SUMMARY OF SAFETY AND EFFECTIVENESS (SSED)

I. General Information

Device Generic Name:	Intraocular Lens (IOL)
Device Trade Name:	AcrySof® IQ ReSTOR® +2.5 D Multifocal Intraocular Lens (MIOL), Model SV25T0
Device Procode:	MFK
Applicant's Name and Address:	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, TX 76134
Date of Panel Recommendation:	None
Premarket Approval (PMA) Application Number	P040020/S050
Date of FDA Notice of Approval:	April 13, 2015

AcrySof® IQ ReSTOR® +2.5 D multifocal IOL (MIOL) Model SV25T0 is based on the parent AcrySof® IQ ReSTOR® +4.0D MIOL Model SA60D3 approved under PMA P040020 on 3/21/2005 with the following Indication for Use: 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. The SSED to support the indication is available on the CDRH website and is incorporated by reference here.

The material used in the AcrySof® IQ ReSTOR® +2.5 D MIOL Model SV25T0 is based on the FDA-approved AcrySof® Natural Single Piece IOL Model SB30AL (PMA P930014/S009 approved on 6/24/2003). The device is indicated for the replacement of the human lens to achieve visual correction of aphakia in adults when extracapsular cataract extraction or phacoemulsification is performed. These lenses are intended for placement

in the capsular bag. This material (AL-37884) was also used in the FDA-approved and clinically studied ACRYSOF® ReSTOR® Aspheric +3 D (SN6AD1) (P040020/S012 approved on 12/22/2008), and+4 D (SN6AD3) (P040020/S003 approved on 1/30/2007) MIOLs.

II. Indication for Use

The AcrySof® IQ ReSTOR® +2.5 D Multifocal IOL is indicated for primary implantation in the capsular bag of the eye 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.

III. Contraindications

None

IV. Warnings and Precautions

The warnings and precautions can be found in the AcrySof® IQ ReSTOR® +2.5 D MIOL labeling.

V. Description of Device

The AcrySof® IQ ReSTOR® +2.5 D MIOL is an ultraviolet and blue light filtering foldable MIOLs. The optical portion consists of a proprietary high refractive index hydrophobic acrylic material with a blue light filtering chromophore which filters light in a manner that approximates the human crystalline lens in the 400-475 nm blue light wavelength range (Boettner and Wolter, 1962). 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. After surgical insertion into the eye, the lens gently unfolds to restore the optical performance. The biconvex optic contains an aspheric apodized diffractive structure with a central refractive zone on the anterior surface. The apodized diffractive structure divides incoming light to provide a range of vision from distance to near. The anterior surface of the AcrySof® IQ ReSTOR® +2.5 D MIOL Model SV25T0 is designed with negative spherical aberration to

compensate for the positive spherical aberration of the cornea. The effects(s) of this aspheric design feature have not been clinically assessed. A summary of the physical characteristics of these lenses are shown in **Table 1**.

Table 1: Physical Characteristics

Physical Characteristic	Description
Optic Type	Apodized Diffractive Aspheric Optic With a Central Refractive Zone
Optic Material	Ultraviolet and blue light filtering Acrylate/Methacrylate Copolymer
Index Of Refraction	1.55
Optic Powers	+6.0 through +30.0 diopters in 0.5 diopter increments and +31.0 through +34.0 diopters in 1.0 Diopter increments with +2.5 diopters of add power
Haptic Configuration	STABLEFORCE® Haptic
Haptic Material	Ultraviolet and blue light filtering Acrylate/Methacrylate Copolymer
Haptic Color	Yellow
Optic Diameter (mm)	6.0
Overall Length (mm)	13.0
Haptic Angle	0º

VI. Alternative Practices and Procedures

Patients who undergo cataract extraction presently have several non-surgical and surgical alternatives for restoring vision of the aphakic eye. Non-surgical options include special cataract glasses or contact lenses. Surgical options such as other multifocal, monofocal, toric, and accommodative IOLs are 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

AcrySof® IQ ReSTOR® +2.5 D MIOLs are currently commercially available in the European Union, Australia, Canada, China, Japan, and multiple other countries within Central and South America, the Middle East and the Far East. The lenses have not been withdrawn from any country for any reason including for any reason related to safety and effectiveness.

VIII. Potential Adverse Effects of the Device on Health

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 Section X below.

IX. Summary of Preclinical Studies

Biocompatibility Testing

The AcrySof® IQ ReSTOR® +2.5 D MIOL (optic and haptic components) are composed of the same AL-37884 IOL material (i.e., AcrySof® Natural IOL Material) and manufacturing contact materials previously qualified with other approved and commercially available Alcon IOL models composed of the AL-37884 IOL material. The differences between the AcrySof® IQ ReSTOR® +2.5 D MIOL and other approved and commercially available Alcon IOL models composed of the AL-37884 IOL material are optical designs and dimensional characteristics only, which do not increase patient risk to material biocompatibility. A comprehensive battery of toxicity studies were performed on the AL-37884 IOL material and demonstrated that the IOL material is non-cytotoxic, non-mutagenic, non-sensitizing and resulted in no untoward tissue pathology following a 30-day muscular implantation study in rabbits (refer to **Table 2**). The toxicology studies conducted meet the requirements of EN ISO 10993:, *Biological evaluation of medical devices – Part 3: Tests for genotoxicity, carcinogenicity, and reproductive toxicity, - Part 6: Test for local effects after implantation, and - Part 10: Tests for irritation and skin sensitization* and EN ISO 11979-5, *Ophthalmic implants – Intraocular lenses – Part 5: Biocompatibility* guidelines. Studies were conducted in accordance with Good Laboratory Practices.

Table 2: Biocompatibility Testing

Test:	**Results:**
Genotoxicity – Mouse Lymphoma Forward Mutation Assay	Non-mutagenic
Cytotoxicity – V79 Colony Inhibition Assay (Extract)	No cell growth inhibition or cytotoxicity
Cytotoxicity – V79 Colony Inhibition Assay (Direct)	No cell growth inhibition or cytotoxicity
Cytotoxicity – Nd:YAG Laser Exposure Test (Extract)	Non-cytotoxic
Muscle Implantation – 7, 30 days	No significant biological responses
Sensitization – Guinea Pig Maximization	Non-sensitizing

Optical / Mechanical Testing

Pre-clinical optical / mechanical tests were performed with the AcrySof® IQ ReSTOR® +2.5 D MIOL), Model SV25T0 and were measured in accordance with EN ISO 11979-2 *Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods* and EN ISO 11979-3 *Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods*. Test results are presented in **Table 3**.

Table 3: Optical / Mechanical Testing

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
Modulation Transfer Function	Passed
Optical Evaluation after Multiple Folds	Passed

No additional new preclinical testing was required for this supplement.

