

# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

Device Generic Name: Intraocular Lens (IOL)

Device Trade Name: AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric Intraocular Lens (IOL) Models SND1T3, SND1T4, SND1T5, and SND1T6

Device Procode: MFK

Applicant's Name and Address: Alcon Laboratories, Inc.  
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Date of Panel Recommendation: November 14, 2014

Premarket Approval Application (PMA) Number: P040020/S049

Date of FDA Notice of Approval: December 22, 2016

The original PMA (PMA #P040020) for the multifocal optical design parent IOL was approved on March 21, 2005 and is indicated for the visual correction of aphakia secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision with increased spectacle independence. The lens is intended to be placed in the capsular bag. The SSED to support the indication is available on the CDRH website at <http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpma/pma.cfm?id=P040020> and is incorporated by reference here. The current supplement was submitted to expand the indication for the AcrySof<sup>®</sup> ReSTOR<sup>®</sup> IOLs. This device is considered a first-of-a-kind device because it is the first multifocal IOL that also corrects corneal astigmatism.

## II. INDICATIONS FOR USE

The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric Posterior Chamber Intraocular Lens (IOL) is indicated for primary implantation in the capsular bag of the eye for the visual correction of aphakia and pre-existing corneal astigmatism secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision, reduction of residual refractive cylinder and increased spectacle independence. The lens is intended to be placed in the capsular bag.

### III. CONTRAINDICATIONS

There are no known contraindications.

### IV. WARNINGS AND PRECAUTIONS

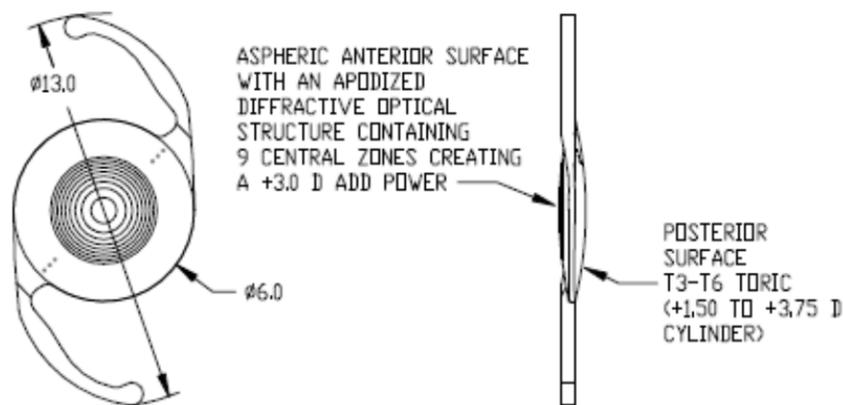
The warnings and precautions can be found in the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric Intraocular Lens labeling.

### V. DEVICE DESCRIPTION

The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Apodized Diffractive Aspheric Multifocal Toric Posterior Chamber IOL is an ultraviolet (UV) and blue light filtering foldable multifocal IOL. The optical portion is biconvex and consists of a soft acrylic material capable of being folded prior to insertion, allowing placement through an incision smaller than the optic diameter of the lens. See Figure 1.

The anterior surface of the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric IOL is designed with negative spherical aberration to compensate for the positive spherical aberration of the cornea. The posterior surface of the optic of the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric IOL is marked with 6 indentations (3 on either side) on the flatter meridian of the optic.

**Figure 1: AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric Drawing**



The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric IOLs studied in the current PMA will be available in four different cylinder powers (1.50 D, 2.25 D, 3.00 D, and 3.75 D) and in spherical equivalent powers of +6 D to +30 D. The four model designations and the associated cylinder powers available are provided in Table 1.

**Table 1: Model Designation and the Associated Cylinder Powers of the AcrySof® IQ ReStor® Multifocal Toric Intraocular Lens (IOL)**

Lens Model	Cylinder Power (D)		Recommend Corneal Astigmatism Range (D)*	
	IOL Plane	Corneal Plane*	Lower	Upper
SND1T3	1.50	1.03	0.75	1.28
SND1T4	2.25	1.55	1.29	1.80
SND1T5	3.00	2.06	1.81	2.32
SND1T6	3.75	2.57	2.33	2.82

\*Based on an average pseudophakic human eye

The physical characteristics of the AcrySof® IQ ReStor® +3.0 D Multifocal Toric IOL are shown in Table 2.

**Table 2: Physical Characteristics of the AcrySof® IQ ReStor® +3.0 D Multifocal Toric IOL**

Characteristics	Model			
	SND1T3	SND1T4	SND1T5	SND1T6
Optic Type	Biconvex Apodized Diffractive Aspheric Toric			
Optics/Haptics Material	Ultraviolet and blue light filtering Acrylate/Methacrylate Copolymer			
UV Cutoff at 10% T	401 nm for 21.0 D			
Index Of Refraction	1.55			
Optic Powers (spherical equivalent diopters)	+6.0 to +30.0 (0.5 D increments) (+3.0 Diopters of add power for near vision)			
IOL Cylinder Power (Diopters)	1.50	2.25	3.00	3.75
Haptic Configuration	STABLEFORCE® Haptic			
Optics/Haptic Color	Yellow			
Optic Diameter (mm)	6.0			
Overall Length (mm)	13.0			
Haptic Angle	0°			

An Alcon web-based calculator is used in conjunction with the AcrySof® IQ ReStor® +3.0 D Multifocal Toric to determine the appropriate intraocular alignment and cylinder power for the patient.

The AcrySof® IQ ReStor® +3.0 D Multifocal Toric IOL is a combination of the previously approved AcrySof® IQ ReStor® +3.0 D Multifocal IOL (P040020/S012) and the previously approved AcrySof® IQ Toric IOL (P930014/S15, S016 and S045).

Except for the addition of the toric component, ReStor® Toric Multifocal IOLs are identical to ReStor® Multifocal IOL in material composition (AcrySof Natural

material) and asphericity. The AcrySof<sup>®</sup> Natural IOL material has also been used in the FDA-approved AcrySof<sup>®</sup> Toric IOLs (SN60T3, SN60T4 and SN60T5; P930014/S016).

## **VI. ALTERNATIVE PRACTICES AND PROCEDURES**

Patients who undergo cataract extraction presently have several non-surgical and surgical alternatives for restoring functional vision of the aphakic eye. Non-surgical options include special cataract glasses or contact lenses. Surgical options such as monofocal, toric, 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 AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric IOLs are currently commercially available in the European Union, Australia, Canada, multiple countries within Central and South America, the Middle East and the Far East. The lenses have been withdrawn from the market in Japan because of reasons related to safety. An investigation of safety issues with the Japanese lenses indicates that they are related to manufacturing processes unique to lenses manufactured for the Japanese market.

## **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.

Potential adverse events and complications accompanying cataract or implant surgery may include, but are not limited to the following: corneal endothelial damage, infection (endophthalmitis), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, cyclitic membrane, iris prolapse, hypopyon, transient or persistent glaucoma, and secondary surgical intervention. Potential 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 study, please see the safety results section for the pivotal study (Section X.D.1).

## **IX. SUMMARY OF PRECLINICAL STUDIES**

### **A. Laboratory Studies**

#### **Biocompatibility**

The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric lenses are made of AcrySof<sup>®</sup> Natural IOL material (AL-37884), the same material that was used with other previously approved IOL designs. The Applicant referenced biocompatibility testing performed on AcrySof<sup>®</sup> Natural IOL material submitted in P930014/S006. The biocompatibility testing met the requirements of International Standard Organization (ISO) 10993, Biological Evaluation of Medical Devices, and ISO 11979-5, Ophthalmic Implants- Intraocular Lenses- Part 5: Biocompatibility, and demonstrated that the AcrySof<sup>®</sup> Natural IOL material does not induce cytotoxicity, sensitization, genotoxicity, or inflammation to muscular and ocular tissue. Studies were conducted in accordance with Good Laboratory Practices.

#### **Sterilization, Packaging and Shelf Life**

The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric lenses are sterilized using 100% ethylene oxide (EO). The sterilization validation was performed according to ANSI/AAMI/ISO 11135 (Sterilization of health care products – Ethylene oxide) using the overkill method. Sterilization validation parameters were designed to achieve a Sterility Assurance Level (SAL) of 10<sup>-6</sup>.

The Multifocal Toric lenses are supplied in a polypropylene “wagon wheel” case inside of a polyester/TYVEK pouch. The pouch is enclosed in a paper box with appropriate labels. Packaging, shipping, and shelf life studies were conducted to verify that the packaging for the Multifocal Toric lenses maintains a sterile barrier and that device performance meets product specifications through a 5 year shelf life. The Applicant performed a microbial aerosol challenge and dye penetration testing on samples aged to an equivalent of 5 years. The shelf life studies conducted were performed in accordance with ISO 11979-6 (Ophthalmic implants – Intraocular lenses – Part 6: Shelf-life and transport stability).

#### **Material/ Chemical Characterization**

Alcon performed material/ chemical characterization testing of the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric lenses.

The material/ chemical characterization tests meet the requirements of ISO 11979-5, Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility and FDA Guidance Document for Multifocal Intraocular Lenses, May 29, 1997, when present. The material/ chemical tests are listed in Table 3.

**Table 3: Summary of Material/Chemical Characterization Tests**

<b>Test:</b>	<b>Acceptance Criteria</b>	<b>Results</b>
Material Stability – aging and leachability	No relevant surface or optical changes	Passed
Material Extraction	None	N/A
Process Extractable Analysis	None	N/A
Heavy Metal Analysis	None	N/A
Fourier Transform/Infrared Spectroscopy	None	N/A
Contact Angle	None	N/A
X-ray photoelectron Spectroscopy	None	N/A

**Optical/ Mechanical characterization**

Alcon performed optical/ mechanical characterization of the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric lenses.

The optical / mechanical tests were conducted and evaluated in accordance with ISO 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods and ISO 11979-3 Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods and ISO 11979-5, Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility. The material/ chemical tests are listed in Table 4.

**Table 4: Summary of Optical / Mechanical Characterization Tests**

<b>Test:</b>	<b>Acceptance Criteria</b>	<b>Results</b>
Haptic Compression Force	None	N/A
Haptic Compression Force Decay	None	N/A
Axial Displacement	None	N/A
Optic Decentration	< 10% of clear optic	Pass
Optic Tilt	< 5°	Pass
Angle of Contact	None	N/A
Fatigue Testing	> 250,000 cycles	Pass
Haptic Strength	> 0.25 N	Pass
Spectral Transmittance	None	N/A
Modulation Transfer Function	MTF specifications at distance and near image planes	Pass
Optical Evaluation after Multiple Folds	Optical specifications	Pass
Test Photostability	Material stability in terms of optical properties and polymer breakdown compounds	Pass
Nd: YAG Laser Exposure Test	No release of cytotoxic compounds	Pass
Refractive Index	None	N/A

**B. Animal Studies**

No animal studies were conducted.

**X. SUMMARY OF PRIMARY CLINICAL STUDY**

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric IOL Models SND1T3, SND1T4, SND1T5, or SND1T6 for primary implantation in the capsular bag for the visual correction of aphakia and pre-existing astigmatism secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision, reduction of residual refractive cylinder and increased spectacle independence. This study was conducted in the US under IDE #G100262.

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**

A prospective, nonrandomized, unmasked, parallel-group study was designed for bilateral implantation of a minimum of 510 (maximum of 600 subjects) subjects in total, with a minimum of 340 subjects implanted with the investigational AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric IOL Models SND1T3-SND1T6 (referred to as the ReSTOR<sup>®</sup> Toric +3.0 D IOL below), and a minimum of 170 subjects implanted with the previously FDA approved AcrySof<sup>®</sup> ReSTOR<sup>®</sup> (+4.0 D Add) Multifocal IOL Model SA60D3 (referred to as the ReSTOR<sup>®</sup> +4.0 D IOL below), at up to 25 investigational sites in the United States (US).

The investigational ReSTOR<sup>®</sup> Toric +3.0 D IOL was designed with a near reading distance of 40 cm and the control ReSTOR<sup>®</sup> +4.0 D IOL was designed with a near reading distance of 33 cm. The parameters expected to be impacted by the near add power difference included intermediate visual acuity and binocular defocus, in favor of the ReSTOR<sup>®</sup> Toric +3.0 D IOL. The rate of severe visual disturbances (e.g., glare and halos) between the ReSTOR<sup>®</sup> Toric +3.0 D IOL and the ReSTOR<sup>®</sup> +4.0 D IOL was also expected to favor the ReSTOR<sup>®</sup> Toric +3.0 D IOL based on the add power difference.

This study included a concurrent, active control arm. The AcrySof<sup>®</sup> ReSTOR<sup>®</sup> Multifocal IOL (Model SA60D3) is an FDA approved posterior chamber IOL. This IOL is intended to be placed in the capsular bag and has no toric component to correct pre-existing corneal astigmatism and does not incorporate asphericity to compensate for corneal spherical aberration. The add power at the IOL plane is +4.0 D.

The investigational and control IOL models were available in IOL powers ranging from 10.0 D to 30.0 D in 0.5 D increments.

According to the study protocol, the primary driver of sample size for the study was the precision of the confidence interval on the rate of actual or potential secondary surgical interventions related to optical properties of the IOL. The study was designed such that the event rate in the ReSTOR<sup>®</sup> Toric IOL group could be estimated to as low as approximately 1% with 95% confidence. Therefore, a minimum of 340 subjects would be enrolled for the ReSTOR<sup>®</sup> Toric IOL group in order to ensure at least 300 eligible subjects to complete the study. An additional 170 subjects were planned for enrollment in the ReSTOR<sup>®</sup> IOL control group.

The study was non-randomized and not masked due to the difference between the control and investigational populations (with regard to the amount of astigmatism that could be present for enrollment) The control group were required to have  $\leq 0.74$  D of preoperative keratometric astigmatism in both eyes. The investigational group included subjects with preoperative astigmatism  $\geq 0.75$  D

### **1. Clinical Inclusion and Exclusion Criteria**

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

- Adults, 21 years of age or older at the time of surgery, of either gender or any race, diagnosed with bilateral cataracts
- Able to comprehend and sign a statement of informed consent
- Calculated lens power and astigmatism within the available range
- Willing and able to complete all required postoperative visits
- Planned cataract removal by phacoemulsification
- Potential postoperative visual acuity of 0.2 logMAR (logarithm of the minimum angle of resolution) or better in both eyes
- Clear intraocular media other than cataract in study eyes
- Preoperative Best Corrected Distance Visual Acuity (BCDVA) worse than 0.2 logMAR in each eye
- Pupil size greater than or equal to 6 mm after dilation
- Able to undergo second eye surgery within 30 days of the first eye surgery.

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

- Significant irregular corneal aberration as demonstrated by corneal topography;
- Keratopathy/Kerectasia - any corneal abnormality, other than regular corneal astigmatism, including, but not limited to the following: keratoconus, keratoglobus, keratolysis, keratomalacia, keratomycosis, and corneal plana;
- Any inflammation or edema (swelling) of the cornea, including but not limited to the following: keratitis, keratoconjunctivitis, and keratouveitis;
- Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted (by subjective assessment of the retina) to cause future acuity losses to a level worse than 0.2 logMAR;
- Subjects who may have reasonably been expected to require a secondary surgical intervention at any time during the study (other than YAG capsulotomy);
- Previous corneal refractive surgery;
- Amblyopia;
- Clinically severe corneal dystrophy (e.g., epithelial, stromal, or endothelial dystrophy);
- Diabetic retinopathy;
- Extremely shallow anterior chamber, not due to swollen cataract;
- Microphthalmos;
- Previous retinal detachment;
- Previous corneal transplant;

- Recurrent severe anterior or posterior segment inflammation of unknown etiology;
- Rubella or traumatic cataract;
- Iris neovascularization;
- Glaucoma (uncontrolled or controlled with medication);
- Aniridia;
- Optic nerve atrophy;
- Pregnancy;
- Any subject participating in another investigational drug or device study;
- Other planned ocular surgery procedures, including, but not limited to LASIK, astigmatic keratotomy and limbal relaxing incisions, for the duration of the study;

The following were intraoperative criteria for not implanting the device:

- Any incision site other than temporal ( $\pm 15^\circ$  from the horizontal meridian);
- Other ocular surgery procedures, including, but not limited to LASIK, astigmatic keratotomy and limbal relaxing incisions, for the duration of the study;
- Mechanical or surgical manipulation required to enlarge the pupil; pupil size was required to be at least 4.5 mm or larger just prior to IOL implantation;
- Significant vitreous loss;
- Significant anterior chamber hyphema;
- Uncontrollable intraocular pressure;
- Zonular or capsular rupture;
- Bag-sulcus, sulcus-sulcus or unknown placement of the haptics.

In the event of zonular damage or capsulorhexis tear during surgery, the subject was to be excluded from the study, the study IOL was not to be implanted, and the surgeon was to make arrangements to implant an alternative non-study IOL.

## 2. Follow-up Schedule

The follow-up visit schedule is presented in Table 5. Specific examinations and scheduled clinical assessments are presented in Table 6. Note that IOL axis orientation was determined using Photographic Assessment of Lens Orientation (PALO) methodology.

**Table 5: Follow-up schedule**

Time From Implantation	1st Implant	2nd Implant
Preoperative	Visit 0 (monocular and binocular)	-
Operative	Visit 00	Visit 00A
1 – 2 days	Visit 1	Visit 1A
7 - 14 days	Visit 2	Visit 2A
30 - 60 days	Visit 3 (monocular-1st eye)	Visit 3A (monocular-2nd eye)
120 - 180 days (after 2nd eye implant)	-	Visit 4A (monocular and binocular)
330 - 420 days (after 2nd eye implant)	-	Visit 5A (monocular and binocular)

**Table 6: Study plan**

PROCEDURES/ MEASUREMENTS/ STATUS	Visit 0 (Preop)	Visit 00 (Op)	Visit 1 (d1-2)	Visit 2 (d7-14)	Visit 3 (d30-60)	Visit 00A (Op)	Visit 1A (d1-2)	Visit 2A (d7-14)	Visit 3A (d30-60)	Visit 4A (d120-180)	Visit 5A (d330-420)
<b>Screening</b>	X										
<b>Informed Consent</b>	X										
<b>Demographics</b>	X										
<b>Ocular and Non-Ocular Medical History</b>	X										
<b>Manifest Refraction</b>	X		X	X	X		X	X	X	X	X
<b>Inclusion/Exclusion Criteria</b>	X	X				X					
<b>Urine Pregnancy Test</b>	X										
<b>Device Deficiencies</b>	X	X	X	X	X	X	X	X	X	X	X
<b>Adverse Events</b>	X	X	X	X	X	X	X	X	X	X	X
<b>Lighting Measurements</b>	X		X	X	X		X	X	X	X	X
<b>Photopic and Mesopic Pupil Size at Distance</b>											X
<b>Photopic and Mesopic Pupil Size at Near (40 cm)</b>											X
<b>Distance Visual Acuity</b>											
Uncorrected	X <sup>b</sup>		X	X	X		X	X	X	XX <sup>b</sup>	XX <sup>b</sup>
Best Corrected	X		X	X	X		X	X	X	XX <sup>b</sup>	XX <sup>b</sup>
<b>Intermediate Visual Acuity- 50 cm</b>											
Uncorrected											X <sup>b</sup>
Distance Corrected											X <sup>b</sup>
<b>Intermediate Visual Acuity-60 cm</b>											
Uncorrected	X <sup>b</sup>										X <sup>b</sup>
Distance Corrected											X <sup>b</sup>
<b>Intermediate Visual Acuity-70 cm</b>											
Uncorrected											X <sup>b</sup>
Distance Corrected											X <sup>b</sup>

