (ANSI/AAMI ST72, USP<85>, FDA Guidance on Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices)	Confirm that Endotoxin present on product is below the permanent intraocular device limit to confirm product is non-pyrogenic.	≤ 0.2 Endotoxin Units (EU)/device	Passed
Bioburden Estimation Testing (ISO 11737-1)	Confirm that naturally occurring Bioburden is controlled on product and in manufacturing environment.	Less than the Specification Limit of < 100 Colony Forming Units (CFU)/device	Passed

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of subjects undergoing cataract extraction and IOL implantation with the RayOne EMV Toric, Model RAO210T for primary implantation in the capsular bag of the eye in adult subjects for visual correction of aphakia and corneal astigmatism following removal of a cataractous lens for improved uncorrected distance vision in the US under IDE # G230072. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

Subjects were treated between August 10, 2023, and June 19, 2024. The database for this Panel Track Supplement reflected data collected through October 23, 2024, and included 274 subjects. There were 9 investigational sites.

This study was a prospective, multi-center, randomized, active controlled, masked (assessor and subject) clinical study for unilateral implantation of low cylinder (1.50 D) toric IOL.

Subjects who met all protocol-specified eligibility criteria were to be randomized to receive either the Rayner RAO210T Toric IOL (1.50 D low cylinder) or the Rayner RAO600C aspheric monofocal IOL in the study eye according to a 1:1 ratio if the study eye's estimated IOL cylinder power using Barrett Toric Calculator was 1.50 D.

If a subject had significant cataract in both eyes, it was recommended that cataract surgery be performed in one eye before the subject enrolled in the study. Once a subject was enrolled, it was also recommended that the fellow eye not undergo cataract surgery (except for a YAG capsulotomy) throughout the duration of the study. At screening, if both eyes qualified for the study, the eye to undergo cataract surgery and IOL implantation was the eye with worse pre-operative best corrected distance visual acuity (BCDVA). If pre-operative BCDVA was the same for each eye, the right eye was to be the study eye.

Subjects completed 6 study visits between the pre-operative visit to completion of Visit 4 (120 to 180 days post-operative).

Nine (9) U.S. sites were to be encouraged to enroll a minimum of 20 subjects in the study. No site could enroll more than 25% of the subjects enrolled in the study.

The control group was treated with Rayner RAO600C aspheric monofocal IOL..

Study sample size was based on the ANSI Standard for Toric IOLs, Z80.30, as well as ISO 11979-7 requirements for a modification of a parent lens, which specify a minimum of 100 evaluable implanted subjects.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the RayOne EMV Toric study was limited to patients who met the following inclusion criteria.

All ocular criteria must have been met in the eye receiving the study lens (only one eye was to be enrolled):

- 1) Male or female, 22 years or older at the pre-operative visit who have cataract with best corrected distance visual acuity of 0.30 logMAR (20/40) or worse in at least one eye with or without a glare source present who are eligible for phacoemulsification cataract surgery
- 2) Subjects who are projected to have best corrected distance visual acuity 0.20 logMAR (20/30) or better after IOL implantation by potential acuity meter (PAM) or Investigator estimation
- 3) Clear intraocular media other than cataract
- 4) Contact lens wearers must demonstrate stability of biometry
- 5) Have the capability to understand and sign an IRB approved informed consent form and privacy authorization in accordance with local regulations
- 6) Female subjects must be 1-year postmenopausal, surgically sterilized, or, if of childbearing potential, have a negative urine pregnancy test at the Pre-operative Visit. Women of childbearing potential must use an acceptable form of contraception throughout the study.
Acceptable methods included at least one of the following: intrauterine (intrauterine device), hormonal (oral, injection, patch, implant, ring), barrier with spermicide (condom, diaphragm), or abstinence.
- 7) Have Investigator selected IOL spherical equivalent power between +10.0 D to +25.0 D in 0.5 D steps and IOL cylinder power of +1.50 D
- 8) Have pre-existing corneal astigmatism of 1.00 D to 1.50 D as determined by keratometry
- 9) Dilated pupil size 5.5 mm or greater to allow visualization of the toric IOL axis markings post-operatively

Patients were not permitted to enroll in the RayOne EMV Toric study if they met any of the following exclusion criteria:

The ocular exclusion criteria applied to both eyes, unless otherwise noted as only the planned operative eye:

- 1) Previous intraocular, corneal, or retinal detachment surgery, including corneal transplant, LASIK / LASEK / PRK, SMILE, astigmatic keratotomy and limbal relaxing incisions in the planned operative eye.
- 2) Diagnosed degenerative visual disorders (e.g., macular degeneration, retinal detachment, proliferative diabetic retinopathy, or other retinal disorders) that

are predicted to cause future acuity losses to a level of 0.20 logMAR (20/30) or worse

- 3) Significant anterior segment pathology that might increase intraoperative risk or compromise IOL stability (e.g., pseudoexfoliation syndrome, any iris pathology)
 - 4) Subjects with conditions associated with increased risk of zonular rupture (that may affect post-operative centration or tilt of IOL) in the planned operative eye
 - 5) Potentially occludable angle or ciliary body tumor, or other pathology that might increase risk to subject safety, based on gonioscopic observation
 - 6) Subjects reasonably expected to require secondary ocular surgical intervention or laser treatment (other than YAG capsulotomy)
 - 7) Subjects with clinically significant corneal pathology, potentially affecting corneal topography
 - 8) Subjects with traumatic cataract in the planned operative eye
 - 9) Participating in a concurrent drug or device clinical trial or who have participated in a drug or device trial within 30 days of the pre-operative visit
 - 10) Subjects with any other serious ocular pathology (e.g., glaucoma, severe dry eye, history of intraocular inflammation, history of retinal surgery or retinal laser procedure) or underlying systemic medical condition (e.g., uncontrolled diabetes) or circumstance that, based on the Investigator's judgment, poses a concern for the subjects' safety or could confound the results of the study
- (History of cataract surgery with PC-IOL in one eye was allowed.)
- 11) Use of medications known to interfere with visual performance, pupil dilation, or iris structure within 30 days of the pre-operative visit, at the discretion of the Investigator
 - 12) Pregnant or nursing females
 - 13) Irregular astigmatism in the planned operative eye

2. Follow-up Schedule

All patients were scheduled to return for follow-up post-operative examinations at:

1. (Form 1) Visit 1 - Postoperative days 1-2
2. (Form 2) Visit 2 - Postoperative days 7-14
3. (Form 3) Visit 3 - Postoperative days 30-60
4. (Form 4) Visit 4 - Postoperative days 120-180

Preoperatively, subjects were evaluated to obtain demographic information and a medical history and to establish a baseline for their ocular condition,

including manifest refraction, uncorrected and best-corrected photopic distance visual acuity using ETDRS chart at 4m, biometry, IOL power calculation, dilated pupil size, and anterior and posterior segment evaluations. In addition, prior to the operative procedure, the intended axis was marked with a corneal marker.

Postoperatively, the objective parameters measured during the study included the following for the study eye:

- Residual manifest cylinder (determined by manifest refraction) – Visits 1, 2, 3 and 4
- IOL axis orientation (retro-illuminated slit lamp images with dilated pupils acquired in Toric group subjects; images were sent to independent reading center for evaluation) – at the conclusion of surgery at the Operative visit and at Visits 1, 2, 3 and 4
- Uncorrected distance visual acuity (UCDVA) (photopic ETDRS, 4m) – Visits 1, 2, 3 and 4
- Best-corrected distance visual acuity (BCDVA) (photopic ETDRS, 4m) – Visits 2, 3 and 4
- Keratometry – Visits 3 and 4
- Lens stability (decentration and tilt) - Visits 2, 3 and 4

In addition, slit lamp biomicroscopy for ocular health, intraocular pressure using applanation tonometry, posterior capsule opacification assessment, PC-IOL observations and fundus examination were performed at all post-operative visits. The Schedule of Events can be found in **TABLE 9** below.