X. Summary of Primary Clinical Study

A. Study Design

A prospective, multicenter, subject-masked, observer-masked, randomized, parallel group, controlled study was conducted following subjects implanted with either the AcrySof® IQ ReSTOR® +2.5 D MIOL Model SV25T0 (referred to as Model SN6AD2 or the +2.5 D MIOL) or the control AcrySof® Monofocal IOL Model SN60WF (referred to as the Monofocal) for 6 months following the second eye implant. A total of 320 subjects were implanted in the study (155 receiving the +2.5 D Multifocal and 165 subjects receiving the Monofocal) at 15 sites.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the primary study was limited to subjects 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
   - Willing and able to complete all required postoperative visits
   - Calculated lens power within the available supply range for the study IOLs
   - Planned cataract removal by phacoemulsification
   - Potential postoperative visual acuity of 0.2 logMAR or better in both eyes
   - Subjects with preoperative astigmatism <1.0 D

     Note: Corneal incisions made to reduce astigmatism were not allowed during the course of the study

   - Clear intraocular media other than cataract in study eyes
   - Preoperative Best Corrected Distance Visual Acuity (BCDVA) worse than 0.2 logMAR
   - The subject were required to undergo second eye surgery within 7 - 30 days of the first eye surgery

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

- Significant irregular corneal aberration as demonstrated by corneal topography
- Any inflammation or edema (swelling) of the cornea
- Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that are predicted to cause future acuity losses to a level worse than 0.2 logMAR
- Subjects who were reasonably expected to require a secondary surgical intervention (SSI) at any time during the study (other than YAG capsulotomy)
- Previous refractive surgery
- Amblyopia
- Clinically severe corneal dystrophy (e.g., epithelial, stromal, or endothelial dystrophy), keratitis, keratoconjunctivitis, keratouveitis, keratopathy, or kerectasia
- 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 currently participating in another investigational drug or device study

In addition, subjects were not to be implanted with the device for the following reasons:

- Other planned ocular surgery procedures, including but not limited to, laser-assisted in situ keratomileusis (LASIK), astigmatic keratotomy and limbal relaxing incisions for the duration of the study
- Mechanical or surgical manipulation required to enlarge the pupil; pupil size must be at least 4.5 mm or larger just prior to implantation
- Excessive iris mobility
- 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, capsulorhexis tear, or decentered capsulorhexis during surgery, the surgeon decided whether the stability of the IOL would be compromised by the complication. If the IOL stability would be compromised, the study IOL was not implanted, the subject was discontinued from the study, and the surgeon made arrangements to implant an alternative non-study IOL.

2. Follow-up Schedule

The follow-up visit schedule is presented in **Table 4**.

Table 4: Clinical Study Visit Schedule

Visit	**Exam**	**Eyes Evaluated**	**Visit Window**
0/0A	Preoperative Exam	Both Eyes	---
00	Operative	1st Eye	---
1	Postop (1 day)	1st Eye	1-2 days post Visit 00
2	Postop (1 week)	1st Eye	7-14 days post Visit 00
3	Postop (1 month)	1st Eye (monocular)	30-60 days post Visit 00
00A	Operative	2nd Eye	7-30 days from Visit 00
1A	Postop (1 day)	2nd Eye	1-2 days post Visit 00A
2A	Postop (1 week)	2nd Eye	7-14 days post Visit 00A

Visit	Exam	Eyes Evaluated	Visit Window
3A	Postop (1 month)	2nd Eye (monocular and binocular defocus testing)	30-60 days post Visit 00A
4A	Postop (6 months)	Both Eyes (monocular and binocular)	120-180 days post Visit 00A

Table 5: Examination Table

Study Activity	Visit 0/0A (Preop)	Visit 00 (Op)	Visit 1 (d1-2)	Visit 2 (d7-14)	Visit 3 (d30-60)	Visit 00A (Op)[a]	Visit 1A (d1-2)	Visit 2A (d7-14)	Visit 3A (d30-60)	Visit 4A (d120-180)
Informed Consent	X									
Demographics	X									
Medical History	X									
Manifest Refraction	X		X	X	X		X	X	X	X
Inclusion/Exclusion	X	X[b]				X[b]				
Urine Pregnancy Test	X									
Device Deficiencies	X	X	X	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X	X	X	X
Light Measurements	X		X	X	X		X	X	X	X
Photopic Pupil Size at Near and Distance	X									X
Mesopic Pupil Size at Near and Distance	X									X
Distance Visual Acuity										
Uncorrected	X		X	X	X		X	X[c]	X[c]	X[c]
Best Corrected	X		X	X	X		X	X[c]	X[c]	X[c]
Visual Acuity @ 33 cm										
Uncorrected									X[c]	X[c]
Distance Corrected									X[c]	X[c]
Visual Acuity @ 53 cm										
Uncorrected									X[c]	X[c]
Distance Corrected									X[c]	X[c]
Mesopic Distance Corrected				X	X			X	X[c]	X[c]
Visual Acuity @ 60 cm										
Uncorrected									X[c]	X[c]
Distance Corrected									X[c]	X[c]

Study Activity	Visit 0/0A (Preop)	Visit 00 (Op)	Visit 1 (d1-2)	Visit 2 (d7-14)	Visit 3 (d30-60)	Visit 00A (Op)[a]	Visit 1A (d1-2)	Visit 2A (d7-14)	Visit 3A (d30-60)	Visit 4A (d120-180)
Near Visual Acuity Standard Distance (40cm)										
Uncorrected			X	X	X		X	X	X[c]	X[c]
Distance Corrected					X				X[c]	X[c]
Best Corrected					X				X[c]	X[c]
Mesopic Distance Corrected				X	X			X	X[c]	X[c]
Mesopic Uncorrected				X	X			X	X[c]	X[c]
Mesopic Best Corrected				X	X			X	X[c]	X[c]
Near Visual Acuity Best Distance										
Uncorrected					X				X[c]	X[c]
Distance Corrected			X	X	X		X	X	X[c]	X[c]
Mesopic Distance Corrected				X	X			X	X[c]	X[c]
Corneal Topography	X									
Target Residual Refractive Error	X									
Contrast Sensitivity Photopic (with and without glare at 3,6,12, &18 cpd)										X[c]
Contrast Sensitivity Mesopic (with and without glare at 1.5, 3, 6 &12 cpd)										X[c]
Binocular Defocus									X[d]	
Anterior Chamber Depth	X									
Axial Length	X									
Keratometry	X									X
Intraocular Pressure	X		X	X	X		X	X	X	X
APPLES	X[d]									X[d]
SILVER	X[d]									X[d]
VISTAS	X[d]									X[d]
Concomitant Medications	X	X	X	X	X	X	X	X	X	X

