SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Device Generic Name: Intraocular Lenses (IOLs)

Device Trade Name: ACRYSOF® Single-Piece Posterior Chamber Intraocular Lenses With Toric Optic

Applicant's Name and Address: Alcon Research Ltd.
6201 South Freeway
Fort Worth, Texas 76134-2099

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P930014/S15

Date of Notice of Approval to Applicant: September 14, 2005

II. INDICATIONS FOR USE

The ACRYSOF® Toric posterior chamber intraocular lenses are intended for primary implantation in the capsular bag of the eye for visual correction of aphakia and pre-existing corneal astigmatism secondary to removal of a cataractous lens in adult patients with or without presbyopia, who desire improved uncorrected distance vision, reduction of residual refractive cylinder and increased spectacle independence for distance vision.

III. CONTRAINDICATIONS

None known.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the ACRYSOF® Toric IOL labeling.

V. DEVICE DESCRIPTION

The ACRYSOF® Toric IOL is a UV-absorbing foldable IOL. The biconvex toric optic consists of a high refractive index soft acrylic material capable of being folded prior to insertion, allowing placement through an incision smaller than the optic diameter of the lens. After surgical insertion into the eye, the lens gently unfolds to original size. The supporting haptics provide for proper positioning and fixation of the IOL optic within the

eye. The sponsor is also providing on the Internet (http://www.acrysoftoriccalculator.com) the ACRYSOF® Toric calculator, which is a software tool designed to assist the surgeon in predicting the amount of post-operative corneal astigmatism that needs to be corrected in order to optimize ACRYSOF® Toric IOL selection and axis placement.

Table 1 provides the physical characteristics of these lenses.

Table 1 - Physical Characteristics of ACRYSOF® Toric IOLs

Characteristics	Model		
	SA60T3	SA60T4	SA60T5
Optic Type	Biconvex Toric Optic		
Optic / Haptic Material	Ultraviolet-absorbing Acrylate/Methacrylate Copolymer UV cutoff at 10% T: 398 nm (+10.0 diopter lens) 400 nm (+30.0 diopter lens)		
IOL Powers (spherical equivalent diopters)	+6.0 through +34.0 D in 0.5 D increments		
IOL Cylinder Power (diopters)	1.50 diopter	2.25 diopter	3.00 diopter
Cylinder Correction at Corneal Plane	1.03	1.55	2.06
Corneal Astigmatism to be Corrected	0.75 – <1.50	≥1.50 – <2.00	≥2.00
Index Of Refraction	1.55		
Haptic Configuration	STABLEFORCE®		
Optic Diameter (mm)	6.0		
Overall Length (mm)	13.0		
Haptic Angle	0°		

VI. ALTERNATIVE PRACTICES OR PROCEDURES

Patients who undergo cataract extraction presently have various 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, multifocal, simultaneous vision or accommodative IOLs are also available.

VII. MARKETING HISTORY

The ACRYSOF® Toric IOL has not been marketed in the United States or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A randomized clinical study was conducted to determine the safety and effectiveness of the ACRYOSOF® Toric IOL (hereafter referred to as Model SA60TT). A total of 494 subjects were implanted in the first operative eye: 244 subjects were implanted with the Model SA60TT and 250 subjects were implanted with the concurrent control lens, Model SA60AT. Adverse events were reported for any subject receiving Model SA60TT or the concurrent control lens, Model SA60AT.

Cumulative Adverse Events: Table 2 presents the cumulative serious adverse events that have occurred in the first operative eye, at rates that exceeded the FDA historical grid rates found in the FDA Intraocular Lens Guidance Document, Annex B (October 14, 1999).

Table 2: Cumulative Adverse Event Incidence Rates, Model SA60TT versus FDA Historical Grid Rate, First Eye – Safety

	Model SA60TT N=244		FDA Grid Rate
Cumulative Adverse Events	N	%	%
Retinal Detachment/Repair	1	0.4	0.3
Surgical Reintervention	4[a]	1.6	0.8
IOL Reposition Due to Rotation	1	0.4	NA
IOL Replacement Due to Rotation	1	0.4	NA
Laser Treatment	2	0.8	NA
Paracentesis	1	0.4	NA

The incidence rates in this table are based upon the number of eyes with an event divided by the number of eyes implanted. Cumulative adverse events are those events that have occurred at any time during the clinical study.
FDA Grid Rate = FDA Grid of Adverse Events with Posterior Chamber Intraocular Lens Historical Controls, FDA Intraocular Lens Guidance Document, Annex B (October 14, 1999)
[a] There were 5 occurrences of surgical reintervention in 4 eyes for Model SA60TT first eye.

The incidence of cumulative adverse events for the Model SA60TT compared favorably to the FDA historical grid rates. Only the rates for retinal detachment/repair and surgical reintervention exceeded the FDA historical grid. However, neither of these rates were statistically significant (p=0.5196 and p= 0.1336, respectively).

The incidence of cumulative adverse events for the Model SA60TT also compared favorably to the concurrent control lens Model SA60AT.

Persistent Adverse Events: No occurrences of persistent adverse events (present at Form 6 or 6A [330 to 420 days postoperative] or later) were observed in any subjects implanted with the Model SA60TT.

Other complications: There were no reports of intraocular infection reported during the clinical study.

Potential complications that did not occur in this clinical trial, but that may accompany cataract or implant surgery include, *but* are not limited to, the following: corneal

endothelial damage, non-pigment precipitates, infection, vitreous loss, iris prolapse, vitreous wick syndrome, uveitis and pupillary membrane.

IX. SUMMARY OF PRECLINICAL STUDIES

Biocompatibility Testing: The ACRYSOF® Toric IOLs are made of the same raw material and manufacturing contact materials previously qualified with other IOL designs. A battery of toxicity studies were performed with the ACRYSOF® raw material and previously qualified ACRYSOF® IOL models. The toxicology studies conducted, identified in Table 3, meet the requirements of ISO 10993, *Biological Evaluation of Medical Devices,* and ISO 11979-5, *Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility* guidelines. Studies were conducted in accordance with Good Laboratory Practices.

Table 3 – Biocompatibility Testing

Test:	Results:
Genotoxicity – Ames Test	Non-mutagenic
Genotoxicity – Chromosome Aberration Assay	Non-clastogenic
Complement Activation	No evidence of complement activation
Hemolysis Test	Non-hemolytic
Cytotoxicity – Agarose Overlay (Extract)	Non-cytotoxic
Cytotoxicity – Agarose Overlay (Direct)	Non-cytotoxic
Cytotoxicity – MEM Elution	Non-cytotoxic
Inhibition of Cell Growth (9 point assay)	Non-inhibitory
Muscle Implantation – 7, 30, 90 days	No significant biological responses
Intracutaneous Toxicity	No significant irritation or toxicity
Intraocular Irritation (extracts)	No evidence of irritation
Sensitization – Guinea Pig Maximization	Non-sensitizing
Acute Systemic Toxicity	No systemic toxicity

Table 3 – Biocompatibility Testing	
Test:	Results:
Implantation – Ocular Implantation (1 Year)	No evidence of irritation

Chemical Characterization: The chemical characterization testing, identified in Table 4, 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.

Table 4 – Chemical Characterization	
Test:	Results:
Material Stability – aging and leachability	Passed
Material Extraction	Passed
Process Extractable Analysis	Passed
Heavy Metal Analysis	Passed
Fourier Transform/Infrared Spectroscopy	Passed
Contact Angle	Passed
X-ray photoelectron Spectroscopy	Passed

Optical / Mechanical Testing: The pre-clinical optical / mechanical tests, identified in Table 5, were performed with the ACRYSOF® raw material and previously qualified ACRYSOF® IOL models and were measured in accordance with the FDA Guidance Document for Multifocal Intraocular Lenses, May 29, 1997, EN ISO 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: *Optical Properties and Test Methods* and EN ISO 13503-3 Ophthalmic Implants – Intraocular Lenses – Part 3: *Mechanical Properties and Test Methods.*

Table 5 – Optical/Mechanical Testing	
Test:	Results:
Haptic Compression Force	Passed

Table 5 – Optical/Mechanical Testing	
Test:	Results:
Haptic Compression Force Decay	Passed
Axial Displacement	Passed
Optic Decentration	Passed
Optic Tilt	Passed
Angle of Contact	Passed
Fatigue Testing	Passed
Haptic Strength	Passed
Spectral Transmittance	Passed
Modulation Transfer Function	Passed
Optical Evaluation after Multiple Folds	Passed
Test Photostability	Passed
Nd: YAG Laser Exposure Test	Passed
Refractive Index	Passed

Microbiology / Sterilization Adoption: The ethylene oxide sterilization cycle was validated in accordance with ISO 11135 Medical Devices – *Validation and Routine Control of Ethylene Oxide Sterilization*, EN 556-1: Sterilization of Medical Devices – *Requirements for Medical Devices to be designated "Sterile,"* and EN 550: *Sterilization of Medical Devices – Validation and Routine Control of Ethylene Oxide Sterilization* and assures a minimum Sterility Assurance Level of 10^{-6}. ACRYSOF® Toric IOLs were successfully adopted into this validated cycle in accordance with Standard Operating Procedure - *Adoption of a Medical Device into a Validated Sterilization Process* (see Table 6). Expiration dating has been established at 5 years.

Table 6 – Sterilization Validation	
Test:	Results:
Device construction, complexity, and configuration	Equivalent
Device Packaging	Equivalent
Sterilant breath ability restrictions	Equivalent

Table 6 – Sterilization Validation	
Test:	Results:
Load aeration characteristics and product EtO residual potential	Equivalent
Sterilizer load configuration and density	Equivalent
Load temperature uniformity	Equivalent
Microbial resistance evaluation	Equivalent
Delivered product lethality using biological indicators (BI's) and product sterility testing	Passed
Package Integrity	Passed
Device cycle compatibility	Equivalent
Device Biocompatibility	Equivalent
EtO and ECH Residuals	Passed
Shelf Life Analysis	Passed

Software Verification Test: A software verification test used to test the ACRYSOF® Toric IOL software check program was submitted by the applicant and found to be adequate. The software tool is designed to assist the surgeon in predicting the amount of post-operative corneal astigmatism that needs to be corrected in order to optimize ACRYSOF® Toric IOL selection and axis placement.