**Table 6: Study plan (continued)**

PROCEDURES/ MEASUREMENTS/ STATUS	Visit 0 (Preop)	Visit 00 (Op)	Visit 1 (d1-2)	Visit 2 (d7-14)	Visit 3 (d30-60)	Visit 00A (Op)	Visit 1A (d1-2)	Visit 2A (d7-14)	Visit 3A (d30-60)	Visit 4A (d120-180)	Visit 5A (d330-420)
<b>Near Visual Acuity- Fixed Distance</b>											
Uncorrected	X <sup>b</sup>				X				X	XX <sup>b</sup>	XX <sup>b</sup>
Distance Corrected					X				X	XX <sup>b</sup>	XX <sup>b</sup>
Best Corrected					X				X	XX <sup>b</sup>	XX <sup>b</sup>
<b>Near Visual Acuity- Best Distance</b>											
Uncorrected					X				X	XX <sup>b</sup>	XX <sup>b</sup>
Distance Corrected					X				X	XX <sup>b</sup>	XX <sup>b</sup>
<b>Mesopic Near Visual Acuity- Best Distance</b>											
Distance Corrected					X				X	X	XX <sup>b</sup>
<b>Corneal Topography</b>	X										
<b>Contrast Sensitivity</b>										X <sup>b</sup>	X <sup>a</sup>
<b>Defocus Curve</b>										X <sup>b</sup>	
<b>Anterior Chamber Depth</b>	X										
<b>Axial Length</b>	X										
<b>ReSTOR Toric Calculator<sup>a</sup></b>	X										
<b>Automated Keratometry</b>	X			X	X			X	X	X	X
<b>Intended Axis Placement<sup>a</sup></b>	X					X					
<b>Current Orientation of Lens Axis<sup>1</sup></b>		X	X	X	X	X	X	X	X	X	X
<b>Target Residual Refractive Error</b>	X										
<b>Intraocular Pressure</b>	X		X	X	X		X	X	X	X	X
<b>APPLES Questionnaire<sup>c</sup></b>	X <sup>b</sup>									X <sup>b</sup>	X <sup>b</sup>
<b>VISTAS Questionnaire</b>	X <sup>b</sup>									X <sup>b</sup>	
<b>SILVER Questionnaire<sup>c</sup></b>	X <sup>b</sup>									X <sup>b</sup>	X <sup>b</sup>
<b>Ocular and Non-Ocular Concomitant Medications</b>	X	X	X	X	X	X	X	X	X	X	X
<b>Operative Eye</b>		X				X					
<b>Problems During Surgery</b>		X				X					
<b>Other Procedures at Surgery</b>		X				X					
<b>Folding Instrument</b>		X				X					
<b>Insertion Instrument</b>		X				X					
<b>Incision Site</b>		X				X					
<b>Final Incision Size</b>		X				X					
<b>Lens Information</b>		X				X					
<b>Slit-Lamp Examination</b>	X		X	X	X		X	X	X	X	X
<b>Dilated Fundus Examination</b>	X				X				X	X	X
<b>Retinal Detail</b>					X				X		
<b>Secondary Surgical Interventions</b>			X	X	X		X	X	X	X	X
<b>IOL Observations</b>			X	X	X		X	X	X	X	X
<b>IOL Position Change</b>			X	X	X		X	X	X	X	X
<b>Subjective Posterior Capsule Opacification</b>			X	X	X		X	X	X	X	X
<b>Posterior Capsulotomy</b>			X	X	X		X	X	X	X	X

<sup>a</sup> Investigational Lens Only

<sup>b</sup> Binocular Testing

<sup>c</sup> APPLES and SILVER prior to any SSI

<sup>d</sup> Contrast testing was repeated at Visit 5A for those subjects that had a posterior capsulotomy after Visit 4A. If the patient was scheduled a posterior capsulotomy at Visit 4A, contrast testing was deferred to Visit 5A.

### 3. Clinical Endpoints

The primary effectiveness outcomes were mean monocular Uncorrected Distance Visual Acuity (UCDVA) and mean monocular Uncorrected Near Visual Acuity (UCNVA) at fixed distance for the first operative eye at 12 months (Visit 5A).

The two primary effectiveness endpoints are evaluated by comparing the two treatment groups using a non-inferiority test. Results would be considered successful if the upper limit for each co-primary parameter was less than the clinical performance target. The clinical performance target was set at 0.1 logMAR (logarithm of the minimum angle of resolution) unit.

The supportive effectiveness variables were:

- Monocular (Best Corrected) and Binocular (Uncorrected and Best Corrected) Distance Visual Acuity
- Monocular (Distance Corrected for optical infinity and Best Corrected) and Binocular (Uncorrected, Distance Corrected for optical infinity and Best Corrected) Near Visual Acuity at Fixed Distance
- Monocular and Binocular Near Visual Acuity at Best Distance: Uncorrected and Distance Corrected for optical infinity
- Monocular and Binocular Mesopic Near Visual Acuity at Best Distance: Distance Corrected for optical infinity
- Binocular Intermediate Visual Acuity (50 cm, 60 cm, and 70 cm): Uncorrected and Distance Corrected for optical infinity
- Orientation of Lens Axis determined by Photographic Assessment of Lens Orientation, PALO (Investigational Lens only)
- Reduction of Cylinder (Investigational Lens only)
- Binocular Defocus (+2.0 D to -5.0 D in 0.5 D increments)
- Contrast Sensitivity (Photopic and Mesopic with and without glare)
- Pupil Size (Photopic Distance and Near and Mesopic Distance and Near)
- Intended Lens Placement (Investigational Lens only)
- Spectacle Independence Lens Vision Evaluation And Repurchase (SILVER) Questionnaire
- Visual Tasks (VISTAS) Questionnaire

The primary safety endpoint is the rate of actual and potential secondary surgical interventions (SSIs) related to the optical properties of the IOL for first and second operative eyes separately at Visit 5A (12 months) for both the investigational and control groups. If an ocular surgical intervention was performed on a subject, it qualified as an actual SSI; however, if a subject met the criteria that would warrant an SSI, but did not actually undergo the SSI during the course of the study, it qualified as a potential SSI.

Therefore, subjects were required to answer the following item on the Assessment of Photic Phenomena and Lens EffectS (APPLES) questionnaire—“Are you experiencing any symptoms bothersome enough that you would want to have

another surgery to reposition or remove the IOL(s), if the lens is determined to be the cause of your symptoms?” This question was administered to subjects in the “Other Concern Section” of the APPLES questionnaire at 6 months, 12 months and at any unscheduled visit. If the subject answered the question in the affirmative, the site was required to fill out the SSI Notification Form and evaluate the subject’s symptoms including the need to perform an ocular intervention. If it was determined that the optical properties of the lens were not the cause of the subject’s symptoms, then alternative etiology was required to be documented.

The predefined SSIs related to the optical properties of the IOL included, but were not limited to the following:

- IOL repositioning due to IOL misalignment - Toric component of the IOL
- IOL repositioning due to IOL instability (e.g., decentration, tilt or rotation)
- IOL explantation/replacement due to incorrect IOL power that is not a result of inaccurate preoperative planning or surgical error
- IOL explantation/replacement due to subject intolerance of visual symptoms or functional impairment

No formal statistical hypotheses were specified for the primary safety endpoints.

The secondary safety endpoint is the rate of severe visual disturbances/distortions as reported by the subjects on the APPLES questionnaire at 12 months (Visit 5A).

Supportive Safety Variables were:

- AEs including SSI
- Slit-Lamp Examination
- Dilated Fundus Examination
- Subjective Posterior Capsule Opacification (PCO)
- Posterior Capsulotomy
- IOL Observations
- IOL Position Change
- IOP
- Retinal Detail
- Surgical Problems
- Device Deficiencies

Additional safety data is incorporated by reference to the parent lens, the ACRYSOFF<sup>®</sup> ReSTOR<sup>®</sup> Apodized Diffractive Optic Posterior Chamber IOL, Models MA60D3 and SA60D3, including results from a driving sub-study.

## **B. Accountability of PMA Cohort**

All subjects with successful IOL implantation in at least one eye were considered evaluable for the “All Implanted” analyses. All subjects with attempted IOL

implantation (successful or aborted after contact with the eye) were considered evaluable for the “Safety” analyses. In addition, all eyes successfully implanted, that had at least one postoperative visit and had no preoperative ocular pathology or macular degeneration at any time, were evaluable for “Best Case” analyses. The “Best Case” data set was the primary data set of analysis for the supportive effectiveness parameters of Defocus Curve and Contrast Sensitivity.

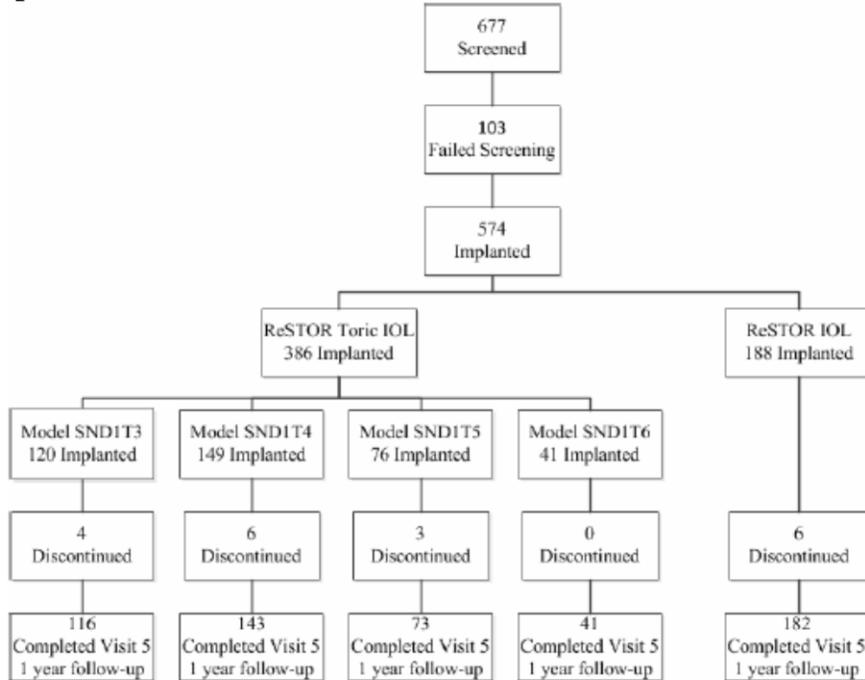
As summarized in the Figure 2 and Table 7, 677 subjects provided informed consent and were enrolled in the clinical study, which began with the first preoperative examination (Form 0) conducted on 28 July 2011. Study enrollment involved consenting the subject and then performing the preoperative (Form 0) study testing, in order to determine the subject’s eligibility for implantation and further participation in the study. Of these, 103 subjects were not implanted (screening failures), while the remaining 574 subjects were implanted with either the ReSTOR Toric +3.0 D IOL (120 – Model SND1T3, 179 – SND1T4, 76 – Model SND1T5, and 41 – Model SND1T6) (386 subjects) or the control ReSTOR +4.0 D IOL (188 subjects). Of these 574 subjects, all but 3 were implanted, or had an attempted implantation, in the second eye. The first implantation occurred on 01 August 2011, and the implantation of the last study subject in the first eye occurred on 22 December 2011. Second eye implantations began on 08 August 2011 and the last second eye implantation was on 29 December 2011.

The primary reasons for the 103 screening failures were due to the inclusion/exclusion criteria. These criteria included: preoperative BCDVA was not worse than 0.2 logMAR in each eye (n = 34); did not meet astigmatism ranges for first and/or second eye (n = 15); consent withdrawn prior to surgery (n = 8); significant irregular corneal aberration as demonstrated by corneal topography (n = 6); calculated lens power and astigmatism not within the available range (n = 4); amblyopia (n = 4); the primary investigator withdrew from the study (n=4); for all other individual criteria leading to screening failures, n ≤ 3.

Among the 574 subjects implanted with an intraocular lens in this clinical study, 19 subjects were discontinued before completion of the study. Four subjects were discontinued due to deaths from causes unrelated to the study IOLs. One subject experienced a stroke. Five subjects were lost to follow-up. Eight subjects no longer wished to participate and one subject moved prior to visit 5A.

Percent accountability at Visit 5 was 96.6% (373/386) in the first eyes of the investigational arm, 95.7% (180/188) in the first eyes of the control arm, 97.1% (371/386) in the second eyes of the investigational arm, and 96.8% (180/188) in the second eyes of the control arm.

**Figure 2: Subject Accountability Flowchart, All Lens Models, First Eye, All Implanted**



**Table 7: Subject Disposition (All Implanted)**

	ReSTOR Toric +3.0 D (N=386)		ReSTOR +4.0 D (N=188)		Combined (N=574)	
	n	(%)	n	(%)	n	(%)
Completed	373	(96.6)	182	(96.8)	555	(96.7)
Discontinued	13	(3.4)	6	(3.2)	19	(3.3)
Adverse Event	1	(0.3)	0	(0.0)	1	(0.2)
Lost to Follow-up	4	(1.0)	1	(0.5)	5	(0.9)
No Longer Wished Participation	4	(1.0)	4	(2.1)	8	(1.4)
Unable to Make Office Visit/Moved	1	(0.3)	0	(0.0)	1	(0.2)
Subject Died	3	(0.8)	1	(0.5)	4	(0.7)

ReSTOR Toric +3.0 D = ACRYSOF IQ ReSTOR +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR +4.0 D = ACRYSOF® ReSTOR Multifocal Lens (+4.0 D Add) Model SN60D3

### C. Study Population Demographics and Baseline Parameters

The study population demographics are reported in Table 8. Baseline characteristics for BCDVA, axial length, and anterior chamber depth were similar between the ReSTOR Toric IOL and the control ReSTOR IOL arms.

**Table 8: Demographic Statistics (All Implanted)**

	ReSTOR Toric +3.0 D (N=386) n (%)	ReSTOR +4.0 D (N=188) n (%)	Overall (N=574) n (%)
<b>Age(Years)</b>			
21-29	2 (0.5)	0 (0.0)	2 (0.3)
30-39	3 (0.8)	0 (0.0)	3 (0.5)
40-49	10 (2.6)	3 (1.6)	13 (2.3)
50-59	57 (14.8)	24 (12.8)	81 (15.1)
60-69	155 (40.2)	73 (38.8)	228 (39.7)
70-79	135 (35.0)	76 (40.4)	211 (36.8)
≥80	24 (6.2)	12 (6.4)	36 (6.3)
<b>Gender</b>			
Male	146 (37.8)	52 (27.7)	198 (34.5)
Female	240 (62.2)	136 (72.3)	376 (65.5)
<b>Race</b>			
White	362 (93.8)	176 (93.6)	538 (93.7)
Black or African American	14 (3.6)	12 (6.4)	26 (4.5)
Asian	5 (1.3)	0 (0.0)	5 (0.9)
Other	5 (1.3)	0 (0.0)	5 (0.9)
<b>Ethnicity</b>			
Hispanic, Latino or Spanish	6 (1.6)	3 (1.6)	9 (1.6)
Not Hispanic, Latino or Spanish	380 (98.4)	185 (98.4)	565 (98.4)

ReSTOR Toric +3.0 D = ACRYSOFF® IQ ReSTOR® +3.0 D Multifocal Toric Intraocular Lens

Models SN61T3/SND1T4/SND1T5/SND1T6

ReSTOR +4.0 D = ACRYSOFF® ReSTOR Multifocal Lens (+4.0 Add) Model SN60D3

## D. Safety and Effectiveness Results

### 1. Safety Results

Primary safety endpoint: Rate of actual and potential secondary surgical interventions (SSIs) due to the optical properties of the IOL

The rate of actual and potential SSIs due to optical properties for ReSTOR® Toric IOL subjects was 1.04% [90% CI:(0.35, 2.36)] in the first eye and 0.52% [90% CI:(0.09, 1.63)] in the second eye. The rate of actual and potential SSIs due to optical properties for the control ReSTOR® IOL subjects was 2.13% [90% CI:(0.73, 4.80)] in the first eye and 2.13% [90% CI:(0.73, 4.80)] in the second eye. See Table 9.

**Table 9: Incidence and Confidence Limits of Actual and Potential SSIs Due to Optical Properties (assuming discontinued subjects having no incidents) Safety Set**

	ReSTOR Toric IOL				ReSTOR IOL				Difference	
	N	n	(%)	90% CI	N	n	(%)	90% CI	(%)	90% CI
First Implanted Eye	386	4	(1.04)	(0.00, 0.02)	188	4	(2.13)	(0.01, 0.05)	(-1.09)	(-0.08, 0.06)
Second Implanted Eye	383	2	(0.52)	(0.00, 0.02)	188	4	(2.13)	(0.01, 0.05)	(-1.61)	(-0.09, 0.06)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

CI = Confidence interval

SSI = Actual and Potential Secondary Surgical Interventions Due to Optical Properties

Difference = ReSTOR Toric IOL Rate - ReSTOR IOL Rate

If an SSI was reported as due to both optical and non-optical properties, Alcon has reported the SSI such that the event was included in the analyses as related to the optical properties of the lens. The most frequently reported reason for an SSI due to optical properties in both arms was visual disturbances. No subjects implanted with the ReSTOR® Toric IOL experienced an actual SSI due to the optical properties of the IOL. In the control ReSTOR® IOL group, 2 subjects experienced an actual SSI in both their first and second eyes. Four subjects in the ReSTOR® Toric group experienced potential SSIs of which two subjects experienced potential SSIs in their first and second eyes. Two subjects in the control ReSTOR® group experienced potential SSIs in both their first and second eyes.

In the ReSTOR® Toric IOL investigational arm, there were no actual SSIs and six potential SSIs. One subject had a potential SSI reported for visual symptoms related to aberrations in the first operative eye. Another subject had a potential SSI reported in the first operative eye at Visit 5A (12 months) for residual astigmatism (manifest refraction - 0.75+0.75x021). The investigator recommended that a PRK procedure be performed if the subject was dissatisfied with his vision. At the conclusion of the study, the subject had not yet scheduled the procedure. A third subject had 2 potential SSIs reported for the first and second operative eyes at Visit 5A (12 months) for complaints of visual disturbances on the APPLES questionnaire that were related to the optical

properties of the IOL. Additionally, the investigator reported an inaccurate preoperative measurement error for the axial length. The investigator recommended that a LASIK procedure be performed; however, the subject decided to postpone treatment. Finally, a fourth subject had 2 potential SSIs reported for the first and second operative eyes at Visit 4A (6 months) for complaints of visual disturbances. In the ReSTOR® IOL control arm, there were four actual SSIs and four potential SSIs. One subject had bilateral SSIs due to severe visual disturbances and answered “yes” to the “Are you experiencing any symptoms bothersome enough that you would want to have another surgery to repositions or remove the IOL(s), if the lens is determined to be the cause of your symptoms?” APPLES question at Visit 4A (6 months). Another subject had bilateral SSIs due to severe visual disturbances and stated that the reading distance with the IOL was too close. Additionally, this subject reported “yes” to the “Are you experiencing any symptoms bothersome enough that you would want to have another surgery to repositions or remove the IOL(s), if the lens is determined to be the cause of your symptoms?” APPLES question.

Two subjects in the control ReSTOR® group experienced potential SSIs. One subject had 2 potential SSIs reported for the first and second operative eyes at Visit 4A (6 months) for visual disturbances. Another subject had two potential SSIs reported for the first operative eye and two potential SSIs reported for the second operative eye at Visits 4A and 5A (6 months and 12 months, respectively). The Investigator completed the SSI Notification Form twice for each eye for this subject; however, for accounting purposes (i.e., in the tables), this subject was only counted once. At Visits 4A and 5A, the subject reported visual disturbances and answered “yes” to the “Are you experiencing any symptoms bothersome enough that you would want to have another surgery to repositions or remove the IOL(s), if the lens is determined to be the cause of your symptoms?” APPLES question.

Secondary safety endpoint: rate of severe visual disturbances/distortions as reported by the subjects on the APPLES questionnaire at 12 months (Visit 5A).

A Patient-Reported Outcomes instrument (APPLES) was developed and used in this clinical study to assess visual disturbances and distortions. Psychometric evaluation did not support this instrument being fit for its purpose of measuring the concept of visual disturbances and distortions in this intended use population. Interpretation of the results from this questionnaire should be made with caution. The frequency of patients reporting specific visual symptoms were similar between the ReSTOR® Toric +3.0 D IOL and the control ReSTOR® +4.0 D IOL groups at 1 year. The highest rate of “severe” reports at 1 year was for halos at 7.5 % for ReSTOR® Toric +3.0 D IOL and 11.0 % for the control ReSTOR® +4.0 D IOL. See Table 10.