Study Activity	Visit 0/0A (Preop)	Visit 00 (Op)	Visit 1 (d1-2)	Visit 2 (d7-14)	Visit 3 (d30-60)	Visit 00A (Op)[a]	Visit 1A (d1-2)	Visit 2A (d7-14)	Visit 3A (d30-60)	Visit 4A (d120-180)
Operative Eye		X				X[a]				
Surgical Problems		X				X				
Other procedures at surgery		X				X				
Folding and Insertion Instrument		X				X				
Incision Site and Size		X				X				
Haptic Placement		X				X				
Lens Information		X				X				
Slit Lamp Examination	X		X	X	X		X	X	X	X
Dilated Fundus Examination	X				X				X	X
Retinal Detail					X				X	
Secondary Surgical Interventions			X	X	X		X	X	X	X
IOL Observations			X	X	X		X	X	X	X
IOL Position Change			X	X	X		X	X	X	X
Posterior Capsulotomy			X	X	X		X	X	X	X
Subjective Posterior Capsule Opacification			X	X	X		X	X	X	X

[a] Second Implantation can be done within 7-30 days of first implantation
[b] Review of inclusion/exclusion criteria prior to surgery
[c] Monocular and Binocular testing
[d] Binocular testing only

3. Clinical Endpoints

Effectiveness

The primary effectiveness endpoint was to demonstrate superiority of the primary eyes of subjects in the +2.5 D Multifocal group to those in the Monofocal group in terms of mean photopic, monocular, distance-corrected visual acuity at 53 cm at visit 4A (120-180 days). The primary eye was the first implanted eye of each subject (the one with the worse cataract).

The first secondary effectiveness endpoint was to demonstrate non-inferiority of the primary eyes of subjects in the +2.5 D Multifocal group to those in the Monofocal group in terms of mean photopic, monocular, best-corrected distance (4 m) visual acuity at visit 4A.

The second secondary effectiveness endpoint was to demonstrate superiority of the primary eyes of the +2.5 D Multifocal group to those in the Monofocal group in terms of mean photopic, monocular, distance-corrected near visual acuity at 40 cm at visit 4A.

The third secondary effectiveness endpoint was to demonstrate superiority of the +2.5 D Multifocal group to Monofocal group in terms of patient-reported overall spectacle independence rates at visit 4A.

The fourth secondary effectiveness endpoint was to demonstrate superiority of the +2.5 D Multifocal group to the Monofocal group in terms of patient-reported near spectacle independence rates at visit 4A (120-180 days).

Safety

The first key safety endpoint was to demonstrate that the adverse event rates for the +2.5D Multifocal group were not worse than Safety Performance Endpoint (SPE) rates as defined in IS EN ISO 11979-7:2006 at visit 4A. This was the last published ISO IOL standard as of the writing of the protocol.

The second key safety endpoint was to estimate contrast sensitivity for the +2.5 D Multifocal group and for the Monofocal group for all binocular, distance, contrast sensitivity tests at visit 4A.

Additional safety data is incorporated by reference to the parent lens, the ACRYSOF® ReSTOR® Apodized Diffractive Optic Posterior Chamber IOL, Models MA60D3 and SA60D3, including results from a driving sub-study, rates of adverse events and rates of visual disturbances.

B. Accountability of PMA-supplement Cohort

As summarized in **Table 6**, 409 subjects provided informed consent and were enrolled in the clinical study, of which 80 failed screening procedures prior to randomization. Three hundred and twenty nine (329) subjects were randomized, with 16 of these subjects discontinuing early from the study. Nine subjects discontinued after randomization but prior to first eye implantation (8 in the +2.5 D Multifocal group and 1 in the Monofocal group) and 7 discontinued after at least one eye had been implanted (2 in the +2.5 D Multifocal group and 5 in the Monofocal group). A total of 320 randomized subjects received IOL implantation in the first eye (155 received the +2.5 D Multifocal and 165 received the Monofocal) and 318 subjects received IOL implantation in the second eye (155 with the +2.5 D Multifocal and 163 with the Monofocal). Three hundred and thirteen (313) subjects completed the study (153 in the +2.5 D Multifocal group and 160 in the Monofocal group).

Table 6: Subject Disposition
(All Enrolled Population)

	Overall	**(%)**	**Multifocal**	**(%)**	**Monofocal**	**(%)**
Enrolled	409					
Screening Failures	80					
Randomized (N)	329	(100.0)	163	(100.0)	166	(100.0)
Early Termination (n)	16	(4.9)	10	(6.1)	6	(3.6)
Completed Study (n)	313	(95.1)	153	(93.9)	160	(96.4)

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D M Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
Percent (%) Early Termination=n/N
Percent (%) Completed Study=n/N

C. Study Population Demographics

The study population demographics for subjects implanted with the test or control device are reported in **Table 7.**

Table 7: Demographic Statistics by Treatment
(All Implanted Population)

	Overall (N=320) n (%)	Multifocal (N=155) n (%)	Monofocal (N=165) n (%)
Age(Years)			
20-29	1 (0.3)	1 (0.6)	0 (0.0)
30-39	2 (0.6)	2 (1.3)	0 (0.0)
40-49	5 (1.6)	2 (1.3)	3 (1.8)
50-59	30 (9.4)	18 (11.6)	12 (7.3)
60-69	115 (35.9)	53 (34.2)	62 (37.6)
70-79	136 (42.5)	65 (41.9)	71 (43.0)
≥80	31 (9.7)	14 (9.0)	17 (10.3)
Gender			
Male	127 (39.7)	59 (38.1)	68 (41.2)
Female	193 (60.3)	96 (61.9)	97 (58.8)
Ethnicity			
Hispanic or Latino	16 (5.0)	8 (5.2)	8 (4.8)
Not Hispanic or Latino	303 (94.7)	146 (94.2)	157 (95.2)
Race			
White	292 (91.3)	138 (89.0)	154 (93.3)
Black or African American	21 (6.6)	12 (7.7)	9 (5.5)
Asian	3 (0.9)	2 (1.3)	1 (0.6)
American Indian or Alaska Native	2 (0.6)	2 (1.3)	0 (0.0)
Multi-Race	1 (0.3)	1 (0.6)	0 (0.0)
Other	1 (0.3)	0 (0.0)	1 (0.6)

N=Number of subjects (All Implanted)
%=n/N
Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
One subject(C10016.3903.1212) did not report an ethnicity

D. Safety and Effectiveness Results

1. Safety Results

According to the protocol, all subjects with attempted IOL implantation in at least one eye (successful or aborted after contact with the eye) were to be considered evaluable for the safety analyses. Additionally, any adverse event that was experienced by a subject during screening procedures was to be listed in the safety analysis.

Adverse Events

The observed rates of serious adverse did not exceed the Safety and Performance Endpoints (SPE) rates shown in EN ISO 11979-7:2006 *Ophthalmic implants -- Intraocular lenses -- Part 7: Clinical investigations* (see **Table 8**). The serious adverse events shown in the table were reported as unrelated to the IOL.

No unanticipated serious adverse device effects were observed in any subjects implanted with the +2.5 D Multifocal.