X. SUMMARY OF CLINICAL STUDIES

Study Objective: The objective of this study was to determine the safety and effectiveness of the ACRYSOF® Toric IOL Intraocular Lenses when implanted into the capsular bag. This study included three Toric IOL models: SA60T3, SA60T4, & SA60T5. The model designation SA60TT is used when all three Toric IOL models are referenced collectively. The study was randomized, open label, parallel group, and multi-centered. Subjects were implanted with either the ACRYSOF® Toric Model SA60TT IOL or the ACRYSOF® control Model SA60AT.

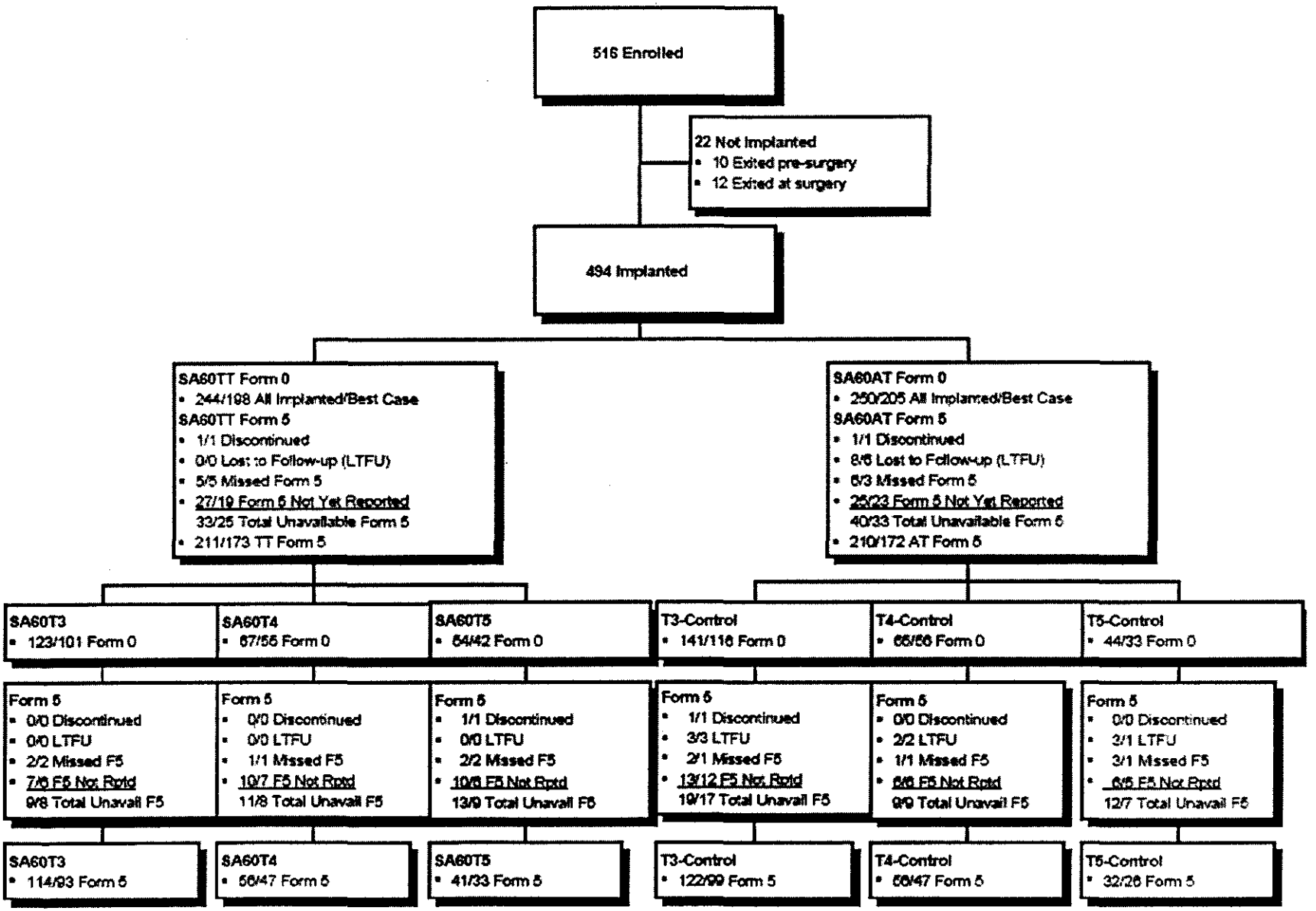
At the eleven investigational sites in the U.S., 494 subjects were implanted (250 control Model SA60AT subjects and 244 Toric Model SA60TT subjects) in the first operative eye. Of the 244 subjects implanted with a Model SA60TT in the first operative eye, 123 were implanted with a Model SA60T3, 67 with a Model SA60T4 and 54 with a Model SA60T5.

Demographics: The mean age of subjects in this clinical study who received either the Model SA60TT or the control lens Model SA60AT in the first operative eye was 71.2 years at the time of surgery; 55.3% female and 44.7% male. The study population was 96.6% Caucasian, 1.8% Black, 0.6% Asian and 1.0% of other race. No statistically significant differences between the subjects receiving Model SA60TT and the control Model SA60AT were found for Race and Age categories, although the subject numbers for Race, other than Caucasian, were too small to evaluate statistically.

Subject Accountability: All eyes with attempted IOL implantation (successful or aborted after contact with the eye) of Model SA60TT or the control lens were included in the safety analysis. All eyes that were implanted with a study lens (either Model SA60TT or Model SA60AT) and had at least one postoperative visit were evaluable for the All Implanted analysis. A subset of the entire population was also used for some analyses; this is the best case data set. The best case data set included all eyes that were implanted with a study lens, had at least one postoperative visit, and did not have preoperative ocular pathology typically considered visually significant or macular degeneration at any postoperative visit.

To provide an overview of the subject data collection, the "Subject Accountability Flow Chart" provided below shows the total subject enrollment and follow-up through the Form 5 (120-180 days postoperative) visit for both lens models and for both the All Implanted and Best Case data sets. Of the 123 subjects implanted with Model SA60T3, 114 subjects have reported for Form 5. Of the 67 subjects implanted with Model SA60T4, 56 subjects have reported for Form 5. Of the 54 subjects implanted with Model SA60T5, 41 subjects have reported for Form 5. In comparison, of the 250 subjects implanted with Model SA60AT, 210 subjects have reported for Form 5.

Subject Accountability Flow Chart



Data Analysis and Results: This report contains safety and effectiveness analysis for the first operative eye of subjects implanted with Model SA60TT lenses.

Data analysis by gender showed no significant differences in results.

Distance Visual Acuity: Uncorrected distance monocular (first eye implanted) visual acuity results obtained at the Form 5 visit for all subjects implanted with a Model SA60TT or Model SA60AT are presented below in Tables 7 and 8, respectively. Comparison between lens models is necessary for uncorrected distance visual acuity (UCDVA), as there is no grid value available.

When examining Tables 7 and 8 (UCDVA breakdown for Models SA60TT and SA60AT, respectively), 38.4% of subjects implanted with a Model SA60TT achieved uncorrected visual acuities of 20/20 or better compared to only 19.0% of those subjects implanted with the control lens Model SA60AT. Also, of the 211 subjects implanted with a Model SA60TT and examined at the Form 5 visit, 140 (66.4%) achieved an uncorrected distance visual acuity of 20/25 or better, compared to only 86 subjects (40.9%) implanted with the control Model SA60AT.

Table 7: Uncorrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60TT, All Implanted

		Visual Acuity											
Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better	
	N	n	%	n	%	n	%	n	%	n	%	n	%
<60	33	15	45.5	11	33.3	2	6.1	4	12.1	1	3.0	32	97.0
60-69	56	25	44.6	11	19.6	14	25.0	6	10.7	0	0.0	56	100.0
70-79	90	32	35.6	29	32.2	15	16.7	7	7.8	7	7.8	83	92.2
≥ 80	32	9	28.1	8	25.0	5	15.6	5	15.6	5	15.6	27	84.4
Total	211	81	38.4	59	28.0	36	17.1	22	10.4	13	6.2	198	93.8

Table 8: Uncorrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60AT, All Implanted

		Visual Acuity											
Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better	
	N	n	%	n	%	n	%	n	%	n	%	n	%
<60	15	2	13.3	6	40.0	2	13.3	1	6.7	4	26.7	11	73.3
60-69	54	14	25.9	10	18.5	13	24.1	5	9.3	12	22.2	42	77.8
70-79	92	18	19.6	16	17.4	12	13.0	28	30.4	18	19.6	74	80.4
≥ 80	49	6	12.2	14	28.6	10	20.4	5	10.2	14	28.6	35	71.4
Total	210	40	19.0	46	21.9	37	17.6	39	18.6	48	22.9	162	77.1

At the Form 5 visit, 93.8% of Model SA60TT subjects achieved 20/40 or better UCDVA (first operative eye of the All Implanted data set) compared to 77.1% of the subjects implanted with the control Model SA60AT. The difference in uncorrected distance visual acuity (UCDVA) rate between the ACRYSOF® Toric IOL and the control Model SA60AT was statistically significant (all p-values ≤ 0.0001) in favor of the Model SA60TT.

A repeated measures analysis of variance was performed to assess lens model difference between the ACRYSOF® Toric IOL Model SA60TT (combination of SA60T3, SA60T4 and SA60T5) and the Model SA60AT control lens. Statistical analyses demonstrate that ACRYSOF® Toric IOL Model SA60TT is significantly higher when compared to the control lens Model SA60AT in logMAR UCDVA when examined at Forms 1 through 6. The resulting least squares (LS) means and differences of LS means of logMAR UCDVA are presented in Table 9 below.

Table 9: Analysis of UCDVA
Differences of Least Square Means Between Lens Models at Each Visit, SA60TT vs SA60AT

			Estimate	Lower	Upper	P-Value
Visit	Lens Model	Lens Model				
Form 1	SA60TT	SA60AT	-0.1108	-0.1441	-0.0774	<.0001
Form 2	SA60TT	SA60AT	-0.1037	-0.1372	-0.0701	<.0001
Form 3	SA60TT	SA60AT	-0.1058	-0.1398	-0.0719	<.0001
Form 4	SA60TT	SA60AT	-0.1129	-0.1477	-0.0781	<.0001
Form 5	SA60TT	SA60AT	-0.1178	-0.1526	-0.0830	<.0001
Form 6	SA60TT	SA60AT	-0.1143	-0.1559	-0.0727	<.0001

A Cochran-Mantel-Haenszel (CMH) Test with rank scores analysis was also performed on the UCDVA (at Form 5) of those subjects implanted with each of the individual Toric models (SA60T3, SA60T4 and SA60T5) and compared to those subjects in the same cylinder range but receiving the control lens. These data are

graphically displayed in Figures 1 through 3 and they show that the UCDVA of subjects receiving each Toric IOL model is clinically significantly better than the UCDVA of subjects implanted with the control Model SA60AT in the same cylinder range.