**Table 10: Reported Frequencies (Percentage) of Visual Disturbances for ReSTOR Toric +3.0 D and ReSTOR +4.0 D 1 year Postoperative (following second eye implantation)**

Visual Disturbance	ReSTOR® Toric +3.0 D					ReSTOR® +4.0 D				
	N	None %	Mild %	Mod <sup>a</sup> %	Severe %	N	None %	Mild %	Mod <sup>a</sup> %	Severe %
Glare	372	40.6	36.3	19.6	3.5	182	35.2	36.8	25.3	2.7
Halos	372	22.6	38.4	31.5	7.5	182	20.9	40.7	27.5	11.0
Starbursts	372	37.4	39.0	19.4	4.3	182	34.6	37.4	19.2	8.8
Hazy vision	372	55.1	33.1	10.5	1.3	182	51.6	30.8	17.0	0.5
Blurred vision	372	70.7	19.1	9.4	0.8	182	69.2	23.6	7.1	0.0
Distortion where straight lines look tilted	372	96.8	2.2	1.1	0.0	182	92.9	4.9	2.2	0.0
Distortion where flat lines look curved	372	96.5	3.2	0.3	0.0	182	94.0	4.9	1.1	0.0
Double vision	372	89.8	7.5	1.9	0.8	182	91.2	6.6	2.2	0.0
Color distortion	371	94.3	5.1	0.5	0.0	182	95.1	3.8	1.1	0.0
Feeling sick due to visual distortion	371	98.4	1.3	0.3	0.0	182	97.8	1.6	0.0	0.5

<sup>a</sup> Mod = Moderate

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric IOL Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal IOL (+4.0 D Add) Model SA60D3

Supportive Safety Variables:

- AEs including SSI

During the clinical study, 39 SSIs actual (excluding potential) were performed across all eyes. Some eyes experienced multiple SSIs. Of these, 20 SSIs occurred in 16 primary eyes (15 in the investigational arm and 5 SSIs in the control arm). In the first implanted eye, the observed rate of secondary surgical interventions exceeded the Safety and Performance Endpoints (SPE) rates for serious and persistent adverse events listed in ISO 11979-7 in the ReSTOR® Toric group (Table 11). This indicates that the observed rate of SSIs was statistically significantly greater than the SPE rate for SSIs (0.8%) In addition, 19 SSIs occurred in 17 second implanted eyes (13 SSIs in the investigational arm and 6 SSIs in the control arm). In the second implanted eye, the observed rate of secondary surgical interventions exceeded the Safety and Performance Endpoints (SPE) rates in both the ReSTOR® Toric IOL and the control ReSTOR® IOL groups. In the investigational ReSTOR® Toric group, twelve first eyes and eleven second eyes experienced a secondary surgical intervention. In the control ReSTOR IOL group, four first eyes and six second eyes experienced a SSI.

Five cases of IOL repositioning were reported in four ReSTOR® Toric subjects. One subject underwent two separate lens repositioning procedures due to floppy iris syndrome. The IOL was still misaligned by 8.141 degrees at the final study visit (Visit 5A) in this subject.

No unanticipated serious adverse device effects were reported. In the first implanted eye, 28 ocular serious AEs (SAE) and ocular adverse device effects were reported among the 386 subjects implanted with the ReSTOR® Toric IOL. Eight ocular SAEs and adverse device effects were reported among the 188 subjects implanted with the control ReSTOR® IOL. The observed rates for all ocular SAEs and ocular adverse device effects were less than or equal to 1.1% in either group. In the second implanted eye, 32 ocular SAEs and adverse device effects were reported among the 383 subjects implanted

with the ReSTOR<sup>®</sup> Toric IOL. Fifteen ocular SAEs and adverse device effects were reported among the 188 subjects implanted with the control ReSTOR<sup>®</sup> IOL. The observed rates for all ocular SAEs and adverse device effects were less than or equal to 1.6% in either group. Persistent adverse events are observed at the final 12 month postoperative visit.

See Tables 11-16.

**Table 11: Serious and Persistent Adverse Events and SPE Rates (Safety)**

	First implanted eye						Second implanted eye					
	ReSTOR <sup>®</sup> Toric +3.0 D (N = 386)			ReSTOR <sup>®</sup> +4.0 D (N = 188)			ReSTOR <sup>®</sup> Toric +3.0 D (N = 383)			ReSTOR <sup>®</sup> +4.0 D (N = 188)		
	n	%	SPE %	n	%	SPE %	n	%	SPE %	n	%	SPE %
<b>Serious Adverse Events</b>												
Cystoid macular edema	1	(0.3)	3.0	0	(0.0)	3.0	3	(0.8)	3.0	1	(0.5)	3.0
Endophthalmitis	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1
Hypopyon	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3
Lens dislocated from posterior chamber	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1
Pupillary block	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1	0	(0.0)	0.1
Retinal detachment	1	(0.3)	0.3	0	(0.0)	0.3	2	(0.5)	0.3	1	(0.5)	0.3
Secondary surgical intervention	12	(3.1)	0.8	4	(2.1)	0.8	11	(2.9)	0.8	6	(3.2)	0.8
<b>Persistent Serious Adverse Events</b>												
Corneal oedema	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3
Cystoid macular oedema	1	(0.3)	0.5	0	(0.0)	0.5	1	(0.3)	0.5	0	(0.0)	0.5
Iritis	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3	0	(0.0)	0.3
Raised IOP requiring treatment	0	(0.0)	0.4	0	(0.0)	0.4	0	(0.0)	0.4	0	(0.0)	0.4

ReSTOR<sup>®</sup> Toric +3.0 D = AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR<sup>®</sup> +4.0 D = AcrySof<sup>®</sup> ReSTOR<sup>®</sup> Multifocal Lens (+4.0 D Add) Model SA60D3

**Table 12: Summaries of Ocular SAEs and Adverse Device Effects by Preferred Term- First Implanted Eye (Safety Set)**

	ReSTOR Toric IOL (N = 386)				ReSTOR IOL (N = 188)				Overall (N = 574)			
	n	(%)	UCL	E	n	(%)	UCL	E	n	(%)	UCL	E
Eye disorder	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Halo vision	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.3)	1.1	2
Iris atrophy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Keratotomy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Photopsia	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Retinal detachment	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Surgical procedure repeated	3	(0.8)	2.0	3	2	(1.1)	3.3	2	5	(0.9)	1.8	5
Vision blurred	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Visual impairment	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.3)	1.1	2
Vitrectomy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Vitreous prolapse	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Glare	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Intraocular lens repositioning	4	(1.0)	2.4	5	0	(0.0)	1.6	0	4	(0.7)	1.6	5
Intra-ocular injection	0	(0.0)	0.8	0	1	(0.5)	2.5	2	1	(0.2)	0.8	2
Eye laser surgery	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Cataract operation complication	2	(0.5)	1.6	2	0	(0.0)	1.6	0	2	(0.3)	1.1	2
Cystoid macular oedema	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Corneal operation	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.3)	1.1	2
Device dislocation	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Age-related macular degeneration	0	(0.0)	0.8	0	1	(0.5)	2.5	1	1	(0.2)	0.8	1
Retinopexy	2	(0.5)	1.6	2	0	(0.0)	1.6	0	2	(0.3)	1.1	2
Keratomileusis	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

Adverse Events coded using MedDRA

UCL - 95% one-sided upper confidence limit using Clopper-Pearson exact test

If an eye has multiple occurrences of an AE, the eye was presented only once in the respective eye count (n).

Events are counted each time in the event (E) column. Events recorded as OU (both eyes) were counted once for the first eye and second eye.

**Table 13: Summaries of Ocular SAEs and Adverse Device Effects by Preferred Term – Second Implanted Eye (Safety Set)**

	ReSTOR Toric IOL (N = 383)				ReSTOR IOL (N = 188)				Overall (N = 571)			
	n	(%)	UCL	E	n	(%)	UCL	E	n	(%)	UCL	E
Eye disorder	3	(0.8)	2.0	3	0	(0.0)	1.6	0	3	(0.5)	1.4	3
Halo vision	1	(0.3)	1.2	1	2	(1.1)	3.3	2	3	(0.5)	1.4	3
Iris atrophy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Macular oedema	0	(0.0)	0.8	0	1	(0.5)	2.5	1	1	(0.2)	0.8	1
Photopsia	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Retinal detachment	2	(0.5)	1.6	3	1	(0.5)	2.5	1	3	(0.5)	1.4	4
Retinal tear	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Surgical procedure repeated	1	(0.3)	1.2	1	3	(1.6)	4.1	3	4	(0.7)	1.6	4
Vision blurred	0	(0.0)	0.8	0	1	(0.5)	2.5	1	1	(0.2)	0.8	1
Visual impairment	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Macular hole	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Glare	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Suture insertion	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Wound complication	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Eye laser surgery	3	(0.8)	2.0	3	0	(0.0)	1.6	0	3	(0.5)	1.4	3
Cataract operation complication	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Cystoid macular oedema	3	(0.8)	2.0	3	1	(0.5)	2.5	1	4	(0.7)	1.6	4
Eye injury	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Corneal operation	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Retinal operation	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Retinopexy	3	(0.8)	2.0	5	1	(0.5)	2.5	1	4	(0.7)	1.6	6
Keratomileusis	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

Adverse Events coded using MedDRA

UCL - 95% one-sided upper confidence limit using Clopper-Pearson exact test

If an eye has multiple occurrences of an AE, the eye was presented only once in the respective eye count (n).

Events are counted each time in the event (E) column. Events recorded as OU (both eyes) were counted once for the first eye and second eye.

**Table 14: Secondary Surgical Interventions – First and Second Eyes**

Secondary Surgical Intervention	First Eye		Second eye	
	ReSTOR <sup>®</sup> Toric +3.0 D (N=386)	ReSTOR <sup>®</sup> +4.0 D (N=188)	ReSTOR <sup>®</sup> Toric +3.0 D (N=383)	ReSTOR <sup>®</sup> +4.0 D (N=188)
Secondary Surgical Intervention	15	5	13	6
IOL repositioning due to IOL misalignment	1 <sup>a</sup>	0	0	0
IOL repositioning due to inaccurate IOL placement	4 <sup>b,c</sup>	0	0	0
IOL repositioning due to haptic outside of the bag	1	0	0	0
IOL replacement due to visual disturbances	0	2	0	2
LASIK to correct residual refractive error	1	0	1	0
Astigmatic keratotomy to correct residual refractive error (astigmatism)	1	0	0	0
Limbal relaxing incision to correct surgically induced astigmatism	1	0	1	0
Limbal relaxing incision to correct pre-existing astigmatism	0	1	0	1
Macular hole repair	0	0	1	0
YAG laser capsulotomy for wrinkles, folds or strands in capsule	1 <sup>b</sup>	0	3	0
Intraocular injection for wet age related macular degeneration	0	2 <sup>d</sup>	0	0
Retinal detachment repair and prophylactic retinopexy	2	0	5 <sup>e</sup>	1
Retained lens removal	2	0	1	1
Corneal wound leak repair	0	0	1	1
Anterior vitrectomy	1	0	0	0

<sup>a</sup> One subject required an IOL repositioning surgery at the 6 month visit. The Investigator considered the event related to the patient's eye anatomy and the IOL rotation was assumed to have occurred within the first 24 hours following surgery.

<sup>b</sup> One subject experienced floppy iris during surgery and required two repositioning procedures. The same subject also experienced a YAG laser capsulotomy for wrinkled capsule in the first eye.

<sup>c</sup> The IOL was implanted at the incorrect axis in two subjects.

<sup>d</sup> One subject was administered two intraocular injections for wet age related macular degeneration in the first eye.

<sup>e</sup> One subject had one prophylactic retinopexy procedure performed in the first eye and three retinopexy procedures performed in the second eye.

**Table 15: Summaries of Ocular SAEs by Preferred Term where Surgical Intervention was Performed - First Implanted Eye (Safety Set)**

	ReSTOR Toric IOL (N = 386)				ReSTOR IOL (N = 188)				Overall (N = 574)			
	n	(%)	UCL	E	n	(%)	UCL	E	n	(%)	UCL	E
Keratotomy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Surgical procedure repeated	3	(0.8)	2.0	3	2	(1.1)	3.3	2	5	(0.9)	1.8	5
Vitrectomy	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Intraocular lens repositioning	4	(1.0)	2.4	5	0	(0.0)	1.6	0	4	(0.7)	1.6	5
Intra-ocular injection	0	(0.0)	0.8	0	1	(0.5)	2.5	2	1	(0.2)	0.8	2
Eye laser surgery	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Corneal operation	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.3)	1.1	2
Retinopexy	2	(0.5)	1.6	2	0	(0.0)	1.6	0	2	(0.3)	1.1	2
Keratomileusis	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

Adverse Events coded using MedDRA

UCL - 95% one-sided upper confidence limit using Clopper-Pearson exact test

If an eye has multiple occurrences of an AE, the eye was presented only once in the respective eye count (n).

Events are counted each time in the event (E) column. Events recorded as OU (both eyes) were counted once for the first eye and second eye.

**Table 16: Summaries of Ocular SAEs by Preferred Term where Surgical Intervention was Performed - Second Implanted Eye (Safety Set)**

	ReSTOR Toric IOL (N = 383)				ReSTOR IOL (N = 188)				Overall (N = 571)			
	n	(%)	UCL	E	n	(%)	UCL	E	n	(%)	UCL	E
Surgical procedure repeated	1	(0.3)	1.2	1	3	(1.6)	4.1	3	4	(0.7)	1.6	4
Suture insertion	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Eye laser surgery	3	(0.8)	2.0	3	0	(0.0)	1.6	0	3	(0.5)	1.4	3
Corneal operation	1	(0.3)	1.2	1	1	(0.5)	2.5	1	2	(0.4)	1.1	2
Retinal operation	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1
Retinopathy	3	(0.8)	2.0	5	1	(0.5)	2.5	1	4	(0.7)	1.6	6
Keratomileusis	1	(0.3)	1.2	1	0	(0.0)	1.6	0	1	(0.2)	0.8	1

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3

Adverse Events coded using MedDRA

UCL - 95% one-sided upper confidence limit using Clopper-Pearson exact test

If an eye has multiple occurrences of an AE, the eye was presented only once in the respective eye count (n).

Events are counted each time in the event (E) column. Events recorded as OU (both eyes) were counted once for the first eye and second eye.

- Slit-Lamp Examination and Dilated Fundus Examination

The incidences of slit-lamp and dilated fundus examination findings were similar between the ACRYSOFF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/SND1T4/SND1T5/SND1T6 and the control ACRYSOFF<sup>®</sup> ReSTOR<sup>®</sup> Multifocal IOL Model SA60D3 groups. The most frequent slit-lamp observation was posterior capsule opacification in both the ReSTOR<sup>®</sup> Toric IOL (1<sup>st</sup> eye – 52.3%) and the control ReSTOR<sup>®</sup> IOL (1<sup>st</sup> eye - 42.9%) groups at Visit 5 (12 months). The most frequent dilated fundus finding was clinically non-significant vitreous detachment observed in both the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL. Overall, no untoward safety issues were identified for subjects implanted with the ReSTOR Toric IOL or the control ReSTOR IOL based on an evaluation of slit lamp and dilated fundus observations.

- Subjective Posterior Capsule Opacification (PCO)

The development of clinically significant PCO requiring a posterior capsulotomy (YAG) was reported in less than 10% of eyes from each IOL group at any scheduled postoperative visit. The incidence of PCO of any grade at the early postoperative visits (Visits 1 and 2) was < 6% in either group. All reports of PCO at Visits 1 and 2 were assessed as clinically non-significant with the exceptions of 1 subject (both eyes) in the ReSTOR<sup>®</sup> Toric IOL group, in whom PCO was assessed as clinically non-significant prior to 1 month postoperative (Visit 3). At subsequent visits, the PCO was graded as clinically significant without a need for YAG, and the BCDVA improved. The first eye did not require posterior capsulotomy during the study, despite the early findings of clinically significant PCO. In the second eye of the same subject, clinically significant PCO was noted at the 1 day postoperative (Visit 1A) with a BCDVA of 0.02 logMAR. At subsequent visits, the PCO was graded as clinically significant (except for the 1 week postoperative visit where it was graded clinically non-significant). The second eye also did not require posterior capsulotomy during the study. See Table 17.

**Table 17: Number and Percentage of Eyes with Subjective PCO by Visit (Safety Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR	ReSTOR	ReSTOR	ReSTOR
		Toric IOL	IOL	Toric IOL	IOL
		n (%)	n (%)	n (%)	n (%)
Visit 1	<b>Total</b>	<b>386</b>	<b>188</b>	<b>382</b>	<b>188</b>
	<b>None</b>	376 (97.4)	187 (99.5)	374 (97.9)	188 (100.0)
	<b>Clinically non-significant</b>	9 (2.3)	1 (0.5)	7 (1.8)	0 (0.0)
	<b>Clinically significant</b>	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
	<b>Clinically significant requiring a YAG</b>	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Visit 2	<b>Total</b>	<b>386</b>	<b>188</b>	<b>382</b>	<b>188</b>
	<b>None</b>	373 (96.6)	182 (96.8)	362 (94.8)	184 (97.9)
	<b>Clinically non-significant</b>	12 (3.1)	6 (3.2)	20 (5.2)	4 (2.1)
	<b>Clinically significant</b>	1 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
	<b>Clinically significant requiring a YAG</b>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visit 3	<b>Total</b>	<b>383</b>	<b>187</b>	<b>382</b>	<b>187</b>
	<b>None</b>	304 (79.4)	154 (82.4)	310 (81.2)	153 (81.8)
	<b>Clinically non-significant</b>	76 (19.8)	30 (16.0)	69 (18.1)	32 (17.1)
	<b>Clinically significant</b>	1 (0.3)	2 (1.1)	1 (0.3)	2 (1.1)
	<b>Clinically significant requiring a YAG</b>	2 (0.5)	1 (0.5)	2 (0.5)	0 (0.0)
Visit 4	<b>Total</b>	<b>379</b>	<b>186</b>	<b>378</b>	<b>186</b>
	<b>None</b>	218 (57.5)	114 (61.3)	215 (56.9)	115 (61.8)
	<b>Clinically non-significant</b>	137 (36.1)	59 (31.7)	143 (37.8)	54 (29.0)
	<b>Clinically significant</b>	11 (2.9)	3 (1.6)	9 (2.4)	3 (1.6)
	<b>Clinically significant requiring a YAG</b>	13 (3.4)	10 (5.4)	11 (2.9)	14 (7.5)
Visit 5	<b>Total</b>	<b>373</b>	<b>182</b>	<b>372</b>	<b>182</b>
	<b>None</b>	178 (47.7)	104 (57.1)	180 (48.4)	108 (59.3)
	<b>Clinically non-significant</b>	169 (45.3)	72 (39.6)	167 (44.9)	71 (39.0)
	<b>Clinically significant</b>	9 (2.4)	1 (0.5)	8 (2.2)	1 (0.5)
	<b>Clinically significant requiring a YAG</b>	17 (4.6)	5 (2.7)	17 (4.6)	2 (1.1)
Unscheduled	<b>Total</b>	<b>16</b>	<b>9</b>	<b>17</b>	<b>7</b>
	<b>None</b>	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	<b>Clinically non-significant</b>	11 (68.8)	7 (77.8)	11 (64.7)	5 (71.4)
	<b>Clinically significant</b>	3 (18.8)	0 (0.0)	2 (11.8)	0 (0.0)
	<b>Clinically significant requiring a YAG</b>	7 (43.8)	3 (33.3)	7 (41.2)	3 (42.9)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

- **Posterior Capsulotomy**

Posterior capsulotomy for the treatment of a posterior capsule opacification was performed at a similar incidence in each of the IOL groups. A review of the individual

patient data revealed that none of the eyes experienced clinically significant raised IOP or an IOL position change following posterior capsulotomy. One eye in the ReSTOR<sup>®</sup> Toric IOL group experienced a retinal detachment and one eye in the control ReSTOR<sup>®</sup> IOL group experienced cystoid macular edema following posterior capsulotomy. See Table 18.