Table 8: Cumulative and Persistent Adverse Events and SPE Rates for First and Second Implanted Eyes with Multifocal Lens (Safety Population)

	Multifocal (N=310)			SPE	Threshold	
	n	(%)	UCL %	%	%	P-value[a]
Cumulative Adverse Events						
Cystoid macular oedema	4	(1.3)	2.9	3.0	5.8	0.9566
Endophthalmitis	0	(0.0)	1.0	0.1	1.0	1.0000
Hypopyon	0	(0.0)	1.0	0.3	1.8	1.0000
Lens dislocated from posterior chamber	0	(0.0)	1.0	0.1	1.0	1.0000
Pupillary block	0	(0.0)	1.0	0.1	1.0	1.0000
Retinal detachment	0	(0.0)	1.0	0.3	1.8	1.0000
Secondary surgical intervention	0	(0.0)	1.0	0.8	2.6	1.0000
Persistent Adverse Events						
Corneal stroma oedema	0	(0.0)	1.0	0.3	1.8	1.0000
Cystoid macular oedema	2	(0.6)	2.0	0.5	2.2	0.4592
Iritis	2	(0.6)	2.0	0.3	1.8	0.2385
Raised IOP requiring treatment	0	(0.0)	1.0	0.4	1.8	1.0000

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
N = Number of eyes evaluable for safety, UCL = Exact (Clopper-Pearson) one-sided 95 % upper confidence limit
SPE = Safety and Performance Endpoints
%=n/N
Threshold rate: The minimum rate detectable as statistically significantly different from the SPE rate. Calculated based on N=155 in multifocal group
155 subjects were evaluable for safety for a total of 310 eyes
[a]One-sided exact binomial test (alpha=5%)
Cases of persistent Uveitis are included under the persistent Iritis category.

The frequency and incidence of all ocular adverse events not included in Table 8 (serious and non-serious) in subjects implanted with the AcrySof® IQ ReSTOR® +2.5 D MIOL Model SV25T0 are presented for first implanted eyes and all implanted eyes (see **Table 9**). The incidence rate is calculated by number of eyes for which adverse events were reported divided by the total number of subjects in the safety cohort MIOL arm. Adverse events belonging to the same category were grouped and listed under headings according to the involved eye structure and the type of condition involved in the adverse event (i.e., Retinal disorders, Corneal disorders, Lacrimal disorders, etc.).

Table 9: Incidence of All Non-SPE* Ocular Adverse Events in Multifocal Subjects by Event Group (Safety Population)

	First Eye (N=155)			All Eyes (N=310)		
	Eyes n	(%)	Events	Eyes n	(%)	Events
Symptoms Reported as Adverse Events	**11**	**(7.10)**	**15**	**21**	**(6.77)**	**27**
Glare	4	(2.58)	4	8	(2.58)	8
Halo vision	4	(2.58)	4	8	(2.58)	8
Eye pain	2	(1.29)	2	3	(0.97)	3
Vision blurred	2	(1.29)	2	3	(0.97)	3
Visual impairment^	2	(1.29)	2	3	(0.97)	3
Photophobia	1	(0.65)	1	1	(0.32)	1
Photopsia	0	(0.00)	0	1	(0.32)	1
Eyelid Disorders	**7**	**(4.52)**	**7**	**13**	**(4.19)**	**13**
Blepharitis	2	(1.29)	2	4	(1.29)	4
Blepharal papilloma	1	(0.65)	1	2	(0.65)	2
Dermatitis allergic	1	(0.65)	1	2	(0.65)	2
Eyelid oedema	1	(0.65)	1	1	(0.32)	1
Hordeolum	1	(0.65)	1	1	(0.32)	1
Meibomianitis	1	(0.65)	1	1	(0.32)	1
Trichiasis	0	(0.00)	0	2	(0.65)	2
Lacrimal Disorders	**6**	**(3.87)**	**7**	**12**	**(3.87)**	**14**
Dry eye	5	(3.23)	5	10	(3.23)	10
Keratoconjunctivitis sicca	1	(0.65)	1	2	(0.65)	2
Lacrimation increased	1	(0.65)	1	2	(0.65)	2
Ocular Hypertension/Glaucoma	**6**	**(3.87)**	**7**	**10**	**(3.23)**	**11**
Intraocular pressure increased	4	(2.58)	5	7	(2.26)	8
Ocular hypertension	2	(1.29)	2	3	(0.97)	3
Conjunctival Disorders	**6**	**(3.87)**	**6**	**10**	**(3.23)**	**10**

	First Eye (N=155)			All Eyes (N=310)		
	Eyes		Events	Eyes		Events
	n	(%)		n	(%)	
Conjunctivitis allergic	3	(1.94)	3	6	(1.94)	6
Conjunctivitis viral	2	(1.29)	2	3	(0.97)	3
Conjunctival haemorrhage	1	(0.65)	1	1	(0.32)	1
Retinal Disorders	**5**	**(3.23)**	**6**	**8**	**(2.58)**	**12**
Retinal haemorrhage	2	(1.29)	2	4	(1.29)	4
Retinal pigment epitheliopathy	2	(1.29)	2	2	(0.65)	2
Diabetic retinopathy	1	(0.65)	1	2	(0.65)	2
Retinal degeneration	1	(0.65)	1	2	(0.65)	2
Retinal artery embolism	0	(0.00)	0	1	(0.32)	1
Retinal exudates	0	(0.00)	0	1	(0.32)	1
Other Eye Disorders	**5**	**(3.23)**	**5**	**5**	**(1.61)**	**5**
Eye naevus	2	(1.29)	2	2	(0.65)	2
Amblyopia[+]	1	(0.65)	1	1	(0.32)	1
Episcleritis	1	(0.65)	1	1	(0.32)	1
Eye discharge	1	(0.65)	1	1	(0.32)	1
Uveitis	**4**	**(2.58)**	**4**	**9**	**(2.90)**	**9**
Iritis	3	(1.94)	3	7	(2.26)	7
Eye inflammation	1	(0.65)	1	2	(0.65)	2
Capsular Opacification	**3**	**(1.94)**	**3**	**4**	**(1.29)**	**4**
Posterior capsule opacification	2	(1.29)	2	3	(0.97)	3
Lenticular opacities	1	(0.65)	1	1	(0.32)	1
Vitreous Disorders	**3**	**(1.94)**	**3**	**8**	**(2.58)**	**8**
Vitreous detachment	3	(1.94)	3	6	(1.94)	6
Vitreous floaters	0	(0.00)	0	2	(0.65)	2
Corneal Disorders	**1**	**(0.65)**	**1**	**6**	**(1.94)**	**6**
Punctate keratitis	1	(0.65)	1	3	(0.97)	3
Corneal abrasion	0	(0.00)	0	2	(0.65)	2
Corneal disorder	0	(0.00)	0	1	(0.32)	1

Multifocal = ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
*SPE = Safety and Performance Endpoints as per ISO 11979-7 (2006)
%=n/N
^One subject experienced bilateral visual disturbances induced by medications. One subject reported an irregular image in vision.
[+]An "adverse event" of amblyopia was reported post-operatively for one subject. A retrospective chart review indicated that the subject had poorer visual acuity in the right eye. Amblyopia is not considered by FDA to be an adverse event.