Figure 1: UCDVA by Lens Model, Form 5, All Implanted SA60T3 vs. T3-control

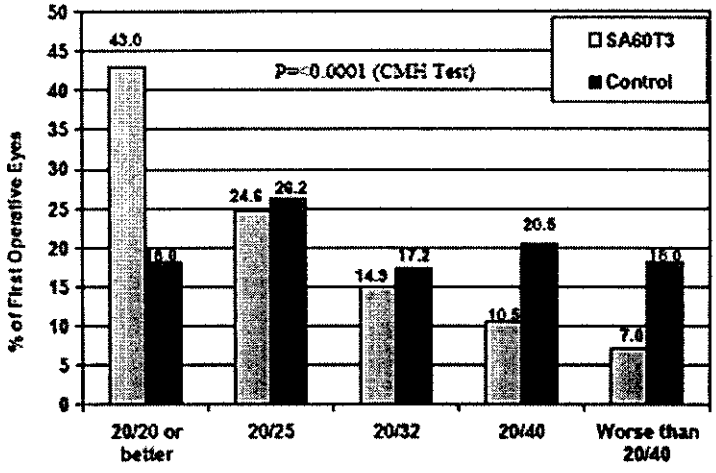


Figure 2: UCDVA by Lens Model, Form 5, All Implanted SA60T4 vs. T4-control

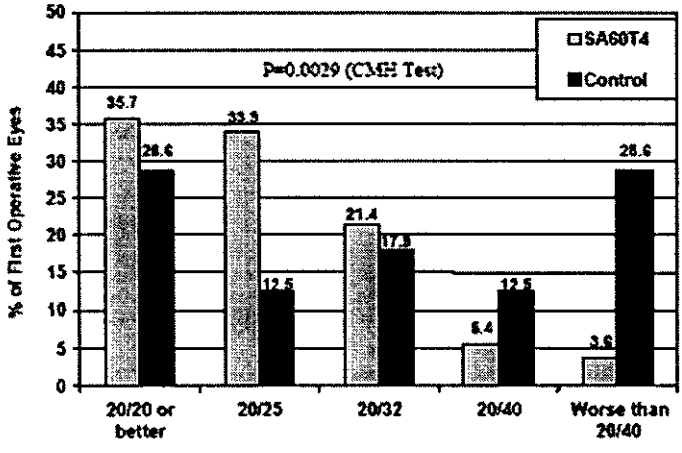
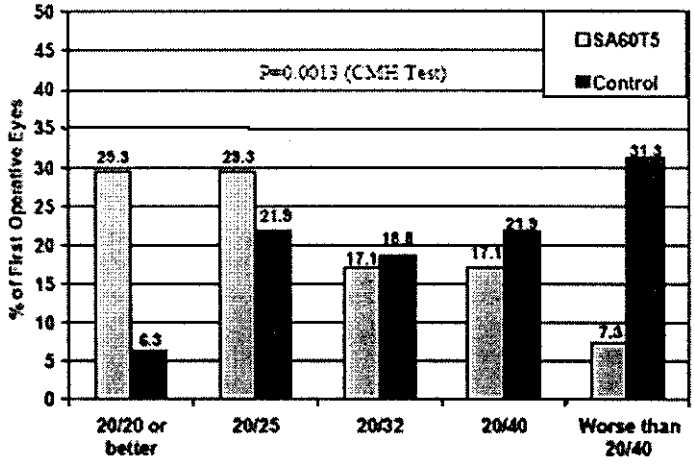
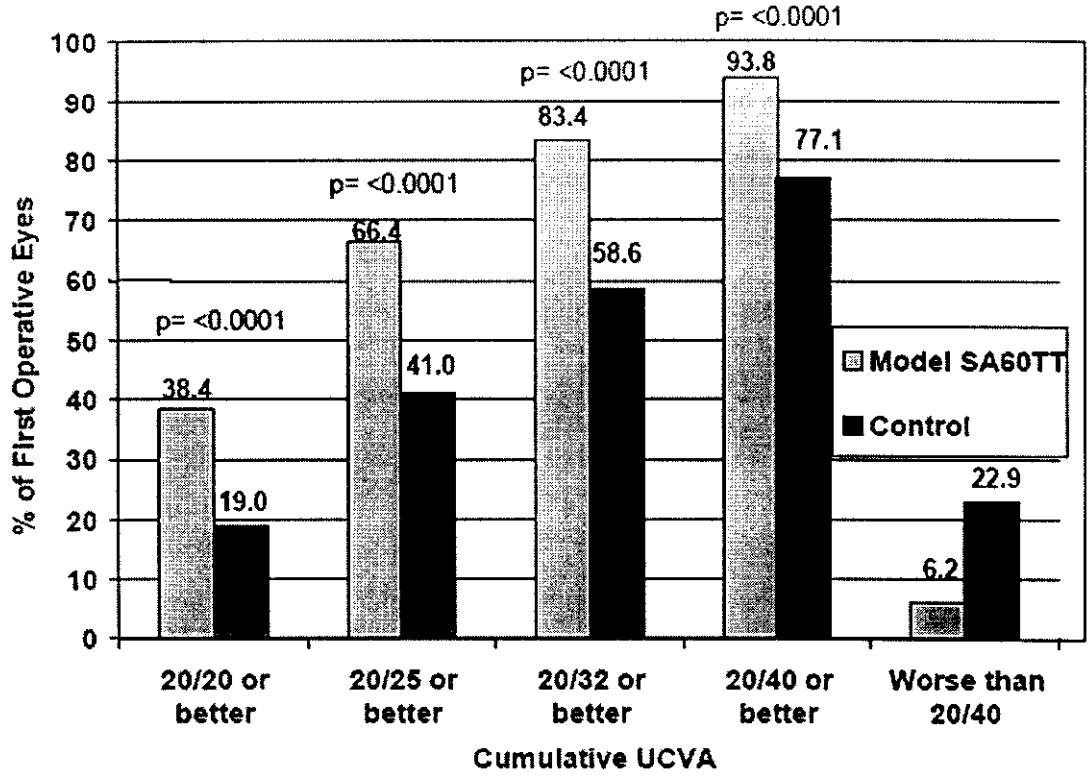


Figure 3: UCDVA by Lens Model, Form 5, All Implanted SA60T5 vs. T5-control



Graphic presentation of cumulative uncorrected distance visual acuity in Snellen line is also presented below. Figure 4 supports the claim that the Model SA60TT lens is more likely to provide a favorable outcome in cumulative UCDVA since all of the cumulative uncorrected visual acuities are statistically significant (all p-values <0.0001) and in favor of the Model SA60TT. The p-values for cumulative data were adjusted for multiplcity.

Figure 4: Cumulative UCDVA, Model SA60TT vs. Control, Form 5, All Implanted



Figures 5 through 7 show a summary of cumulative uncorrected visual acuities for each Toric cylinder model compared to the control subjects in the same cylinder range. These figures show that each Toric cylinder model is statistically higher to the control model for each visual acuity category (20/20 or better, 20/25 or better, 20/32 or better and 20/40 or better) with the exception of the Model SA60T4 at 20/20 or better where the difference was not statistically significant.