**Table 18: Number and Percentage of Eyes with Posterior Capsulotomy (Safety Set)**

	First Implanted Eye						Second Implanted Eye					
	ReSTOR Toric IOL			ReSTOR IOL			ReSTOR Toric IOL			ReSTOR IOL		
	N	n	(%)	N	n	(%)	N	n	(%)	N	n	(%)
Visit 1	386	0	(0.0)	188	0	(0.0)	382	0	(0.0)	188	0	(0.0)
Visit 2	386	0	(0.0)	188	0	(0.0)	382	0	(0.0)	188	0	(0.0)
Visit 3	386	1	(0.3)	188	1	(0.5)	382	2	(0.5)	188	0	(0.0)
Visit 4	386	7	(1.8)	188	2	(1.1)	383	5	(1.3)	188	3	(1.6)
Visit 5	386	42	(10.9)	188	21	(11.2)	383	39	(10.2)	188	21	(11.2)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

Surgeries occurring after Visit 5 were mapped to Visit 5.

- IOL Observations

Overall, no unexpected safety issues were identified for subjects implanted with the ReSTOR<sup>®</sup> Toric IOL or the control ReSTOR<sup>®</sup> IOL based on an evaluation of IOL observations. At Visit 5, 95.7 % (357/373) of ReSTOR<sup>®</sup> Toric and 97.3% (177/182) of ReSTOR<sup>®</sup> subjects had no observation of glistenings in the first implanted eye and 96.0% (357/372) of ReSTOR<sup>®</sup> Toric and 97.3% (177/182) of ReSTOR<sup>®</sup> subjects had no observation of glistenings in the second implanted eye. None of the observed glistenings were reported as clinically significant by the implanting surgeons.

- IOL Position Change

IOL position was stable following IOL implantation. No occurrence of decentration or tilt in either IOL group was observed after the 1 week visit (Visit 2). Decentration of the IOL by > 0.5 mm was observed in 2 eyes, which included 1 eye from each IOL group. These IOL position changes occurred within 1 week after surgery and stabilized at subsequent visits. In one eye, the ReSTOR<sup>®</sup> Toric IOL (Model SND1T3) was decentered by 0.8 mm at Visit 2 (1 week postoperative). The investigator stated that the IOL decentration was due to the configuration of the capsular bag. In another eye, the control ReSTOR<sup>®</sup> IOL was decentered by 2 mm at Visit 1 (1 day postoperative). The investigator stated that the IOL decentration occurred due to the absence of nasal zonules in the eye. A capsular tension ring was used during the surgery to correct the decentration. Lens tilt > 10° was observed in 2 eyes in the ReSTOR<sup>®</sup> Toric IOL group, which occurred at the 1 day visit after surgery. One eye with a tilt of 180 degrees required surgical intervention. In this eye the lens tilt was attributed to surgical error and the subject was noted to have floppy iris syndrome. In another study eye, with IOL tilt of 15 degrees, the IOL position stabilized without intervention. In this case the tilt was believed to have been caused by retained viscoelastic. See Table 19.

**Table 19: Number and Percentage of Eyes with IOL Position Change since Last Visit (Safety Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
		n (%)	n (%)	n (%)	n (%)
Visit 1	Total	386	188	382	188
	None	384 (99.5)	188 (100.0)	382 (100.0)	187 (99.5)
	Tilted >10 degrees	2 (0.5)	0 (0.0)	0 (0.0)	0 (0.0)
	Decentered >0.5 mm	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.5)
Visit 2	Total	386	188	382	188
	None	386 (100.0)	188 (100.0)	381 (99.7)	188 (100.0)
	Tilted >10 degrees	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Decentered >0.5 mm	0 (0.0)	0 (0.0)	1 (0.3)	0 (0.0)
Visit 3	Total	383	187	382	187
	None	383 (100.0)	187 (100.0)	382 (100.0)	187 (100.0)
	Tilted >10 degrees	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Decentered >0.5 mm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visit 4	Total	379	186	377	186
	None	379 (100.0)	186 (100.0)	377 (100.0)	186 (100.0)
	Tilted >10 degrees	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Decentered >0.5 mm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visit 5	Total	373	182	371	182
	None	373 (100.0)	182 (100.0)	371 (100.0)	182 (100.0)
	Tilted >10 degrees	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Decentered >0.5 mm	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

- IOP

Transient increases in IOP were observed in both IOL groups following cataract surgery but returned to baseline values by the one week postoperative visit and remained stable at subsequent visits throughout the study for both IOL groups. Among the first and second eyes for each IOL group, the mean IOP increased at Visit 1 (1 day postoperative) by approximately 4 mmHg. The mean IOP returned to near the preoperative baseline by Visit 2 (1 week postoperative) and remained stable at subsequent visits. The mean IOP for eyes with the ReSTOR<sup>®</sup> Toric IOL was within 1 mmHg of that for eyes with the control ReSTOR<sup>®</sup> IOL at all scheduled visits. No SAEs for raised IOP requiring treatment were reported, and 9 non-serious AEs of IOP increased were reported. Eight of these AEs occurred in the ReSTOR<sup>®</sup> Toric IOL, and 1 AE of IOP increased occurred in the control ReSTOR<sup>®</sup> IOL group.

None of the AEs were related to the study device. For 6 cases, the investigator provided an etiology: cataract surgery (n = 1 eye), phacoemulsification during cataract surgery (n = 3 eyes), and steroid response (n = 2 eyes). All of the AEs were reported in the first month postoperative with 6 of the 9 AEs reported on 1 day postoperative. All 9 AEs of

IOP increased required treatment: medication (n = 7 eyes), a change in medication (n = 1 eye), and wound burping with added medication (n = 1 eye). The AEs of increased IOP resolved with treatment within 1 month of event onset. IOP measurements for these 9 eyes were within 10 mmHg of the preoperative baseline measurement at the final study visit.

- Retinal Detail

As per the protocol, the investigators were asked to indicate whether the ReSTOR<sup>®</sup> Toric IOL or the control ReSTOR<sup>®</sup> IOL caused any loss in retinal detail that would alter a surgeon's ability to administer retinal treatment, as compared to their experience with monofocal IOLs. The postoperative dilated fundus examination utilized for the assessment of retinal detail was performed at Visit 3/3A (1 month). No loss of retinal detail was observed in either IOL group.

- Surgical Problems

In only one study subject did the Applicant consider a surgical problem to warrant exclusion of the subject's eye from participation in the study (as outlined in the protocol). This subject developed a capsulorhexis tear secondary to breaking of a haptic following implantation of a ReSTOR<sup>®</sup> Toric IOL). The IOL was explanted at the operative visit and a non-study IOL was implanted. Seven eyes in 6 subjects in the ReSTOR<sup>®</sup> Toric IOL group experienced a capsulorhexis tear and/or an "other" - anterior radial tear at the operative visit. One subject experienced floppy iris syndrome during surgery and a pupil size less than 2.5 mm at the conclusion of the surgery in the second operative eye. Five subjects implanted with a ReSTOR<sup>®</sup> Toric IOL experienced pupil constriction in one or both eyes (n = 8 eyes) during surgery.

The "Other" types of surgical problems included the following:

- In the ReSTOR<sup>®</sup> Toric group, the "other" types of surgical problems included: floppy iris (n = 4 eyes), wound leak (n = 1 eye), partial zonular dehiscence after IOL was implanted (n = 1 eye), transillumination defect (n = 1 eye), corneal abrasion (n = 1 eye), and an IOL that needed to be reloaded into the C cartridge (n = 1 eye).
- In the ReSTOR<sup>®</sup> control group, the "other" types of surgical problems included: wound leak (n = 1 eye), inadequate zonular support (n = 1 eye), corneal abrasion (n = 1 eye), iris chaffing (n = 1 eye), and enlarged incision (n = 1 eye).

While a slightly higher incidence of surgical problems was reported in the ReSTOR<sup>®</sup> Toric IOL group relative to the control ReSTOR<sup>®</sup> IOL (1.8% versus 1.6%), overall, surgical problems occurred infrequently in both IOL groups.

There is no increased risk associated with the implantation and/or manipulation of the investigational ReSTOR<sup>®</sup> Toric IOL based on an evaluation of subjects who

experienced a capsulorhexis tear and/or an anterior capsular tear and zonular damage at the operative visit. Although a numerical increase in the number of subjects who experienced a capsulorhexis tear and anterior radial tear is observed in the investigational arm, a closer inspection into the etiology and timing of these events indicates no relationship to the device being implanted. Of the nine events identified, eight occurred in seven subjects in the investigational arm and one event in one subject in the control arm.

See Table 20 – 21.

**Table 20: Number and Percentage of Eyes with Surgical Problem (Safety Set)**

**Table 9.2.1.10.-1:  
Number and Percentage of Eyes With Surgical Problems  
(Safety Set)**

	First Implanted Eye		Second Implanted Eye	
	ReSTOR Toric IOL (N = 386)	ReSTOR IOL (N = 188)	ReSTOR Toric IOL (N = 383)	ReSTOR IOL (N = 188)
	n (%)	n (%)	n (%)	n (%)
None	379 (98.2)	185 (98.4)	371 (96.9)	185 (98.4)
Capsulorhexis tear	0 (0.0)	0 (0.0)	3 (0.8)	0 (0.0)
Other	7 (1.8)	3 (1.6)	9 (2.3)	3 (1.6)

ReSTOR, Toric IOL = ACRYSOF IQ ReSTOR, Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR, IOL = ACRYSOF ReSTOR, Multifocal Lens Model SA60D3

**Table 21: Number and Percentage of Eyes with Capsulorhexis Tear and Anterior Radial Tear or Zonular Damage (Safety Set)**

	First Implanted Eye		Second Implanted Eye	
	ReSTOR Toric IOL (N = 386)	ReSTOR IOL (N = 188)	ReSTOR Toric IOL (N = 383)	ReSTOR IOL (N = 188)
	n (%)	n (%)	n (%)	n (%)
Capsulorhexis tear & Anterior radial tear	3 (0.8)	1 (0.5)	5 (1.3)	0 (0.0)
Zonular damage	1 (0.3)	0 (0.0)	0 (0.0)	1 (0.5)

ReSTOR, Toric IOL = ACRYSOF IQ ReSTOR, Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR, IOL = ACRYSOF ReSTOR, Multifocal Lens Model SA60D3

- Device Deficiencies

A total of four IOL device deficiencies were reported in this study. Three IOLs (2 ReSTOR<sup>®</sup> Toric IOLs and 1 control ReSTOR<sup>®</sup> IOL) scheduled to be used in this clinical study demonstrated a device deficiency due to damage of the haptics from manufacturing or handling of the lens either prior to, during or after the surgical procedure in both IOL groups. One device deficiency was reported for the control ReSTOR<sup>®</sup> IOL due to a damaged IOL box. Of the damaged IOLs, in only one case did the damage occur following implantation of the IOL (this is the case discussed under “Surgical Problems” above which resulted in exclusion of the subject from the study). In the other two cases, the damage was noted prior to insertion in the eye.

## 2. Effectiveness Results

Primary effectiveness outcomes: Mean monocular Uncorrected Distance Visual Acuity (UCDVA) and mean monocular Uncorrected Near Visual Acuity (UCNVA) at fixed distance for the first operative eye at 12 months (Visit 5A)

The two primary effectiveness endpoints are evaluated by comparing the two treatment groups using a non-inferiority test. Results would be considered successful if the upper limit for each co-primary parameter was less than the clinical performance target. The clinical performance target was set at 0.1 logMAR (logarithm of the minimum angle of resolution) unit. All visual acuity data is presented in logMAR units except in tables 25-26 which use Snellen units.

Both primary effectiveness outcomes of mean monocular UCDVA and mean monocular UCNVA at fixed distance for the first operative eye at Visit 5A (12 months) were successfully met. See Tables 22 - 23.

**Table 22: Comparison of Monocular UCDVA at Visit 5 Using Least Squares Estimates (All Implanted Population)**

		<b>ReSTOR Toric IOL (N=386)</b>	<b>ReSTOR IOL (N=186)</b>	<b>Difference (95%UCL)</b>
<b>First Implanted Eye</b>	<b>N</b>	373	180	
	<b>Mean</b>	0.126	0.125	0.001 (0.030)
	<b>SE</b>	0.013	0.015	
<b>Second Implanted Eye</b>	<b>N</b>	371	180	
	<b>Mean</b>	0.113	0.102	0.011 (0.038)
	<b>SE</b>	0.011	0.013	

**Table 23: Comparison of Monocular UCNVA at Visit 5 at Fixed Distance Using Least Squares Estimates (All Implanted Population)**

		ReSTOR Toric IOL (N=386)	ReSTOR IOL (N=186)	Difference (95% UCL)
<b>First Implanted Eye</b>	<b>N</b>	373	180	
	<b>Mean</b>	0.193	0.236	-0.044 (- 0.017)
	<b>SE</b>	0.015	0.017	
<b>Second Implanted Eye</b>	<b>N</b>	371	180	
	<b>Mean</b>	0.181	0.234	-0.052 (- 0.026)
	<b>SE</b>	0.013	0.015	

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3  
 Difference = ReSTOR Toric IOL – ReSTOR IOL  
 Estimates were based on the repeated measure analysis of covariance  
 UCL = 95% Upper Confidence Limit; SE = Standard Error  
 “(N= )” in column header is number in the treatment groups.  
 Subjects who discontinued before Visit 5 are excluded from this analysis. Numbers with data are indicated in the table body.

Supportive effectiveness variables:

- Monocular (Best Corrected) and Binocular (Uncorrected and Best Corrected) Distance Visual Acuity

With regard to supportive effectiveness parameters, there were no clinically relevant differences in the mean binocular UCDVA between the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL at Visit 5 (12 months). Furthermore, mean binocular distance visual acuity results were 20/20 (equivalent Snellen acuity) at Visit 5 (12 months) for both lens models. The observed percentage of ReSTOR<sup>®</sup> Toric IOL subjects who achieved monocular and binocular UCDVA of 20/40 or better was similar to the control ReSTOR<sup>®</sup> IOL subjects at all postoperative visits. The monocular and binocular UCDVA results were similar between the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL over all age ranges.

There were no clinically relevant differences in the mean BCDVA for subjects implanted with the ACRYSOF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 compared with subjects implanted with the control ACRYSOF<sup>®</sup> ReSTOR<sup>®</sup> Multifocal IOL Model SA60D3. The mean monocular BCDVA results for ReSTOR<sup>®</sup> Toric IOL Models SND1T3/ SND1T4

and Models SND1T5/ SND1T6 were within 2 letters on an ETDRS chart (0.03 logMAR) at all first and second eye postoperative visits.

One subject in each arm had worse than 20/40 Snellen binocular BCDVA for reasons unrelated to the IOL at Visit 5 (12 months). Four subjects lost one or more lines of BCDVA between the preoperative visit and Visit 5. Only one of these case occurred in a subject implanted with the investigational ReSTOR<sup>®</sup> Toric IOL, and three cases occurred in subjects implanted with the control ReSTOR<sup>®</sup> IOL. The subject in the investigational arm who lost one line of BCDVA from Visit 0 (preoperative) to Visit 5 (12 months) experienced clinically significant posterior capsular opacification (requiring YAG laser treatment) at Visit 5 (12 months). In the three control subjects, the vision loss was attributed to retinal pathologies.

See Tables 24 – 26.

**Table 24: Descriptive Statistics for Monocular BCDVA (all Implanted Set) by Lens Model**

		First Implanted Eye		Second Implanted Eye	
		SND1T3/ SND1T4	SND1T5/ SND1T6	SND1T3/ SND1T4	SND1T5/ SND1T6
Screening	n	269	117	316	66
	Mean (SD)	0.37 (0.17)	0.38 (0.16)	0.35 (0.15)	0.37 (0.18)
	(Min, Max)	(0.20, 1.40)	(0.22, 1.40)	(0.16, 1.40)	(0.22, 1.40)
	95% CI	(0.35, 0.39)	(0.35, 0.41)	(0.34, 0.37)	(0.33, 0.42)
Visit 1	n	269	117	316	66
	Mean (SD)	0.12 (0.15)	0.14 (0.18)	0.10 (0.13)	0.10 (0.17)
	(Min, Max)	(-0.12, 0.60)	(-0.14, 1.00)	(-0.18, 0.84)	(-0.14, 0.82)
	95% CI	(0.10, 0.14)	(0.11, 0.18)	(0.09, 0.12)	(0.06, 0.14)
Visit 2	n	269	117	316	66
	Mean (SD)	0.04 (0.10)	0.06 (0.13)	0.03 (0.10)	0.03 (0.11)
	(Min, Max)	(-0.20, 0.36)	(-0.18, 0.70)	(-0.22, 0.52)	(-0.18, 0.40)
	95% CI	(0.03, 0.05)	(0.04, 0.08)	(0.02, 0.04)	(0.00, 0.05)
Visit 3	n	267	116	316	66
	Mean (SD)	0.01 (0.10)	0.02 (0.09)	0.00 (0.09)	0.03 (0.10)
	(Min, Max)	(-0.18, 0.60)	(-0.14, 0.28)	(-0.20, 0.40)	(-0.12, 0.36)
	95% CI	(0.00, 0.03)	(0.00, 0.04)	(-0.00, 0.01)	(0.00, 0.05)
Visit 4	n	265	114	311	66
	Mean (SD)	0.01 (0.09)	0.01 (0.09)	0.00 (0.09)	0.02 (0.11)
	(Min, Max)	(-0.20, 0.30)	(-0.18, 0.32)	(-0.20, 0.34)	(-0.18, 0.44)
	95% CI	(-0.00, 0.02)	(-0.01, 0.03)	(-0.01, 0.01)	(-0.01, 0.04)
Visit 5	n	260	113	306	65
	Mean (SD)	0.02 (0.10)	0.02 (0.10)	0.01 (0.10)	0.02 (0.10)
	(Min, Max)	(-0.18, 0.50)	(-0.20, 0.40)	(-0.20, 0.40)	(-0.18, 0.46)
	95% CI	(0.01, 0.03)	(-0.00, 0.04)	(-0.00, 0.02)	(-0.01, 0.04)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

**Table 25: Number and Percentage of Subjects with Monocular BCDVA (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL		ReSTOR IOL	
		n	(%)	n	(%)
Screening	Total	386	188	382	188
	20/20 or better	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
	Worse than 20/20	386 (100.0)	188 (100.0)	382 (100.0)	188 (100.0)
Visit 1	Total	386	187	382	188
	20/20 or better	151 (39.1)	69 (36.9)	169 (44.2)	84 (44.7)
	Worse than 20/20	235 (60.9)	118 (63.1)	213 (55.8)	104 (55.3)
Visit 2	Total	386	188	382	187
	20/20 or better	233 (60.4)	120 (63.8)	266 (69.6)	132 (70.6)
	Worse than 20/20	153 (39.6)	68 (36.2)	116 (30.4)	55 (29.4)
Visit 3	Total	383	187	382	187
	20/20 or better	283 (73.9)	148 (79.1)	290 (75.9)	137 (73.3)
	Worse than 20/20	100 (26.1)	39 (20.9)	92 (24.1)	50 (26.7)
Visit 4	Total	379	186	377	186
	20/20 or better	277 (73.1)	143 (76.9)	290 (76.9)	142 (76.3)
	Worse than 20/20	102 (26.9)	43 (23.1)	87 (23.1)	44 (23.7)
Visit 5	Total	373	180	371	180
	20/20 or better	264 (70.8)	140 (77.8)	273 (73.6)	144 (80.0)
	Worse than 20/20	109 (29.2)	40 (22.2)	98 (26.4)	36 (20.0)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

**Table 26: Number and Percentage of Subjects with Binocular BCDVA (All Implanted Set)**

		ReSTOR Toric IOL		ReSTOR IOL	
		n	(%)	n	(%)
		Visit 4	Total	377	186
20/20 or better	335 (88.9)		173 (93.0)		
Worse than 20/20	42 (11.1)		13 (7.0)		
Visit 5	Total	371	180		
	20/20 or better	335 (90.3)	173 (96.1)		
	Worse than 20/20	36 (9.7)	7 (3.9)		

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models  
 SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

- Monocular (Distance Corrected for optical infinity and Best Corrected) and Binocular (Uncorrected, Distance Corrected for optical infinity and Best Corrected) Near Visual Acuity at Fixed Distance

The mean monocular BCNVA (at fixed distance) results for ReSTOR<sup>®</sup> Toric IOL Models SND1T3/ SND1T4 and Models SND1T5/ SND1T6 were within one letter on an ETDRS chart (0.01 logMAR) at all first and second eye postoperative visits.