TABLE 9 SCHEDULE OF EVENTS

Procedure	Both Eyes	Study Eye ¹				
	Visit 00 Pre-Op	Visit 0 Operative	Visit 1 Post-Op	Visit 2 Post-Op	Visit 3 Post-Op	Visit 4 Post-Op
	Day -90 - 0	Day 0	Day 1-2	Day 7-14	Day 30-60	Day 120- 180
Informed Consent/HIPAA	X					
Inclusion/Exclusion Criteria Review	X	X ²				
Demographics	X					
Ocular and Significant Non-ocular Medical History	X*	X				
Urine Pregnancy Test (if applicable)	X					
Potential Visual Acuity	X*					
Corneal Topography	X*					
Axial length/ Anterior chamber depth (biometry)/ Target refraction/ IOL power calc	X*					

Procedure	Both Eyes	Study Eye ¹				
	Visit 00 Pre-Op	Visit 0 Operative	Visit 1 Post-Op	Visit 2 Post-Op	Visit 3 Post-Op	Visit 4 Post-Op
	Day -90 - 0	Day 0	Day 1-2	Day 7-14	Day 30-60	Day 120- 180
(Barrett Toric and any non-toric Monofocal IOL formula)						
Keratometry	X*				X	X
Gonioscopy	X*					
Dilated Pupil size	X*					
Randomization (for subjects with estimated IOL cyl power of 1.50 D with Barrett Toric)	X					
Operative Procedures ³		X				
Manifest Refraction ⁴	X			X	X	X
UCDVA - Monocular (ETDRS) – 4 m ⁴	X		X	X	X	X
BCDVA - Monocular (ETDRS) – 4 m ⁴	X			X	X	X
Intraocular Pressure ⁴	X*		X	X	X	X
Slit lamp Biomicroscopy ⁴	X*		X	X	X	X
Posterior Capsule Opacification (PCO) Assessment ⁴ (dilated)			X	X	X	X
IOL Observations ⁴ (dilated)			X	X	X	X
Lens Stability - decentration and tilt (dilated)				X	X	X
IOL Axis Orientation - retroilluminated slit lamp photo ⁵ (dilated)		X	X	X	X	X
Dilated Fundus Exam ^[4]	X*		X	X	X	X
Adverse Events ⁴	X	X	X	X	X	X
Device Deficiencies ⁴		X	X	X	X	X
Concomitant Medications ⁴	X	X	X	X	X	X
Exit from Study						X

1. If both eyes qualify, the study eye will be the eye with the worse preoperative BCDVA. If BCDVA of both eyes is the same, the study eye will be the right eye
2. Review of inclusion/exclusion criteria before surgery
3. Surgical incision will be standardized to the temporal horizontal meridian and approximately 2.4 mm incision size to minimize variations in changes in corneal astigmatism between toric and control subjects; incision location and size information should be noted in Form 0. The intended axis will be marked preoperatively with two marks, 180 degrees apart in the peripheral cornea near the limbus, using a corneal marker such as a pre-inked RoboMarker (Surgilum, Wilmington, NC) or similar device.
4. Additionally, to be completed at any post-operative Unscheduled Visit
5. Subjects implanted with RAO210T toric IOL only. Images will be evaluated by an independent Reading center to assess IOL axis orientation from IOL axis marks correlated with intended axis and anatomic landmarks at Day 0 and all subsequent visits.

*Assessments performed as standard of care within the -90 – 0 pre-operative visit screening window may be used as qualifying assessments prior to date of informed consent.

[] Optional at Unscheduled Visit, based on Investigator's discretion

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:

Co-primary safety endpoints

- Rates of IOL adverse events through 120 to 180 days post-operatively (Visit 4) for eyes implanted with Toric IOLs compared to ISO Safety and Performance Endpoint (SPE) rates as defined in ISO 11979-7. Per the performance criteria specified in Annex E of ISO 11979-7, the null and alternative hypotheses for each IOL adverse event were structured as follows:

$$H_{0s}: p_{ts} \leq p_0$$

$$H_{1s}: p_{ts} > p_0$$

Where p_{ts} denoted the true proportion of Toric test group eyes at Visit 4 suffering from the adverse event, and p_0 represented the corresponding SPE rate specified in ISO 11979-7. If none of the null hypotheses were rejected at a one-sided 0.05 significance level using exact binomial test, then it would be concluded that the Toric IOL successfully met this endpoint according to the ISO 11979-7 performance criteria.

- Rates of all other adverse events not included in IOL adverse event list from ISO 11979-7 through 120 to 180 days post-operatively (Visit 4). These rates were planned to be descriptively summarized.
- Rates of secondary surgical interventions for IOL repositioning due to IOL misalignment through 120 to 180 days post-operatively (Visit 4). These rates were planned to be descriptively summarized.
- Rate of BCDVA 0.30 logMAR or better at 120 to 180 days post-operatively (Visit 4) in eyes implanted with Toric IOLs compared to the ISO SPE rate specified in ISO 11979-7. For the proportion of Toric test group eyes with 0.30 logMAR or better at Visit 4, the null and alternative hypotheses were as follows:

$$H_{0s}: p_{ts} \geq p_0$$

$$H_{1s}: p_{ts} < p_0$$

Where p_{ts} denoted the true proportion of Toric test group eyes achieving a BCDVA of 0.30 logMAR or better at Visit 4 and p_0 was the corresponding SPE rate specified in ISO 11979-7. If the null hypothesis was not rejected at a one-sided 0.05 significance level using exact binomial test for both the Safety and Best Case Sets (defined in Section X.A.4), then it would be concluded that the Toric IOL successfully met this endpoint according to the ISO 11979-7 performance criteria.

With regards to effectiveness:

Co-primary effectiveness endpoints

- Mean magnitude of residual manifest cylinder (as measured by manifest refraction) at 120 to 180 days post-operatively (Visit 4). The primary effectiveness hypotheses were:

$$H_{0e}: \mu_{te} - \mu_{ce} \geq 0$$

$$H_{1e}: \mu_{te} - \mu_{ce} < 0$$

Where μ_{te} and μ_{ce} denoted the population mean magnitude of residual manifest cylinder at Visit 4 for the Toric test group and Monofocal control group, respectively. If the null hypothesis was rejected at a one-sided 0.025 significance level, then it would be concluded that the 1.50 D Toric IOL is statistically successful in this endpoint.

- Percentage of Toric IOLs with axis misalignment at Visit 4 (as determined by photographic method) less than
 - 10 degrees and
 - 20 degrees

Per ANSI Z80.30, the co-primary endpoint for axis misalignment would be considered successful if IOL axis misalignment was less than 10 degrees for 90% of eyes and less than 20 degrees for 95% of eyes from the Toric test group.

- Stability of Toric IOL axis orientation, expressed as percentage of Toric IOLs that rotate ≤ 5 degrees postoperatively between 30 to 60 days (Visit 3) and 120 to 180 days (Visit 4). Per ANSI Z80.30, the co-primary endpoint for axis stability would be considered successful at Visit 4 if at least 90% of the Toric IOL eyes rotated less than or equal to five degrees between Visits 3 and 4.