Figure 5: Cumulative UCDVA, Model SA60T3 vs. Control, Form 5, All Implanted

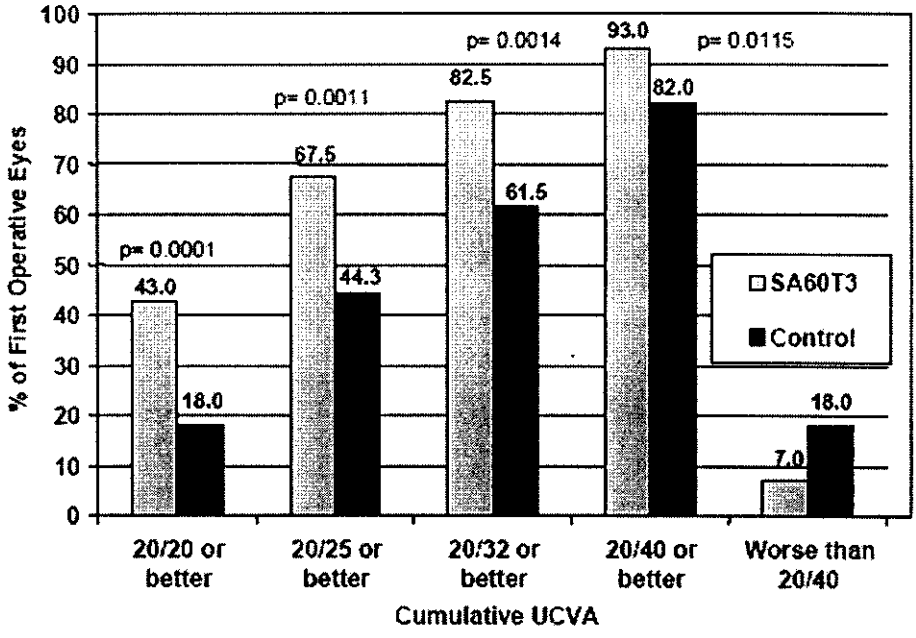


Figure 6: Cumulative UCDVA, Model SA60T4 vs. Control, Form 5, All Implanted

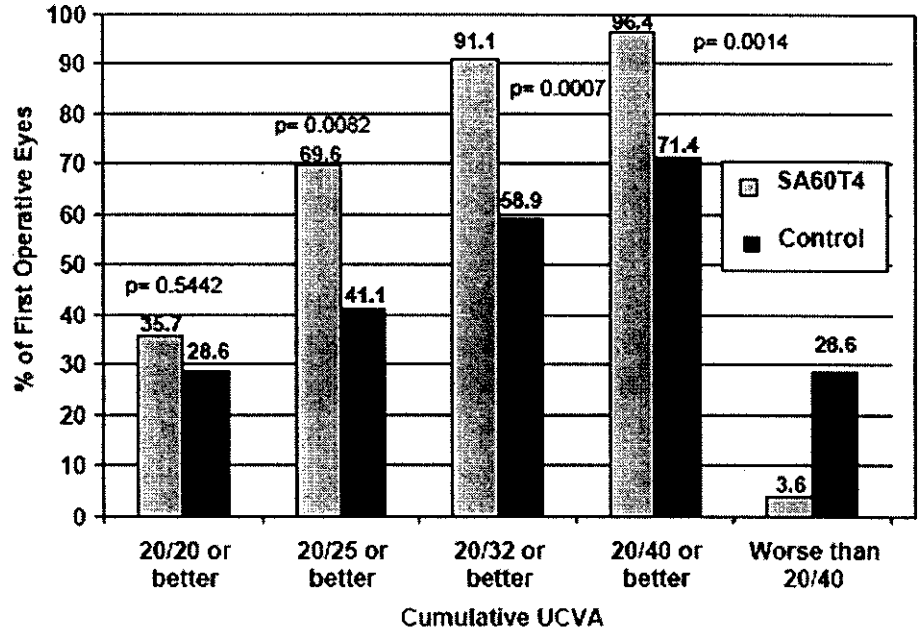
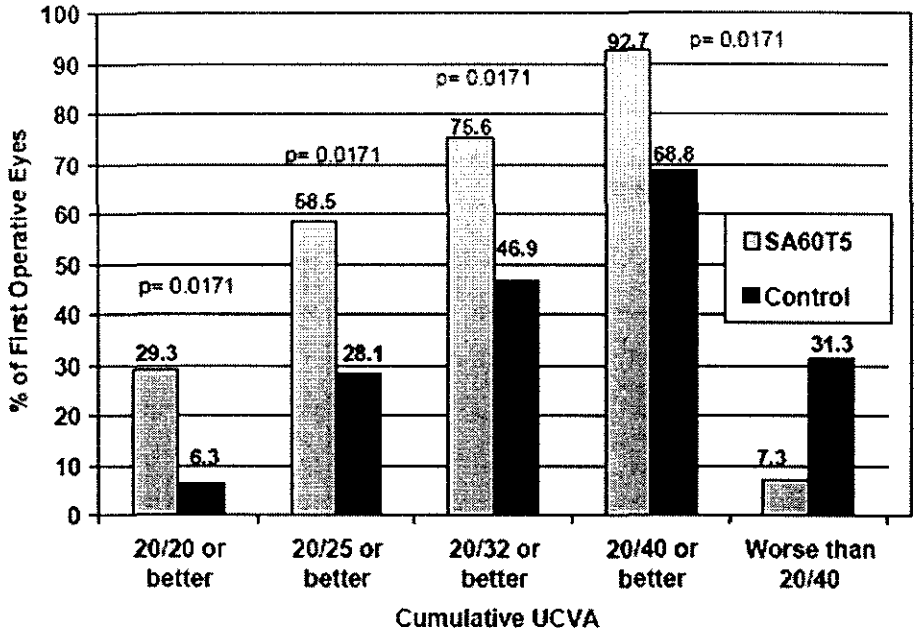


Figure 7: Cumulative UCDVA, Model SA60T5 vs. Control, Form 5, All Implanted



The Model SA60TT IOL group achieved higher uncorrected distance visual acuity compared to the Model SA60AT IOL control group. This difference provides evidence that the Model SA60TT IOL can correct both spherical and cylindrical refractive error simultaneously compared to the standard, non-toric monofocal Model SA60AT control, which is designed to correct spherical refractive error only.

The best spectacle corrected distance visual acuities (BSCDVA) achieved by the first operative eyes implanted with a Model SA60TT in the All Implanted data set at the Form 5 visit are tabulated below in Table 10 and compared to the FDA grid.

Of the first operative eyes implanted with a Model SA60TT and examined at the Form 5 visit, 100.0% achieved a BSCDVA of 20/40 or better in the All Implanted data set. These rates exceed the FDA grid rates of 92.5%.

Table 10: Best Spectacle Corrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60TT, All Implanted

Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better		FDA Grid
	N	n	%	n	%	n	%	n	%	n	%	N	%	%
<60	33	30	90.9	2	6.1	1	3.0	0	0.0	0	0.0	33	100.0	97.9
60-69	56	47	83.9	7	12.5	2	3.6	0	0.0	0	0.0	56	100.0	95.7
70-79	90	72	80.0	15	16.7	3	3.3	0	0.0	0	0.0	90	100.0	93.4
≥ 80	32	22	68.8	5	15.6	4	12.5	1	3.1	0	0.0	32	100.0	86.5
Total	211	171	81.0	29	13.7	10	4.7	1	0.5	0	0.0	211	100.0	92.5

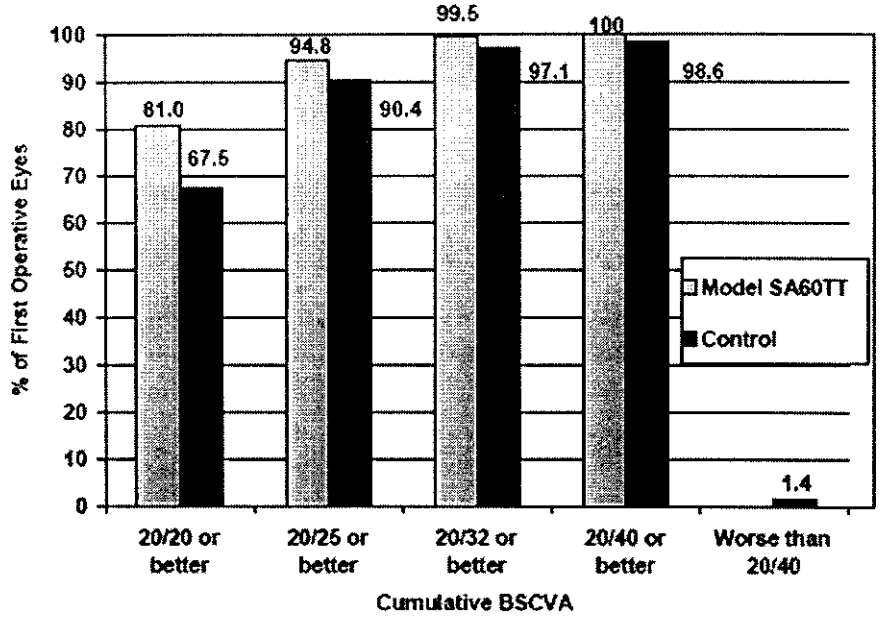
In comparison, Table 11 shows the best spectacle corrected distance visual acuities achieved by the first operative eyes implanted with the control Model SA60AT in the All Implanted data set at the Form 5 visit. Of the first operative eyes implanted with the control Model SA60AT and examined at the Form 5 visit, 98.6% in the All Implanted data set achieved 20/40 or better. Table 11 also shows that 67.5% of the control Model SA60AT subjects in the All Implanted data set achieved 20/20 or better.

Table 11: Best Spectacle Corrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60AT, All Implanted

Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better		FDA Grid
	N	n	%	n	%	n	%	n	%	n	%	N	%	%
<60	15	13	86.7	1	6.7	1	6.7	0	0.0	0	0.0	15	100.0	97.9
60-69	54	41	75.9	12	22.2	1	1.9	0	0.0	0	0.0	54	100.0	95.7
70-79	91	59	64.8	22	24.2	10	11.0	0	0.0	0	0.0	91	100.0	93.4
≥ 80	49	28	57.1	13	26.5	2	4.1	3	6.1	3	6.1	46	93.9	86.5
Total	209	141	67.5	48	23.0	14	6.7	3	1.4	3	1.4	206	98.6	92.5

Figure 8 shows a summary of cumulative best spectacle corrected distance visual acuities for the Model SA60TT vs. the control.

Figure 8: Cumulative BSCDVA, Model SA60TT vs. Control, Form 5, All Implanted



Figures 9 through 11 show a summary of cumulative best spectacle corrected distance visual acuities for each Toric cylinder model compared to the control subjects in the same cylinder range for the All Implanted data set.