At fixed distance, the mean monocular DCNVA results for ReSTOR® Toric IOL Models SND1T3/ SND1T4 and Models SND1T5/ SND1T6 were within two letters on an ETDRS acuity chart (0.03 logMAR) at all first and second eye postoperative visits. There were no clinically relevant differences in the mean monocular and binocular DCNVA at fixed distance between the ReSTOR® Toric IOL and the control ReSTOR® IOL at all postoperative visits.

See Tables 27 – 30.

**Table 27: Descriptive Statistics for Monocular BCNVA at Fixed Distance (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
Visit 3	<b>n</b>	378	187	377	187
	<b>Mean (SD)</b>	0.12 (0.13)	0.15 (0.13)	0.11 (0.13)	0.16 (0.14)
	<b>(Min, Max)</b>	(-0.18, 0.70)	(-0.08, 0.72)	(-0.18, 0.70)	(-0.06, 0.80)
	<b>95% CI</b>	(0.11, 0.13)	(0.14, 0.17)	(0.10, 0.13)	(0.14, 0.18)
Visit 4	<b>n</b>	379	186	377	186
	<b>Mean (SD)</b>	0.12 (0.12)	0.16 (0.13)	0.11 (0.12)	0.16 (0.14)
	<b>(Min, Max)</b>	(-0.14, 0.64)	(-0.02, 0.70)	(-0.20, 0.52)	(-0.12, 0.78)
	<b>95% CI</b>	(0.10, 0.13)	(0.14, 0.18)	(0.10, 0.12)	(0.14, 0.18)
Visit 5	<b>n</b>	373	180	371	180
	<b>Mean (SD)</b>	0.11 (0.13)	0.14 (0.16)	0.10 (0.14)	0.14 (0.14)
	<b>(Min, Max)</b>	(-0.12, 0.70)	(-0.22, 1.28)	(-0.12, 0.84)	(-0.18, 0.82)
	<b>95% CI</b>	(0.09, 0.12)	(0.11, 0.16)	(0.09, 0.11)	(0.12, 0.16)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

**Table 28: Descriptive Statistics for Binocular BCNVA at Fixed Distance (All Implanted Set)**

		ReSTOR Toric IOL	ReSTOR IOL
		Visit 4	<b>n</b>
	<b>Mean (SD)</b>	0.05 (0.10)	0.10 (0.12)
	<b>(Min, Max)</b>	(-0.20, 0.42)	(-0.12, 0.88)
	<b>95% CI</b>	(0.04, 0.06)	(0.08, 0.12)
Visit 5	<b>n</b>	371	180
	<b>Mean (SD)</b>	0.04 (0.11)	0.07 (0.11)
	<b>(Min, Max)</b>	(-0.20, 0.50)	(-0.22, 0.50)
	<b>95% CI</b>	(0.03, 0.05)	(0.06, 0.09)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

**Table 29: Descriptive Statistics for Monocular BCNVA at Fixed Distance (All Implanted Set) By Lens Model**

		First Implanted Eye		Second Implanted Eye	
		SND1T3/ SND1T4	SND1T5/ SND1T6	SND1T3/ SND1T4	SND1T5/ SND1T6
Visit 3	<b>n</b>	262	116	311	66
	<b>Mean (SD)</b>	0.12 (0.13)	0.13 (0.13)	0.11 (0.13)	0.11 (0.14)
	<b>(Min, Max)</b>	(-0.18, 0.70)	(-0.10, 0.50)	(-0.18, 0.70)	(-0.12, 0.52)
	<b>95% CI</b>	(0.10, 0.13)	(0.11, 0.16)	(0.10, 0.13)	(0.08, 0.15)
Visit 4	<b>n</b>	265	114	311	66
	<b>Mean (SD)</b>	0.12 (0.12)	0.12 (0.12)	0.11 (0.12)	0.12 (0.13)
	<b>(Min, Max)</b>	(-0.14, 0.64)	(-0.10, 0.56)	(-0.20, 0.52)	(-0.10, 0.44)
	<b>95% CI</b>	(0.10, 0.13)	(0.10, 0.14)	(0.09, 0.12)	(0.09, 0.15)
Visit 5	<b>n</b>	260	113	306	65
	<b>Mean (SD)</b>	0.11 (0.14)	0.10 (0.12)	0.10 (0.13)	0.10 (0.14)
	<b>(Min, Max)</b>	(-0.12, 0.70)	(-0.12, 0.52)	(-0.10, 0.84)	(-0.12, 0.52)
	<b>95% CI</b>	(0.09, 0.12)	(0.08, 0.13)	(0.09, 0.12)	(0.07, 0.13)

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3

**Table 30: Descriptive Statistics for Binocular UCNVA at Fixed Distance (All Implanted Set)**

		ReSTOR	ReSTOR
		Toric IOL	IOL
Screening	<b>n</b>	384	188
	<b>Mean (SD)</b>	0.63 (0.29)	0.69 (0.30)
	<b>(Min, Max)</b>	(-0.18, 1.38)	(0.12, 1.30)
	<b>95% CI</b>	(0.60, 0.66)	(0.65, 0.73)
Visit 4	<b>n</b>	377	186
	<b>Mean (SD)</b>	0.11 (0.12)	0.15 (0.12)
	<b>(Min, Max)</b>	(-0.16, 0.54)	(-0.12, 0.58)
	<b>95% CI</b>	(0.09, 0.12)	(0.14, 0.17)
Visit 5	<b>n</b>	371	180
	<b>Mean (SD)</b>	0.10 (0.13)	0.14 (0.13)
	<b>(Min, Max)</b>	(-0.10, 0.60)	(-0.10, 0.68)
	<b>95% CI</b>	(0.08, 0.11)	(0.12, 0.16)

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models  
 SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3

- Monocular and Binocular Near Visual Acuity at Best Distance: Uncorrected and Distance Corrected for optical infinity

The mean monocular UCNVA at best distance for ReSTOR<sup>®</sup> Toric IOL Models SND1T3/SND1T4 and Models SND1T5/ SND1T6 were within one letter on an ETDRS chart (0.02 logMAR), at all first and second eye postoperative visits. There were no clinically relevant differences in the mean monocular and

binocular UCNVA at best distance between the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL at all postoperative visits. The mean distance identified by subjects as providing the best binocular UCNVA was approximately 5.57 cm greater for the ReSTOR<sup>®</sup> Toric IOL subjects than for the control ReSTOR<sup>®</sup> IOL subjects (as opposed to the expected 7 cm difference between 33 cm and 40 cm). The observed percentage of ReSTOR<sup>®</sup> Toric IOL subjects who achieved monocular and binocular UCNVA at best distance of 20/40 or better was similar to that of the control ReSTOR<sup>®</sup> IOL subjects at all postoperative visits.

See Tables 31 – 32.

**Table 31: Descriptive Statistics for Monocular UCNVA at Best Distance (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
Visit 3	<b>n</b>	383	187	382	187
	<b>Mean (SD)</b>	0.17 (0.14)	0.20 (0.15)	0.16 (0.14)	0.21 (0.17)
	<b>(Min, Max)</b>	(-0.18, 0.75)	(-0.09, 0.72)	(-0.13, 0.81)	(-0.07, 0.80)
	<b>95% CI</b>	(0.15, 0.18)	(0.18, 0.22)	(0.15, 0.18)	(0.19, 0.24)
Visit 4	<b>n</b>	379	186	377	186
	<b>Mean (SD)</b>	0.18 (0.15)	0.19 (0.14)	0.16 (0.14)	0.19 (0.15)
	<b>(Min, Max)</b>	(-0.18, 0.74)	(-0.12, 0.68)	(-0.19, 0.62)	(-0.08, 0.94)
	<b>95% CI</b>	(0.17, 0.20)	(0.17, 0.21)	(0.15, 0.18)	(0.17, 0.21)
Visit 5	<b>n</b>	373	180	371	180
	<b>Mean (SD)</b>	0.17 (0.14)	0.19 (0.17)	0.16 (0.14)	0.18 (0.16)
	<b>(Min, Max)</b>	(-0.10, 0.68)	(-0.10, 1.34)	(-0.10, 0.76)	(-0.09, 0.98)
	<b>95% CI</b>	(0.15, 0.18)	(0.16, 0.21)	(0.15, 0.18)	(0.16, 0.20)

ReSTOR Toric IOL = ACRYSOFT IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR IOL = ACRYSOFT ReSTOR Multifocal Lens Model SA60D3

**Table 32: Number and Percentage of Subjects with Monocular UCNVA at Best Distance (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
		<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>	<b>n (%)</b>
Visit 3	<b>Total</b>	383	187	382	187
	<b>20/40 or better</b>	335 (87.5)	155 (82.9)	340 (89.0)	154 (82.4)
	<b>Worse than 20/40</b>	48 (12.5)	32 (17.1)	42 (11.0)	33 (17.6)
Visit 4	<b>Total</b>	379	186	377	186
	<b>20/40 or better</b>	331 (87.3)	160 (86.0)	335 (88.9)	162 (87.1)
	<b>Worse than 20/40</b>	48 (12.7)	26 (14.0)	42 (11.1)	24 (12.9)
Visit 5	<b>Total</b>	373	180	371	180
	<b>20/40 or better</b>	332 (89.0)	157 (87.2)	339 (91.4)	164 (91.1)
	<b>Worse than 20/40</b>	41 (11.0)	23 (12.8)	32 (8.6)	16 (8.9)

ReSTOR Toric IOL = ACRYSOFT IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR IOL = ACRYSOFT ReSTOR Multifocal Lens Model SA60D3

No clinically relevant differences in DCNVA at best distance were observed for the ACRYSOFF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/SND1T6 and the control ACRYSOFF<sup>®</sup> ReSTOR<sup>®</sup> Multifocal IOL Model SA60D3 under photopic conditions. The mean monocular DCNVA (at best distance) results for ReSTOR<sup>®</sup> Toric IOL Models SND1T3/ SND1T4 and Models SND1T5/ SND1T6 were within 1 letter on an ETDRS acuity chart (0.02 logMAR), at first and second eye postoperative visits.

There were no clinically relevant differences in the mean monocular and binocular DCNVA, at best distance, between the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL at postoperative visits.

- Monocular and Binocular Mesopic Near Visual Acuity at Best Distance: Distance Corrected for optical infinity

No clinically relevant differences in Distance Corrected Near Visual Acuity at best distance were observed for the ACRYSOFF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/SND1T4/ SND1T5/ SND1T6 and the control ACRYSOFF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal IOL Model SA60D3 under mesopic conditions. The observed percentage of ReSTOR<sup>®</sup> Toric IOL subjects who achieved monocular and binocular mesopic DCNVA (at best distance) of 20/40 or better was similar to the control ReSTOR IOL subjects at all postoperative visits.

- Binocular Intermediate Visual Acuity (50 cm, 60 cm, and 70 cm): Uncorrected and Distance Corrected for optical infinity

Clinically relevant differences favoring the AcyrSof<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 were observed for mean Uncorrected Intermediate Visual Acuity (UCIVA) at all testing distances (50 cm, 60 cm, and 70 cm). At all 3 intermediate testing distances (50 cm, 60 cm, and 70 cm), the mean binocular UCIVA for the ReSTOR<sup>®</sup> Toric IOL compared favorably to the control ReSTOR<sup>®</sup> IOL resulting in approximately 1 line visual acuity increase ( $\geq 0.1$  logMAR). At Visit 5 (12 months), the observed difference in UCIVA between lens models favored the ReSTOR<sup>®</sup> Toric IOL at all distances, with the greatest observed difference being 1.5 lines at 50 cm and 60 cm. See Table 33.

**Table 33: Descriptive Statistics for Binocular UCIVA at Visit 5 (All Implanted Set)**

		ReSTOR Toric IOL	ReSTOR IOL
VA at 50 cm	n	371	180
	Mean (SD)	0.13 (0.14)	0.28 (0.17)
	(Min, Max)	(-0.20, 0.60)	(-0.18, 0.74)
	95% CI	(0.11, 0.14)	(0.26, 0.31)
VA at 60 cm	n	371	180
	Mean (SD)	0.17 (0.15)	0.32 (0.15)
	(Min, Max)	(-0.26, 0.54)	(-0.24, 0.64)
	95% CI	(0.16, 0.19)	(0.29, 0.34)
VA at 70 cm	n	371	180
	Mean (SD)	0.21 (0.14)	0.32 (0.15)
	(Min, Max)	(-0.30, 0.68)	(-0.22, 0.76)
	95% CI	(0.19, 0.22)	(0.29, 0.34)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models  
SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR IOL = ACRYSOF ReSTOR Multifocal Lens Model SA60D3

We note that the control IOL has a +4 D add power and the investigational IOLs have a +3 D add power. A difference favoring the +3 D add power is to be expected in this measurement. Therefore, this result is likely reflecting the difference in the add powers rather than the addition of a toric feature.

Clinically relevant differences favoring the ACRYSOF® IQ ReSTOR® Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 were observed for mean Distance Corrected Intermediate Visual Acuity at all testing distances (50 cm, 60 cm, and 70 cm). All differences between groups were greater than 0.15 logMAR (1.5 lines on an ETDRS visual acuity chart).

- Orientation of Lens Axis determined by Photographic Assessment of Lens Orientation, PALO (Investigational Lens only) and Intended Lens Placement (Investigational Lens only)

Supportive effectiveness parameters also included orientation of Lens Axis determined by Photographic Assessment of Lens Orientation, PALO (Investigational Lens only) and Intended Lens Placement (Investigational Lens only).

Subjects who underwent SSIs were included in all analyses of IOL rotation and misalignment with their pre- and post-SSI data. For subjects who had SSIs, no imputations of PALO data were conducted for calculating IOL orientation and misalignment, as specified in the statistical analysis plan.

Misalignment:

The mean absolute difference between intended axis orientation and achieved axis orientation at surgery was  $5.0^\circ \pm 6.1$  for the 362 ReSTOR® Toric IOL subjects in the first operative eyes. See Tables 34 – 36.

**Table 34: Number and Percentage of Subjects with Absolute Misalignment Categories (All Implanted Set) 10 degrees**

		1st Implanted Eye		2nd Implanted Eye	
		n	(%)	n	(%)
<b>Surgery</b>	<b>Total</b>	<b>363</b>		<b>366</b>	
	<b>&lt;10 degrees</b>	329	(90.6)	335	(91.5)
	<b>≥10 degrees</b>	34	(9.4)	31	(8.5)
<b>Visit 1</b>	<b>Total</b>	<b>376</b>		<b>375</b>	
	<b>&lt;10 degrees</b>	336	(89.4)	338	(90.1)
	<b>≥10 degrees</b>	40	(10.6)	37	(9.9)
<b>Visit 2</b>	<b>Total</b>	<b>377</b>		<b>370</b>	
	<b>&lt;10 degrees</b>	342	(90.7)	337	(91.1)
	<b>≥10 degrees</b>	35	(9.3)	33	(8.9)
<b>Visit 3</b>	<b>Total</b>	<b>370</b>		<b>370</b>	
	<b>&lt;10 degrees</b>	333	(90.0)	337	(91.1)
	<b>≥10 degrees</b>	37	(10.0)	33	(8.9)
<b>Visit 4</b>	<b>Total</b>	<b>366</b>		<b>366</b>	
	<b>&lt;10 degrees</b>	331	(90.4)	337	(92.1)
	<b>≥10 degrees</b>	35	(9.6)	29	(7.9)
<b>Visit 5</b>	<b>Total</b>	<b>360</b>		<b>360</b>	
	<b>&lt;10 degrees</b>	326	(90.6)	328	(91.1)
	<b>≥10 degrees</b>	34	(9.4)	32	(8.9)

**Table 35: Number and Percentage of Subjects with Absolute Misalignment Categories (All Implanted Set) 30 degrees**

		1st Implanted Eye		2nd Implanted Eye	
		n	(%)	n	(%)
Surgery	<b>Total</b>	<b>363</b>		<b>366</b>	
	<30 degrees	362	(99.7)	365	(99.7)
	≥30 degrees	1	(0.3)	1	(0.3)
Visit 1	<b>Total</b>	<b>376</b>		<b>375</b>	
	<30 degrees	373	(99.2)	375	(100.0)
	≥30 degrees	3	(0.8)	0	(0.0)
Visit 2	<b>Total</b>	<b>377</b>		<b>370</b>	
	<30 degrees	374	(99.2)	370	(100.0)
	≥30 degrees	3	(0.8)	0	(0.0)
Visit 3	<b>Total</b>	<b>370</b>		<b>370</b>	
	<30 degrees	370	(100.0)	370	(100.0)
	≥30 degrees	0	(0.0)	0	(0.0)
Visit 4	<b>Total</b>	<b>366</b>		<b>366</b>	
	<30 degrees	365	(99.7)	366	(100.0)
	≥30 degrees	1	(0.3)	0	(0.0)
Visit 5	<b>Total</b>	<b>360</b>		<b>360</b>	
	<30 degrees	360	(100.0)	360	(100.0)
	≥30 degrees	0	(0.0)	0	(0.0)

**Table 36: Descriptive Statistics for the Differences between Lens Axis Orientation at the Post-Operative Visit and Intended Placement (Degrees) (All Implanted Set)**

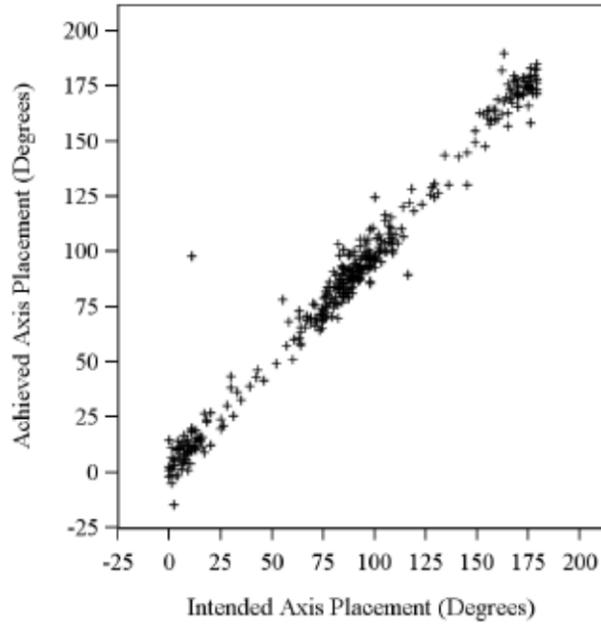
		Absolute Misalignment		Signed Misalignment	
		1st Implanted Eye	2nd Implanted Eye	1st Implanted Eye	2nd Implanted Eye
<b>Surgery</b>	<b>n</b>	363	366	363	366
	<b>Mean (SD)</b>	5.0 (6.1)	4.7 (4.0)	-1.3 (7.7)	-1.5 (6.0)
	<b>(Min, Max)</b>	(0.0, 87.1)	(0.0, 35.8)	(-87.1, 26.5)	(-35.8, 22.3)
	<b>95% CI</b>	(4.3, 5.6)	(4.2, 5.1)	(-2.1, -0.5)	(-2.1, -0.9)
<b>Visit 1</b>	<b>n</b>	376	375	376	375
	<b>Mean (SD)</b>	5.4 (6.7)	4.9 (4.2)	-1.2 (8.5)	-1.6 (6.2)
	<b>(Min, Max)</b>	(0.0, 86.2)	(0.0, 25.2)	(-86.2, 45.6)	(-22.1, 25.2)
	<b>95% CI</b>	(4.7, 6.1)	(4.4, 5.3)	(-2.1, -0.4)	(-2.2, -0.9)
<b>Visit 2</b>	<b>n</b>	377	370	377	370
	<b>Mean (SD)</b>	5.3 (6.7)	4.7 (3.9)	-0.5 (8.5)	-1.0 (6.0)
	<b>(Min, Max)</b>	(0.0, 85.4)	(0.0, 21.8)	(-85.4, 48.2)	(-20.0, 21.8)
	<b>95% CI</b>	(4.6, 6.0)	(4.3, 5.1)	(-1.4, 0.3)	(-1.6, -0.4)
<b>Visit 3</b>	<b>n</b>	370	370	370	370
	<b>Mean (SD)</b>	4.9 (4.2)	4.7 (4.0)	-0.3 (6.5)	-0.5 (6.2)
	<b>(Min, Max)</b>	(0.0, 24.3)	(0.0, 24.4)	(-24.3, 23.9)	(-21.1, 24.4)
	<b>95% CI</b>	(4.5, 5.3)	(4.3, 5.1)	(-1.0, 0.3)	(-1.2, 0.1)
<b>Visit 4</b>	<b>n</b>	366	366	366	366
	<b>Mean (SD)</b>	5.2 (4.6)	4.7 (4.0)	-0.1 (7.0)	-0.5 (6.1)
	<b>(Min, Max)</b>	(0.0, 44.4)	(0.0, 25.6)	(-24.1, 44.4)	(-17.9, 25.6)
	<b>95% CI</b>	(4.7, 5.7)	(4.3, 5.1)	(-0.8, 0.6)	(-1.1, 0.1)
<b>Visit 5</b>	<b>n</b>	360	360	360	360
	<b>Mean (SD)</b>	5.1 (4.0)	4.7 (3.9)	-0.1 (6.5)	-0.9 (6.0)
	<b>(Min, Max)</b>	(0.0, 24.0)	(0.0, 24.4)	(-21.7, 24.0)	(-23.3, 24.4)
	<b>95% CI</b>	(4.7, 5.5)	(4.3, 5.1)	(-0.8, 0.6)	(-1.5, -0.3)

Nine subjects (7 first eyes and 2 second eyes) had actual misalignments of 20 degrees or more at the operative visit (ranging from 20-87 degrees misalignment). Of these, 3 subjects were actual misplacements at the time of surgery.

