SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

A. Generic Name of Device: Multifocal Posterior Chamber Intraocular Lens (IOL)

B. Trade Name of Device: AcrySof® ReSTOR® Apodized Diffractive Optic Posterior Chamber Intraocular Lenses

C. Applicant's Name and Address:

Alcon Research Ltd.
6201 South Freeway
Fort Worth, TX 76134

D. Premarket Approval Application (PMA) Number: P040020
Date Filed: April 19, 2004

E. Date of Ophthalmic Devices Panel Recommendation: None

F. Date of Notice of Approval to Applicant: March 21, 2005

II. INDICATIONS

AcrySOF® ReSTOR® IOLs are 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.

III. CONTRAINDICATIONS

None known.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AcrySof® ReSTOR® IOL labeling.

V. DEVICE DESCRIPTION

The AcrySOF® ReSTOR® Apodized Diffractive Optic Posterior Chamber Intraocular Lens (IOL) is a UV-absorbing foldable multifocal intraocular lens (IOL). The optical portion is biconvex and 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 restore the optical performance. The supporting haptics provide for proper positioning of the IOL optic within the eye.

The AcrySOF® ReSTOR® Apodized Diffractive Optic Posterior Chamber Intraocular Lens (IOL) is available in both a multi-piece (MA60D3) and single-piece (SA60D3) design. The asymmetric biconvex design features a 13.0mm overall diameter (6.0mm optic diameter) with an apodized diffractive pattern in the central region of the anterior surface of the optic. AcrySOF® material (single-piece) or PMMA (multi-piece) haptics secure the lens within the posterior capsule.

VI. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

A total of eight hundred two (802) patients were enrolled in the clinical trials to determine the safety of the AcrySof® ReStor® diffractive optic posterior chamber IOL, and 760 patients were evaluated at the one year follow-up. Of the 760 cohort patients, 566 first eyes were implanted with the AcrySOF® ReSTOR® IOL (440 of the multi-piece design, 126 of the single-piece design) and 194 first eyes were implanted with a monofocal control IOL (AcrySOF® Model MA60BM). Of the first eyes implanted with each lens model, the fellow eye was also implanted with the same lens model in 549 eyes (426 multi-piece, 123 single-piece) and 181 eyes (monofocal control).

The incidence of cumulative adverse events for the AcrySof® ReSTOR® IOL compared favorably to the FDA historical grid rates. A single occurrence of pupillary block exceeded the FDA Grid rate. No occurrences of persistent adverse events were observed in any patients implanted with the AcrySof®ReSTOR® IOL.

Table 1:
ReSTOR® IOL versus FDA Historical Grid, First Eye - Safety

	ReSTOR MA60D3 (N=440)		ReSTOR SA60D3 (N=126)		FDA Grid rate*
	N	%	N	%	%
Cumulative Adverse Events					
Endophthalmitis	0	0	0	0	0.1
Macular Edema	12	2.7	1	0.8	3.0
Retinal Detachment/Repair	0	0	1	0.8	0.3
Hyphema	0	0	0	0	2.2
Pupillary block	1	0.2	0	0	0.1
Lens Dislocation	0	0	0	0	0.1
Surgical reintervention	10	2.3	2	1.6	0.8

	ReSTOR MA60D3 (N=440)		ReSTOR SA60D3 (N=126)		FDA Grid rate*
	N	%	N	%	%
IOL replacement for biometry error	2	0.5	0	0	NA
IOL replacement for incorrect power/ operating room error	2	0.5	0	0	NA
IOL replacement for visual disturbance	1	0.2	0	0	NA
IOL replacement for decentered IOL due to trauma	1	0.2	0	0	NA
IOL replacement due to patient dissatisfaction	0	0	1	0.8	NA
Laser treatment	3	0.7	1	0.8	NA
Fibrin removal	1	0.2	0	0	NA
Persistent Adverse Events:					
Macular Edema	0	0	0	0	0.5
Raised IOP Requiring Treatment	0	0	0	0	0.4
Corneal Edema	0	0	0	0	0.3
Iritis	0	0	0	0	0.3

*FDA draft guidance on Monofocal Intraocular Lenses, Annex B (October 14, 1999)

Contrast Acuity: Mean contrast acuities and contrast sensitivity under various lighting conditions was clinically equivalent between the AcrySof® ReSTOR® IOL and the monofocal control patients. While there was a tendency for reduced contrast sensitivity and low contrast acuity in AcrySof® ReSTOR® IOL patients in low lighting (mesopic) conditions when exposed to a glare source, no differences in low contrast acuity exceeded more than 2 Snellen lines.

Visual Disturbances: Tables 2 and 3 summarize findings for Visual disturbances after monocular implantation at Forms 4 and 5. Glare/flare, problems with night vision, and halos were reported significantly ($p<0.05$) more often by monocularly implanted ReSTOR subjects compared to subjects implanted with the monofocal control IOL.

Table 2:
Visual Disturbances Mean Impact Ratings, Form 3 - 1st Eye, Safety, All Implanted

Visual Disturbances	MA60D3			SA60D3			MA60BM		
	Mean	Std. D.	N	Mean	Std. D.	N	Mean	Std. D.	N
Glare/Flare	1.73	1.96	422	1.25	1.80	125	1.22	1.89	186
Problems with Night Vision	0.89	1.67	420	1.00	1.76	125	0.85	1.71	186
Problems with Color Perception	0.06	0.43	421	0.09	0.60	125	0.09	0.68	186
Halos	1.22	1.79	422	1.48	1.90	125	0.76	1.69	186
Distorted Near Vision	0.20	0.87	422	0.13	0.62	125	0.44	1.23	186
Distorted Far Vision	0.14	0.72	422	0.07	0.36	125	0.15	0.84	186
Blurred Near Vision	1.05	1.68	421	0.91	1.56	125	2.34	2.00	186
Blurred Far Vision	0.68	1.43	421	0.49	1.10	125	0.61	1.29	186
Double Vision with Both Eyes	0.25	0.97	421	0.16	0.78	125	0.18	0.73	186

No assessments reported for Subject 1434.601, 1434.602, 1434.604.
None=0, Mild=1-2, Moderate=3-5, Severe=6-7

Table 3:
Visual Disturbances Mean Impact Ratings, Form 4 - 1st Eye, Safety, All Implanted