The following secondary effectiveness endpoints were planned to be descriptively summarized:

- Residual manifest cylinder by subgroups of 0.25 D preoperative keratometric cylinder at 120 to 180 days post-operatively (Visit 4)
- Percent reduction in absolute cylinder (calculated as reduction of magnitude of residual manifest cylinder relative to preoperative keratometric cylinder)

at 120 to 180 days post-operatively (Visit 4)

Additional effectiveness variables were:

- Percentage of eyes achieving UCDVA at 4 m at 120 to 180 days post-operatively (Visit 4): ≤ 0.30 logMAR, ≤ 0.20 logMAR, ≤ 0.00 logMAR
- Percentage of eyes achieving BCDVA at 4 m at 120 to 180 days post-operatively (Visit 4): ≤ 0.30 logMAR, ≤ 0.20 logMAR, ≤ 0.00 logMAR
- Percentage of eyes achieving accuracy of cylinder (to target) at 120 to 180 days post-operatively (Visit 4) within: ± 0.25 D, ± 0.50 D, ± 0.75 D
- Lens axis misalignment (with toric IOLs) (compared to intended) at 120 to 180 days post-operatively (Visit 4): Absolute value of misalignment, Signed value of misalignment, Two-sided tolerance interval around mean of the signed value of misalignment, Percentage of eyes with lens axis misalignment: < 10 degrees, < 20 degrees, > 30 degrees
- Reduction in cylinder power at 120 to 180 days post-operatively (Visit 4), defined as the difference between pre-operative magnitude of keratometric cylinder and magnitude of manifest cylinder at Visit 4
- Reduction in cylinder power by subgroups of 0.25 D preoperative keratometric cylinder at 120 to 180 days post-operatively (Visit 4)
- Percentage of eyes with reduction of cylinder, at 120 to 180 days post-operatively (Visit 4), within 0.50 D and within 1.00 D of intended
- Descriptive statistics concerning the distribution of surgically induced astigmatism (at Visit 4)
- Scatterplots and regression analyses of the change in magnitude of corneal astigmatism (at Visit 4) from preop as a function of the incision location
- Scatterplots and regression analyses of change in corneal cylinder axis (at Visit 4) from preop, as a function of preoperative corneal cylinder magnitude
- Double-angle plots and vector analyses (intended refractive correction, surgically induced refractive correction, error vector, correction ratio, error ratio) at Visit 4, stratified by preoperative corneal cylinder magnitude

4. Analysis Sets

- All Enrolled Set – All subjects who signed informed consent. This set would be used for disposition summaries.
- Intent-to-Treat (ITT) Set – All enrolled subjects who were randomized. All ITT analyses would be done according to randomized lens assignment.
- Safety Set (SAF) – All ITT subjects who underwent surgery. Summaries and analyses based on the Safety Set would be analyzed according to IOL actually implanted. If no IOL was successfully implanted, but the IOL touched the eye, the subject would be analyzed by the attempted lens. If a subject underwent surgery yet no IOL touched the eye, the subject would be analyzed in a separate Not Treated group. If it was confirmed that a subject did not undergo surgery, then the subject would be excluded from all safety

analyses.

- Per Protocol (PP) Set – All SAF subjects who were successfully implanted with a study lens and who had no major protocol deviations.
- Best Case Set (BCS) – All PP subjects who also met the following criteria:
 - o No clinically significant pre-operative ocular pathology
 - o No macular degeneration detected at any time
 - o No previous surgery for the correction of refractive errors, which would have resulted in exclusion of the subject from the study

B. Accountability of PMA Cohort

At the time of database lock, of 274 patients enrolled (consented) in the PMA study, 85.0% (233) patients were available for analysis at the completion of the study, the 6-month post-operative visit (Day 120-180, Visit 4).

Refer to **TABLE 10** for accountability at each scheduled visit and **TABLE 11** for the number and percentage of subjects included in the study analysis sets. In all tables, ‘N’ refers to the total number of subjects (Toric or Monofocal) in the specified analysis set (e.g., ITT or Safety, as indicated).

TABLE 10 ACCOUNTABILITY OF SUBJECTS AT EACH FORM VISIT (ITT SET)

Randomized Lens	Accountability	Operative n (%)	Visit 1 (Day 1-2) n (%)	Visit 2 (Day 7-14) n (%)	Visit 3 (Day 30-60) n (%)	Visit 4 (Day 120-180) n (%)
Toric IOL (N=118)	Available for Analysis (in Window)	117 (99.2%)	117 (99.2%)	116 (98.3%)	115 (97.5%)	117 (99.2%)
	Visit Out of Window	0	0	0	1 (0.8%)	0
	Missed Visit	0	0	1 (0.8%)	1 (0.8%)	0
	Discontinued	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)	1 (0.8%)
	Lost to Follow-up	0	0	0	0	0
	% Accountability	117 (100%)	117 (100%)	116 (99.1%)	115 (98.3%)	117 (100%)
Monofocal IOL (N=120)	Available for Analysis (in Window)	117 (97.5%)	115 (95.8%)	115 (95.8%)	113 (94.2%)	116 (96.7%)
	Visit Out of Window	0	1 (0.8%)	1 (0.8%)	3 (2.5%)	0
	Missed Visit	0	0	0	0	0
	Discontinued	3 (2.5%)	4 (3.3%)	4 (3.3%)	4 (3.3%)	4 (3.3%)
	Lost to Follow-up	0	0	0	0	0
	% Accountability	117 (100%)	115 (99.1%)	115 (99.1%)	113 (97.4%)	116 (100%)

N = total eyes in the analysis set

n = total number of eyes in the specified row category at that visit

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 11 ANALYSIS SETS

Population (N=238 Randomized)	n (%)
Intent-to-Treat Set ^[1]	238
Toric IOL	118 (49.6%)
Monofocal IOL	120 (50.4%)
Safety Set ^[2]	234 (98.3%)
Toric IOL	117 (50.0%)
Monofocal IOL	116 (49.6%)
Not Treated	1 (0.4%)
Per Protocol Set ^[3]	226 (95.0%)
Toric IOL	111 (49.1%)
Monofocal IOL	115 (50.9%)
Best Case Set ^[4]	222 (93.3%)
Toric IOL	111 (50.0%)
Monofocal IOL	111 (50.0%)

^[1]All randomized subjects (eyes).

^[2]All ITT subjects who undergo surgery.

^[3]All Safety Set subjects who are implanted with the randomized study lens and who have no major protocol deviations.

^[4]All Per Protocol Set subjects meeting the conditions specified in the SAP.

All subjects with Major Protocol Deviations are excluded from the PP Set.

Per Protocol Subjects were excluded from the BCS due to significant pre-operative ocular pathology in the study eye.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an IOL study performed in the US. The proportions enrolled were consistent with the sex, age, racial and ethnic prevalence of disease in the US.

TABLE 12 shows the distribution of demographics of all ITT subjects in the study. Subjects ranged in age from 48 to 85 years in the Toric group (Mean: 67.7 ± 7.4 years) and 44 to 85 years in the Monofocal group (Mean: 69.4 ± 7.0 years). Females comprised 56% (66/118) in the Toric group and 58% (70/120) of the subjects enrolled in the Monofocal group. The study eye was the right eye in a majority of subjects in both groups.

TABLE 13 shows the key baseline parameters for the Toric and Control groups. The distribution of axial length, pre-operative keratometry cylinder, and the grade of cataract are similar between randomized groups.

TABLE 12 DEMOGRAPHICS (ITT SET)

		Randomized Lens	
Demographic Parameter		Toric IOL (N=118)	Monofocal IOL (N=120)
Age (years)	N	118	120
	Mean ± SD	67.7 ± 7.4	69.4 ± 7.0
	Median	68	70
	Min, Max	48, 85	44, 85
Age Group, n (%)	< 65 years	36 (30.5%)	23 (19.2%)
	≥ 65 years	82 (69.5%)	97 (80.8%)
Sex, n (%)	Male	52 (44.1%)	50 (41.7%)
	Female	66 (55.9%)	70 (58.3%)
Study Eye, n (%)	OD	62 (52.5%)	73 (60.8%)
	OS	56 (47.5%)	47 (39.2%)

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 13 BASELINE PARAMETERS (ITT SET)