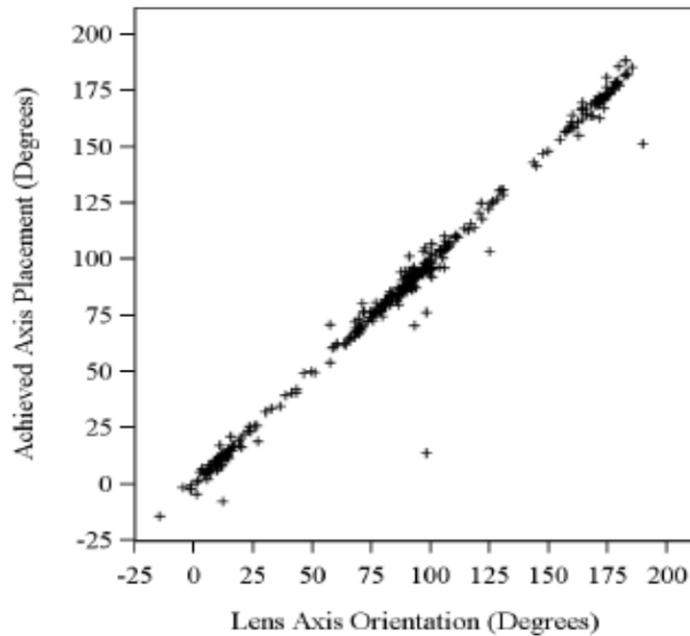
In addition to poor photograph quality at the operative visit, intra-operative factors also contribute to whether an accurate placement of the lens at the intended location/orientation is achieved. Careful wound construction, IOP fluctuations, and removal of ophthalmic viscosurgical devices (OVD) can contribute to the misalignment of IOLs during surgery. Additionally, while IOL misalignment may be related to the axis of implantation, axial length, and capsular bag diameter results from this study could neither confirm nor refute such correlation.

See Figures 3 – 6.

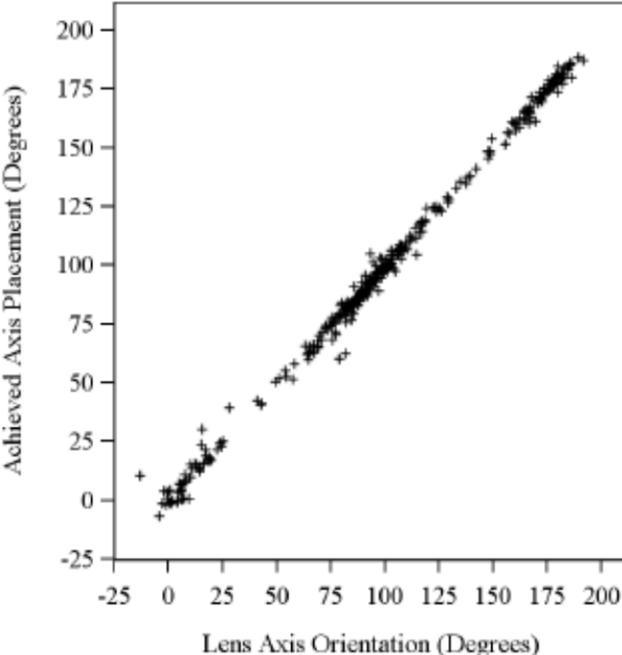
**Figure 3: Intended Axis Placement versus Achieved Axis Placement (Degrees) at the Operative Visit First Implanted Eye (All Implanted Set)**



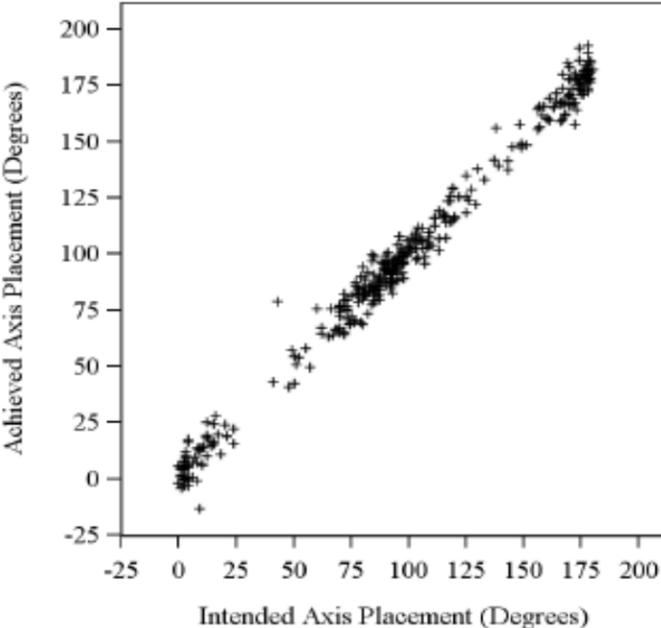
**Figure 4: Achieved Axis Placement (Degrees) at the Operative Visit versus Lens Axis Orientation at the Month 12 Visit First Implanted Eye (All Implanted Set)**



**Figure 5: Achieved Axis Placement (Degrees) at the Operative Visit versus Lens Axis Orientation at the Month 12 Visit Second Implanted Eye (All Implanted Set)**



**Figure 6: Intended Axis Placement versus Achieved Axis Placement (Degrees) at the Operative Visit Second Implanted Eye (All Implanted Set)**



Over 90% of first (329/363) and second eyes (335/366) had no more than 10 degrees of misalignment from the intended IOL axis calculated prior to surgery. However, 11 primary eyes and 7 second implanted eyes (total of 18 eyes) had lens misalignment >20 degrees at any visit. The Applicant reports a total of 5 SSI's for IOL misalignment performed in 4 subjects. For two of these five subjects, anatomical factors - torticollis and floppy iris syndrome were probably responsible for the IOL misalignment. For another subject the Investigator stated that the IOL misalignment was due to eye anatomy without more specific detail being provided.

Rotation:

At least 97.2% (346/356) of subjects demonstrated absolute lens rotation of less than 10° between the operative visit and Visit 5. IOL rotation, the mean absolute difference between the achieved lens axis orientation at Visit 5 and the achieved axis placement at surgery, was 2.7° ± 5.8 in the first operative eyes and 2.2° ± 2.7 in the second operative eyes. Furthermore, the mean actual difference between the achieved lens axis orientation and the achieved axis placement at surgery was ~ 1.0° ± 6.3 in the first and second operative eyes at all postoperative visits. A post-hoc analysis was performed to confirm that the rotational stability of the ReSTOR® Toric IOL was maintained between 2 consecutive visits at least 3 months apart (between Visits 3 and 4). See Table 37.

**Table 37: Number and Percentage of Subjects by Lens Axis Rotation between Visit 3 and Visit 4 (All Implanted Set)**

		ReSTOR Toric n (%)
<b>First Implanted Eye</b>	<b>Total</b>	<b>359</b>
	<b>Lens Movement ≤5 degrees</b>	<b>338 (94.2)</b>
	<b>Lens Movement &gt;5 degrees</b>	<b>21 (5.8)</b>
<b>Second Implanted Eye</b>	<b>Total</b>	<b>361</b>
	<b>Lens Movement ≤5 degrees</b>	<b>339 (93.9)</b>
	<b>Lens Movement &gt;5 degrees</b>	<b>22 (6.1)</b>

ReSTOR Toric = ACRYSOF IQ ReSTOR Multifocal Lens Models  
SND1T3/SND1T4/SND1T5/SND1T6  
Subjects with missing observations at either Visit 3 or Visit 4 were excluded

The data demonstrate that at least 90% of ReSTOR® Toric IOL subjects achieved a rotational stability of 5 degrees or less between 2 consecutive visits, at least 3 months apart. However, eight subjects had a lens rotation of 20 degrees or more at the 12 month visit. Note that three of these subjects had lens repositioning surgeries after their initial implantation due to a worsening of visual acuity and observed lens axis rotation however, the 12 month rotation results for these 3 subjects calculated between the surgical visit (Visit 00/00A) and the 12 month visit (Visit 5A), without taking into account the IOL orientation following the repositioning surgery.

While three subjects (three primary eyes) were noted to have absolute lens axis rotation of thirty degrees or more at seven visits (ranging from 31-85 degrees absolute rotation), the mean rotation and mean misalignment observed in the study were less than 3 degrees in the majority of subjects, indicating that the achieved placement was close (on average) to the intended placement, and little rotation generally occurred after placement.

See Table 38.

**Table 38: Descriptive Statistics for the Difference between Lens Axis Orientation at the Postoperative Visit and Achieved Axis Placement (Degrees) at the Operative Visit (All Implanted Set)**

		Absolute Misalignment		Actual Misalignment	
		First Implanted Eye	Second Implanted Eye	First Implanted Eye	Second Implanted Eye
Visit 1	n	376	375	376	375
	Mean (SD)	1.4 (1.8)	1.5 (1.7)	-0.1 (2.3)	-0.0 (2.2)
	(Min, Max)	(0, 18)	(0, 14)	(-11, 18)	(-6, 14)
	95% CI	(1.2, 1.6)	(1.3, 1.6)	(-0.3, 0.2)	(-0.2, 0.2)
Visit 2	n	375	366	375	366
	Mean (SD)	1.8 (2.3)	2.0 (2.7)	0.5 (2.9)	0.6 (3.3)
	(Min, Max)	(0, 23)	(0, 30)	(-11, 23)	(-23, 30)
	95% CI	(1.6, 2.0)	(1.7, 2.2)	(0.2, 0.8)	(0.2, 0.9)
Visit 3	n	367	368	367	368
	Mean (SD)	2.2 (5.1)	2.1 (2.7)	0.8 (5.5)	0.9 (3.3)
	(Min, Max)	(0, 85)	(0, 24)	(-17, 85)	(-24, 24)
	95% CI	(1.6, 2.7)	(1.8, 2.4)	(0.3, 1.4)	(0.6, 1.3)
Visit 4	n	363	364	363	364
	Mean (SD)	2.3 (5.2)	2.3 (3.0)	1.0 (5.6)	1.0 (3.6)
	(Min, Max)	(0, 85)	(0, 27)	(-13, 85)	(-24, 27)
	95% CI	(1.7, 2.8)	(2.0, 2.6)	(0.4, 1.6)	(0.7, 1.4)
Visit 5	n	356	357	356	357
	Mean (SD)	2.7 (5.8)	2.2 (2.7)	1.0 (6.3)	0.7 (3.4)
	(Min, Max)	(0, 84)	(0, 24)	(-36, 84)	(-24, 19)
	95% CI	(2.1, 3.3)	(1.9, 2.5)	(0.4, 1.7)	(0.4, 1.1)

For subjects with missing Operative Visit axis placement data, Day 1 (Visit 1) data were used as baseline

- Reduction of Cylinder (Investigational Lens only)

Subjects implanted with the ReSTOR<sup>®</sup> Toric IOL demonstrated a mean percent reduction in cylinder with respect to target cylinder of at least 76.6% in the first and second operative eyes at all postoperative visits. At least 74.5% (278/373) of subjects implanted with the ReSTOR<sup>®</sup> Toric IOL achieved a reduction in cylinder within 0.5 D of the target cylinder in the first and second operative eyes at Visit 5. Furthermore, at least 94.1% (351/373) of subjects implanted with the ReSTOR<sup>®</sup> Toric IOL achieved a reduction in cylinder within 1.0 D of the target cylinder in the first and second operative eyes at Visit 5.

Analysis of the current pivotal Clinical Study (C-09-036) surgically induced astigmatism (SIA) results demonstrated that the mean scalar SIA magnitude is similar for both treatment groups, 0.45 D for the investigational ReSTOR<sup>®</sup> Toric IOL and 0.43 D for the control ReSTOR<sup>®</sup> IOL. Both the observed average magnitude SIA, ~0.45D with the rule (WTR), and the observed vector SIA, ~0.05 D WTR, differed from the assumed 0.25 D WTR SIA by 0.20 D. The fixed 0.0 D SIA assumption for the ReSTOR<sup>®</sup> Toric study calculator input impacted study results (manifest refractive astigmatism) by approximately 0.20 D against the rule (ATR) for both the investigational and control lenses.

Note that the SIA input value and incision location were fixed in Clinical Study (C-09-036) to minimize potential variability of clinical study outcomes due to differences in the surgical procedure. The proposed ReSTOR<sup>®</sup> Toric IOL calculator intended to be marketed will allow customized SIA and incision location inputs based on the surgeon’s clinical judgment and surgical plan.

See Tables 39 – 41.

**Table 39: Descriptive Statistics for Percent Reduction in Cylinder with Respect to Target Cylinder (All Implanted Set)**

		First Implanted Eye	Second Implanted Eye	Overall
Visit 1	n	386	382	768
	Mean (SD)	86.5 (28.0)	85.7 (33.6)	86.1 (30.9)
	(Min, Max)	(-49, 137)	(-43, 160)	(-49, 160)
	95% CI	(83.7, 89.3)	(82.3, 89.0)	(83.9, 88.3)
Visit 2	n	386	382	768
	Mean (SD)	84.8 (28.2)	86.5 (36.0)	85.6 (32.3)
	(Min, Max)	(-45, 155)	(-133, 160)	(-133, 160)
	95% CI	(82.0, 87.6)	(82.9, 90.1)	(83.4, 87.9)
Visit 3	n	383	382	765
	Mean (SD)	83.3 (28.4)	84.2 (32.1)	83.8 (30.3)
	(Min, Max)	(-34, 155)	(-69, 160)	(-69, 160)
	95% CI	(80.5, 86.2)	(80.9, 87.4)	(81.6, 85.9)
Visit 4	n	379	377	756
	Mean (SD)	81.7 (29.0)	78.0 (35.1)	79.9 (32.2)
	(Min, Max)	(-37, 155)	(-84, 160)	(-84, 160)
	95% CI	(78.8, 84.6)	(74.5, 81.6)	(77.6, 82.2)
Visit 5	n	373	371	744
	Mean (SD)	77.6 (31.1)	76.6 (36.8)	77.1 (34.0)
	(Min, Max)	(-63, 155)	(-118, 151)	(-118, 155)
	95% CI	(74.5, 80.8)	(72.9, 80.4)	(74.7, 79.6)

**Table 40: Descriptive Statistics for Percent Reduction in Cylinder with Respect to Target Cylinder by Lens Model (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		SND1T3/ SND1T4	SND1T5/ SND1T6	SND1T3/ SND1T4	SND1T5/ SND1T6
Visit 1	<b>n</b>	269	117	316	66
	<b>Mean (SD)</b>	84.8 (31.2)	90.3 (17.8)	84.1 (36.0)	93.0 (16.6)
	<b>(Min, Max)</b>	(-49, 137)	(39, 116)	(-43, 160)	(36, 115)
	<b>95% CI</b>	(81.1, 88.6)	(87.0, 93.6)	(80.1, 88.1)	(88.9, 97.1)
Visit 2	<b>n</b>	269	117	316	66
	<b>Mean (SD)</b>	84.0 (31.2)	86.6 (19.7)	85.4 (38.7)	91.8 (16.4)
	<b>(Min, Max)</b>	(-45, 155)	(18, 114)	(-133, 160)	(52, 116)
	<b>95% CI</b>	(80.3, 87.8)	(83.0, 90.2)	(81.1, 89.7)	(87.7, 95.8)
Visit 3	<b>n</b>	267	116	316	66
	<b>Mean (SD)</b>	82.2 (31.3)	86.0 (19.9)	82.7 (34.3)	91.1 (16.1)
	<b>(Min, Max)</b>	(-34, 155)	(17, 114)	(-69, 160)	(51, 116)
	<b>95% CI</b>	(78.4, 86.0)	(82.3, 89.7)	(78.9, 86.5)	(87.1, 95.0)
Visit 4	<b>n</b>	265	114	311	66
	<b>Mean (SD)</b>	81.0 (32.2)	83.4 (19.7)	75.8 (37.3)	88.5 (18.3)
	<b>(Min, Max)</b>	(-37, 155)	(-4, 113)	(-84, 160)	(38, 116)
	<b>95% CI</b>	(77.1, 84.9)	(79.7, 87.0)	(71.6, 80.0)	(84.0, 93.0)
Visit 5	<b>n</b>	260	113	306	65
	<b>Mean (SD)</b>	76.0 (34.6)	81.3 (20.9)	74.7 (39.4)	85.7 (18.2)
	<b>(Min, Max)</b>	(-63, 155)	(18, 114)	(-118, 151)	(22, 116)
	<b>95% CI</b>	(71.8, 80.3)	(77.4, 85.2)	(70.3, 79.1)	(81.2, 90.2)