Visual Disturbances	MA60D3			SA60D3			MA60BM		
	Mean	Std. D.	N	Mean	Std. D.	N	Mean	Std. D.	N
Glare/Flare	1.30	1.88	282	1.22	1.87	110	0.73	1.48	175
Problems with Night Vision	0.83	1.74	282	0.93	1.80	110	0.41	1.27	175
Problems with Color Perception	0.01	0.19	282	0.03	0.29	110	0.07	0.62	175
Halos	1.60	1.94	282	1.93	2.07	110	0.45	1.28	175
Distorted Near Vision	0.06	0.51	282	0.02	0.13	110	0.05	0.39	175
Distorted Far Vision	0.03	0.37	282	0.04	0.30	110	0.05	0.39	175
Blurred Near Vision	0.67	1.40	282	0.45	1.28	110	1.60	2.01	175
Blurred Far Vision	0.45	1.18	282	0.34	1.19	110	0.31	1.04	175
Double Vision with Both Eyes	0.09	0.58	282	0.05	0.39	110	0.07	0.47	175

Data are from clinical study C-01-63 (US Study) only because clinical study C-01-21 (EU study) did not collect visual disturbance data at Form 4.
No assessments reported for Subject 1434.615, 1434.617, 1434.658.
None=0, Mild=1-2, Moderate=3-5, Severe=6-7

Following second eye implantation, AcrySof® ReSTOR® IOL patients reported a rate of severe observation no greater than their Monofocal Control counterparts in every category of visual disturbance evaluated (Table 4).

Table 4:
Visual Disturbances, 6 Months Postoperative
(Following second eye implantation)

Visual Disturbance	ReSTOR Model MA60D3		ReSTOR Model SA60D3		Monofocal Control	
	% Moderate	% Severe	% Moderate	% Severe	% Moderate	% Severe
Glare/Flare	20.1	4.9	23.2	4.3	7.1	1.9
Problems with Night Vision	8.5	4.1	10.1	2.9	3.8	1.9
Halos	18.0	4.4	23.2	7.2	1.9	1.3
Distorted Near Vision	0.8	0.8	0	0	0.6	0
Distorted Far Vision	1.0	0.3	0	0	0.6	0
Blurred Near Vision	5.9	0.8	7.2	0	12.8	3.8
Blurred Far Vision	5.9	1.0	5.8	0	3.2	0.6
Double Vision in both eyes	1.5	0.8	1.4	0	1.3	0
Problems with Color Perception	0.5	0	0	0	0	0

Of the 440 subjects implanted with AcrySof® ReSTOR Model MA60D3 and 126 subjects implanted with Model SA60D3, one subject implanted with AcrySof® ReSTOR Model MA60D3 required lens explantation due to visual disturbances.

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

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, retinal detachment, vitreous loss, iris prolapse, vitreous wick syndrome, uveitis and pupillary membrane.

VII. SUMMARY OF NONCLINICAL STUDIES

Biocompatibility Testing: AcrySOF® ReSTOR® Apodized Diffractive Optic Intraocular Lenses (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 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.

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

Test:	Results:
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 evidence if irritation or inflammation
Intracutaneous Toxicity	No intracutaneous reactivity
Intraocular Irritation (extracts)	No evidence of irritation
Sensitization – Guinea Pig Maximization	Non-sensitizing
Acute Systemic Toxicity	No systemic toxicity
Implantation – Ocular Implantation (1 Year)	No evidence of irritation

Chemical Characterization: The 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.

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 performance of the AcrySOF® ReSTOR® IOLs 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.*

Test:	Results:
Haptic Compression Force	Passed
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

Test:	Results:
Modulation Transfer Function	Passed
Optical Evaluation after Multiple Folds	Passed
Test Photostability	Passed
Nd: YAG Laser Exposure Test	Passed
Refractive Index	Passed
Optical Equivalency Testing (MA60D3 versus SA60D3)	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® ReSTOR® IOLs were successfully adopted into this validated cycle in accordance with Standard Operating Procedure - *Adoption of a Medical Device into a Validated Sterilization Process*. Expiration dating for this device has been established and approved at 5 years.

Test:	Results:
Device construction, complexity, and configuration	Equivalent
Device Packaging	Equivalent
Steriliant breath ability restrictions	Equivalent
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

VIII. SUMMARY OF CLINICAL STUDIES

Objective and Study Design: Multicenter clinical studies were conducted in the United States and Europe to establish the safety and effectiveness of the AcrySof® ReSTOR® Apodized

Diffractive Optic IOL (Models MA60D3 and SA60D3). Sixteen (16) investigators located in the U.S. bilaterally implanted subjects with either the AcrySOF® ReSTOR® IOL Model MA60D3, AcrySOF® ReSTOR® IOL Model SA60D3, or AcrySOF® monofocal IOL Model MA60BM. Eight (8) investigators located in Europe bilaterally implanted subjects with AcrySOF® ReSTOR® IOL Model MA60D3.

A total of 566 first-eye implanted AcrySof® ReSTOR® IOL (440 MA60D3 and 126 SA60D3) and 194 AcrySof® ReSTOR® MA60BM Monofocal Control patients comprise the All Implanted cohort. A Best Case cohort (no clinically significant preoperative ocular pathology or postoperative macular degeneration) consists of 391 MA60D3 and 109 SA60D3 AcrySof® ReSTOR® IOL patients and 172 Monofocal Control patients.

Information regarding physical appearance and health of the eye and visual acuity was collected during the preoperative visit and each postoperative visit. Information regarding pupil size, subjective questionnaire and quality of life questionnaires were administered at several, but not all, examination visits. In addition, subjects at specific sites in the U.S. were selected to complete additional testing for clinical substudies of Contrast Sensitivity, Contrast Acuity, Defocus, and Night Driving Simulation.