Figure 9: Cumulative BSCDVA, Model SA60T3 vs. Control, Form 5, All Implanted

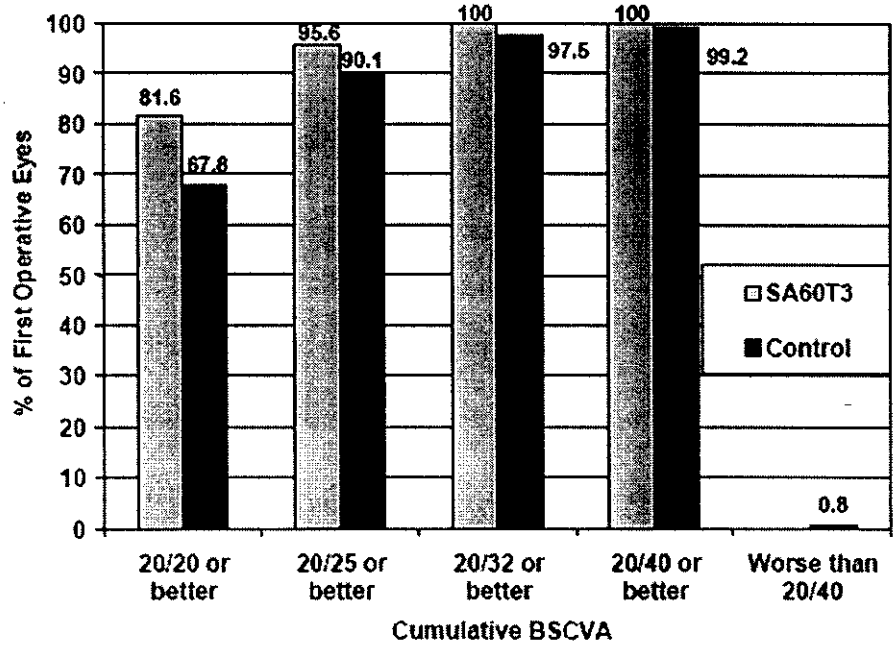


Figure 10: Cumulative BSCDVA, Model SA60T4 vs. Control, Form 5, All Implanted

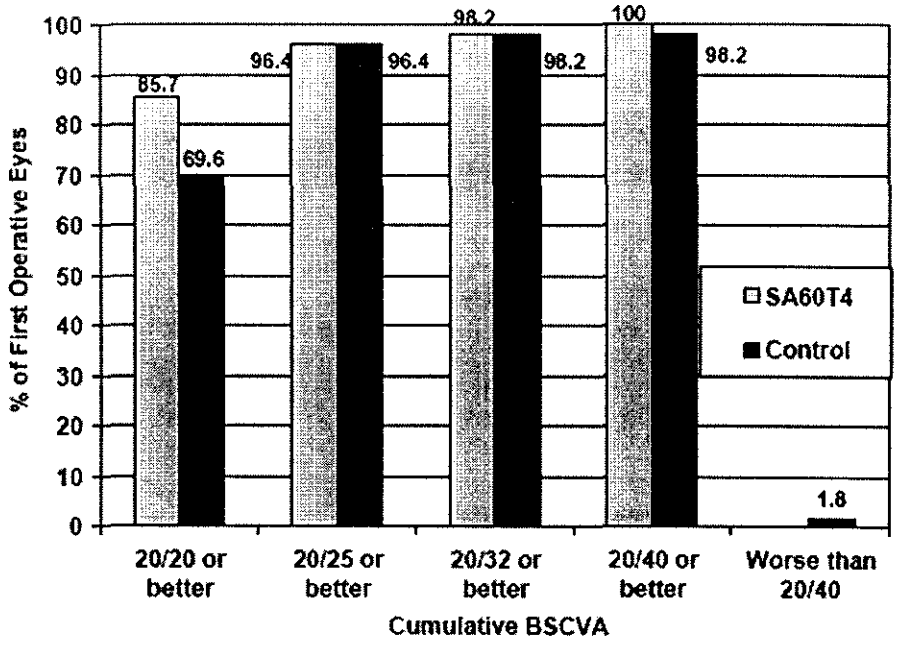
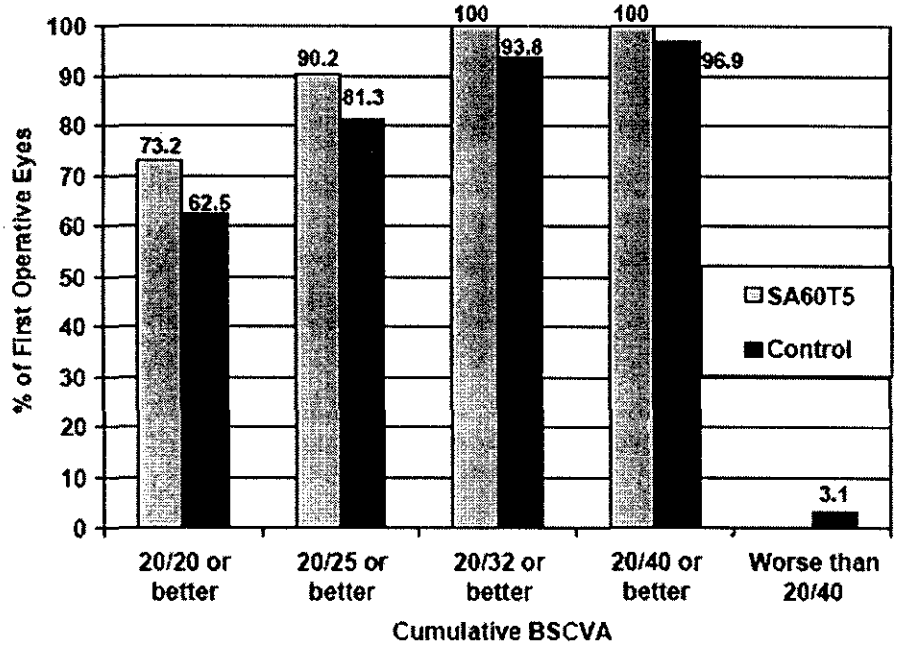


Figure 11: Cumulative BSCDVA, Model SA60T5 vs. Control, Form 5, All Implanted



A summary of best spectacle corrected distance visual acuity (BSCDVA) achieved at six months postoperatively among subjects who did not have any visually significant preoperative pathology or macular degeneration at any time (Best Case) is presented in

Tables 12 and 13. Of the first operative eyes implanted with a Model SA60TT or Model SA60AT that were examined at the Form 5 visit, 100.0% achieved a BSCDVA of 20/40 or better in the Best Case dataset. These rates exceed the FDA grid rates of 96.7%.

Table 12: Best Spectacle Corrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60TT, Best Case

Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better		FDA Grid
	N	n	%	n	%	n	%	n	%	n	%	N	%	%
<60	29	27	93.1	1	3.4	1	3.4	0	0.0	0	0.0	29	100.0	98.5
60-69	51	42	82.4	7	13.7	2	3.9	0	0.0	0	0.0	51	100.0	96.5
70-79	73	57	78.1	13	17.8	3	4.1	0	0.0	0	0.0	73	100.0	97.5
≥ 80	20	14	70.0	4	20.0	1	5.0	1	5.0	0	0.0	20	100.0	94.8
Total	173	140	80.9	25	14.5	7	4.0	1	.06	0	0.0	173	100.0	96.7

Table 13: Best Spectacle Corrected Distance Visual Acuity by Age Category, Status at Form 5 – Lens Model SA60AT, Best Case

Age	Sample Size	20/20 or better		20/25		20/32		20/40		Worse than 20/40		20/40 or better		FDA Grid
	N	n	%	n	%	n	%	n	%	n	%	N	%	%
<60	15	13	86.7	1	6.7	1	6.7	0	0.0	0	0.0	15	100.0	98.5
60-69	49	38	77.6	11	22.4	0	0.0	0	0.0	0	0.0	49	100.0	96.5
70-79	75	48	64.0	21	28.0	6	8.0	0	0.0	0	0.0	75	100.0	97.5
≥ 80	32	19	59.4	8	25.0	2	6.3	3	9.4	0	0.0	32	100.0	94.8
Total	171	118	69.0	41	24.0	9	5.3	3	1.8	0	0.0	171	100.0	96.7

Tables 12 and 13 also show that 80.9% of the Model SA60TT subjects and 69.0% of the Model SA60AT subjects in the Best Case data set achieved a best spectacle corrected distance visual acuity of 20/20 or better. Therefore, the ACRYSOF® Toric Model SA60TT showed a higher rate of subjects who achieved 20/20 or better when compared to the control Model SA60AT IOL.

Absolute Residual Refractive Cylinder: In the clinical study, residual refractive cylinder was determined by the postoperative manifest refraction used to obtain best spectacle corrected distance visual acuity.

Figures 12 through 14 demonstrate that cumulative residual refractive cylinder values were lower among those subjects implanted with either an ACRYSOF® Toric Model SA60T3, SA60T4 or SA60T5 IOL when compared to the corresponding subjects implanted with the control Model SA60AT.

Figure 12: Cumulative Absolute Residual Refractive Cylinder, Model SA60T3 vs. Control, Form 5, All Implanted

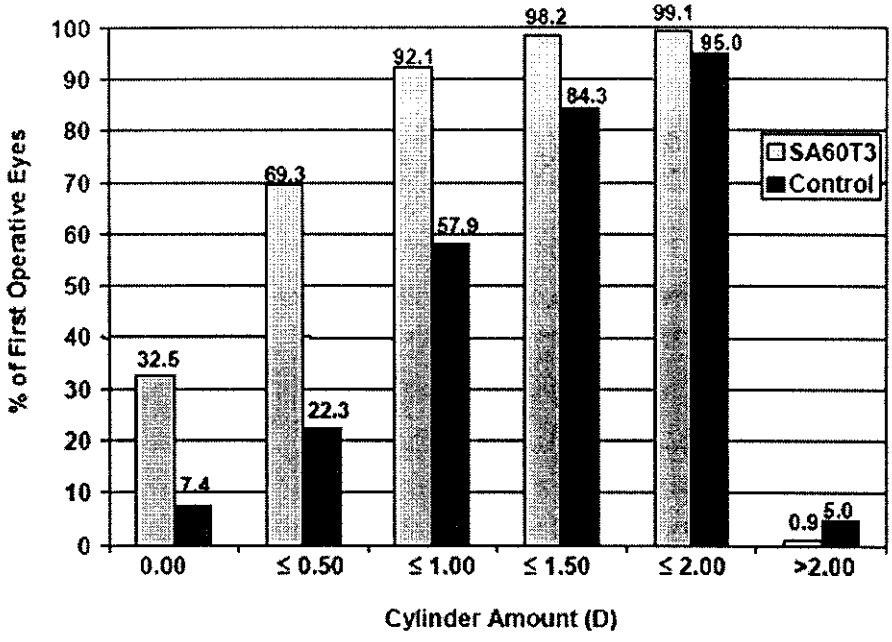


Figure 13: Cumulative Absolute Residual Refractive Cylinder, Model SA60T4 vs. Control, Form 5, All Implanted

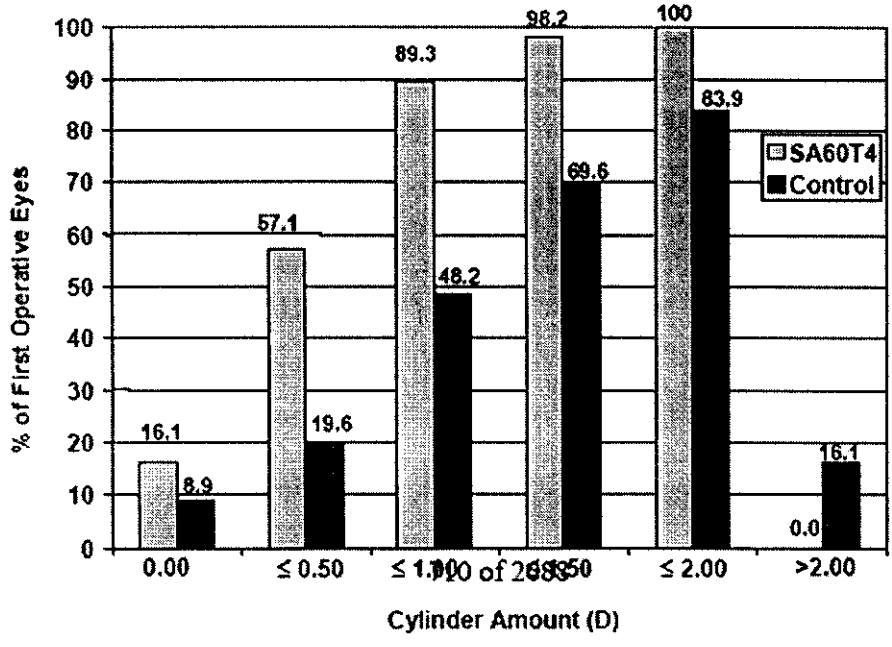


Figure 14: Cumulative Absolute Residual Refractive Cylinder, Model SA60T5 vs. Control, Form 5, All Implanted