		Randomized Lens	
Parameter	Statistic	Toric IOL (N=118)	Monofocal IOL (N=120)
Axial Length (mm)	N	118	120
	Mean ± SD	24.2 ± 1.1	24.1 ± 1.1
	Median	24.1	24.1
	Min, Max	21.9, 27.5	21.8, 26.7
Keratometric Cylinder (D) ^[1]	N	118	120
	Mean ± SD	1.21 ± 0.15	1.25 ± 0.14
	Median	1.18	1.23
	Min, Max	1.00, 1.50	1.02, 1.50
LOCS III: Nuclear Opalescence, n (%)	N	117	120
	NO1	11 (9.4%)	7 (5.8%)
	NO2	31 (26.5%)	38 (31.7%)
	NO3	44 (37.6%)	43 (35.8%)
	NO4	6 (5.1%)	7 (5.8%)
	NO5	6 (5.1%)	4 (3.3%)
	NO6	1 (0.9%)	0

		Randomized Lens	
Parameter	Statistic	Toric IOL (N=118)	Monofocal IOL (N=120)
	N/A	18 (15.4%)	21 (17.5%)
LOCS III: Cortical Opacity, n (%)	N	117	120
	C1	28 (24.1%)	29 (24.4%)
	C2	20 (17.2%)	34 (28.6%)
	C3	18 (15.5%)	18 (15.1%)
	C4	4 (3.4%)	3 (2.5%)
	C5	2 (1.7%)	1 (0.8%)
	N/A	44 (37.9%)	34 (28.6%)
LOCS III: Posterior Subcapsular, n (%)	N	117	120
	P1	27 (23.3%)	27 (22.9%)
	P2	12 (10.3%)	13 (11.0%)
	P3	5 (4.3%)	4 (3.4%)
	P4	3 (2.6%)	4 (3.4%)
	P5	0	0
	N/A	69 (59.5%)	70 (59.3%)

^[1]One subject was randomized (Toric IOL) but not treated due to a Screen Failure upon re-screening due to a preop keratometric cylinder of 0.61 D. The subject's initial preop value of 1.14 D is used for all keratometric cylinder tables and analyses.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the Safety set cohort (117 subjects implanted with Toric IOL and 116 subjects implanted with Monofocal IOL) of 233 subjects available for the 6-month (Visit 4) evaluation (Day 120-180).

The key safety outcomes for this study are presented below in **TABLE 14** and **TABLE 18**. The results of adverse events analyses based on the consensus definitions as set forth by American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) are shown in **TABLE 15**. All ocular adverse events (serious and non-serious combined) are reported in **TABLE 16**. Secondary Surgical Interventions (SSIs) due to IOL misalignment are reported in **TABLE 17**.

Adverse effects that occurred in the PMA clinical study:

The first co-primary safety endpoint was to evaluate rates of cumulative and persistent adverse events in first operative eyes at Visit 4 in comparison to ISO 11979-7 Safety and Performance Endpoints grid (SPE rates), and the results are summarized in **TABLE 14**. Of the AEs listed in the ISO grid, the two cumulative AEs observed in this study were cystoid macular edema (2/117 subjects, 1.7%) and secondary surgical interventions (SSIs) (2/117 subjects, 1.7%). There were no persistent AEs observed in the trial among those listed in the ISO grid. At Visit 4, no rates of the adverse events in the Toric group were identified to be statistically higher than the ISO grid at one-sided 0.05 significance level, and this endpoint was successfully met according to the ISO performance criteria.

TABLE 14 RATES OF IOL ADVERSE EVENTS COMPARED TO ISO 11979-7 SAFETY AND PERFORMANCE ENDPOINTS (SPE) RATES (SAFETY, TORIC IOLS)

Adverse Event	n/N (%)	SPE Rate (%)	P-value ^[1]	95% Confidence Interval ^[2]
Cumulative				
Cystoid macular edema	2/117 (1.7%)	3.0	0.8691	(0.208%, 6.039%)
Hypopyon	0/117 (0.0%)	0.3	>.9999	(0%, 3.104%)
Endophthalmitis*	0/117 (0.0%)	0.1	>.9999	(0%, 3.104%)
Lens dislocation from posterior chamber	0/117 (0.0%)	0.1	>.9999	(0%, 3.104%)
Mechanical pupillary block	0/117 (0.0%)	0.1	>.9999	(0%, 3.104%)
Retinal detachment	0/117 (0.0%)	0.3	>.9999	(0%, 3.104%)
Secondary Surgical Intervention ^[3]	2/117 (1.7%)	0.8	0.2406	(0.208%, 6.039%)
Persistent				
Cornea stroma edema	0/117 (0.0%)	0.3	>.9999	(0%, 3.104%)
Cystoid macular edema	0/117 (0.0%)	0.5	>.9999	(0%, 3.104%)
Iritis	0/117 (0.0%)	0.3	>.9999	(0%, 3.104%)
Increased IOP	0/117 (0.0%)	0.4	>.9999	(0%, 3.104%)

^[1]One-sided Exact Binomial Test comparing the proportion of Toric eyes to the SPE Rate, without multiplicity adjustment.

^[2]Two-sided 95% Exact (Clopper-Pearson) confidence interval for the Toric IOL AE Rate, without multiplicity adjustment.

^[3]Excludes Wound Burp SSI. Posterior capsulotomies were excluded as SSIs.

* Endophthalmitis is defined as inflammatory reaction (sterile or infectious) involving the vitreous body.

n=number of subjects that experienced the event; N = total number of subjects in the Safety Set implanted with the Toric IOL.

The second co-primary safety endpoint was to evaluate the rates of all other adverse events not included in the IOL adverse event list from ISO 11979-7 through Visit 4. The results of adverse events analyses based on the consensus

definitions as set forth by American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) are shown in **TABLE 15**. All ocular adverse events (serious and non-serious combined) are reported in **TABLE 16**. The most common adverse events reported (out of an N=117) were posterior capsular opacification (n=14 subjects, 12.0%), posterior vitreous detachment (n=7 subjects, 6.06%) and corneal edema (n=7 subjects, 6.0%). No unexpected safety concerns were identified with the RayOne EMV Toric.

TABLE 15 RATES OF ADVERSE EVENTS BASED ON A MODIFIED VERSION OF THE AAO TASK FORCE CONSENSUS (MASKET ET AL, 2017), SAFETY SET

Adverse Event	Toric IOL (N=117)			Monofocal IOL (N=116)		
Subjects with at least one Masket et al Study Eye AE	5 (4.3%)			4 (3.4%)		
	n (%)	Two-sided 95% CI ^[1]	E ^[2]	n (%)	Two-sided 95% CI ^[1]	E ^[2]
Chronic anterior uveitis	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Clinically significant cystoid macular edema: Macular edema diagnosed by exam and testing (e.g., OCT, FA) resulting in BCDVA of 0.30 logMAR or worse at $\geq$ Visit 3	1 (0.9%)	[0.0%, 4.7%]	1	0	[0.0%, 3.1%]	0
Visually significant corneal edema	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Endophthalmitis	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Mechanical pupillary block	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Increased IOP: Elevation of IOP by $\geq$ 10 mmHg above baseline to a minimum of 25 mmHg	3 (2.6%)	[0.5%, 7.3%]	3	4 (3.4%)	[0.9%, 8.6%]	4
Rhegmatogenous RD	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Toxic anterior segment syndrome	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Secondary IOL Intervention	1 (0.9%)	[0.0%, 4.7%]	1	0	[0.0%, 3.1%]	0
Exchange (the investigational device is replaced with the same lens model)	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
Removal (the investigational device is removed and replaced with a non-investigational lens or no lens is implanted)	0	[0.0%, 3.1%]	0	0	[0.0%, 3.1%]	0
IOL repositioning (existing IOL is surgically moved to another location or rotated)	1 (0.9%)	[0.0%, 4.7%]	1	0	[0.0%, 3.1%]	0

^[1] Two-sided 95% Exact (Clopper-Pearson) confidence interval for the AE Rate, without multiplicity adjustment.