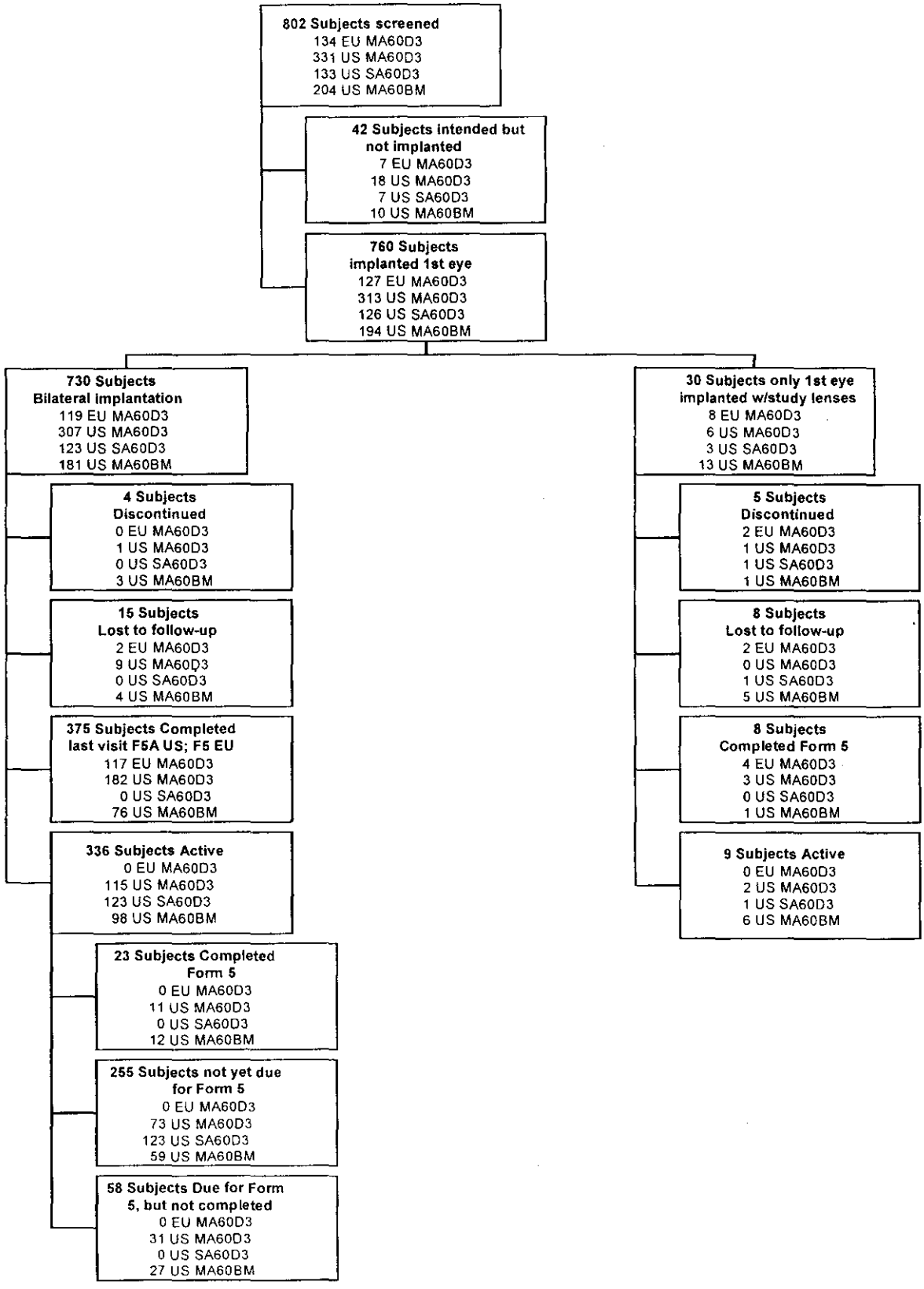
In addition to the clinical studies supporting the safety and effectiveness of AcrySOF® ReSTOR® IOL Models MA60D3 and SA60D3 as described above, a parallel group, non-randomized, multi-center study was conducted in the U.S. to evaluate the performance of AcrySOF® ReSTOR® lens Model MA60D3 for intermediate vision compared to the monofocal control, AcrySOF ReSTOR® IOL Model MA60BM.

Demographics: The study population was 496/760 (65.3%) female and 264/760 (34.7%) male. Of the 760 patients, 714 (93.9%) were Caucasian, 20 (2.6%) were Black, 7 (0.9%) were Asian, and 19 (2.5%) were designated as "Other" race. The mean age was 68.8 years (range of 22 to 88 years) at the time of surgery.

Data analysis by gender showed no significant differences in results.

Subject Accountability: The flowchart given below provides the number of subjects for each lens model and each clinical study (including 12 subjects implanted in Phase 1) followed from enrollment through status at the final study visit at the time of this report. Form 5A is the final study visit for the US subjects that were implanted bilaterally, and Form 5 is the final study visit for all European subjects and US subjects with implantation in the first eye only. The flowchart does not reflect subject status for any follow-up visits other than Form 5/5A.

Subject Accountability Flowchart for Form 5 / 5A



Data Analysis and Results: The safety and effectiveness data contained in the report represents six months monocular postoperative, one year monocular postoperative, and six months binocular postoperative visits. Results for the one year postoperative visit include data on the multi-piece AcrySof® ReSTOR® IOL only (MA60D3).

Visual Acuity:

Distance visual acuity was tested without visual correction and with best correction using a logMAR chart positioned 4 meters away from the subject under photopic lighting conditions. For uncorrected distance visual acuity (UCDVA), +0.25 D was applied to correct for optical infinity. For best corrected distance visual acuity (BCDVA), visual correction via manifest refraction was applied. Best corrected distance visual acuity results for the AcrySOF® ReSTOR® IOL compared favorably to the FDA grid of historical data Table 5).

Table 5
Best Corrected Distance Visual Acuity, Percentage 20/40 or Better
All Implanted and Best Case

	FDA Grid	ReSTOR		Monofocal Control	
	%	N	%	N	%
6 months postoperative (monocular)					
All Implanted	92.5	407	99.3	176	99.4
Best Case	96.7	359	99.7	155	100.0
1 year postoperative (monocular)					
All Implanted	92.5	319	99.1	89	100.0
Best Case	96.7	282	99.6	80	100.0
6 months postoperative (binocular)					
All Implanted	92.5	387	100.0	157	100.0
Best Case	96.7	334	100.0	132	100.0

Distance visual acuities for patients implanted with the AcrySOF® ReSTOR® IOL were also compared to the distance visual acuities for patients implanted with the monofocal control IOL Tables 6 and 7 depict outcomes for Distance Visual acuity at 6 and 12 months respectively after monocular implantation. When implanted monocularly, a statistically significant decrease (≤2 letters) in mean uncorrected and best corrected distance visual acuity was observed in subjects with AcrySof® ReSTOR® IOL as compared to the monofocal controls. Table 8 summarizes Distance Visual Acuity outcomes for subjects implanted bilaterally. Binocularly implanted AcrySof® ReSTOR® subjects achieved uncorrected and best corrected distance visual acuities similar to monofocal control subjects.