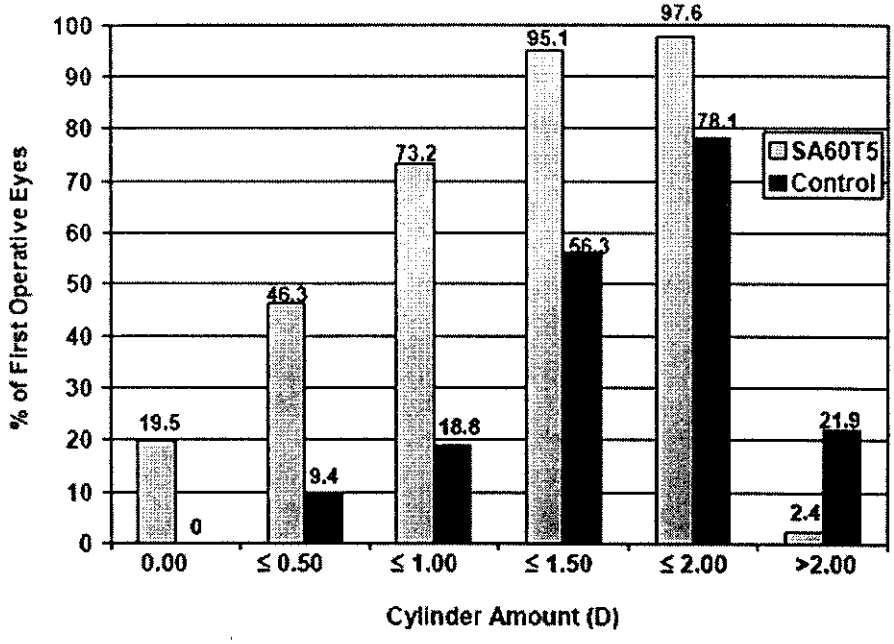
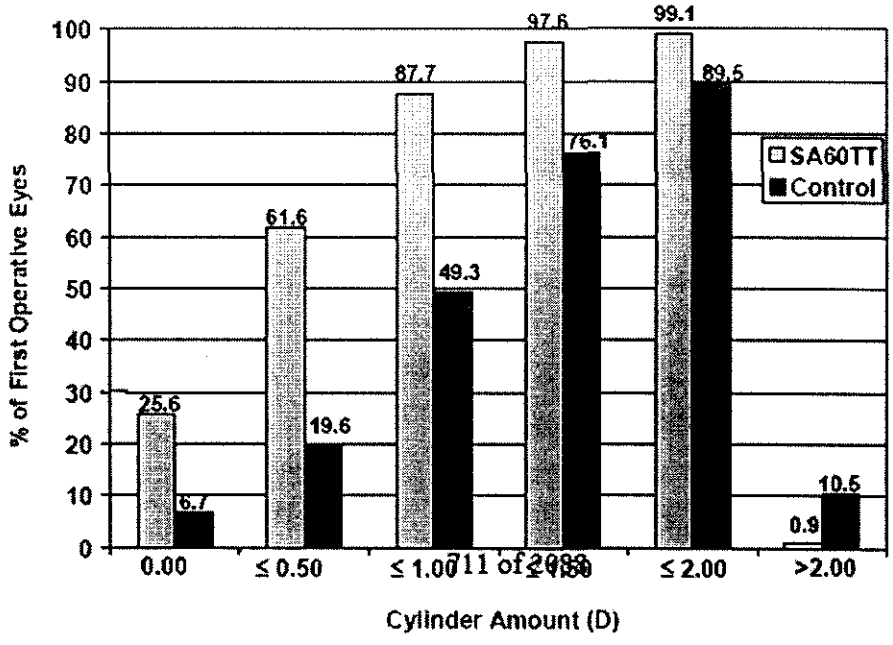


Figure 15 shows a comparison between Model SA60TT (three Toric models combined) and the control Model SA60AT for residual refractive cylinder at Form 5. The residual refractive cylinder values were lower among those subjects implanted with an ACRYSOF® Toric Model SA60TT when compared to the subjects implanted with the control Model SA60AT.

Figure 15: Cumulative Absolute Residual Refractive Cylinder, Model SA60TT vs. Control, Form 5, All Implanted



The CMH test with rank scores was performed to test whether the mean rank scores are equal for the two groups, aimed at comparing the amount of residual cylinder at postoperative visits between the ACRYSOF® Toric IOL and control lens models.

At Form 5, residual refractive cylinder values were statistically significantly lower among those implanted with a ACRYSOF® Toric Model SA60TT IOL compared to the control Model SA60AT subjects (p-value <0.0001 for SA60T3 vs. SA60AT, p-value<0.0001 for SA60T4 vs. SA60AT and p-value<0.0001 for SA60T5 vs. SA60AT). These results are shown graphically in Figures 16 through 18 for Models SA60T3, SA60T4 and SA60T5 respectively. Each of the ACRYSOF® Toric Lens Models SA60T3, SA60T4 and SA60T5 had at least a 3-fold increase in the likelihood of achieving residual refractive cylinder of 0.5 D or less as compared to the corresponding control model.

Figure 16: Residual Refractive Cylinder, SA60T3 and T3-Control at Form 5, All Implanted

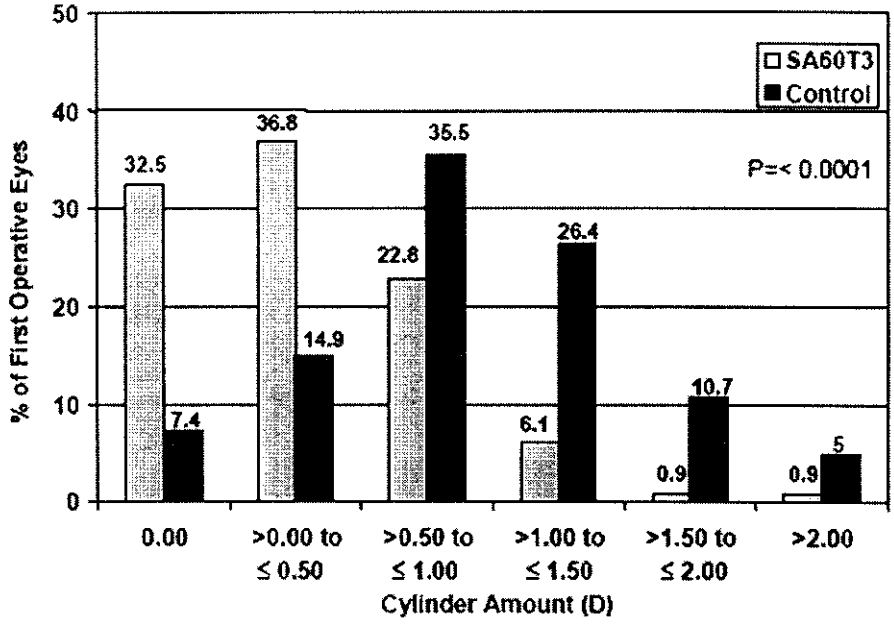


Figure 17: Residual Refractive Cylinder, SA60T4 and T4-Control at Form 5, All Implanted

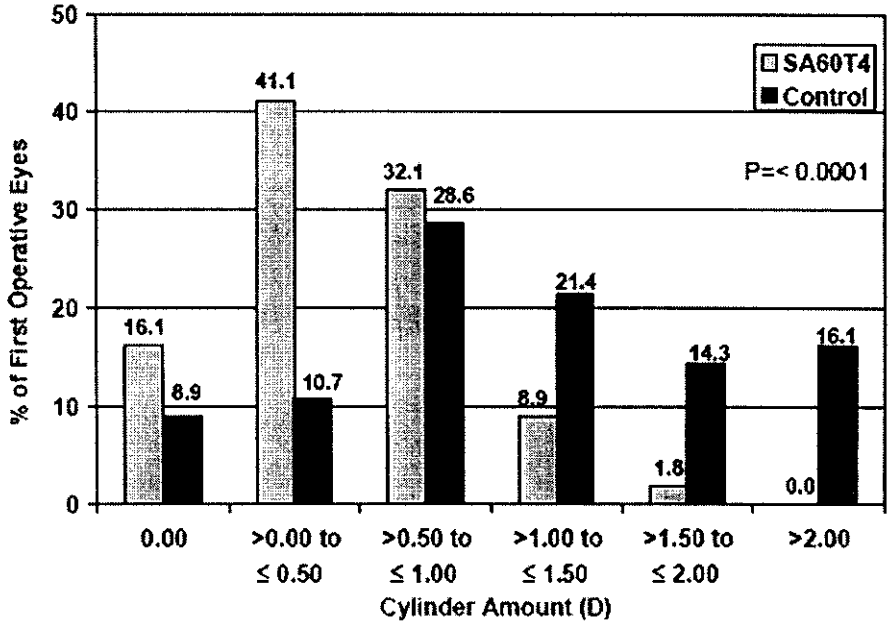
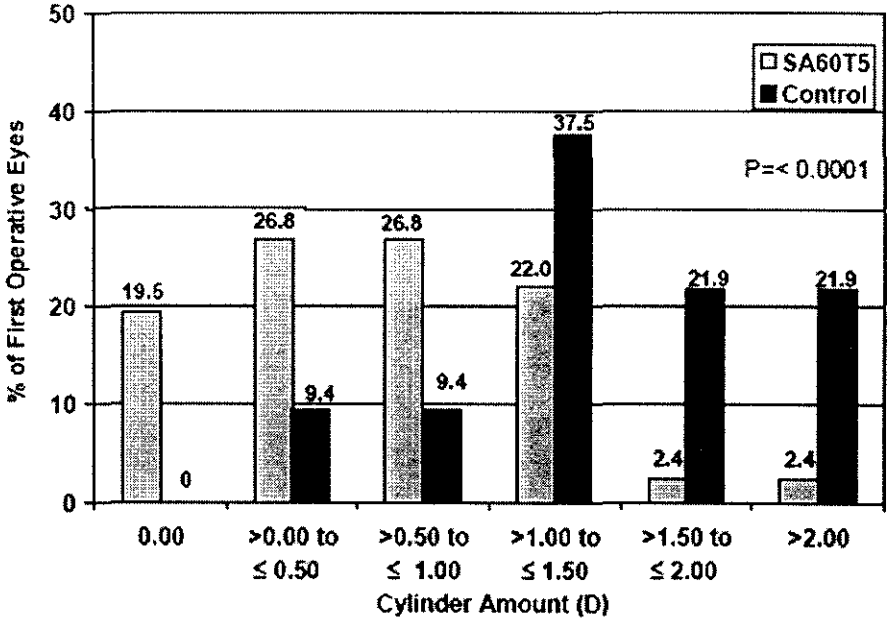


Figure 18: Residual Refractive Cylinder, SA60T5 and T5-Control at Form 5, All Implanted



The performance of Model SA60TT was also compared to the performance of Model SA60AT by calculating a mean and standard deviation residual refractive cylinder for each lens model. These results are illustrated in Table 14.