^[2] E = Number of events.

n=number of subjects that experienced the event; N = total number of subjects in the Safety Set (N=117 Toric; N=116 Monofocal)

TABLE 16 OCULAR ADVERSE EVENTS (SERIOUS AND NON-SERIOUS COMBINED), SAFETY SET

	Toric IOL (N=117)			Monofocal IOL (N=116)		
Adverse Event	n (%)	Two-sided 95% CI ^[1]	E ^[2]	n (%)	Two-sided 95% CI ^[1]	E ^[2]
Subjects with at least one Study Eye AE	49 (41.9%)	[32.8%, 51.4%]	75	40 (34.5%)	[25.9%, 43.9%]	49
Posterior capsular opacification requiring YAG capsulotomy	14 (12.0%)	[6.7%, 19.3%]	14	4 (3.4%)	[0.9%, 8.6%]	4
Posterior vitreous detachment	7 (6.0%)	[2.4%, 11.9%]	7	11 (9.5%)	[4.8%, 16.3%]	11
Corneal edema ^[3]	7 (6.0%)	[2.4%, 11.9%]	7	7 (6.0%)	[2.5%, 12.0%]	7
Cornea stroma edema ^[4]	6 (5.1%)	[1.9%, 10.8%]	6	5 (4.3%)	[1.4%, 9.8%]	5
Increased IOP	4 (3.4%)	[0.9%, 8.5%]	4	7 (6.0%)	[2.5%, 12.0%]	7
Anterior chamber cells greater than Grade 2 at Visit 1	5 (4.3%)	[1.4%, 9.7%]	5	1 (0.9%)	[0.0%, 4.7%]	1
Corneal abrasion	3 (2.6%)	[0.5%, 7.3%]	3	0	[0%, 3.1%]	0
Cystoid macular edema	2 (1.7%)	[0.2%, 6.0%]	2	1 (0.9%)	[0.0%, 4.7%]	1
Epithelial defect	2 (1.7%)	[0.2%, 6.0%]	2	1 (0.9%)	[0.0%, 4.7%]	1
Epiretinal membrane	2 (1.7%)	[0.2%, 6.0%]	2	0	[0%, 3.1%]	0
Choroidal nevus	1 (0.9%)	[0.0%, 4.7%]	1	1 (0.9%)	[0.0%, 4.7%]	1
Corneal dellen	1 (0.9%)	[0.0%, 4.7%]	1	1 (0.9%)	[0.0%, 4.7%]	1
Dermatochalasis	1 (0.9%)	[0.0%, 4.7%]	1	1 (0.9%)	[0.0%, 4.7%]	1
Subconjunctival hemorrhage	1 (0.9%)	[0.0%, 4.7%]	1	1 (0.9%)	[0.0%, 4.7%]	1
Worsening dry eye disease	1 (0.9%)	[0.0%, 4.7%]	1	1 (0.9%)	[0.0%, 4.7%]	1
Conjunctival injection	0	[0%, 3.1%]	0	2 (1.7%)	[0.2%, 6.1%]	2
Central capsular wrinkle	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Chemosis	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Double vision secondary to neurological adjustment following cataract surgery	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Epithelial basement membrane dystrophy	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
IOL decentration/malposition resulting in secondary surgical intervention	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0

	Toric IOL (N=117)			Monofocal IOL (N=116)		
Adverse Event	n (%)	Two-sided 95% CI ^[1]	E ^[2]	n (%)	Two-sided 95% CI ^[1]	E ^[2]
IOL repositioning (existing IOL is surgically moved to another location or rotated)	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Intraretinal hemorrhage	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Iris pigment epithelium loss	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Photophobia	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Progression or onset diabetic retinopathy	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Retained lens material	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Retinal pigment epithelial mottling	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Superficial punctate keratitis	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Surgical removal of retained lens fragment	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Trace punctate epithelial erosions	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Visually significant corneal edema resulting in BCDVA of 0.3 or worse	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Worsening punctate epithelial erosion	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Wound burp (aqueous tap, or paracentesis)	1 (0.9%)	[0.0%, 4.7%]	1	0	[0%, 3.1%]	0
Dry eye disease	0	[0%, 3.1%]	0	1 (0.9%)	[0.0%, 4.7%]	1
Iritis	0	[0%, 3.1%]	0	1 (0.9%)	[0.0%, 4.7%]	1
Keratoconjunctivitis Sicca, not specified as Sjogrens	0	[0%, 3.1%]	0	1 (0.9%)	[0.0%, 4.7%]	1
Retinal pigment epithelial changes	0	[0%, 3.1%]	0	1 (0.9%)	[0.0%, 4.7%]	1

^[1]Two-sided 95% Exact (Clopper-Pearson) confidence interval for the AE Rate, without multiplicity adjustment.

^[2]E = Number of events.

^[3] Corneal edema of grade 2+ or more reported after IOL surgery in the early post-operative period (prior to one week).

^[4] Edema of corneal stroma of any degree at any location regardless of effect on BCDVA at Visit 2 (Day 7-14) or later.

n=number of subjects that experienced the event; N = total number of subjects in the Safety Set (N=117 Toric; N=116 Monofocal)

The third co-primary safety endpoint was to evaluate the rates of secondary surgical interventions for IOL repositioning due to IOL misalignment through Visit 4 (TABLE 17). One out of 117 (0.9%) toric subjects underwent IOL

repositioning surgery within the first few weeks. The need for repositioning was not attributed to the device itself, but to the initial placement.

TABLE 17 RATE OF SECONDARY SURGICAL INTERVENTION (SSI) DUE TO IOL MISALIGNMENT (SAFETY, TORIC IOLS)

	n/N (%)	95% Confidence Interval ^[1]
Secondary Surgical Intervention for IOL Repositioning due to IOL Misalignment	1/117 (0.9%)	(0.022%, 4.670%)

^[1]Two-sided 95% Exact (Clopper-Pearson) confidence interval for the Toric IOL AE Rate, without multiplicity adjustment.

n=number of subjects that experienced the event; N = total number of subjects in the Safety Set implanted with the Toric IOL.

The fourth co-primary safety endpoint was to evaluate the rate of BCDVA of 0.30 logMAR or better at Visit 4 compared to the ISO SPE rates as described in ISO 11979-7, and the results are summarized in **TABLE 18**. All Toric subjects achieved BCDVA of 0.30 logMAR (20/40) or Month 6 post-operatively based the Safety set (117/117, 100%, 95% CI [96.9%, 100%]) and the Best-Case set (111/111, 100%, 95% CI [96.7%, 100%]). The rate of BCDVA of 0.30 logMAR or better at Visit 4 for the test Toric group was not identified to be statistically significantly lower than the corresponding ISO SPE rate based on both the Safety (92.5%) and Best Case sets (96.7%), therefore this endpoint was successfully met per the ISO performance criteria.

Therefore, all co-primary safety endpoints were met.

TABLE 18 RATE OF BCDVA OF 0.30 LOGMAR OR BETTER AT VISIT 4 (SAFETY AND BEST-CASE SETS)

Analysis Population	Implanted Lens	n/N (%)	SPE Rate (%)	P-value ^[1]	95% Confidence Interval ^[2]
Safety Set	Toric IOL	117/117 (100.0%)	92.5	>.9999	(96.90%, 100%)
	Monofocal IOL	116/116 (100.0%)	92.5	>.9999	(96.87%, 100%)
Best Case Set	Toric IOL	111/111 (100.0%)	96.7	>.9999	(96.73%, 100%)
	Monofocal IOL	111/111 (100.0%)	96.7	>.9999	(96.73%, 100%)

^[1]One-sided Exact Binomial Test comparing the proportion of Toric eyes to the SPE Rate, without multiplicity adjustment.

^[2]Two-sided 95% Exact (Clopper-Pearson) confidence interval for the Toric IOL AE Rate, without multiplicity adjustment.

2. Effectiveness Results

The analysis of effectiveness was based on the 238 evaluable patients at the 6-month time point (Day 120-180). Key effectiveness outcomes are presented in **TABLE 19**, **TABLE 20** and **TABLE 21**.