Table 6:
Cumulative Monocular Photopic Distance Vision by Lens Model, All Implanted, 6 Months Postoperative

		Sample size	20/20 or better	20/25 or better	20/32 or better	20/40 or better	Worse than 20/40
		N	%	%	%	%	%
Uncorrected	MA60D3	407	33.2	59.2*	77.1*	90.2	9.8
	SA60D3	110	29.1	53.6*	80.0*	92.7	7.3
	Monofocal	176	42.0	71.6	85.8	94.9	5.1
Best Corrected	MA60D3	407	73.5*	92.6	97.1	99.3	0.7
	SA60D3	110	77.3*	92.7	98.2	100.0	0.0
	Monofocal	176	84.7	96.0	98.3	99.4	0.6

*Statistically significant difference versus monofocal control

Table 7:
Cumulative Monocular Photopic Distance Vision by Lens Model, All Implanted, 1 Year Postoperative

		Sample size	20/20 or better	20/25 or better	20/32 or better	20/40 or better	Worse than 20/40
		N	%	%	%	%	%
Uncorrected	MA60D3	319	30.1	58.9*	76.8*	90.0	10.0
	Monofocal	89	42.7	78.7	89.9	95.5	4.5
Best corrected	MA60D3	319	74.6*	93.4	97.8	99.1	0.9
	Monofocal	89	87.6	94.4	98.9	100.0	0.0

*Statistically significant difference versus monofocal control

Table 8:
Cumulative Binocular Photopic Distance Visual Acuity by Lens Model, All Implanted, 6 Months Postoperative

		Sample size	20/20 or better	20/25 or better	20/32 or better	20/40 or better	Worse than 20/40
		N	%	%	%	%	%
Uncorrected	MA60D3	388	64.2	88.1	95.1	99.2	0.8
	SA60D3	69	58.0	88.4	95.7	100.0	0
	Monofocal	157	70.7	91.7	94.9	97.5	2.5
Best Corrected	MA60D3	387	89.4	97.9	100.0	100.0	0.0
	SA60D3	69	88.4	100.0	100.0	100.0	0.0
	Monofocal	157	93.0	97.5	98.7	100.0	0.0

Near visual acuity was measured under three different conditions: uncorrected, distance corrected, and best corrected. Uncorrected near visual acuity (UCNVA) and distance corrected near visual acuity (DCNVA) measurements were obtained using a hand-held ETDRS chart at a standard distance of 33 cm and at a distance the subject identified as providing the best near vision (best distance). Best corrected near visual acuity (BCNVA) measurements were obtained using a hand-held ETDRS chart at a standard distance of 33 cm only. Primary near vision measurements were made under photopic lighting conditions. In addition, DCNVA and BCNVA were measured under mesopic lighting conditions for subjects implanted in the United States only. Tables 9 and 10 depict outcomes for Photopic Near Visual acuity at 6 and 12 months respectively after monocular implantation. Table 11 summarizes Photopic Near Visual Acuity

outcomes for subjects implanted bilaterally. The improvement in distance corrected near vision was greater under photopic than mesopic conditions. Mean spherical add power needed to achieve best corrected near visual acuity was higher under mesopic conditions (mean value of 2.5 D) than photopic conditions (range of mean values: 0.09 to 0.16 D). The average distance of best focus for near vision was approximately 2 cm closer than the predicted distance of 33 cm.

Table 9:
Cumulative Monocular Photopic Near Vision by Lens Model,
All Implanted, 6 Months Postoperative

		Sample size	20/20 (J0) or better	20/25 (J1) or better	20/32 (J2) or better	20/40 (J3) or better	Worse than 20/40 (J3)
		N	%	%	%	%	%
Uncorrected (Best Distance)	MA60D3	407	27.3	51.8	74.9	86.2	13.8
	SA60D3	110	28.2	53.6	79.1	90.0	10.0
	Monofocal	176	1.1	5.7	12.5	26.1	73.9
Uncorrected (Standard Distance)	MA60D3	407	19.2	42.5	67.6	84.5	15.5
	SA60D3	110	19.1	41.8	67.3	85.5	14.5
	Monofocal	176	0	0.6	6.8	11.9	88.1
Distance Corrected (Best Distance)	MA60D3	407	30.2	58.2	83.0	92.1	7.9
	SA60D3	110	30.9	63.6	86.4	94.5	5.5
	Monofocal	176	0.6	2.3	9.1	21.6	78.4
Distance Corrected (Standard Distance)	MA60D3	407	26.8	59.0	81.1	92.9	7.1
	SA60D3	110	30.0	64.5	80.9	96.4	3.6
	Monofocal	176	0.6	1.1	3.4	11.4	88.6
Best Corrected (Standard Distance)	MA60D3	406	35.5	70.7	88.4	95.6	4.4
	SA60D3	110	36.4	77.3	90.0	97.3	2.7
	Monofocal	176	34.7	67.0	85.2	94.9	5.1

Table10:
Cumulative Monocular Photopic Near Vision by Lens Model,
All Implanted, 1 Year Postoperative

		Sample size	20/20 (J0) or better	20/25 (J1) or better	20/32 (J2) or better	20/40 (J3) or better	Worse than 20/40 (J3)
		N	%	%	%	%	%
Uncorrected (Best Distance)	MA60D3	319	21.0	53.6	74.9	85.6	14.4
	Monofocal	89	3.4	4.5	11.2	19.1	80.9
Uncorrected (Standard Distance)	MA60D3	319	17.9	43.6	69.6	79.6	20.4
	Monofocal	89	0	0	2.2	12.4	87.6
Distance Corrected (Best Distance)	MA60D3	318	30.5	62.9	82.1	90.9	9.1
	Monofocal	89	0.0	1.1	3.4	14.6	85.4
Distance Corrected (Standard Distance)	MA60D3	319	29.5	60.5	80.6	90.3	9.7
	Monofocal	89	0	1.1	2.2	9.0	91.0
Best Corrected (Standard Distance)	MA60D3	319	36.4	70.2	89.3	94.7	5.3
	Monofocal	89	50.6	79.8	94.4	95.5	4.5

Table 11:
Cumulative Binocular Photopic Near Visual Acuity by Lens Model, All Implanted, 6 Months Postoperative