Table 14:
Mean Absolute Residual Refractive Cylinder, Status at Form 5, All Implanted

Corneal Astigmatism		Residual Refractive Cylinder (D)				
		Mean	Std	N	Min	Max
Form 5	SA60TT	0.55	0.50	211	0.0	2.75
	SA60AT	1.22	0.73	209	0.0	4.25

Subjects implanted with an ACRYSOF® Toric Model SA60T3 showed a 62.4% mean reduction in refractive cylinder from the preoperative visit (keratometric cylinder) as compared to the 10.8% mean reduction for subjects implanted with the concurrent control Model SA60AT. Subjects implanted with an ACRYSOF® Toric Model SA60T4 or SA60T5 showed similar results with a mean reduction in refractive cylinder of 54.8% and 67.8%, respectively, as compared to subjects implanted with the concurrent control model who had a mean reduction in refractive cylinder of 22.1% and 27.7%, respectively. These results are illustrated in Table 15.

Table 15: Mean % Change of Refractive Cylinder from Baseline to Form 5, All Implanted

		% Change of Refractive Cylinder from Baseline				
		Mean	Std	N	Min	Max
Targeted Corneal Astigmatism	Lens Model					
<1.50 D	SA60T3	62.40	37.86	114	-42.86	100.00
	SA60AT	10.83	46.35	121	-99.12	100.00
≥1.50-<2.0 D	SA60T4	54.80	33.16	56	-50.00	100.00
	SA60AT	22.13	42.28	56	-83.33	100.00
≥2.0 D	SA60T5	67.80	24.50	41	7.98	100.00
	SA60AT	27.96	27.35	32	-70.00	87.50

IOL Rotational Stability: The cylindrical component of the Toric IOL requires careful placement to ensure retention of the IOL Model SA60TT in the appropriate orientation within the capsular bag. The flat meridian (indicated by axis marks) of the IOL must be aligned with the steep meridian of the post-operative corneal astigmatism to provide optimal vision correction. Misalignment of the IOL reduces the astigmatic correction and results in a shift in the axis of the refractive cylinder. Extreme cases, such as misalignment or postoperative rotation > 30° from the intended axis of placement, may result in an increase in refractive cylinder (Shimizu et al., 1994).

In the clinical study, the orientation of the IOL cylinder for Model SA60TT was measured at the operative visit and at each postoperative visit. The operative visit results were compared to the intended axis orientation in order to demonstrate the accuracy and ease of placement of the Model SA60TT in the capsular bag.

As illustrated in Table 16, the mean difference between intended axis orientation and achieved axis orientation at Form 00 (operative visit) was 0.4° ± 1.4 for the subjects implanted with a Model SA60TT. Table 16 also demonstrates that the accuracy of placement was independent of IOL cylinder power.

Table 16: Mean Absolute Difference Between Intended Axis Orientation and Achieved Axis Orientation at Surgery (degrees), All Implanted

Lens Model	Accuracy of Placement (degrees)				
	Mean	STD	N	Min	Max
SA60T3	0.4	1.5	123	0.0	10.0
SA60T4	0.1	0.3	66	0.0	2.0
SA60T5	0.5	1.8	53	0.0	11.0
SA60TT	0.4	1.4	242	0.0	11.0

The postoperative results at Form 5 were compared to the operative visit results to determine rotational stability. Figures 19 and 20 demonstrate the rotational stability of

the ACRYSOF® Toric Model SA60TT IOL with the majority of the lenses (81.1%) rotating ≤ 5°.

Figure 19: Change in Axis Orientation from Operative Visit to Form 5, All Implanted

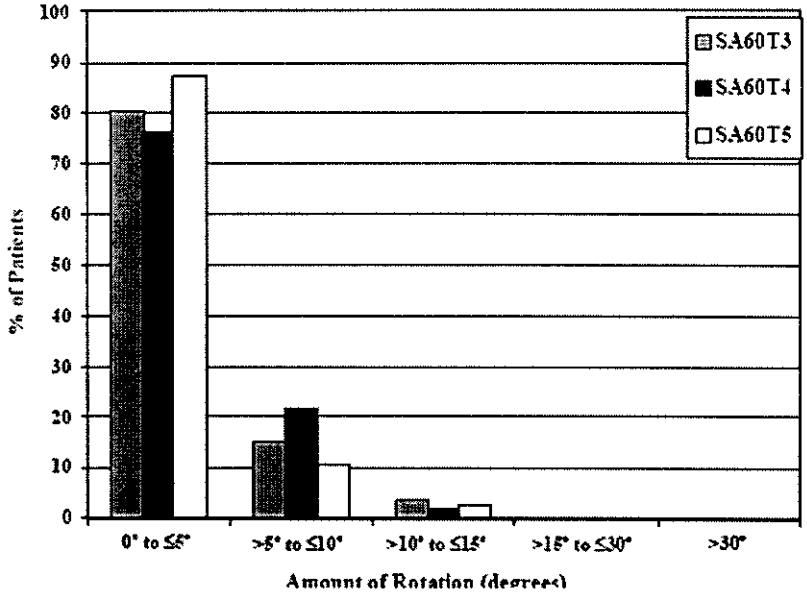
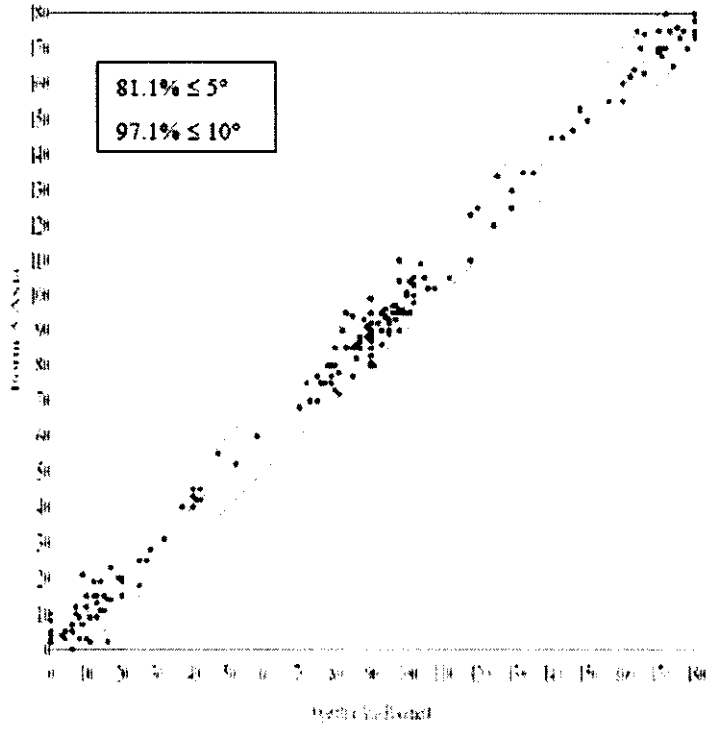


Figure 20: Model SA60TT Absolute Change in Axis Orientation from Operative Visit to Form 5, All Implanted



The mean change in axis orientation from the operative visit to the Form 5 visit (Table 17) was also calculated to demonstrate that the amount of rotation seen with ACRYSOF® Toric IOLs is independent of the cylinder power.

Table 17: Mean Absolute Change in Axis Orientation from Operative Visit to Form 5, All Implanted

Lens Model	Change in Axis Orientation				
	Mean	Std	N	Min	Max
SA60T3	3.4	3.1	112	0	14
SA60T4	3.7	2.9	55	0	11
SA60T5	2.9	2.8	39	0	12
SA60TT	3.4	3.0	206	0	14

No assessments reported for Subject 3470.142 (Form 00), 3470.154 (Form 00), 3481.554 (Form 5), 1204.708 (Form 5).

A two way analysis of variance on axis rotation from the operative visit demonstrates that there were no statistically significant lens model main effects or cylinder power main effects, and that the differences between lens models are consistent across visit. The minimal amounts of rotation presented in the tables above were independent of the lens model or the amount of cylinder being corrected. Rotation of the lens for postoperative visits Form 3, 4 and 5 are compared among lens models in Table 18. There is no significant difference in rotation between lens models at any visit.

Table 18: Comparison of Lens Models by Visit for Axis Rotation, 1st Eye, All Implanted Difference in Least Square Means between Lens Models at Each Visit

			Difference	Lower	Upper	P-Value
Visit	Lens Model	Lens Model				
Form 3	SA60T3	SA60T4	-0.1522	-1.1884	0.8840	0.7728
		SA60T5	0.2943	-0.8151	1.4038	0.6020
	SA60T4	SA60T5	0.4466	-0.8127	1.7058	0.4859
Form 4	SA60T3	SA60T4	0.3112	-0.7450	1.3674	0.5626
		SA60T5	0.2304	-0.9083	1.3691	0.6909
	SA60T4	SA60T5	-0.0808	-1.3692	1.2076	0.9019
Form 5	SA60T3	SA60T4	-0.0571	-1.1120	0.9977	0.9152
		SA60T5	0.2620	-0.8927	1.4166	0.6557
	SA60T4	SA60T5	0.3191	-0.9883	1.6265	0.6315

Stability of Cylinder: Subjects implanted with lens model SA60TT exhibited stability of cylinder at Form 4 (3 months) with greater than 90% of all subjects changing less than or equal to 1.00 diopter at consecutive visits between Form 3 (one month) and Form 6 (twelve months). Tables 19 and 20 demonstrate stability of cylinder for eyes

that had two consecutive exams (but not necessarily every follow-up exam), and stability of cylinder for every follow-up exam up to 12 months postoperatively.