ReSTOR Toric IOL = ACRYSOF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6

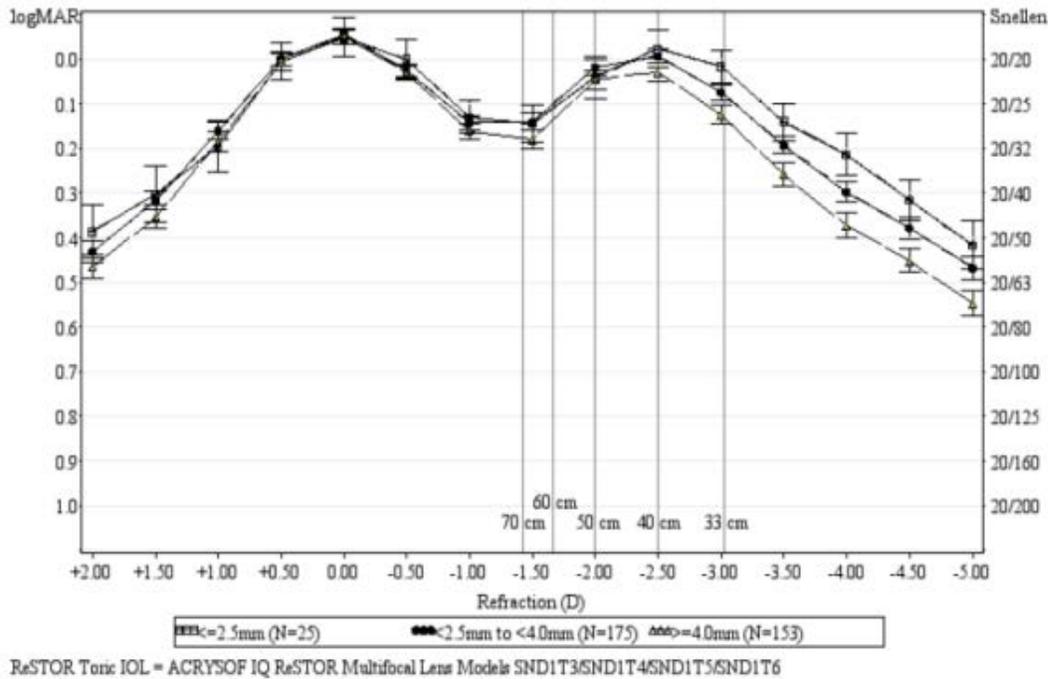
**Table 41: Number and Percentage of Subjects with Reduction of Cylinder within the Target Cylinder Correction Categories (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye		Overall	
		n	(%)	n	(%)	n	(%)
Visit 1	<b>Total</b>	386		382		768	
	<b>Within 0.5D</b>	331	(85.8)	325	(85.1)	656	(85.4)
	<b>Within 1.0D</b>	376	(97.4)	379	(99.2)	755	(98.3)
	<b>&gt; 1.0D</b>	10	(2.6)	3	(0.8)	13	(1.7)
Visit 2	<b>Total</b>	386		382		768	
	<b>Within 0.5D</b>	316	(81.9)	329	(86.1)	645	(84.0)
	<b>Within 1.0D</b>	374	(96.9)	378	(99.0)	752	(97.9)
	<b>&gt; 1.0D</b>	12	(3.1)	4	(1.0)	16	(2.1)
Visit 3	<b>Total</b>	383		382		765	
	<b>Within 0.5D</b>	304	(79.4)	339	(88.7)	643	(84.1)
	<b>Within 1.0D</b>	369	(96.3)	378	(99.0)	747	(97.6)
	<b>&gt; 1.0D</b>	14	(3.7)	4	(1.0)	18	(2.4)
Visit 4	<b>Total</b>	379		377		756	
	<b>Within 0.5D</b>	301	(79.4)	302	(80.1)	603	(79.8)
	<b>Within 1.0D</b>	366	(96.6)	370	(98.1)	736	(97.4)
	<b>&gt; 1.0D</b>	13	(3.4)	7	(1.9)	20	(2.6)
Visit 5	<b>Total</b>	373		371		744	
	<b>Within 0.5D</b>	278	(74.5)	295	(79.5)	573	(77.0)
	<b>Within 1.0D</b>	351	(94.1)	362	(97.6)	713	(95.8)
	<b>&gt; 1.0D</b>	22	(5.9)	9	(2.4)	31	(4.2)

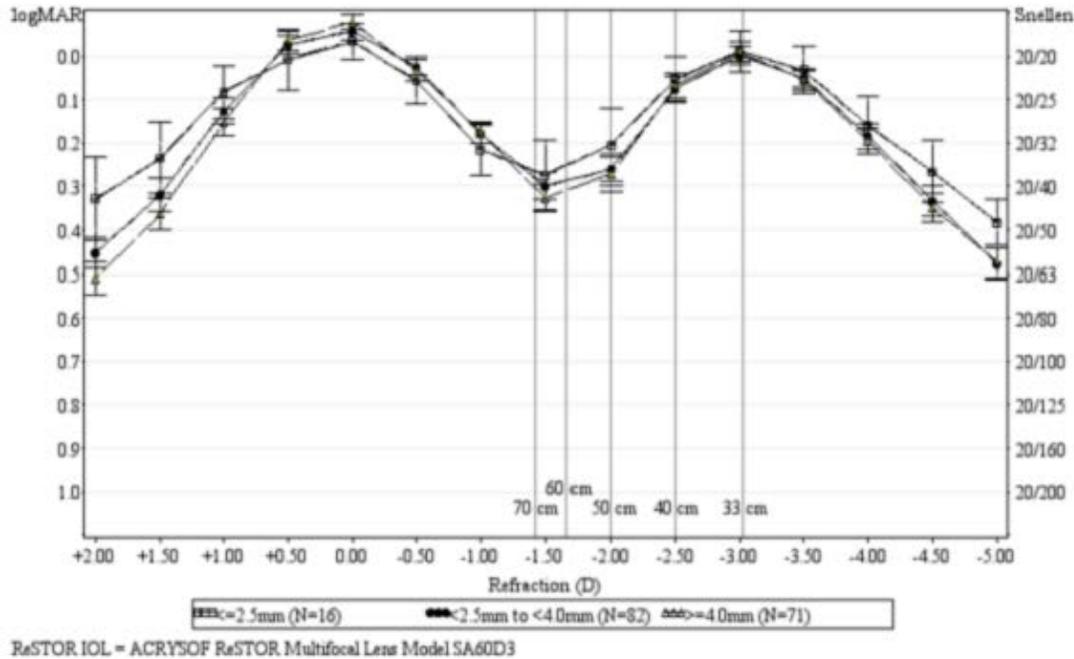
- Binocular Defocus (+2.0 D to -5.0 D in 0.5 D increments)

The mean binocular defocus curves obtained at Visit 4A demonstrate that subjects implanted with the ReSTOR<sup>®</sup> Toric IOL achieved mean 20/40 or better vision (depth of focus) from approximately +1.25 D to -3.75 D, while the control ReSTOR<sup>®</sup> IOL maintained 20/40 or better vision from approximately +1.25 D to -4.25 D. As expected, a shift in the near peak of the defocus curve was observed, with peak near vision for the ReSTOR<sup>®</sup> Toric IOL at -2.5 D (which corresponds to an equivalent distance of 40 cm) of defocus compared to -3.0 D (which corresponds to an equivalent distance of 33 cm) of defocus for the ReSTOR<sup>®</sup> IOL. The ReSTOR<sup>®</sup> Toric IOL curve, from -1.50 D to -2.00 D of defocus, showed a mean binocular intermediate visual acuity of 20/32 or better, which is more than a 1 line improvement in visual acuity compared with the control ReSTOR<sup>®</sup> IOL. The distance peaks of both curves demonstrated a mean distance visual acuity of 20/20. The mean depth of focus, analyzed by pupil size subgroups, for the ReSTOR<sup>®</sup> Toric IOL subjects demonstrated no significant differences at most defocus values, as measured using the defocus curves for the small ( $\leq 2.5$  mm), medium ( $> 2.5$  mm to  $< 4.0$  mm), and large ( $\geq 4.0$  mm) pupil sizes. At a spherical defocus of -3.0 D, an expected pupil size effect was observed, with improvement of binocular visual acuity with decreasing pupil size. See Figures 7 – 8.

**Figure 7: Mean Defocus Curves with 95% Confidence Limits by Pupil Size Category Visit 4A ReSTOR Toric IOL (Best Case Population)**



**Figure 8: Mean Defocus Curves with 95% Confidence Limits by Pupil Size Category Visit 4A ReSTOR IOL (Best Case Population)**



- Contrast Sensitivity

Binocular best corrected distance contrast sensitivity was performed using a sine wave grating acuity chart (VectorVision CSV1000E) at the 4-6 month exam under four conditions: photopic without glare, photopic with glare, mesopic without glare, and mesopic with glare.

Descriptive statistics including mean contrast scores and standard deviations (SD) are provided for the ReSTOR<sup>®</sup> Toric +3.0 D IOL and for the ReSTOR<sup>®</sup> +4.0 D IOL groups under each photopic lighting condition and spatial frequency (Table 42) and each mesopic lighting condition and spatial frequency (Table 43). The number and percent of subjects unable to see at least one grating are shown in the tables in the “Number Scoring (-1)” rows. As per ISO 11979-9:2006, these analyses were performed using data from the best case data set (defined as all eyes successfully implanted that had at least 1 postoperative visit and had no preoperative ocular pathology or macular degeneration at any time).

**Table 42: Descriptive Statistics for Binocular Photopic Contrast Sensitivity at 6 months Postoperative (Best Case Population)**

		Photopic without glare		Photopic with glare	
		ReSTOR Toric +3.0 D	ReSTOR +4.0 D	ReSTOR Toric +3.0 D	ReSTOR +4.0 D
<b>3.0 CPD</b>	<b>n</b>	360	173	360	173
	<b>Number scoring (-1)</b>	0 (0.0%)	0 (0.0%)	2 (0.6%)	1 (0.6%)
	<b>Mean (SD)</b>	1.68 (0.22)	1.71 (0.23)	1.59 (0.27)	1.62 (0.28)
	<b>(Min, Max)</b>	(1.18, 2.08)	(0.70, 2.08)	(0.40, 2.08)	(0.40, 2.08)
	<b>95% CI</b>	(1.65, 1.70)	(1.67, 1.74)	(1.56, 1.61)	(1.58, 1.66)
<b>6.0 CPD</b>	<b>N</b>	360	173	360	173
	<b>Number scoring (-1)</b>	1 (0.3%)	0 (0.0%)	24 (6.7%)	6 (3.5%)
	<b>Mean (SD)</b>	1.78 (0.24)	1.81 (0.23)	1.61 (0.39)	1.66 (0.36)
	<b>(Min, Max)</b>	(0.61, 2.29)	(0.90, 2.29)	(0.61, 2.29)	(0.61, 2.29)
	<b>95% CI</b>	(1.76, 1.81)	(1.78, 1.85)	(1.57, 1.65)	(1.61, 1.71)
<b>12.0 CPD</b>	<b>N</b>	360	173	360	173
	<b>Number scoring (-1)</b>	5 (1.4%)	3 (1.7%)	18 (5.0%)	7 (4.0%)
	<b>Mean (SD)</b>	1.38 (0.35)	1.37 (0.32)	1.25 (0.41)	1.24 (0.38)
	<b>(Min, Max)</b>	(0.31, 2.00)	(0.31, 2.00)	(0.31, 2.00)	(0.31, 2.00)
	<b>95% CI</b>	(1.34, 1.42)	(1.32, 1.42)	(1.21, 1.29)	(1.18, 1.30)
<b>18.0 CPD</b>	<b>N</b>	360	173	360	173
	<b>Number scoring (-1)</b>	4 (1.1%)	1 (0.6%)	8 (2.2%)	2 (1.2%)
	<b>Mean (SD)</b>	0.87 (0.31)	0.88 (0.30)	0.84 (0.33)	0.81 (0.32)
	<b>(Min, Max)</b>	(-0.13, 1.56)	(-0.13, 1.56)	(-0.13, 1.56)	(-0.13, 1.56)
	<b>95% CI</b>	(0.84, 0.90)	(0.83, 0.92)	(0.80, 0.87)	(0.77, 0.86)
ReSTOR Toric +3.0 D = AcrySof IQ ReSTOR +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6 ReSTOR +4.0 D = AcrySof ReSTOR Multifocal Lens (+4.0 D Add) Model SA60D3					

**Table 43: Descriptive Statistics for Binocular Mesopic Contrast Sensitivity at 6 months Postoperative (Best Case Population)**

		Mesopic without glare		Mesopic with glare	
		ReSTOR Toric +3.0 D	ReSTOR +4.0 D	ReSTOR Toric +3.0 D	ReSTOR +4.0 D
<b>1.5 CPD</b>	<b>N</b>	359	172	359	172
	<b>Number scoring (-1)</b>	5 (1.4%)	2 (1.2%)	7 (1.9%)	3 (1.7%)
	<b>Mean (SD)</b>	1.57 (0.26)	1.55 (0.25)	1.51 (0.29)	1.50 (0.28)
	<b>(Min, Max)</b>	(0.30, 1.97)	(0.30, 1.97)	(0.30, 1.97)	(0.30, 1.97)
	<b>95% CI</b>	(1.54, 1.59)	(1.51, 1.59)	(1.48, 1.54)	(1.46, 1.55)
<b>3.0 CPD</b>	<b>N</b>	360	172	360	172
	<b>Number scoring (-1)</b>	0 (0.0%)	0 (0.0%)	3 (0.8%)	0 (0.0%)
	<b>Mean (SD)</b>	1.57 (0.25)	1.57 (0.24)	1.55 (0.28)	1.55 (0.26)
	<b>(Min, Max)</b>	(0.70, 2.08)	(0.85, 2.00)	(0.40, 2.08)	(0.70, 2.08)
	<b>95% CI</b>	(1.54, 1.59)	(1.53, 1.61)	(1.52, 1.58)	(1.52, 1.59)
<b>6.0 CPD</b>	<b>N</b>	360	172	360	172
	<b>Number scoring (-1)</b>	9 (2.5%)	5 (2.9%)	41 (11.4%)	19 (11.0%)
	<b>Mean (SD)</b>	1.51 (0.31)	1.50 (0.31)	1.41 (0.37)	1.40 (0.37)
	<b>(Min, Max)</b>	(0.61, 2.29)	(0.61, 2.29)	(0.61, 2.29)	(0.61, 2.21)
	<b>95% CI</b>	(1.47, 1.54)	(1.46, 1.55)	(1.37, 1.45)	(1.35, 1.46)
<b>12.0 CPD</b>	<b>N</b>	360	172	360	172
	<b>Number scoring (-1)</b>	52 (14.4%)	31 (18.0%)	94 (26.1%)	50 (29.1%)
	<b>Mean (SD)</b>	0.92 (0.39)	0.89 (0.40)	0.81 (0.40)	0.80 (0.41)
	<b>(Min, Max)</b>	(0.31, 2.00)	(0.31, 2.00)	(0.31, 2.00)	(0.31, 2.00)
	<b>95% CI</b>	(0.88, 0.96)	(0.83, 0.95)	(0.76, 0.85)	(0.74, 0.87)

ReSTOR Toric +3.0 D = AcrySof IQ ReSTOR +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
ReSTOR +4.0 D = AcrySof ReSTOR Multifocal Lens (+4.0 D Add) Model SA60D3

- Pupil Size (Photopic Distance and Near and Mesopic Distance and Near)

Distance visual acuity was assessed in conjunction with pupil size under photopic and mesopic conditions. At Visit 5 (12 months), the mean pupil size measured with the subject focusing on a far ETDRS visual acuity target under photopic and mesopic lighting conditions was similar for the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL.

Near visual acuity results for the ACRYSOFF<sup>®</sup> IQ ReSTOR<sup>®</sup> Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 and the control ACRYSOFF<sup>®</sup> ReSTOR<sup>®</sup> Multifocal IOL Model SA60D3 were similar across all pupil size categories. The observed percentage of subjects achieving 20/40 or better binocular UCNVA was similar between the ReSTOR<sup>®</sup> Toric IOL and the control ReSTOR<sup>®</sup> IOL across all pupil size categories.

See Tables 44 – 46.

**Table 44: Descriptive Statistics for Pupil Size at Visit 5 (All Implanted Set)**

		First Implanted Eye		Second Implanted Eye	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
Photopic pupil size far	n	373	180	371	180
	Mean (SD)	3.7 (0.8)	3.6 (0.8)	3.7 (0.8)	3.6 (0.7)
	(Min, Max)	(2, 7)	(2, 6)	(2, 7)	(2, 6)
Photopic pupil size near	n	373	180	371	180
	Mean (SD)	3.6 (0.8)	3.5 (0.7)	3.5 (0.8)	3.5 (0.7)
	(Min, Max)	(2, 6)	(2, 6)	(2, 6)	(2, 6)
Mesopic pupil size far	n	372	180	370	180
	Mean (SD)	4.5 (1.0)	4.6 (1.0)	4.5 (1.0)	4.6 (1.0)
	(Min, Max)	(2, 7)	(2, 7)	(2, 7)	(2, 7)
Mesopic pupil size near	n	373	180	371	180
	Mean (SD)	4.3 (1.0)	4.3 (1.0)	4.3 (1.0)	4.3 (1.0)
	(Min, Max)	(2, 7)	(2, 7)	(2, 7)	(2, 7)

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3

**Table 45: Frequency and Percentage of Subjects with Binocular BCDVA (All Implanted Set) By Pupil Size**

		≤2.5 mm		>2.5 mm to <4.0 mm		≥4.0 mm	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Visit 4	Total	26	17	183	89	160	76
	20/20 or better	23 (88.5)	13 (76.5)	162 (88.5)	84 (94.4)	143 (89.4)	73 (96.1)
	20/25	3 (11.5)	4 (23.5)	18 (9.8)	4 (4.5)	12 (7.5)	1 (1.3)
	20/32	0 (0.0)	0 (0.0)	3 (1.6)	1 (1.1)	4 (2.5)	2 (2.6)
	20/40	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1 (0.6)	0 (0.0)
	20/50	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)
Visit 5	Total	26	17	184	88	161	75
	20/20 or better	25 (96.2)	16 (94.1)	162 (88.0)	83 (94.3)	148 (91.9)	74 (98.7)
	20/25	1 (3.8)	0 (0.0)	15 (8.2)	3 (3.4)	10 (6.2)	0 (0.0)
	20/32	0 (0.0)	1 (5.9)	5 (2.7)	2 (2.3)	2 (1.2)	0 (0.0)
	20/40	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	1 (0.6)	0 (0.0)
	20/50	0 (0.0)	0 (0.0)	1 (0.5)	0 (0.0)	0 (0.0)	1 (1.3)

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3  
 Mean pupil size of both eye were used to determine the pupil size category

**Table 46: Number and Percentage of Subjects with Binocular Mesopic DCNVA at Best Distance (All Implanted Set) By Pupil Size**

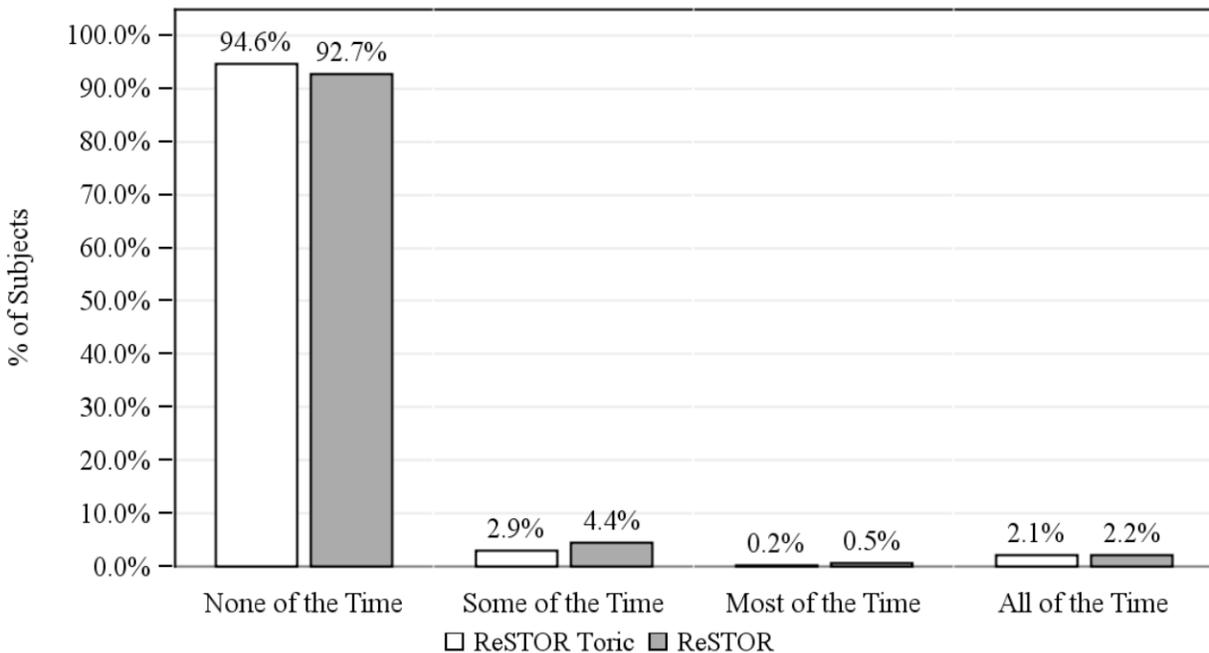
		≤2.5 mm		>2.5 mm to <4.0 mm		≥4.0 mm	
		ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL	ReSTOR Toric IOL	ReSTOR IOL
		n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Visit 5	Total	26	17	184	88	161	75
	20/20 or better	2 (7.7)	0 (0.0)	23 (12.5)	3 (3.4)	6 (3.7)	3 (4.0)
	20/25 or better	4 (15.4)	3 (17.6)	47 (25.5)	13 (14.8)	24 (14.9)	8 (10.7)
	20/32 or better	8 (30.8)	5 (29.4)	75 (40.8)	24 (27.3)	45 (28.0)	20 (26.7)
	20/40 or better	15 (57.7)	9 (52.9)	110 (59.8)	46 (52.3)	76 (47.2)	35 (46.7)
	20/50 or better	23 (88.5)	13 (76.5)	140 (76.1)	58 (65.9)	105 (65.2)	49 (65.3)
	20/63 or better	26 (100.0)	15 (88.2)	169 (91.8)	71 (80.7)	137 (85.1)	57 (76.0)
	Worse than 20/63	0 (0.0)	2 (11.8)	15 (8.2)	17 (19.3)	24 (14.9)	18 (24.0)

ReSTOR Toric IOL = ACRYSOFF IQ ReSTOR Multifocal Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR IOL = ACRYSOFF ReSTOR Multifocal Lens Model SA60D3  
 Mean pupil size of both eye were used to determine the pupil size category

- Spectacle Independence Lens Vision Evaluation And Repurchase (SILVER) Questionnaire and Visual Tasks (VISTAS) Questionnaire

A sponsor developed questionnaire was used in the study with the intent to assess spectacle independence following implantation with the IOLs. The questionnaire was not determined to be a valid assessment of the concept “spectacle independence”. In addition, the study was not masked. These two factors limit the interpretability of the participant’s responses to this questionnaire. Responses to individual items on this questionnaire did not appear to be meaningfully different between the two groups. See Figure 9.