		Sample size	20/20 (J0) or better	20/25 (J1) or better	20/32 (J2) or better	20/40 (J3) or better	Worse than 20/40 (J3)
		N	%	%	%	%	%
Uncorrected (Best Distance)	MA60D3	388	38.9	74.5	90.5	96.4	3.6
	SA60D3	69	46.4	69.6	87.0	98.6	1.4
	Monofocal	157	3.2	14.0	23.6	40.8	59.2
Uncorrected (Standard Distance)	MA60D3	388	36.9	69.1	87.9	95.9	4.1
	SA60D3	69	42.0	69.6	87.0	98.6	1.4
	Monofocal	157	0.6	2.5	8.9	26.1	73.9
Distance Corrected (Best Distance)	MA60D3	387	45.5	76.2	92.5	97.9	2.1
	SA60D3	69	43.5	76.8	88.4	97.1	2.9
	Monofocal	157	1.9	5.7	15.9	33.8	66.2
Distance Corrected (Standard Distance)	MA60D3	387	47.5	77.5	93.8	97.9	2.1
	SA60D3	69	44.9	76.8	89.9	98.6	1.4
	Monofocal	157	0.6	3.8	8.3	21.0	79.0
Best Corrected (Standard Distance)	MA60D3	387	54.3	85.0	96.4	98.4	1.6
	SA60D3	68	58.8	85.3	95.6	98.5	1.5
	Monofocal	157	52.9	79.6	94.3	96.8	3.2

Older subjects implanted with the AcrySof®ReSTOR® lens (e.g. ≥ 80 years old), demonstrated a trend for poorer uncorrected distance visual acuity than the monofocal control patients.

Results from a controlled clinical study revealed that maximum visual performance is achieved when implanted bilaterally. Figures 1 A and B are a summary of binocular distance and near photopic visual acuity results for patients who completed the Form 4A (120-180 days after second eye implantation).

Figure 1-A:
Combined 20/40 or Better Distance & Near Photopic Visual Acuity Binocular, Best Case 6 Months Postoperative

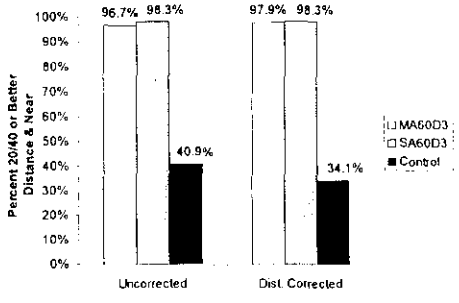
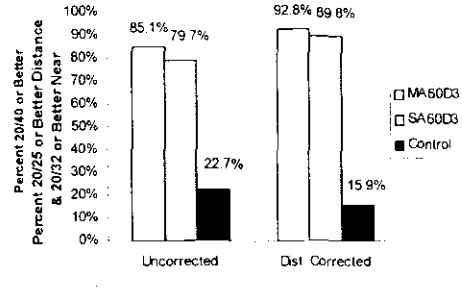


Figure 1-B:
Combined 20/25 or Better Distance & 20/32 or Better Near Photopic Visual Acuity Binocular, Best Case 6 Months Postoperative



Intermediate Visual Acuity was assessed in a non-randomized, multi-center substudy. In this substudy, visual acuity was tested without visual correction (uncorrected) and with the manifest refraction obtained for best corrected distance visual acuity

(distance correction) applied. Intermediate vision was tested with a hand-held 100% contrast ETDRS chart set at 50 cm, at 60 cm, and at 70 cm on the nearpoint rod, respectively. All testing parameters were performed binocularly under photopic lighting conditions.

At a distance of 70 cm, the percentage of eyes achieving 20/20 or better uncorrected vision and 20/25 or better distance corrected vision was significantly worse for the AcrySof® ReSTOR® IOL as compared to the monofocal control. No statistical differences were observed between the AcrySof® ReSTOR® IOL and the monofocal control lens for uncorrected and distance corrected vision 20/32 or better when tested at 50, 60 or 70 cm. Uncorrected intermediate visual acuities at 50 cm of 20/40 or better, however, were achieved by 82.4% of AcrySof® ReSTOR® IOL patients vs. 59.3% of monofocal control patients (Table 12).

Table 12:
Intermediate Photopic Visual Acuity,
Binocular, All Implanted

			Percent 20/40 or better		
		Total Sample Size	50 cm	60 cm	70 cm
Uncorrected	ReSTOR	34	82.4*	85.3	67.6
	Control	27	59.3	66.7	63.0
Distance Corrected	ReSTOR	34	64.7	70.6	52.9
	Control	27	59.3	66.7	77.8

*=Statistically different from control at 0.05 level

Contrast Sensitivity

A Vector Vision (CSV1000) contrast sensitivity chart that employs a full range of sine wave gratings at 9 contrast levels and 4 spatial frequencies (3, 6, 12, and 18 cpd) was used to assess contrast sensitivity under photopic (85 cd/m^2) and mesopic (2-5 cd/m^2) conditions, with and without a glare source.

Statistical and descriptive comparisons of contrast sensitivity of the AcrySOF® ReSTOR® IOL versus the Monofocal Control IOL indicate that, while there are measurable differences between the two groups at higher spatial frequencies when tested under the same photopic and mesopic conditions with and without glare, none of these differences exceeded 0.3 log units. At certain spatial frequencies, the AcrySOF® ReSTOR® IOL Model SA60D3 performed statistically significantly better than the AcrySOF® ReSTOR® IOL Model MA60D3 by at least 0.128 log units under monocular mesopic with and without glare conditions and by 0.143 log units under binocular mesopic with glare conditions. Additionally, for monocular contrast sensitivity testing, there was no difference in the percentage of AcrySof® ReSTOR and monofocal control patients who were not able to see any of the gratings (Table 13).

For binocular contrast sensitivity testing at least 85% of patients in both the AcrySof® ReSTOR® and monofocal control groups were able to see at least one grating, with the exception of mesopic with glare testing at 12 and 18 cycles per degree. At these spatial frequencies, the

percentage of AcrySof® ReSTOR® patients able to see at least one grating ranged from 85.9% - 75.0% as compared to 95.8% - 90.6% of Monofocal Control patients (Table 14).