Binocular Contrast Sensitivity

Test procedure: Contrast sensitivity testing was conducted using the CSV-1000 (VectorVision Inc., Greenville, OH) contrast sensitivity test under photopic and

mesopic conditions with and without a glare source. The CSV-1000 contrast sensitivity test uses sine-wave gratings at nine contrast levels. The photopic chart luminance was 85 cd/m^2 and the mesopic chart luminance was 3 cd/m^2. Testing was performed at 8 feet with best spectacle correction at the chart distance in place for each of four spatial frequencies; 3, 6, 12 and 18 cycles per degree (cpd) for photopic conditions and 1.5, 3, 6 and 12 cpd for mesopic conditions. For photopic conditions, the last correct response at each spatial frequency was recorded as the contrast sensitivity. For mesopic conditions, two consecutive sessions were run and the mean of the two individual measurements was recorded as the contrast sensitivity.

Results and analysis: Prior to statistical analysis, raw test scores were converted to the common logarithm of the reciprocal of the threshold contrast. If the subject could not see the grating at the highest available contrast, the measurement was assigned a score of (-1) and the measurement was excluded from statistical calculations. In order to provide a qualitative indication of the amount of resulting bias, the number and percentage of -1 scores was tabulated for each condition. The percentage of -1 scores gives a rough indication of the degree of bias in the remaining data (Note that nearly one-third of the multifocal eyes in Table 10 received a -1 score for the 12 cpd condition.). Also, statistics that excluded -1 scores were marked as less than (<) or greater than (>) the calculated value, as appropriate. Representative binocular contrast sensitivity estimates are shown in **Tables 10 and 11**.

The presence of unmeasurable sensitivities limits the interpretability of the results. However, it is clear that, at least for the higher spatial frequencies, log contrast sensitivity is more than 0.1 log unit lower for the multifocal test IOL than for the monofocal control. Although the study was not designed to assess clinical significance, the calculated mean differences are large enough to justify a warning in the labeling about the possibility of visual performance impairment under low-contrast or low-light conditions.

Table 10: Descriptive Statistics for Binocular Photopic Contrast Sensitivity at Visit 4A (Best Case Population)

		Without Glare		With Glare	
		Multifocal (N=133)	Monofocal (N=137)	Multifocal (N=133)	Monofocal (N=137)
Frequency		n (%)	n (%)	n (%)	n (%)
3 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (1)	1 (0.8%)	0 (0.0%)	2 (1.5%)	2 (1.5%)
	Number with Data for Analysis	131 (98.5%)	133 (97.1%)	130 (97.7%)	131 (95.6%)
	Mean	<1.676	1.743	<1.608	<1.692
	Median	<1.633	1.785	<1.633	<1.785
	SD	>0.259	0.203	>0.307	>0.274
	(Min, Max)	(<0.70, 2.08)	(1.18, 2.08)	(<0.70, 2.08)	(<0.70, 2.08)
	CI	(<1.639, 1.714)	(1.714, 1.773)	(<1.563, 1.653)	(<1.652, 1.732)
6 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	2 (1.5%)	0 (0.0%)	15 (11.3%)	8 (5.8%)
	Number with Data for Analysis	130 (97.7%)	133 (97.1%)	117 (88.0%)	125 (91.2%)
	Mean	<1.816	1.938	<1.684	<1.844
	Median	<1.845	1.996	<1.699	<1.845
	SD	>0.256	0.251	>0.316	>0.309
	(Min, Max)	(<0.90, 2.29)	(1.20, 2.29)	(<0.90, 2.29)	(<0.90, 2.29)
	CI	(<1.778, 1.853)	(1.902, 1.974)	(<1.636, 1.733)	(<1.798, 1.889)
12 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	3 (2.3%)	1 (0.7%)	15 (11.3%)	6 (4.4%)
	Number with Data for Analysis	129 (97.0%)	132 (96.4%)	117 (88.0%)	127 (92.7%)
	Mean	<1.460	<1.555	<1.334	<1.475
	Median	<1.544	<1.544	<1.398	<1.544
	SD	>0.312	>0.312	>0.321	>0.336
	(Min, Max)	(<0.60, 2.00)	(<0.60, 2.00)	(<0.60, 2.00)	(<0.60, 2.00)
	CI	(<1.414, 1.505)	(<1.510, 1.599)	(<1.285, 1.383)	(<1.426, 1.524)
18 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	2 (1.5%)	2 (1.5%)	13 (9.8%)	5 (3.6%)
	Number with Data for Analysis	130 (97.7%)	131 (95.6%)	119 (89.5%)	128 (93.4%)
	Mean	<0.970	<1.109	<0.914	<1.043
	Median	<0.978	<1.114	<0.978	<1.114
	SD	>0.348	>0.325	>0.333	>0.361
	(Min, Max)	(<0.18, 1.56)	(<0.18, 1.56)	(<0.18, 1.56)	(<0.18, 1.56)
	CI	(<0.919, 1.021)	(<1.062, 1.156)	(<0.863, 0.964)	(<0.990, 1.096)

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
%=n/N
SD = Standard Deviation
CI = Two-sided 90% Confidence Interval
CPD = Cycles Per Degree
The score was set to (-1) when a subject could not complete a sensitivity measurement.
For mean and variability estimations, scores of (-1) were excluded from the calculations. Hence the corresponding mean and median measures are overestimated and variability measures are underestimated.
Column header is number of subjects in the best case population
Number assessed is number in the best case population minus number not assessed.
Number with data for analysis is number assessed minus number scoring (-1).

Table 11: Descriptive Statistics for Binocular Mesopic Contrast Sensitivity at Visit 4A (Best Case Population)