The primary analysis was based on the Intent to Treat Analysis Set (ITT) with missing data being handled using multiple imputation (MI) method. Visual acuity was measured in this study with the Early Treatment of Diabetic Retinopathy Study (ETDRS) charts using the M&S Clinical Trial Suite system (M&S Technologies, Niles, IL) at 4 meters.

All three co-primary effectiveness endpoints were met according to the ANSI Z80.30 performance criteria: the adjusted mean difference in magnitude of residual manifest cylinder between the randomized groups (Test-Control) was -0.430 D (95% CI [-0.544, -0.316]), which was statistically ($P < 0.0001$) and clinically significant, meeting the minimum clinically important difference (MCID) of 0.40 D recommended by FDA (**TABLE 19**); the percentages of Toric IOL axis misalignment (from pre-operatively marked intended axis) under 10 degrees and 20 degrees exceeded the minimum percentages of 90% and 95%, respectively, (93.1%, 95% CI [86.1%, 96.8%] less than 10 degrees and 99.99%, 95% CI [96.9%, 100%] less than 20 degrees) per the primary imputation analysis (**TABLE 20**) and the percentage of Toric IOLs that rotated $\leq$ five degrees between Visit 3 (Day 30-60) and Visit 4 (Day 120-180) was 99.0% (95% CI [93.5%, 99.9%]) and exceeded the pre-specified success criteria of 90% for rotational stability using the primary imputation strategy (**TABLE 21**).

The results of the secondary effectiveness endpoints are as follows: at Visit 4, the magnitude of residual manifest cylinder was stratified by preoperative keratometric cylinder for the Toric group compared with the Monofocal group, with between-group differences of $-0.381 \text{ D} \pm 0.078 \text{ D}$ in the 1.00 to $<1.25 \text{ D}$ subgroup and $-0.478 \text{ D} \pm 0.088 \text{ D}$ in the 1.25 to 1.50 D subgroup. Percent reduction in absolute cylinder at Visit 4 was 68.6% in the Toric group versus 36.1% in the Monofocal group (**TABLE 22** and **TABLE 23**).

In addition to the co-primary and secondary effectiveness endpoints, several additional effectiveness analyses were performed to further characterize visual and refractive outcomes. These included uncorrected and best-corrected distance visual acuity (**TABLE 24** and **TABLE 25**), accuracy of cylinder to target (**TABLE 26**), lens axis misalignment (**TABLE 27**), mean reduction in cylinder power overall and by preoperative keratometric cylinder subgroup (**TABLE 28** and **TABLE 29**), and the percentage of eyes with

reduction in cylinder within 0.50 D and 1.00 D of intended (**TABLE 30**).
These analyses were evaluated descriptively using summary statistics.

TABLE 19 RESIDUAL MANIFEST CYLINDER (D) AT VISIT 4 – PRIMARY IMPUTATION STRATEGY (ITT SET)

Statistic	Result
<u>Observed data</u>	
Toric IOL	117/118
Mean $\pm$ SD	0.368 $\pm$ 0.334
Median	0.25
Min, Max	0.00, 1.25
Q1, Q3	0.00, 0.50
Monofocal (Control) IOL	116/120
Mean $\pm$ SD	0.780 $\pm$ 0.532
Median	0.75
Min, Max	0.00, 2.50
Q1, Q3	0.38, 1.25
Difference in Means $\pm$ SE	-0.413 $\pm$ 0.0582
<u>With Imputation</u>	
Number of Imputations ^[1]	50
LS Mean Difference $\pm$ SE	-0.430 $\pm$ 0.058 ^[2]
95% Confidence Interval	[-0.544, -0.316]
t Value	-7.39
P-value	<.0001

Results are presented in absolute cylinder (D); more negative differences are more favorable for the Toric lens. One toric IOL subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4.

^[1]Missing values imputed with the Markov chain Monte Carlo (MCMC) method.

Following imputation, the primary hypothesis was tested using an Analysis of Covariance (ANCOVA) model with randomized treatment as factor and preoperative keratometric cylinder as covariate.

^[2]Meets the minimum clinically significant difference of -0.40 D

TABLE 20 ABSOLUTE IOL AXIS MISALIGNMENT (DEGREES) AT VISIT 4 – PRIMARY IMPUTATION STRATEGY (ITT SET)

	< 10 Degrees Misalignment at V4	< 20 Degrees Misalignment at V4
Absolute Misalignment (degrees), at Visit 4		
% (n/N), observed	93.9% (92/98)	100% (98/98)
%, with imputation ^[1]	93.1%	99.99%
95% Confidence Interval ^[2] , with imputation ^[1,3]	[86.1%, 96.8%]	[96.9%, 100%]

IOL Axis Misalignment is the difference in intended axis of orientation, marked pre-operatively on the day of surgery (Day 0), and the IOL axis at the postoperative visit.

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last IOL Misalignment (9.04°) prior to the SSI was carried forward to subsequent Visits 3 and 4.

The IOL axis misalignment endpoint is successful if IOL axis misalignment is less than 10 degrees for 90% of eyes and less than 20 degrees for 95% of eyes from the Toric test group in the fifty imputed datasets.

^[1] Missing values were handled through multiple imputation (50 sets) using with the Markov chain Monte Carlo (MCMC) method.

^[2] 95% Exact (Clopper-Pearson) confidence interval (CI), without multiplicity adjustment.

^[3] All Missing data were imputed as <20 degrees misalignment in 49/50 imputations. The 95% CI presented for the percent of eyes with <20 degrees misalignment is based on a single imputation with 118/118 successes.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 21 STABILITY OF TORIC IOL AXIS ORIENTATION (DEGREES) AT VISIT 4 - PRIMARY IMPUTATION STRATEGY (ITT SET)

	Absolute IOL Axis Rotation ≤ 5 degrees between Visit 3 and Visit 4
Stability of Toric IOL Axis Orientation (degrees) at Visit 4	
% (n/N), observed	99.0% (100/101)
%, with imputation ^[1]	99.0%
95% Confidence Interval ^[2] , with imputation ^[1]	[93.5%, 99.9%]

Absolute IOL Axis Rotation is the absolute difference in the actual IOL axis at the postoperative visits

The IOL axis stability endpoint is successful if at least 90% of all toric lenses in the fifty imputed datasets rotate less than or equal to five degrees between Visits 3 and 4.

^[1] Missing values were handled through multiple imputation (50 sets) using with the Markov chain Monte Carlo (MCMC) method.

^[2] 95% Exact (Clopper-Pearson) confidence interval (CI), without multiplicity adjustment.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 22 RESIDUAL MANIFEST CYLINDER (D) AT VISIT 4 STRATIFIED BY PREOPERATIVE KERATOMETRIC CYLINDER (ITT SET)

	Residual Manifest Cylinder (D) at Visit 4		
Pre-operative Keratometric cylinder	Toric IOL Mean ± SD	Monofocal IOL Mean ± SD	Difference Difference in means (± SE)
1.00 to < 1.25 D			
n	75	62	
	0.413 ± 0.333	0.794 ± 0.535	-0.381 (± 0.078)
1.25 to 1.50 D			
n	42	54	
	0.286 ± 0.325	0.764 ± 0.533	-0.478 (± 0.088)

Abbreviations: D=Diopter; SD=Standard deviation; SE=Standard Error

Results are presented in absolute cylinder (D); more negative differences are more favorable for the Toric lens.

For one subject who underwent an SSI for IOL repositioning, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4, per ANSI Z80.30.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 23 PERCENT REDUCTION IN ABSOLUTE CYLINDER (ITT SET)

Percent Reduction in cylinder at Visit 4	Toric IOL Mean ± SD	Monofocal IOL Mean ± SD
n	117	116
Mean ± SD	68.59% ± 29.17 %	36.11% ± 45.69 %
Difference		
Difference in means (± SE)	32.48% (± 5.03) %	

Abbreviations: SD=Standard deviation; SE=Standard Error

Percent Reduction in absolute cylinder is calculated for each eye as $(1 - |\text{residual manifest cylinder}| / (\text{preoperative keratometric cylinder})) \times 100\%$.