Table 13:
Mean Log Decrease in Contrast Sensitivity
ReSTOR Compared to Monofocal Control Under Photopic, Mesopic and Glare Conditions, Monocular, All Implanted, 6 Months Postoperative

		Spatial Frequency (c/d)			
Light Source	Model	A(3)	B(6)	C(12)	D(18)
Photopic w/o Glare	MA60D3	-0.02	-0.04	-0.09	-0.05
	SA60D3	0.01	-0.03	-0.12	-0.09
Photopic w/ Glare	MA60D3	-0.06	-0.15	-0.15	-0.15
	SA60D3	-0.05	-0.14	-0.18	-0.16
Mesopic w/o Glare	MA60D3	-0.00	-0.12	-0.13	-0.09
	SA60D3	-0.00	-0.02	0.00	-0.04
Mesopic w/ Glare	MA60D3	-0.08	-0.11	-0.12	-0.12
	SA60D3	-0.01	-0.04	-0.02	-0.06

Table 14:
Mean Log Decrease in Contrast Sensitivity
ReSTOR Compared to Monofocal Control Under Photopic, Mesopic and Glare Conditions, Binocular, All Implanted, 6 Months Postoperative

		Spatial Frequency (c/d)			
Light Source	Model	A(3)	B(6)	C(12)	D(18)
Photopic w/o Glare	MA60D3	-0.03	-0.11	-0.17	-0.12
	SA60D3	-0.06	-0.15	-0.21	-0.16
Photopic w/ Glare	MA60D3	-0.07	-0.23	-0.22	-0.17
	SA60D3	-0.10	-0.24	-0.23	-0.24
Mesopic w/o Glare	MA60D3	-0.06	-0.12	-0.26	-0.18
	SA60D3	-0.07	-0.17	-0.23	-0.19
Mesopic w/ Glare	MA60D3	-0.15	-0.24	-0.25	-0.19
	SA60D3	-0.07	-0.24	-0.23	-0.21

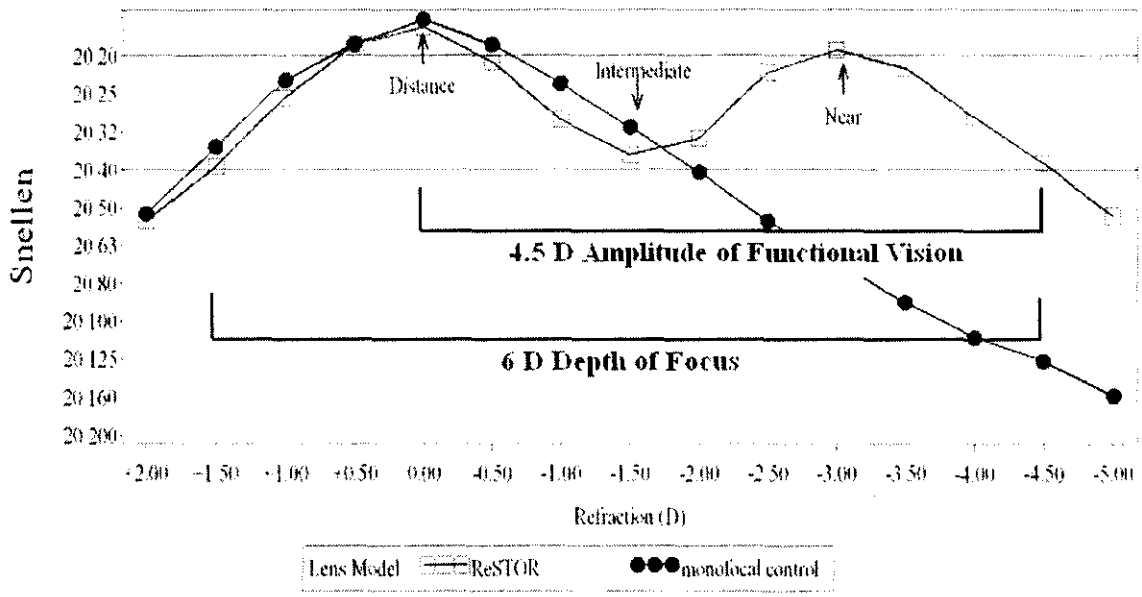
Contrast Acuity: Distance and near visual acuity (in logMAR) testing under photopic and mesopic conditions with and without glare was performed on Best Case AcrySof® ReSTOR® IOL and monofocal control patients using 100%, 25% and 9% low contrast charts.

Low contrast distance acuity of the AcrySof® ReSTOR® IOL was comparable to the monofocal control at all light sources and gray scales, with bilateral patients maintaining 20/40 or better for all gray scales for photopic conditions with and without glare as well as the 100% and 25% gray scales for mesopic conditions with and without glare.

Patients implanted unilaterally and bilaterally with the AcrySof® ReSTOR® IOL also maintained near vision of 20/40 or better under 100% and 25% gray scales for photopic conditions with and without glare.

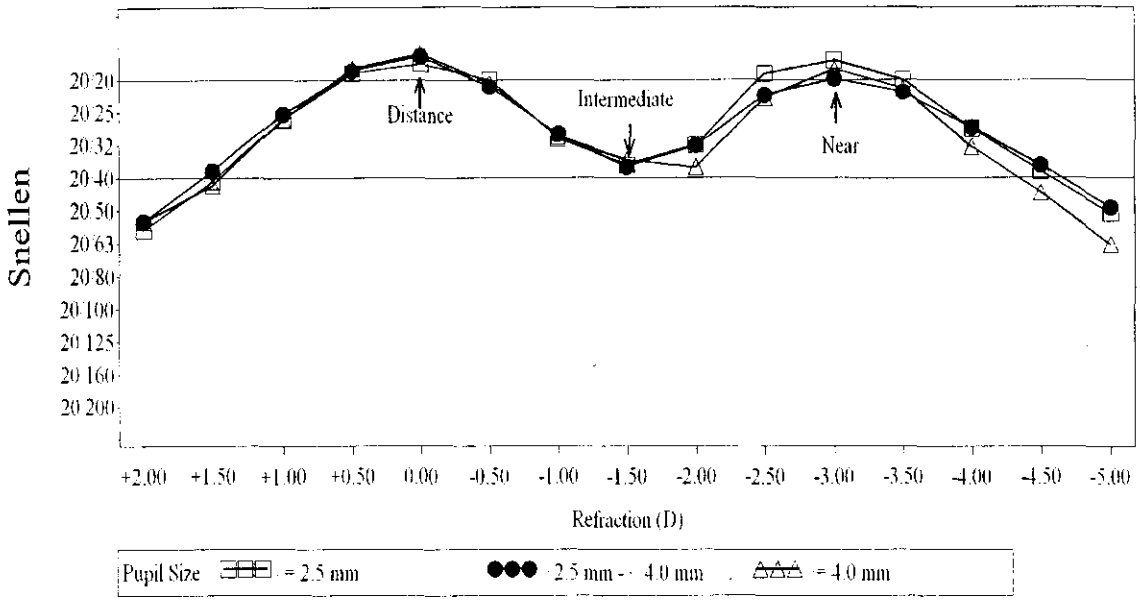
Defocus: A binocular refraction defocus curve from the United States Intermediate Vision Study (34 AcrySOF® ReSTOR® MA60D3 All Implanted patients) displays two peaks, with one at the zero baseline corresponding to the distance focal point of the lens and one near the –3.0 D of correction, which corresponds to the near focal point of the lens. The distance peak of this curve demonstrates that AcrySof® ReSTOR® IOL patients achieved a mean distance visual acuity of 20/20 or better, with an additional increased depth of focus from -2.0 D to -4.5 D as compared to monofocal control patients (N = 27). This additional increased depth of focus translates to a mean intermediate visual acuity of 20/40 or better and is most pronounced at near, with up to a five-line visual acuity improvement for patients implanted with an AcrySof® ReSTOR® IOL versus the Monofocal Control (Figure 2).