**Figure 9: Frequency of Spectacle Wear for Distance Vision, Bilateral Comparison**



ReSTOR<sup>®</sup> +4.0 D = AcrySof<sup>®</sup> ReSTOR<sup>®</sup> Multifocal Lens (+4.0 D Add) Model SA60D3

Additionally, another questionnaire (VISTAS) was also administered during the study. The VISTAS questionnaire was exploratory and the responses were not interpretable.

### 3. Pediatric Extrapolation

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

## **E. 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 21 investigators of which none were full-time or part-time employees of the sponsor and 11 investigators 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 investigators
- Significant payment of other sorts: 11 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 0 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.

## **XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION**

Additional safety data is incorporated in the product labeling by reference to the parent lens, the ACRYSOF<sup>®</sup> ReSTOR<sup>®</sup> Apodized Diffractive Optic Posterior Chamber IOL, Models MA60D3 and SA60D3, including results from a driving sub-study.

The following figures represent supplemental information of parameters assessed during the trial and are provided in the physician labeling:

- Binocular Visual Acuity

See Tables 47 – 51 and Figure 10.

**Table 47: Overall Comparison of ReSTOR<sup>®</sup> Toric +3.0 D and ReSTOR<sup>®</sup> +4.0 D IOLs Mean Binocular Distance-Corrected Visual Acuity (logMAR), All Implanted, 1 Year Postoperative**

<b>Model</b>	<b>Near VA @ Best Distance</b>	<b>Intermediate VA @ 50 cm</b>	<b>Intermediate VA @ 60 cm</b>	<b>Intermediate VA @ 70 cm</b>	<b>Distance VA</b>
<b>ReSTOR<sup>®</sup> +3.0 D Toric</b>	0.08 (20/25)	0.08 (20/25)	0.14 (20/25)	0.20 (20/32)	-0.04 (20/20)
<b>ReSTOR<sup>®</sup> +4.0 D</b>	0.09 (20/25)	0.28 (20/40)	0.35 (20/50)	0.36 (20/50)	-0.04 (20/20)

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal Lens (+4.0 D Add) Model SA60D3

**Table 48: Cumulative Binocular Photopic Near Visual Acuity of ReSTOR® Toric +3.0 D and ReSTOR® +4.0 D IOLs by Lens Model, All Implanted, 1 Year Postoperative**

		N	20/20 or better %	20/25 or better %	20/32 or better %	20/40 or better %	20/50 or better %	20/63 or better %	Worse than 20/63 %
<b>Uncorrected (Best Distance*)</b>	<b>ReSTOR® Toric +3.0 D</b>	371	35.6	69.5	89.5	97.8	98.7	99.5	0.5
	<b>ReSTOR® +4.0 D</b>	180	25.6	67.8	88.9	96.1	98.3	99.4	0.6
<b>Uncorrected (Standard Distance**)</b>	<b>ReSTOR® Toric +3.0 D</b>	371	42.3	70.9	89.5	96.2	98.1	99.7	0.3
	<b>ReSTOR® +4.0 D</b>	180	23.9	56.1	84.4	92.2	97.8	98.9	1.1
<b>Distance Corrected (Best Distance*)</b>	<b>ReSTOR® Toric +3.0 D</b>	371	37.5	73.9	94.6	97.8	99.2	99.5	0.5
	<b>ReSTOR® +4.0 D</b>	180	35.0	72.2	93.9	95.6	99.4	100.0	0.0
<b>Distance Corrected (Standard Distance**)</b>	<b>ReSTOR® Toric +3.0 D</b>	371	44.5	80.6	94.1	98.1	98.9	99.5	0.5
	<b>ReSTOR® +4.0 D</b>	180	31.1	65.6	88.9	97.2	98.3	98.9	1.1
<b>Best Corrected (Standard Distance**)</b>	<b>ReSTOR® Toric +3.0 D</b>	371	58.2	86.0	97.3	99.2	99.5	100.0	0.0
	<b>ReSTOR® +4.0 D</b>	180	41.7	81.1	92.8	98.3	99.4	100.0	0.0

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/ SND1T6

ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal Lens (+4.0 D Add) Model SA60D3

\*Best distance: The distance selected by the subject as the distance of best near vision

\*\*Standard distance: 33 cm for the ReSTOR® +4.0 D IOL and 40 cm for ReSTOR® +3.0 D Toric IOL

**Table 49: Cumulative Binocular Photopic Distance Visual Acuity of ReSTOR® Toric +3.0 D and ReSTOR® +4.0 D IOLs by Lens Model, All Implanted, 1 Year Postoperative**

			20/20 or better	20/25 or better	20/32 or better	20/40 or better	20/50 or better	20/63 or better	Worse than 20/63
N			%	%	%	%	%	%	%
<b>Uncorrected</b>	<b>ReSTOR® Toric +3.0 D</b>	371	65.0	88.7	96.0	98.9	99.2	99.5	0.5
	<b>ReSTOR® +4.0 D</b>	180	68.9	91.7	97.8	99.4	99.4	100.0	0.0
<b>Best Corrected</b>	<b>ReSTOR® Toric +3.0 D</b>	371	90.3	97.3	99.2	99.7	100.0	100.0	0.0
	<b>ReSTOR® +4.0 D</b>	180	96.1	97.8	99.4	99.4	100.0	100.0	0.0

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/ SND1T6

ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal Lens (+4.0 D Add) Model SA60D3

**Table 50: Intermediate Photopic Visual Acuity for ReSTOR® +3.0 D Toric and ReSTOR® +4.0 D IOLs by Lens Model, All Implanted, 1 Year Postoperative**

		N	Percent 20/40 or better		
			50 cm	60 cm	70 cm
<b>Uncorrected</b>	<b>ReSTOR® Toric +3.0 D</b>	371	93.3	86.3	79.8
	<b>ReSTOR® +4.0 D</b>	180	63.3	47.2	50.6
<b>Distance Corrected</b>	<b>ReSTOR® Toric +3.0 D</b>	371	96.5	88.4	79.0
	<b>ReSTOR® +4.0 D</b>	180	66.7	37.8	38.9

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal Lens (+4.0 D Add) Model SA60D3

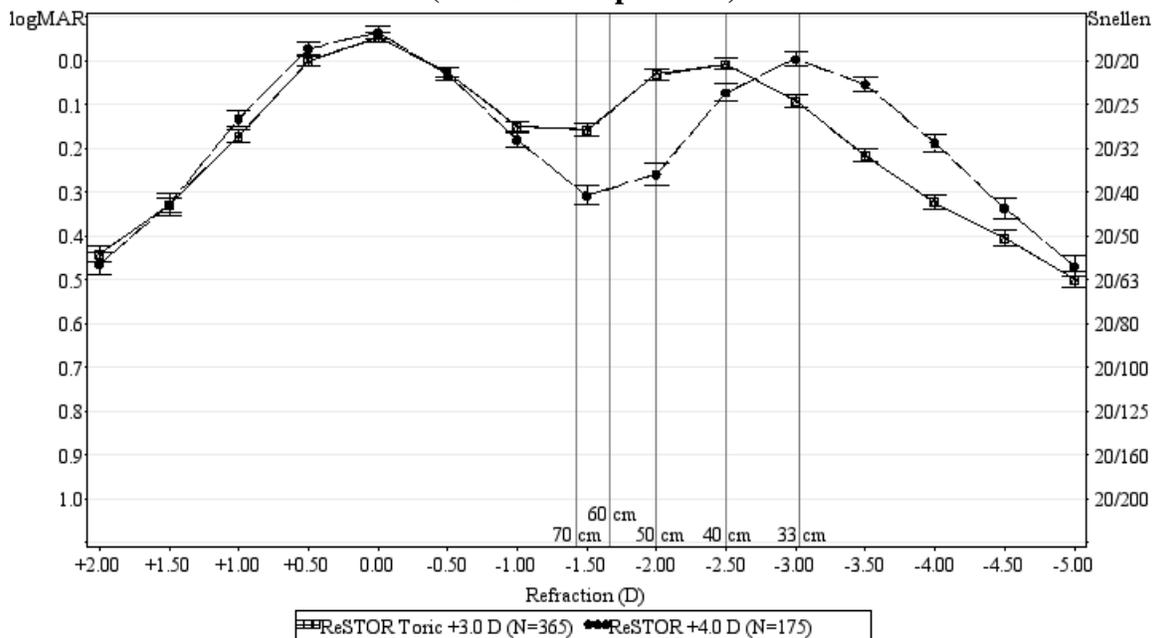
**Table 51: Mean LogMAR Binocular Distance Corrected Intermediate Visual Acuity, for ReSTOR® Toric +3.0 D and ReSTOR® +4.0 D IOLs, All Implanted, 1 Year Postoperative**

Intermediate VA	ReSTOR® Toric +3.0 D	ReSTOR® +4.0 D
50 cm	0.08	0.28
60 cm	0.14	0.35
70 cm	0.20	0.36

ReSTOR® Toric +3.0 D = AcrySof® IQ ReSTOR® +3.0 D Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6

ReSTOR® +4.0 D = AcrySof® ReSTOR® Multifocal Lens (+4.0 D Add) Model SA60D3

**Figure 10: Mean Defocus Curves with 95% Confidence Limits by Lens Model at 6 Months Postoperative Overall (Best Case Population)**



ReSTOR Toric +3.0 D= ACRYSOF IQ ReSTOR (+3.0 D) Multifocal Toric Lens Models SND1T3/SND1T4/SND1T5/SND1T6  
 ReSTOR +4.0 D= ACRYSOF ReSTOR Multifocal Lens (+4.0 D Add) Model SA60D3

## **XII. PANEL MEETING RECOMMENDATION AND FDA’S POST-PANEL ACTION**

### **A. Panel Meeting Recommendation**

At an advisory meeting held on November 14, 2014, the Ophthalmic Devices Panel voted 12-0-0 (yes, no, abstain) that there is reasonable assurance the device is safe, 11-1-0 (yes, no, abstain) that there is reasonable assurance that the device is effective, and 12-0-0 (yes, no, abstain) that the benefits of the device do outweigh the risks in patients who meet the criteria specified in the proposed indication.

The meeting summary can be found at the following:

<http://www.fda.gov/downloads/AdvisoryCommittees/CommitteesMeetingMaterials/MedicalDevices/MedicalDevicesAdvisoryCommittee/OphthalmicDevicesPanel/UCM423457.pdf>

### **B. FDA’s Post-Panel Action**

Subsequent to the Advisory Panel, the applicant submitted a two Major Amendments to the premarket application. The first Major Amendment included a literature review. This literature review summarized factors potentially impacting the rotational

stability of the IOL platform relevant to the ReSTOR Toric +3.0 D IOL. The second Major Amendment summarized the investigation of the safety issues associated with the Japanese version of the multifocal toric IOL and the steps taken to insure that these safety issues (intraocular inflammation) do not occur with the U.S. version of this lens. This new information was key to FDA's decisions regarding the post-approval study requirement.

### **XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES**

#### **A. Effectiveness Conclusions**

The ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 met the clinical performance target for Uncorrected Distance Visual Acuity. There were no clinically relevant differences in the mean Best Corrected Distance Visual Acuity for subjects implanted with the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 compared with subjects implanted with the control ACRYSOF ReSTOR Multifocal IOL Model SA60D3. The observed percentage of subjects achieving a 2 or greater line improvement in Best Corrected Distance Visual Acuity was similar among the 2 lens models (ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 and the control ACRYSOF ReSTOR Multifocal IOL Model SA60D3). The ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 met the clinical performance target for Uncorrected Near Visual Acuity at fixed distance. No clinically relevant differences in Uncorrected Near Visual Acuity at best distance were observed for the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 and the control ACRYSOF ReSTOR Multifocal IOL Model SA60D3.

The ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 is effective in the reduction of cylinder in the range of 0.75 D to 2.82 D. Accuracy of lens placement was demonstrated with the mean absolute difference between intended axis orientation and achieved axis orientation at surgery being  $5.0^{\circ} \pm 6.1$  for the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 in the first operative eyes. The rotational stability of the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 was demonstrated as at least 97.2% (346/356) of subjects demonstrated absolute lens rotation of less than  $10^{\circ}$  between the operative visit and Visit 5.

No clinically relevant differences in binocular contrast sensitivity under photopic and mesopic conditions with and without a glare source were observed between the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 and the control ACRYSOF ReSTOR Multifocal IOL Model SA60D3.

#### **B. Safety Conclusions**

Based on a comparison of all safety parameters assessed on the surgery day and at postoperative visits, no untoward safety issues were identified and similar safety profiles were observed for the ACRYSOF IQ ReSTOR Multifocal Toric IOL and the control ACRYSOF ReSTOR Multifocal Lens Model SA60D3. The incidences of serious adverse events for each IOL group were not statistically significantly different from the Safety and Performance Endpoints (SPE) control rates (BS EN ISO 11979-7: 2006: Ophthalmic Implants – Intraocular Lenses – Part 7: Clinical Investigations) for posterior chamber IOLs with the exception of secondary surgical interventions (see Table 11). No unanticipated serious adverse device effects were reported. Premium IOLs, like this IOL, often have higher rates of secondary surgical interventions to explant or reposition the IOL due to visual disturbances, misalignment or rotational instability. The highest rate of “severe” visual symptoms at Visit 5 (12 months) was for halos at 7.5 % (28/372) for ReSTOR Toric IOL and 11.0 % (20/182) for the control ReSTOR IOL. Reports of other visual symptoms were similar between the ReSTOR Toric IOL and the control ReSTOR IOL at Visit 5 (12 months).

### 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 device is a first of a kind option combining the benefits of a multifocal with the benefits of a toric IOL. Patients who are currently interested in obtaining a multifocal IOL with correction of astigmatism must undergo two procedures, whereas this device could combine such benefit into a single intervention.

Patient perspectives considered during the review included a patient-reported outcome measure (APPLES) developed and implemented during this trial to assess visual disturbances and distortions. The qualitative and quantitative development work for the APPLES questionnaire did not support this measure as being fit for its stated purpose. Therefore, the results of this questionnaire were interpreted with caution. In addition, a measure to assess the use of glasses and a measure of satisfaction (SILVER questionnaire) as well as visual tasks (VISTAS) was used in the trial. Because of the concerns about the questionnaire’s ability to measure the specified concepts, this information was not considered during the review.

In conclusion, given the available information above, the data support that for primary implantation in the capsular bag of the eye for the visual correction of aphakia and pre-existing astigmatism secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision, reduction of residual refractive cylinder and increased spectacle independence, the probable benefits outweigh the probable risks. As this is a first-of-a-kind device, the added probable benefits associated with better distance-corrected intermediate and near visual acuity in comparison to (1) a multifocal IOL without astigmatism correction or (2) a toric IOL without multifocal features or a (3) monofocal without either multifocal or toric benefits outweigh the added probable risks of lower contrast sensitivity, visual

disturbances, and the potential for additional secondary surgical interventions to explant or reposition the IOL.

#### **D. Overall Conclusions**

The preclinical and clinical data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The clinical data indicates that the ACRYSOF IQ ReSTOR Multifocal Toric IOL Models SND1T3/ SND1T4/ SND1T5/ SND1T6 are effective in the reduction of cylinder in the range of 0.75 D to 2.82 D without any significant effect on visual performances measures compared to the control ACRYSOF ReSTOR Multifocal IOL Model SA60D3. Based on a comparison of all safety parameters assessed on the surgery day and at postoperative visits, no untoward safety issues were identified and similar safety profiles were observed for the ACRYSOF IQ ReSTOR Multifocal Toric IOL and the control ACRYSOF ReSTOR Multifocal Lens Model SA60D3.

#### **XIV. CDRH DECISION**

CDRH issued an approval order on December 22, 2016. The final conditions of approval cited in the approval order are described below.

PMA Post-Approval Study: Post Approval Study for the AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Toric IOLs to Assess Post-Surgical Intraocular Inflammation:

The AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Toric Post Approval Study is designed to evaluate the rate of post-surgical intraocular inflammation (based on a specified case definition) observed following implantation of an AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Toric IOL, compared to the rate of post-surgical intraocular inflammation (based on ICD-9 codes) observed from the 2011-2013 Medicare Beneficiary Encrypted Files (BEF). The study is intended to assess the safety of the approved device, and will be conducted in two phases. The two phases may be conducted in parallel.

Phase A:

Phase A of the study consists of a multi-center active surveillance study in 3,000 eyes that have been implanted with an AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> +3.0 D Toric IOL for up to 180 days. The primary endpoint is the rate (per 1,000) of post-surgical intraocular inflammation (based on the predefined case definition) reported within a 180 day post-surgical period following implantation of AcrySof<sup>®</sup> IQ ReSTOR<sup>®</sup> Toric IOLs. The case definition of post-surgical intraocular inflammation is as follows: Exacerbated intraocular inflammation within 180 days after IOL implantation as indicated by:

- $\geq 3+$  aqueous cell within the first two weeks post-op (collected on Forms 1 and 2 or at an unscheduled visit between Form 0 and Form 2), and/or
- $\geq 2+$  aqueous cell between 14 days and 60 days post-op (collected on Form 3 or at an unscheduled visit between Form 2 and Form 3), and/or

- $\geq 1+$  aqueous cell after 60 days post-op or later (collected on Form 4 or at an unscheduled visit between Form 3 and Form 4)

There is no study hypothesis.

A minimum of 3,000 eyes will be enrolled. Patients will be followed for 180 days postoperatively. Study visits/assessments will occur at 1 day, 1-2 week, 1-2 month, and 3-6 month postoperatively, according to the premarket post op assessment schedule (Forms 1 through 4).

Phase B:

Phase B of the study consists of a secondary data analysis of the 2011-2013 Medicare Beneficiary Encrypted Files (BEF). All cataract surgeries reported in 2011 through 2013 Medicare BEF will be reviewed to determine the background rate of post-surgical intraocular inflammation (based on the associated coding of endophthalmitis, uveitis, postsurgical intraocular inflammation or other related codes) within a 180 day post-surgical period following implantation of an intraocular lens. It is anticipated that there will be approximately 180,000 surgeries available to estimate the background rate.

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**

International Standard Organization 10993, Biological Evaluation of Medical Devices

International Standard Organization 11979-5, Ophthalmic Implants- Intraocular Lenses- Part 5: Biocompatibility

ANSI/AAMI/ISO 11135 (Sterilization of health care products – Ethylene oxide)

International Standard Organization 11979-6 (Ophthalmic implants – Intraocular lenses – Part 6: Shelf-life and transport stability).

International Standard Organization 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods

International Standard Organization 13503-3 Ophthalmic Implants – Intraocular Lenses –  
Part 3: Mechanical Properties and Test Methods