For one subject who underwent an SSI for IOL repositioning, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4, per ANSI Z80.30.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal); subjects implanted with the Toric IOL (N=117) and Monofocal IOL (N=116).

TABLE 2423 UNCORRECTED DISTANCE VISUAL ACUITY (4M) AT VISIT 4 (ALL TORIC IOLS, ITT SET)

UCDVA (logMAR) Outcomes	UCDVA (Snellen Equivalent)	Visit 4 (Day 120-180) n (%)
N (eyes)		117
-0.20 or better	20/12	1 (0.9%)
-0.10 or better	20/15	10 (8.5%)
0.00 or better	20/20	44 (37.6%)
0.10 or better	20/25	83 (70.9%)
0.20 or better	20/32	102 (87.2%)
0.30 or better	20/40	112 (95.7%)
Count Fingers	Worse than 20/800	0

UCDVA (logMAR) Outcomes	UCDVA (Snellen Equivalent)	Visit 4 (Day 120-180) n (%)
n	117	
Mean ± SD	0.061 ± 0.130	
Median	0.02	
Min, Max	-0.20, 0.52	
Q1, Q3	-0.02, 0.14	
Not Done	0	

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 2524 BEST CORRECTED DISTANCE VISUAL ACUITY (4M) AT VISIT 4 (ALL IOLS, ITT SET)

Randomized Lens	BCDVA (logMAR) Outcomes	UCDVA (Snellen Equivalent)	Visit 4 (Day 120-180) n (%)
Toric IOL	N (eyes)		117
	-0.20 or better	20/12	7 (6.0%)
	-0.10 or better	20/15	43 (36.8%)
	0.00 or better	20/20	90 (76.9%)
	0.10 or better	20/25	114 (97.4%)
	0.20 or better	20/32	116 (99.1%)
	0.30 or better	20/40	117 (100%)
	Mean ± SD		-0.055 ± 0.084
	Median		-0.06
	Min, Max		-0.20, 0.24
	Q1, Q3		-0.10, 0.00
	Not Done		0
Monofocal IOL	N (eyes)		116

Randomized Lens	BCDVA (logMAR) Outcomes	UCDVA (Snellen Equivalent)	Visit 4 (Day 120-180) n (%)
	-0.20 or better	20/12	3 (2.6%)
	-0.10 or better	20/15	34 (29.3%)
	0.00 or better	20/20	83 (71.6%)
	0.10 or better	20/25	114 (98.3%)
	0.20 or better	20/32	116 (100%)
	0.30 or better	20/40	116 (100%)
	Mean $\pm$ SD		-0.039 $\pm$ 0.081
	Median		-0.04
	Min, Max		-0.20, 0.20
	Q1, Q3		-0.10, 0.02
	Not Done		0

Categorical outcomes include count and percentage (%).

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 2625 ACCURACY OF CYLINDER TO TARGET (ITT SET)

Randomized Lens	Accuracy of Cylinder to Target	Visit 4 (Day 120-180)
Toric IOL	± 0.25 D	66/117 (56.4%)
	± 0.50 D	100/117 (85.5%)
	± 0.75 D	110/117 (94.0%)
	> 0.75 D	7/117 (6.0%)
Monofocal IOL	± 0.25 D	32/116 (27.6%)

Randomized Lens	Accuracy of Cylinder to Target	Visit 4 (Day 120-180)
	±0.50 D	56/116 (48.3%)
	±0.75 D	76/116 (65.5%)
	>0.75 D	40/116 (34.5%)

Accuracy of Cylinder is calculated for each eye as the difference between the magnitude of the postoperative manifest refraction cylinder and the magnitude of the target postoperative residual astigmatism per the Toric IOL calculator.

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 2726 IOL AXIS MISALIGNMENT (DEGREES) BY VISIT (ITT SET)

	Statistic	Op	Visit 1 (Day 1-2)	Visit 2 (Day 7-14)	Visit 3 (Day 30-60)	Visit 4 (Day 120-180)
Absolute Misalignment (degrees)	N	106	99	97	97	98
	Mean ± SD	3.101 ± 3.787	3.086 ± 3.598	3.125 ± 3.306	3.071 ± 3.261	3.481 ± 3.418
	Median	1.88	1.94	1.93	1.90	2.61
	Min, Max	0.01, 20.33	0.01, 18.07	0.05, 16.67	0.02, 16.40	0.01, 16.50
	Q1, Q3	0.59, 4.25	0.68, 4.22	0.62, 3.88	0.86, 4.24	1.18, 4.29
	Ungradable Op Image	11	NA	NA	NA	NA
	Ungradable Op Image and Ungradable Postop Image	NA	4	4	4	4
	Ungradable Op Image and Gradable Postop Image	NA	6	6	7	7
	Gradable Op Image and Ungradable Postop Image	NA	5	7	5	8
	Data Not Available	NA	3	2	3	0
Absolute Misalignment (degrees), n (%)	< 5 degrees	84 (79.2%)	82 (82.8%)	77 (79.4%)	78 (80.4%)	76 (77.6%)
	< 10 degrees	101 (95.3%)	95 (96.0%)	92 (94.8%)	93 (95.9%)	92 (93.9%)
	< 20 degrees	105 (99.1%)	99 (100%)	97 (100%)	97 (100%)	98 (100%)

	Statistic	Op	Visit 1 (Day 1-2)	Visit 2 (Day 7-14)	Visit 3 (Day 30-60)	Visit 4 (Day 120-180)
	≤ 30 degrees	106 (100%)	99 (100%)	97 (100%)	97 (100%)	98 (100%)
	> 30 degrees	0	0	0	0	0
Signed IOL Misalignment	N	106	99	97	97	98
	Mean ± SD	1.583 ± 4.639	1.345 ± 4.554	1.183 ± 4.403	1.104 ± 4.351	1.041 ± 4.778
	Median	0.64	0.68	0.57	0.61	0.16
	Min, Max	-9.54, 20.33	-10.62, 18.07	-10.83, 16.67	-10.93, 16.40	-10.95, 16.50
	Q1, Q3	-0.57, 3.60	-0.73, 2.82	-1.01, 3.09	-1.11, 2.88	-1.55, 3.16

IOL Axis Misalignment is the difference in intended axis of orientation, marked pre-operatively on the day of surgery (Day 0), and the IOL axis at the postoperative visit

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last IOL Misalignment (9.04°) prior to the SSI was carried forward to subsequent Visits 3 and 4.

^[1]The image was gradable, but Operative visit image was not gradable / not done.

^[2]For signed misalignment, Clockwise=Negative, Counterclockwise=Positive

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 2827 REDUCTION IN CYLINDER POWER (D) (ITT SET)

Randomized Lens	Statistic	Visit 4 (Day 120-180)
Toric IOL	n	117
	Mean ± SD	0.839 ± 0.385
	Median	0.84
	Min, Max	-0.24, 1.48
	Q1, Q3	0.60, 1.13
Monofocal IOL	n	116
	Mean ± SD	0.466 ± 0.565
	Median	0.52
	Min, Max	-1.40, 1.49
	Q1, Q3	0.08, 0.92
	Difference in Means ± SE	0.373 ± 0.0634

Reduction in Cylinder Power is calculated for each eye as the difference between the magnitude of the preoperative keratometric cylinder and the magnitude of the postoperative manifest refraction cylinder.