Figure 2:
Mean Defocus Curves by Lens Model, Binocular, All Implanted



These data demonstrate that the AcrySof® ReSTOR® IOL provides a 4.5 diopter amplitude of functional (20/40 or better) vision (from optical infinity to approximately 22 cm). Binocular performance of the AcrySof® ReSTOR® IOL was approximately 0.5 lines better for near vision and 1.5 lines better for intermediate vision than the monocular performance of the AcrySof® ReSTOR® IOL. Additionally, the defocus curves were within 1 line among groups when stratified by pupil size (Figure 3).

Figure 3:
Mean Defocus Curves by Pupil Size
Binocular, All Implanted (N=34)



Driving Performance: Night driving performance was tested using the NDS (Night Driving Simulator) developed and validated by Vision Sciences Research, Corp. Bilaterally implanted patients (23 AcrySof®ReSTOR® IOL Model MA60D3 Patients and 25 monofocal controls) were tested to determine visibility distances for the detection and identification of road warning signs, message signs and road hazards under various conditions. The simulated driving scenes were a city street at night with streetlights and a rural highway with low beam headlights. Testing in both driving scenes was conducted under clear (normal), inclement weather (fog) and glare conditions

It is important to realize that there are no absolute detection and identification distances for all targets to determine safety and efficacy. Actual visibility distances, excluding individual differences, will depend upon the target size, contrast (sign age, clean or dirty sign), background clutter (oncoming vehicle headlights, street and store lights) and vehicle headlight condition (low or high beams, clean or dirty lens). The NDS was designed to provide similar visibility distances to that of similar targets reported in the literature. One could use other targets in the real world and obtain other visibility distances; however, those distances would be relevant only for the conditions noted above such as age and condition of the target and would change over time. Therefore, safety and efficacy analysis can only be based on relative differences between the lenses, not absolute values. Visibility distance values could be biased to allow a very large difference between lenses to satisfy stopping distance requirements by making the simulator targets visible at very large distances or, conversely, visibility distance values could be biased to allow a very small difference between lenses to satisfy stopping distance requirements by

making the simulator targets visible at very small distances. With this in mind, further analysis uses the actual target visibility distance examples first reported in the validation study literature for the NDS.

The ability of AcyrSof® ReSTOR® IOL patients to detect and identify road signs and hazards at night was similar to the monofocal controls under normal visibility driving conditions.

Sign Identification:

Rural Driving Conditions: The mean visibility distances, standard deviation and percentage difference of monofocal and AcrySof® ReSTOR® IOL subjects for sign identification under normal, fog and glare conditions in the rural scene are shown in Table 15.

Both fog and glare are seen to cause larger differences between the monofocal and AcrySof®ReSTOR® lens subject performance than the clear night condition. However, in all instances the mean differences were less than 15%.

Table 15:
Mean (± SD) Sign Identification Distances in Rural Scene

Identification Distance (feet)		Lens		Difference	% Loss over Control
		Control	ReSTOR		
Visibility Condition	Targets				
Normal	Text	249 ± 57	230 ± 41	19	7.5 %
	Warning	523 ± 68	476 ± 81	47	8.9 %
Fog	Text	248 ± 42	215 ± 50	33	13.4 %
	Warning	512 ± 89	453 ± 88	60	11.6 %
Glare	Text	228 ± 56	195 ± 52	33	14.1 %
	Warning	512 ± 89	448 ± 83	64	12.5 %

City Driving Conditions: The mean visibility distances, standard deviation and percentage difference of monofocal and AcrySof® ReSTOR® IOL subjects for sign identification under normal, fog and glare conditions in the city scene are shown in Table 16.

Under glare conditions, the ability of the AcrySof® ReSTOR® lens subjects to identify the text sign is reduced on average by 28%, however there was only a small difference under these conditions for the warning sign.

Table 16:
Sign Identification Distances in City Scene

Identification Distance (feet)		Lens		Difference	% Loss Over Control
		Control	ReSTOR		
Visibility Condition	Targets				
Normal	Text	160 ± 30	143 ± 31	17	10.8 %
	Warning	211 ± 26	201 ± 25	10	4.7 %
Fog	Text	159 ± 24	138 ± 34	21	13.2 %
	Warning	208 ± 23	184 ± 31	24	11.7 %
Glare	Text	142 ± 33	102 ± 46	40	28 %
	Warning	194 ± 26	170 ± 28	24	12.5 %

Detecting Hazards:

Rural Conditions: The mean visibility distances, standard deviation and percentage difference of monofocals and AcrySof® ReSTOR® IOLs for hazard detection under normal, fog and glare conditions in the rural scene are shown in Table 17. All differences were less than 20%.

Table 17:
Hazard Detection Distances in Rural Scene

Detection Distance (feet)	Lens		Difference	% Loss Over Control
	Control	ReSTOR		
Visibility Condition				
Normal	511 ± 80	474 ± 87	37	7.2 %
Fog	507 ± 92	465 ± 101	42	8.5 %
Glare	480 ± 98	386 ± 150	94	19.7 %

City Conditions: The mean hazard detection, standard deviation and percentage differences for control and AcyrSof® ReSTOR® IOL subject groups for hazard detection under normal, fog and glare conditions in the city scene are shown in Table 18. In all instances the mean differences were less than 15%.