Frequency		Without Glare Multifocal (N=133) n (%)	Without Glare Monofocal (N=137) n (%)	With Glare Multifocal (N=133) n (%)	With Glare Monofocal (N=137) n (%)
1.5 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	4 (3.0%)	2 (1.5%)	5 (3.8%)	4 (2.9%)
	Number with Data for Analysis	128 (96.2%)	131 (95.6%)	127 (95.5%)	129 (94.2%)
	Mean	<1.594	<1.622	<1.536	<1.596
	Median	<1.595	<1.595	<1.520	<1.670
	SD	>0.224	>0.204	>0.237	>0.238
	(Min, Max)	(<0.83, 1.97)	(<1.07, 1.97)	(<0.90, 1.97)	(<0.98, 1.97)
	CI	(<1.562, 1.627)	(<1.593, 1.652)	(<1.501, 1.570)	(<1.561, 1.631)
3 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	1 (0.8%)	1 (0.7%)	4 (3.0%)	3 (2.2%)
	Number with Data for Analysis	131 (98.5%)	132 (96.4%)	128 (96.2%)	130 (94.9%)
	Mean	<1.563	<1.618	<1.542	<1.600
	Median	<1.564	<1.633	<1.562	<1.599
	SD	>0.267	>0.226	>0.292	>0.296
	(Min, Max)	(<0.70, 2.08)	(<1.00, 2.08)	(<0.70, 2.08)	(<-0.35, 2.08)
	CI	(<1.525, 1.602)	(<1.586, 1.651)	(<1.499, 1.585)	(<1.557, 1.643)
6 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	10 (7.5%)	3 (2.2%)	18 (13.5%)	7 (5.1%)
	Number with Data for Analysis	122 (91.7%)	130 (94.9%)	114 (85.7%)	126 (92.0%)
	Mean	<1.581	<1.673	<1.543	<1.617
	Median	<1.628	<1.663	<1.556	<1.620
	SD	>0.296	>0.275	>0.329	>0.277
	(Min, Max)	(<0.90, 2.29)	(<0.90, 2.29)	(<0.90, 2.29)	(<0.90, 2.29)
	CI	(<1.537, 1.625)	(<1.633, 1.713)	(<1.492, 1.594)	(<1.577, 1.658)
12 CPD	Not Assessed	1 (0.8%)	4 (2.9%)	1 (0.8%)	4 (2.9%)
	Number Assessed	132 (99.2%)	133 (97.1%)	132 (99.2%)	133 (97.1%)
	Number Scoring (-1)	30 (22.6%)	21 (15.3%)	42 (31.6%)	28 (20.4%)
	Number with Data for Analysis	102 (76.7%)	112 (81.8%)	90 (67.7%)	105 (76.6%)
	Mean	<1.077	<1.208	<1.043	<1.153
	Median	<1.079	<1.167	<0.929	<1.079
	SD	>0.363	>0.345	>0.385	>0.375
	(Min, Max)	(<0.60, 2.00)	(<0.60, 2.00)	(<0.60, 2.00)	(<0.60, 2.00)
	CI	(<1.017, 1.136)	(<1.154, 1.262)	(<0.975, 1.110)	(<1.092, 1.214)

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
%=n/N
SD = Standard Deviation
CI = Two-sided 90% Confidence Interval
CPD = Cycles Per Degree
The score was set to (-1) when a subject could not complete a sensitivity measurement.
For mean and variability estimations, scores of (-1) were excluded from the calculations. Hence the corresponding mean and median measures are overestimated and variability measures are underestimated.
Column header is number of subjects in the best case population
Number assessed is number in the best case population minus number not assessed.
Number with data for analysis is number assessed minus number scoring (-1).
Mesopic contrast tests were conducted twice and the official sensitivity was defined as the mean of the two individual measures. The mean score was (-1) if either or both of the individual scores were (-1).

Visual Disturbances

A new Patient-Reported Outcomes questionnaire (Assessment of Photic Phenomena & Lens EffectS, abbreviated APPLES) was developed and used in this clinical study. This questionnaire was not determined to be a psychometrically valid assessment of the concept of photic phenomena. Patient-reported rates of moderate or severe levels of visual disturbances are presented in **Table 12**.

The highest rate of "severe" reports of visual disturbances/distortions at Visit 4A was for halos at 10.5% for the +2.5 D Multifocal and 3.8% for the Monofocal.

Table 12: Visual Disturbances, Safety, Visit 4A

	+2.5 D Multifocal (N=153)				Monofocal (N=160)			
	None n (%)	**Mild n (%)**	**Mod n (%)**	**Severe n (%)**	**None n (%)**	**Mild n (%)**	**Mod n (%)**	**Severe n (%)**
Glare	61 (39.9)	55 (35.9)	32 (20.9)	5 (3.3)	79 (49.4)	54 (33.8)	21 (13.1)	6 (3.8)
Halos	57 (37.3)	46 (30.1)	34 (22.2)	16 (10.5)	99 (61.9)	43 (26.9)	12 (7.5)	6 (3.8)
Starbursts	85 (55.6)	38 (24.8)	18 (11.8)	12 (7.8)	99 (61.9)	43 (26.9)	12 (7.5)	6 (3.8)
Hazy vision	101 (66.0)	41 (26.8)	10 (6.5)	1 (0.7)	107 (66.9)	39 (24.4)	12 (7.5)	2 (1.3)
Blurred vision	113 (73.9)	30 (19.6)	10 (6.5)	0 (0.0)	115 (71.9)	37 (23.1)	8 (5.0)	0 (0.0)
Distortion where straight lines look tilted	139 (90.8)	11 (7.2)	3 (2.0)	0 (0.0)	149 (93.1)	9 (5.6)	0 (0.0)	2 (1.3)
Distortion where flat lines look curved	146 (95.4)	4 (2.6)	3 (2.0)	0 (0.0)	152 (95.0)	5 (3.1)	1 (0.6)	2 (1.3)
Double vision	142 (92.8)	7 (4.6)	3 (2.0)	1 (0.7)	153 (95.6)	4 (2.5)	1 (0.6)	2 (1.3)
Color distortion	144 (94.1)	8 (5.2)	1 (0.7)	0 (0.0)	150 (93.8)	9 (5.6)	1 (0.6)	0 (0.0)
Feeling sick due to distortion	146 (95.4)	6 (3.9)	1 (0.7)	0 (0.0)	147 (91.9)	10 (6.3)	3 (1.9)	0 (0.0)

%=n/N

The safety of the device for the indication for use was not based on the results of this clinical trial alone. The safety was based mainly on the clinical evaluation of the parent IOL, Model SA60D3, with the current trial being confirmatory.

2. Effectiveness Results

All eyes with successful IOL implantation were considered evaluable for the All Implanted analyses. This was the primary data set for analysis of effectiveness endpoints. Subjects in whom failure to successfully implant the IOL was due to device-related reasons were included in the analysis of the 3rd and 4th secondary effectiveness endpoints.

All eyes successfully implanted that had at least one postoperative visit, had no preoperative pathology or macular degeneration, and had no major protocol deviations at any time were evaluable for Best Case analyses. Female subjects who became pregnant at any time during the study period were excluded from the Best Case analysis. Determination of whether preoperative pathology excluded a subject from Best Case analysis was based on medical monitor assessment. The Best Case data set was the primary data set for analysis of the supportive effectiveness parameter of binocular defocus and contrast sensitivity and was a supportive data set for the primary and secondary effectiveness analyses. In addition, binocular visual acuity was collected as supportive data. The tables below summarize the information for the pre-specified endpoints of the clinical study. The results of binocular visual acuity were somewhat better than the monocular visual acuity as expected due to binocular summation.

Primary Endpoint: Monocular Visual Acuity at 53 cm

The +2.5 D Multifocal group was superior to the Monofocal group in terms of mean, photopic, monocular, distance-corrected visual acuity at 53 cm. The mean photopic monocular distance corrected visual acuity at the 53 cm test distance for first eyes of subjects implanted with the +2.5 D Multifocal was 0.190 logMAR better (~2 lines)

than for those implanted with the Monofocal ($p < 0.0001$). The data are presented in **Table 13** for the first eye (first implanted).