Table 19: Stability of Cylinder
(Eyes that had 2 consecutive exams, but not necessarily every follow-up exam)

Recommended Corneal Astigmatism Correction Ranges	Toric IOL Model	Magnitude of Vector Change in Cylinder	1 and 3 Months n/N,%	3 and 6 Months n/N,%	6 and 12 Months n/N,%
< 1.5 D	SA60T3	≤ 1.00 D	106/107,99.07%	101/105,96.19%	55/55,100.00%
		Mean Change	0.28	0.29	0.20
		SD	0.32	0.33	0.25
≥ 1.5 - < 2.0 D	SA60T4	≤ 1.00 D	54/56,96.43%	53/54,98.15%	25/27,92.59%
		Mean Change	0.40	0.27	0.46
		SD	0.35	0.22	0.45
≥ 2.0 D	SA60T5	≤ 1.00 D	40/45,88.89%	35/40,87.50%	27/30,90.00%
		Mean Change	0.43	0.42	0.41
		SD	0.44	0.45	0.38
Combined	SA60TT	≤ 1.00 D	200/208,96.15%,(93.54,98.77)	189/199,94.97%,(91.94,98.01)	107/112,95.54%,(91.71,99.36)
		Mean Change	0.35	0.31	0.32
		SD	0.36	0.34	0.36
		95% CI	0.30,0.39	0.26,0.36	0.25,0.39
n/N,%,(%CI) are for percent with change between ± 1.00D					

Table 20: Stability of Cylinder
(Eyes that had every follow-up exam up to Form 6, 12 months)

Recommended Corneal Astigmatism Correction Ranges	Toric IOL Model	Magnitude of Vector Change in Cylinder	1 and 3 Months n/N,%	3 and 6 Months n/N,%	6 and 12 Months n/N,%
< 1.5 D	SA60T3	≤ 1.00 D	34/34,100.00%	34/34,100.00%	34/34,100.00%
		Mean Change	0.25	0.24	0.21
		SD	0.23	0.22	0.24
≥ 1.5 - < 2.0 D	SA60T4	≤ 1.00 D	17/17,100.00%	16/17,94.12%	16/17,94.12%
		Mean Change	0.27	0.25	0.35
		SD	0.25	0.26	0.33
≥ 2.0 D	SA60T5	≤ 1.00 D	17/19,89.47%	15/19,78.95%	16/19,84.21%
		Mean Change	0.44	0.56	0.52
		SD	0.47	0.50	0.43
Combined	SA60TT	≤ 1.00 D	68/70,97.14%,(93.23,100.00)	65/70,92.86%,(86.82,98.90)	66/70,94.29%,(88.84,99.73)
		Mean Change	0.31	0.33	0.33
		SD	0.32	0.35	0.34
		95% CI	0.23,0.38	0.24,0.41	0.25,0.41
n/N,%,(%CI) are for percent with change between ± 1.00D					

Table 21: Stability of Absolute Cylinder for TT Lens Models
(Eyes that had 2 consecutive exams, but not necessarily every follow-up exam)

Recommended Corneal Astigmatism Correction Ranges	Toric IOL Model	Magnitude of Change in Absolute Cylinder	1 and 3 Months n/N,%	3 and 6 Months n/N,%	6 and 12 Months n/N,%
< 1.5 D	SA60T3	≤ 1.00 D	107/107,100.00%	104/105,99.05%	55/55,100.00%
		Mean Change	0.04	0.02	0.05
		SD	0.32	0.38	0.29
≥ 1.5 - < 2.0 D	SA60T4	≤ 1.00 D	54/56,96.43%	54/54,100.00%	27/27,100.00%
		Mean Change	0.18	0.05	-0.12
		SD	0.42	0.27	0.41
≥ 2.0 D	SA60T5	≤ 1.00 D	44/45,97.78%	37/40,92.50%	29/30,96.67%
		Mean Change	0.09	0.06	0.00
		SD	0.38	0.49	0.45
Combined	SA60TT	≤ 1.00 D	205/208,98.56%,(96.93,100.00)	195/199,97.99%,(96.04,99.94)	111/112,99.11%,(97.36,100.00)
		Mean Change	0.09	0.03	-0.01
		SD	0.37	0.38	0.37
		95% CI	0.04,0.14	-0.02,0.09	-0.08,0.06
n/N,%,(%CI) are for percent with change between ± 1.00D					

Table 22: Stability of Absolute Cylinder for TT Lens Models
(Eyes that had every follow-up exam up to Form 6, 12 months)

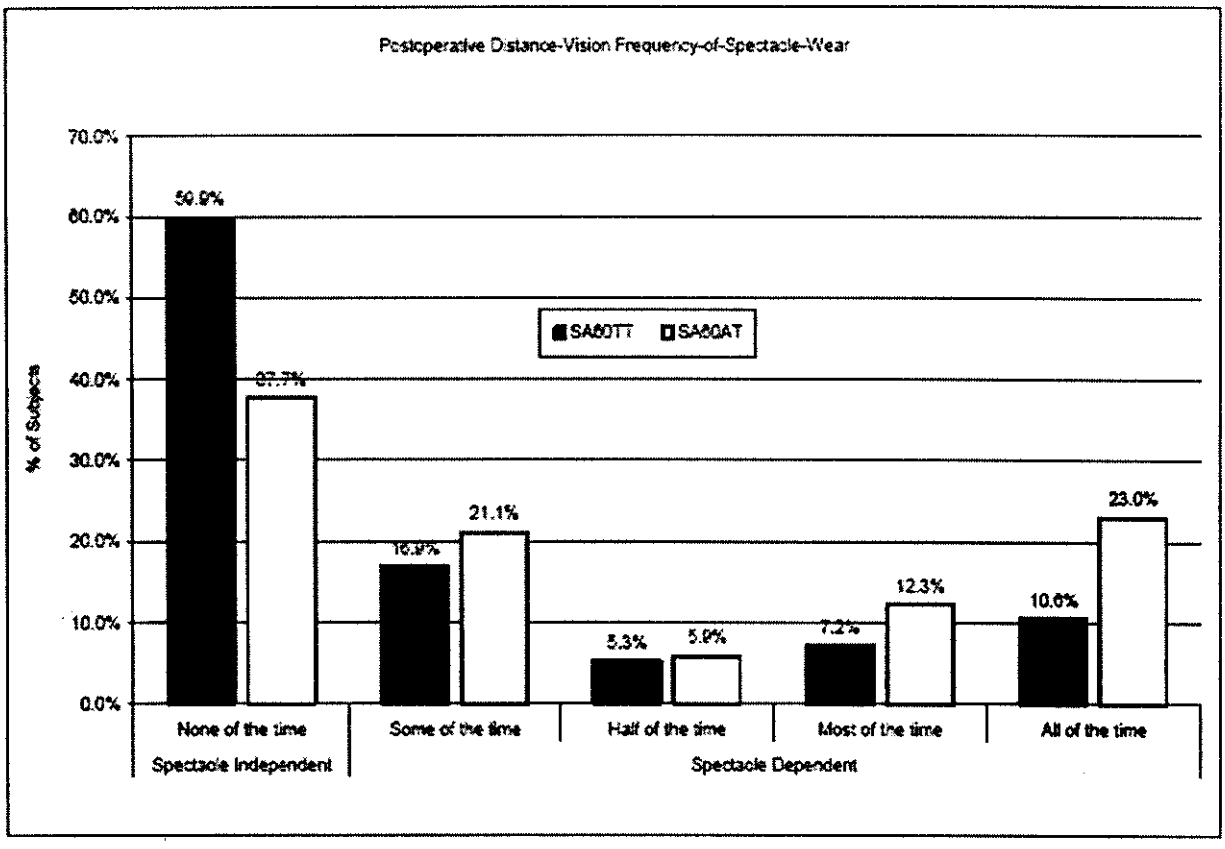
Recommended Corneal Astigmatism Correction Ranges	Toric IOL Model	Magnitude of Change in Absolute Cylinder	1 and 3 Months n/N,%	3 and 6 Months n/N,%	6 and 12 Months n/N,%
< 1.5 D	SA60T3	≤ 1.00 D	34/34,100.00%	34/34,100.00%	34/34,100.00%
		Mean Change	0.01	-0.01	0.07
		SD	0.28	0.31	0.28
≥ 1.5 - < 2.0 D	SA60T4	≤ 1.00 D	17/17,100.00%	17/17,100.00%	17/17,100.00%
		Mean Change	0.06	0.19	-0.04
		SD	0.30	0.21	0.42
≥ 2.0 D	SA60T5	≤ 1.00 D	18/19,94.74%	17/19,89.47%	18/19,94.74%
		Mean Change	0.17	0.05	0.01
		SD	0.45	0.54	0.55
Combined	SA60TT	≤ 1.00 D	69/70,98.57%,(95.78,100.00)	68/70,97.14%,(93.23,100.00)	69/70,98.57%,(95.78,100.00)
		Mean Change	0.07	0.05	0.03
		SD	0.34	0.38	0.40
		95% CI	-0.01,0.15	-0.04,0.14	-0.07,0.12
n/N,%,(%CI) are for percent with change between ± 1.00D					

Patient Reported Outcomes:

Postoperative Comparison of Distance-Vision Spectacle Independence: There was a statistically significant difference in distance-vision frequency-of-spectacle-wear between the SA60TT group and the control group at the postoperative (Form 5) comparison. The SA60TT group indicated greater spectacle independence compared to the control group. Spectacle independence is defined as the proportion of subjects selecting the "none of the time" frequency-of-spectacle-wear response. Approximately 60% of the SA60TT subjects indicated spectacle independence for distance-vision compared to 38% in the control group. Conversely, approximately 40% of the SA60TT subjects indicated some degree of spectacle dependence compared to 62% in

the control group. Figure 21 compares the distance vision frequency-of-spectacle-wear distributions between the SA60TT group and the control group.

Figure 21: Distance-Vision Spectacle Independence: Postoperative Frequency-of-Spectacle-Wear



$p < 0.0001$ CMH test

The results show that substantially more SA60TT subjects were spectacle independent and indicated reduced spectacle wear compared to control subjects at the postoperative (Form 5) assessment for distance-vision.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The data in this application demonstrate a reasonable level of safety and effectiveness of the ACRYSOF® Toric IOL Models SA60TT (SA60T3, SA60T4, and SA60T5) for their intended use

XII. PANEL RECOMMENDATION

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices

Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XIII. CDRH DECISION

The Center for Devices and Radiological Health (CDRH) reviewed the PMA and concluded that the PMA contained sufficient valid scientific evidence to provide reasonable assurance of the safety and effectiveness of the device under the prescribed indications for use. The applicant's manufacturing facilities were also inspected and found to be in compliance with the Quality System Regulation (21 CFR 820). CDRH approved this PMA in a letter to the PMA applicant dated September 14, 2005.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.