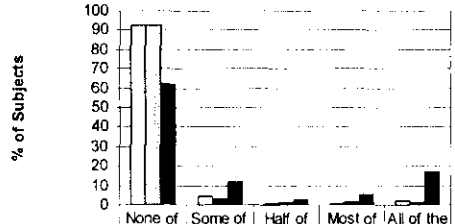
Table 18:
Hazard Detection Distances in City Scene

Detection Distance (feet)	Lens		Difference	% Loss Over Control
	Control	ReSTOR		
Visibility Condition				
Normal	200 ± 52	183 ± 38	17	8.5 %
Fog	229 ± 66	211 ± 65	18	7.9 %
Glare	190 ± 67	166 ± 48	24	12.6 %

Retinal Detail Evaluation: Starting at Form 3 and Form 3A (30 to 60 days postoperative) visit, investigators were asked to report whether the IOL was causing any loss in retinal detail that would alter the surgeon's ability to administer treatment, compared to their experience with monofocal lenses. No difficulties in retinal treatment were encountered by any investigator in the study. However, one investigator had 20 reports of loss of retinal detail (i.e., the fundus appeared more anterior).

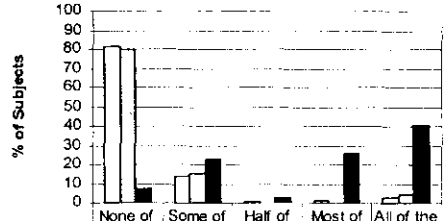
Quality Of Life Evaluation: Quality of Life (QoL) data was collected using the modified cataract TyPE specification instrument designed to measure QoL endpoints (Javitt et al, 1997; Javitt and Steinert, 2000). During the course of the study, QoL was assessed at three study visits: Form 0 Visit (preoperative), Form 3 Visit (30-60 days postoperative after the 1st eye surgery), and Form 4A Visit (120-180 days postoperative after the 2nd eye surgery). Figures 4- 6 depict outcomes for the frequency of spectacle wear after bilateral implantation with MA60D3, SA60D3 and the control monofocal IOL. ReSTOR® IOL spectacle independence rates were statistically better ($p<0.0001$) than the control rates.

Figure 4:
Frequency of Spectacle Wear
Distance Vision, Bilateral Comparison



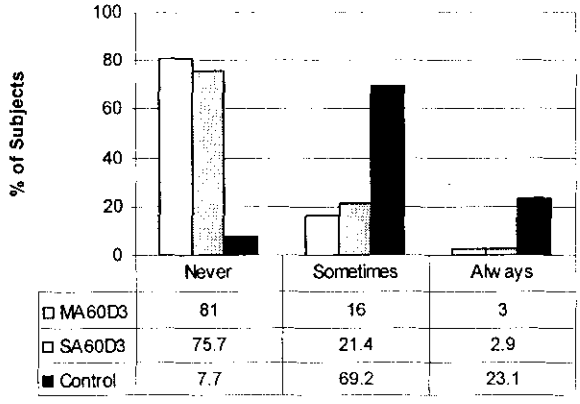
	None of the time	Some of the time	Half of the time	Most of the time	All of the time
MA60D3	92.5	4.5	0.4	0.8	1.9
SA60D3	92.9	2.9	1.4	1.4	1.4
Control	62.2	12.2	3.2	5.1	17.3

Figure 5:
Frequency of Spectacle Wear
Near Vision, Bilateral Comparison



	None of the time	Some of the time	Half of the time	Most of the time	All of the time
MA60D3	81.2	13.9	0.4	1.5	3
SA60D3	80	15.7	0	0	4.3
Control	7.7	23.2	2.6	25.8	40.6

Figure 6:
Overall Frequency of Spectacle Wear, Bilateral Comparison



Satisfaction with vision was measured on a continuous scale of 0-4 where 0 equated to "not at all satisfied" and 4 equated to "completely satisfied." There were no statistical differences between treatment groups in "overall satisfaction with vision (without glasses)" at the baseline measure. The AcrySof® ReSTOR® treatment groups reported significantly (p=0.0029) better satisfaction with vision without glasses as compared to the monofocal control group (Table 19).

Table 19:
Patient Satisfaction with Vision (without glasses)

		MA60D3	SA60D3	Control
Overall	Baseline	0.6 (N=311)	0.5 (N=126)	0.6 (N=193)
	Unilateral	2.6* (N=309)	2.5 (N=124)	2.4 (N=184)
	Bilateral	3.5** (N=268)	3.4** (N=69)	3.0 (N=155)
Day Vision	Baseline	0.9 (N=311)	0.7 (N=126)	0.8 (N=194)
	Unilateral	2.7* (N=309)	2.6 (N=123)	2.5 (N=185)
	Bilateral	3.5** (N=269)	3.4** (N=68)	3.0 (N=156)
Night Vision	Baseline	0.6 (N=311)	0.5 (N=126)	0.6 (N=193)
	Unilateral	2.4 (N=309)	2.5 (N=124)	2.4 (N=185)
	Bilateral	3.3** (N=269)	3.2* (N=69)	2.9 (N=156)

Satisfaction Scale (0-4): 0=not at all satisfied, 4=completely satisfied.
* = Significantly different from control at 0.05 level.
** = Significantly different from control at 0.01 level

Self-rating of vision was measured on a continuous scale of 1-10, where 1 equated to the "worst possible vision" and 10 equated to the "best possible vision." There were no significant differences between treatment groups for self-rating of vision (without

glasses) at the baseline comparison. There were no significant differences between treatment groups for self-rating of vision (without glasses) at the unilateral measure. At the bilateral measure, AcrySof® ReSTOR® subjects rated their vision (without glasses) significantly better ($p \leq 0.0003$) than the monofocal subjects (Table 20).

Table 20:
Self Rating of Vision (without glasses)

	MA60D3	SA60D3	Control
Baseline	4.2	4.1	4.1
Unilateral	7.1	7.1	6.9
Bilateral	8.7**	8.9**	7.9

Rating Scale (0-10): 0=worst possible vision, 10=best possible vision
* = Significantly different from control at 0.05 level.
** = Significantly different from control at 0.01 level

IX. CONCLUSIONS DRAWN FROM THE CLINICAL STUDY

The data in this application provide a reasonable level of safety and effectiveness of the AcrySof® ReSTOR® IOL for its intended use.

X. 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.

XI. CENTER FOR DEVICES AND RADIOLOGICAL HEALTH 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 March 21, 2005.

XII. APPROVAL SPECIFICATIONS

Directions for use: See product labeling
Hazards to health from the use of the device: See Indications, Contraindications, Warnings, Precautions and Adverse Events in Labeling.
Postapproval Requirements and Restrictions: See approval order.