Table 13: Mean Monocular Distance Corrected Visual Acuity (logMAR) at 53 cm at Visit 4A (All Implanted Population)

	Multifocal (N=155) Mean (SD)	Monofocal (N=165) Mean (SD)	Differences (CI)	P value
First Implanted Eye	0.322 (0.014)	0.512 (0.013)	-0.190 (-0.221,-0.158)	<0.0001

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Monofocal IOL Model SN60WF
Difference=Multifocal - Monofocal
CI=Two-sided 90% Confidence Interval on the difference
All values reported are Least-Squares estimates from the mixed model
The treatment * investigator interaction was not found to be significant at alpha = 0.15

First Secondary Endpoint: Monocular Best Corrected Distance Visual Acuity (4 meters)

The +2.5 D Multifocal group was non-inferior to the Monofocal group in terms of mean, photopic, monocular, best-corrected distance visual acuity at 4 meters (using a non-inferiority margin of 1 line of acuity). The data are provided in **Table 14**.

Table 14: Mean Monocular Best Corrected Distance Visual Acuity (logMAR)
(All Implanted Population)

	Multifocal (N = 155) Mean (SD)	**Monofocal (N = 165) Mean (SD)**	**Difference (CI)**
First Implanted Eye	0.025 (0.009)	0.003 (0.009)	0.022 (0.002,0.043)

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
Difference=SN6AD2 - SN60WF
CI=Two-sided 90% Confidence Interval on the difference, logMAR
All values reported are Least-Squares estimates from the mixed model
Non-inferiority is demonstrated if the upper bound of the confidence interval on the difference is less than the margin of0.1 logMAR

Second Secondary Endpoint: Monocular Distance Corrected Near Visual Acuity at Standard Distance (40 centimeters)

The +2.5 D Multifocal group was superior to Monofocal group in terms of mean photopic, monocular, distance-corrected near visual acuity at 40 cm at visit 4A. The mean photopic monocular distance corrected visual acuity at 40 cm for first eyes of subjects implanted with the +2.5 D Multifocal was 0.206 logMAR (~2 lines on an ETDRS visual acuity chart) better than those implanted with the Monofocal ($p < 0.001$). The data are provided in **Table 15**.

Table 15: Mean Monocular Distance Corrected Near Visual Acuity at 40 cm Visit 4A (All Implanted Population)

	Multifocal (N = 155) Mean (SD)	Monofocal (N = 165) Mean (SD)	Difference (CI)	Pvalue
First Implanted Eye	0.426 (0.014)	0.632 (0.013)	-0.206 (-0.238,-0.175)	<0.0001

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2
Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
Difference=SN6AD2 - SN60WF
CI=Two-sided 90% Confidence Interval on the difference, logMAR
All values reported are Least-Squares estimates from the mixed model

Overall Spectacle Independence Using SILVER Patient Reported Outcome (PRO) Questionnaire

A new Patient-Reported Outcomes questionnaire (Spectacle Independence Lens Vision Evaluation Repurchase, abbreviated SILVER) was developed and used in this clinical study. This questionnaire was not determined to be a psychometrically valid assessment of the concept of spectacle independence. The third secondary effectiveness endpoint was overall spectacle independence using the SILVER patient reported outcome questionnaire. The rates of subjects who reported "None of the time" to the SILVER question regarding overall spectacle or contact lens use did not show a statistically significant difference.

Near Spectacle Independence Using SILVER Patient Reported Outcome (PRO) Questionnaire

The rates of subjects who reported "None of the time" to the SILVER question regarding near spectacle or contact lens use did not show a statistically significant difference between the +2.5 D Multifocal and the Monofocal.

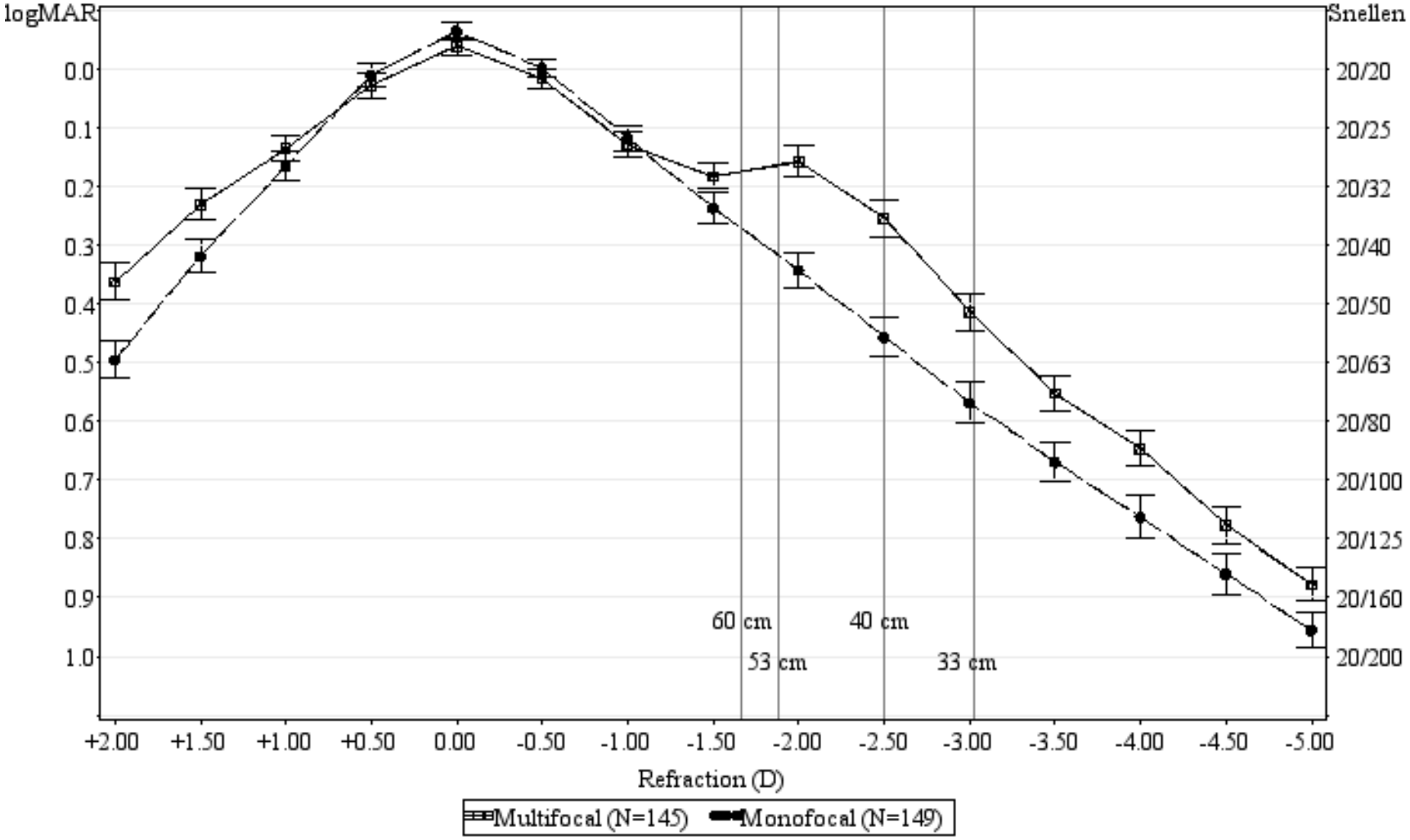
3. Supportive Effectiveness Results

Binocular Defocus Curves

Binocular depth of focus (Defocus) testing was performed under photopic lighting conditions using a 100% contrast ETDRS visual acuity chart at 4 m at Visit 3A (30-60 days postoperative). Each subject was initially defocused with a spherical power of -5.00 D from their best distance corrected manifest refraction, and their visual acuity was measured. Visual acuity testing continued by decreasing the negative spherical power in 0.50 D increments until the point of best distance correction (manifest refraction) was reached. This testing was repeated beginning with a spherical defocus of +2.00 D, decreasing by +0.50 D increments.