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 28 REDUCTION IN CYLINDER POWER (D) BY PREOPERATIVE KERATOMETRIC CYLINDER (ITT SET)

Preoperative Keratometric Cylinder	Randomized Lens	Statistic	Visit 4 (Day 120-180)
1.0 to <1.25 D	Toric IOL	n	75
		Mean $\pm$ SD	0.699 $\pm$ 0.342
		Median	0.73
		Min, Max	-0.24, 1.24
		Q1, Q3	0.51, 0.95
	Monofocal IOL	n	62
		Mean $\pm$ SD	0.346 $\pm$ 0.547
		Median	0.46
		Min, Max	-1.40, 1.21
		Q1, Q3	-0.03, 0.73
	Difference in Means $\pm$ SD		0.353 $\pm$ 0.0799
1.25 to 1.5 D	Toric IOL	n	42
		Mean $\pm$ SD	1.089 $\pm$ 0.330
		Median	1.23
		Min, Max	0.00, 1.48
		Q1, Q3	0.92, 1.34
	Monofocal IOL	n	54
		Mean $\pm$ SD	0.604 $\pm$ 0.558
		Median	0.65
		Min, Max	-0.72, 1.49
		Q1, Q3	0.25, 1.02
	Difference in Means $\pm$ SD		0.486 $\pm$ 0.0914

Preoperative Keratometric Cylinder	Randomized Lens	Statistic	Visit 4 (Day 120-180)
------------------------------------	-----------------	-----------	-----------------------

Reduction in Cylinder Power is calculated for each eye as the difference between the magnitude of the preoperative keratometric cylinder and the magnitude of the postoperative manifest refraction cylinder.

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

TABLE 3029 PERCENTAGE OF EYES WITH REDUCTION OF CYLINDER POWER (D) (ITT SET)

Randomized Lens	Reduction of Cylinder Power within Intended	Visit 4 (Day 120-180)
Toric IOL	≤ 0.50 D	100/117 (85.5%)
	≤ 1.00 D	113/117 (96.6%)
	> 1.00 D	4/117 (3.4%)
Monofocal IOL	≤ 0.50 D	56/116 (48.3%)
	≤ 1.00 D	92/116 (79.3%)
	> 1.00 D	24/116 (20.7%)

Reduction in Cylinder Power is calculated for each eye as the difference between the magnitude of the preoperative keratometric cylinder and the magnitude of the postoperative manifest refraction cylinder. Intended Reduction in Cylinder Power is calculated for each eye as the difference between the magnitude of the preoperative keratometric cylinder and the magnitude of the target postoperative residual astigmatism per the Toric IOL calculator.

One subject underwent an SSI for IOL repositioning; Per ANSI Z80.30, the last Residual Manifest cylinder (1.25 D) prior to the SSI was carried forward to subsequent Visits 3 and 4.

Total number of subjects (Toric or Monofocal) in the ITT Set (N=118 Toric; N=120 Monofocal)

3. Subgroup Analyses

The following baseline characteristics were evaluated for potential association with effectiveness outcomes: sex, age group and site. Additionally, the manifest refractive cylinder outcome was descriptively evaluated by 0.25 D strata of pre-operative keratometric cylinder subgroups. The performance of the Toric IOL regarding all co-primary effectiveness endpoints appeared to be similar between two sex subgroups (male vs. Female) and between two age subgroups (<65 years vs. ≥ 65 years). For axis misalignment and axial stability, data appeared to be poolable across different sites; while there appeared to be a signal of heterogeneity across sites regarding refractive manifest cylinder (P=0.0254 for the site poolability

test, excluding sites with six or fewer subjects implanted). The study was not specifically powered for sex-, age-, site or pre-operative keratometric cylinder-specific subgroups.

4. Pediatric Extrapolation

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

XI. FINANCIAL DISCLOSURE

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 9 investigators of which none were full-time or part-time employees of the sponsor and 2 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: None
- Significant payment of other sorts: 1 investigator
- Proprietary interest in the product tested held by the investigator: None
- Significant equity interest held by investigator in sponsor of covered study: 2 investigators

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.

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

In accordance with the provisions of section 515(c)(3) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The effectiveness results of this study demonstrate that the RayOne EMV Toric is

effective for implantation in the capsular bag for the visual correction of aphakia and for reduction of residual refractive astigmatism in adult patients with greater than or equal to 1.00 diopter (D) of corneal astigmatism, compared to a monofocal IOL. All primary effectiveness endpoints (residual manifest cylinder, IOL axis misalignment, and stability of toric IOL axis orientation) were met. The adjusted mean difference in the magnitude of residual manifest cylinder, as measured by manifest refraction, at Visit 4 was -0.43 D ($P < 0.0001$), which was statistically and clinically significant. Using primary imputation analysis, the percentage of IOL axis misalignment (from pre-operatively marked intended axis) was less than 10 degrees in 93.1% and less than 20 degrees in 99.99% of the subjects; the percentage of Toric lenses that rotated $\leq$ five degrees between Visits 3 and 4 was 99.0%.

B. Safety Conclusions

The risks of the device are based on non-clinical laboratory and animal testing as well as data collected in a clinical study conducted to support PMA approval as described above. The results of the nonclinical laboratory testing including biocompatibility testing, dimensional, optical and mechanical testing, sterility testing, and chemical testing on the Rayacryl material and RayOne EMV Toric support safety. All primary clinical safety endpoints of the clinical trial were met. The rates of cumulative and persistent serious adverse events were not identified to be statistically higher than the ISO 11979-7 SPE rates and this endpoint was successfully met. One Toric subject (1/117, 0.9%) underwent IOL repositioning surgery, the rate of which is comparable to approved Toric lenses. All subjects (100%) achieved 0.30 logMAR BCDVA or better at Visit 4. The rate of BCDVA of 0.30 logMAR or better at Visit 4 for the test Toric group was not identified to be statistically significantly lower than the corresponding ISO SPE rate based on both the Safety and Best Case sets, and this endpoint was successfully met. The safety results of the study provide reasonable evidence that the RayOne Toric IOL is safe for implantation in the capsular bag for the visual correction of aphakia and to provide reduction of residual refractive astigmatism in adult patients with greater than or equal to 1.00 diopter (D) of corneal astigmatism, compared to a monofocal IOL. No unanticipated risks associated with the RayOne EMV Toric were identified.

C. Benefit-Risk Determination

The probable benefits of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The clinical benefits of the RAO 210T IOL are based on the data collected in this clinical study (IDE# G230072), of subjects implanted with the lowest toric power (1.50 D) of the RayOne EMV Toric in comparison to a monofocal control (RAO 600C), which demonstrated that the RayOne EMV Toric is safe and effective when used as intended and according to the instructions for use. The study has demonstrated statistically significant and clinically meaningful results in favor of RayOne EMV Toric regarding visual correction of aphakia and reduction of residual refractive astigmatism in adult subjects with greater than or equal to 1.00 diopter (D) of preoperative corneal astigmatism.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. Adverse events were

comparable to those associated with other intraocular lenses.

1. Patient Perspective

This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, the data provided support that the probable benefits outweigh the probable risks for the primary implantation of the RayOne EMV Toric in the capsular bag of the eye in adult subjects in whom a cataractous lens has been removed by phacoemulsification and provide reduction of residual refractive astigmatism in adult patients with greater than or equal to 1.00 diopter (D) of corneal astigmatism, compared to a monofocal IOL.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of the RayOne EMV Toric when used in accordance with the indications for use. The above-described clinical study was a prospective, multicenter, randomized, active controlled, masked (assessor and subject) pivotal investigation for unilateral implantation of low cylinder (1.50 D) toric IOL in 274 subjects at 9 US sites. The study was conducted consistent with recognized ISO standard and typical enrollment criteria for an IOL study. Bias was minimized by inclusion and exclusion criteria, protocol-standardized clinical assessments and surgical procedure, and safety and effectiveness performance criteria endpoints in accordance with the ISO standard. Success was based on protocol-specified safety and effectiveness endpoints. Safety and effectiveness findings from the clinical study, support that a significant portion of the patient population will achieve clinically significant results. The benefits of using the device outweigh the risks.

XIV. CDRH DECISION

CDRH issued an approval order on [date of approval order].

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

XV. 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.

XVI. REFERENCES

None.