Two peaks are seen in the binocular defocus curve for this multifocal IOL. One is at the zero defocus position, which corresponds to the distance focal point of the lens, and the other is at the –2.0 D defocus position, which generally corresponds to the intermediate focal point of the lens (53 cm). This is in contrast to the binocular depth of focus curve for the monofocal IOL which peaks only around the zero defocus point (**Figure 1**).

Figure 1: Mean Defocus Curves with 95% Confidence Limits by Lens Model at Visit 3A
(Best Case)



Photopic Uncorrected Visual Acuity

Table 16 provides a summary of monocular (for first eye, second eye and both first and second eyes combined) and binocular photopic uncorrected visual acuity results at 4 m, 53 cm, and 40 cm at Visit 4A (6 months post-operative).

At distance (4 m), monocular and binocular mean visual acuities were similar between the AcrySof® IQ ReSTOR® +2.5 D Multifocal IOL Model SV25T0 and AcrySof® IQ Monofocal IOL Model SN60WF (the largest difference was 0.02 logMAR).

At near (40 cm) and intermediate (53 cm) distances, in both monocular and binocular conditions, the mean visual acuity results for the AcrySof® IQ ReSTOR® +2.5 D Multifocal IOL Model SV25T0 were one line better in all conditions compared to the AcrySof® IQ Monofocal IOL Model SN60WF.

Table 16: Uncorrected Visual Acuity (logMAR) at Visit 4A

(All Implanted Population)

			Multifocal (N=155)			**Monofocal (N=165)**		
			n	**Mean**	**SD**	**n**	**Mean**	**SD**
VA @ 4 m	Monocular	First Eye	153	0.10	0.139	160	0.09	0.131
		Second Eye	153	0.08	0.127	159	0.07	0.139
		All Eyes	306	0.09	0.133	319	0.08	0.135
	Binocular		153	0.01	0.126	159	-0.01	0.103
VA @ 53 cm	Monocular	First Eye	153	0.36	0.166	159	0.45	0.194
		Second Eye	153	0.35	0.175	158	0.46	0.178
		All Eyes	306	0.36	0.170	317	0.46	0.186
	Binocular		153	0.25	0.148	158	0.34	0.170
VA @ 40 cm	Monocular	First Eye	153	0.45	0.193	160	0.57	0.188
		Second Eye	153	0.43	0.177	159	0.57	0.182
		All Eyes	306	0.44	0.186	319	0.57	0.185
	Binocular		153	0.34	0.163	159	0.46	0.190

Multifocal=ACRYSOF® IQ ReSTOR® +2.5 D MIOL Model SN6AD2Monofocal=ACRYSOF® IQ Aspheric Natural Intraocular Lens Model SN60WF
N = Number evaluable; n = Number with data
SD=Standard Deviation

XI. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 15 investigators of which 2 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: 2 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 reviewed by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XII. Summary of Supplemental Clinical Information

A study was conducted between November 26, 2012 and August 27, 2013 at 8 investigational sites in the Netherlands, Germany, Spain, Argentina, and Chile. This was a prospective, randomized, parallel-group, subject-masked study that required implantation of the AcrySof® IQ ReSTOR® +2.5 D MIOL in the dominant eye and 1-to-1 randomization of the fellow eye to receive either the AcrySof® IQ ReSTOR® +2.5 D MIOL (bilateral group) or AcrySof® IQ ReSTOR® +3.0 D MIOL (contralateral group). One hundred and three subjects were randomized – 53 were bilaterally implanted with the +2.5 D MIOL and 50 were implanted with the +2.5 D MIOL in the dominant eye and with

the +3 D MIOL in the contralateral eye. All randomized subjects completed the study [follow-up through Visit 3A (90 ± 14 days)]. The safety and effectiveness outcomes of the subjects implanted with the +2.5 D MIOL support the safety and effectiveness of the AcrySof® IQ ReSTOR® +2.5 D MIOL.

XIII. Panel Meeting Recommendation and FDA's Post-Panel Action

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.

XIV. Conclusions Drawn From Preclinical and Clinical Studies

A. Effectiveness Conclusions

The AcrySof® IQ ReSTOR® +2.5 D MIOL was superior to the AcrySof® IQ Monofocal IOL in mean photopic, monocular distance-corrected visual acuity both at 53 cm and at 40 cm.

The AcrySof® IQ ReSTOR® +2.5 D MIOL was noninferior to the AcrySof® IQ Monofocal IOL in mean photopic, monocular best-corrected distance visual acuity in the first eye, within a margin of 0.1 logMAR.

The binocular defocus curve demonstrates the expected near visual acuity peak at approximately 53 cm.

B. Safety Conclusions

The reasonable safety of the device was based upon the clinical investigation of the parent IOLs and supported by the clinical data from the pivotal trial of the +2.5 D MIOL. In the pivotal trial, in comparison to the historical Safety Performance Endpoint (SPE) adverse event rates in ISO 11979-7:2006, the rates for these events at visit 4A in the +2.5D MIOL group were not statistically significantly worse. At the higher spatial frequencies, log contrast sensitivity was lower for the+2.5D MIOL group than for the monofocal control group warranting inclusion of a warning in the labeling about the possibility of visual performance impairment under low-contrast or low-light conditions. The safety information submitted in this PMA supplement is consistent with safety information of previously approved related MIOLs.

C. Benefit-Risk Conclusions

The added probable benefits associated with better distance-corrected intermediate and near visual acuity in comparison to a monofocal IOL outweigh the added probable risks of lower contrast sensitivity and visual disturbances.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the directions for use.

XV. CDRH Decision

CDRH issued an approval order on April 13, 2015.

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

XVI. Approval Specifications

Directions for use: See device labeling.

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

XVII. Reference

Boettner EA, Fralick FB, Wolter JR. Conjunctival concretions of sulfadiazine. An unusual clinical problem solved with modern analytical techniques. Arch Ophthalmol. 1962 Nov; 92(5):446-8.