SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Multifocal Intraocular Lens
Device Trade Name:	AcrySof® IQ PanOptix® Trifocal Intraocular Lens (Model TFNT00) AcrySof® IQ PanOptix® Toric Trifocal Intraocular Lens (Model TFNT30, TFNT40, TFNT50, TFNT60)
Device Procode:	Multifocal Intraocular (MFK)
Applicant's Name and Address:	Alcon Laboratories, Inc. 6201 South Freeway Fort Worth, Texas 76134-2099

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P040020/S087

Date of FDA Notice of Approval: 8/26/2019

The AcrySof® IQ PanOptix® Trifocal Intraocular Lens (Model TFNT00) and AcrySof® IQ PanOptix® Toric Trifocal Intraocular Lens (Model TFNT30, TFNT40, TFNT50, TFNT60) are based on the parent devices AcrySof IQ ReSTOR +3.0D Multifocal IOL Model SN6AD1 and AcrySof IQ ReSTOR +3.0D Toric IOL Model SND1T3-T6 approved under PMAs P040020/S012 and P040020/S049 on December 22, 2008 and December 22, 2016, respectively, with the following Indications for Use:

> The Acrysof IQ ReSTOR +3.0D is indicated for primary implantation for the visual correction of aphakia secondary to removal of a cataractous lens in adult patietns with and without presbyopia, who desire near, intermediate, and distance vision with increased spectacle independence. This lens is intended to be placed in the capsular bag.
>
> The AcrySof IQ ReSTOR +3.0D Toric is indicated for primary implantation in the capsular bag of the eye for the visual correction of aphakia and pre-existing corneal astigmatism secondary to removal of a cataractous lens in adult patients with and without presbyopia, who desire near, intermediate and distance vision, reduction of residual refractive cylinder and increased spectacle independence. The lens is intended to be placed in the capsular bag.

The SSED to support these indications is available on the CDRH website and is incorporated by reference here (https://www.accessdata.fda.gov/cdrh_docs/pdf4/P040020S049B.pdf). The current

supplement was submitted to modify the indications and include the AcrySof® IQ PanOptix® Trifocal Intraocular lens (Model TFNT00) and AcrySof® IQ PanOptix® Toric Trifocal Intraocular lens (Model TFNT30, TFNT40, TFNT50, TFNT60).

II. INDICATIONS FOR USE

AcrySof® IQ PanOptix® Trifocal Intraocular lens
The AcrySof® IQ PanOptix® Trifocal Intraocular lens is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia, in adult patients with less than 1 diopter of pre-existing corneal astigmatism, in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near visual acuity while maintaining comparable distance visual acuity with a reduced need for eyeglasses, compared to a monofocal IOL.

AcrySof® IQ PanOptix® Trifocal Toric Intraocular lens
The AcrySof® IQ PanOptix® Toric Trifocal intraocular lens is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia and the reduction of residual refractive astigmatism, in adult patients in whom a cataractous lens has been removed. The lens mitigates the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity with a reduced need for eyeglasses, compared to a monofocal IOL.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the AcrySof® IQ PanOptix® Trifocal Intraocular lens labeling.

V. DEVICE DESCRIPTION

The AcrySof® IQ PanOptix® Trifocal and AcrySof® IQ PanOptix® Toric Trifocal intraocular lenses (IOLs) are ultraviolet absorbing and blue light filtering foldable multifocal IOLs. Each IOL model is a single-piece design with a central optic and two open-loop haptics (Figure 1). The optic 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. The optic 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. The optic is 6.0 mm in diameter and the lens has an overall diameter of 13.0 mm. After surgical insertion into the eye, the lens unfolds to its intended shape. The optic diffractive structure is in the central 4.5 mm portion of the optic and divides the incoming light to create a +2.17 D intermediate and a +3.25 D near add power at the IOL plane (representing approximately +1.65 D and +2.35 D at the corneal

plane after implantation, respectively, for an average human eye). The anterior surface is designed with negative spherical aberration to compensate for the positive spherical aberration of the cornea. The posterior surface of the optic of the AcrySof® IQ PanOptix® Trifocal Toric IOLs are marked with 6 indentations (3 on either side) on the flatter meridian of the optic. The physical properties of this lens are described in Table 1 and Figures 1, 2, and 3.

Table 1: Physical Characteristics of AcrySof® IQ PanOptix® Trifocal IOLs

Physical Characteristic	Description
Optic Type	Single-piece IOL with diffractive aspheric optic
UV Cutoff at 10% T	401 nm for 21 D
Index Of Refraction	1.55
Spherical Powers	6.0 D - 30.0 D in 0.5 D increments; 31.0 D - 34.0 D diopter in 1.0 D increments
Add Powers	2.17 diopter intermediate and a +3.25 diopter near add power at the IOL plane (representing approximately +1.65 D and +2.35 D at the corneal plane after implantation, respectively, for an average human eye)
Cylinder Powers	Model: Cylinder Power, D TFNT00: 0 TFNT30: 1.50 TFNT40: 2.25 TFNT50: 3.00 TFNT60: 3.75
Haptic Configuration	STABLEFORCE™ Modified-L Haptics
Lens Material	Ultraviolet light absorbing and blue light filtering Acrylate/Methacrylate Copolymer
Optic Diameter (mm)	6.0
Overall Length (mm)	13.0
Haptic Angle	0º

Figure 1: Physical Characteristics

All dimensions in millimeters

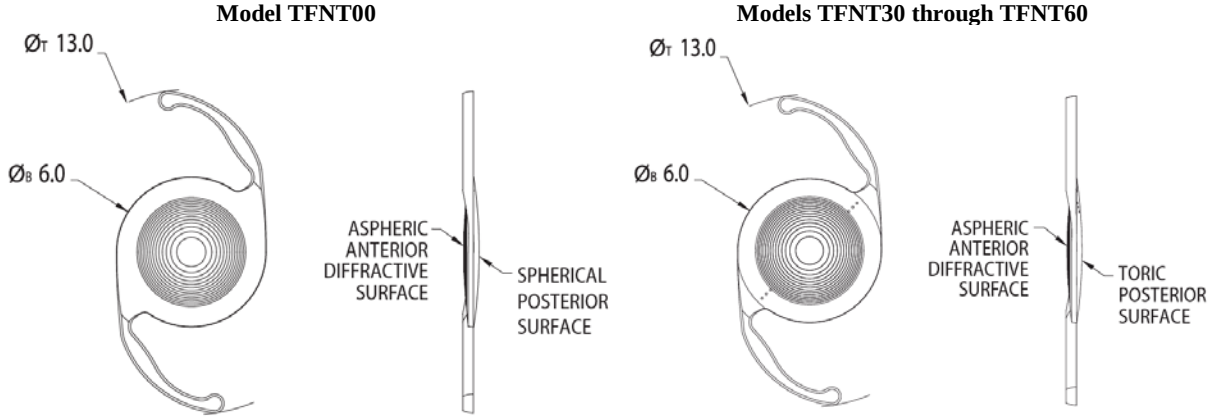
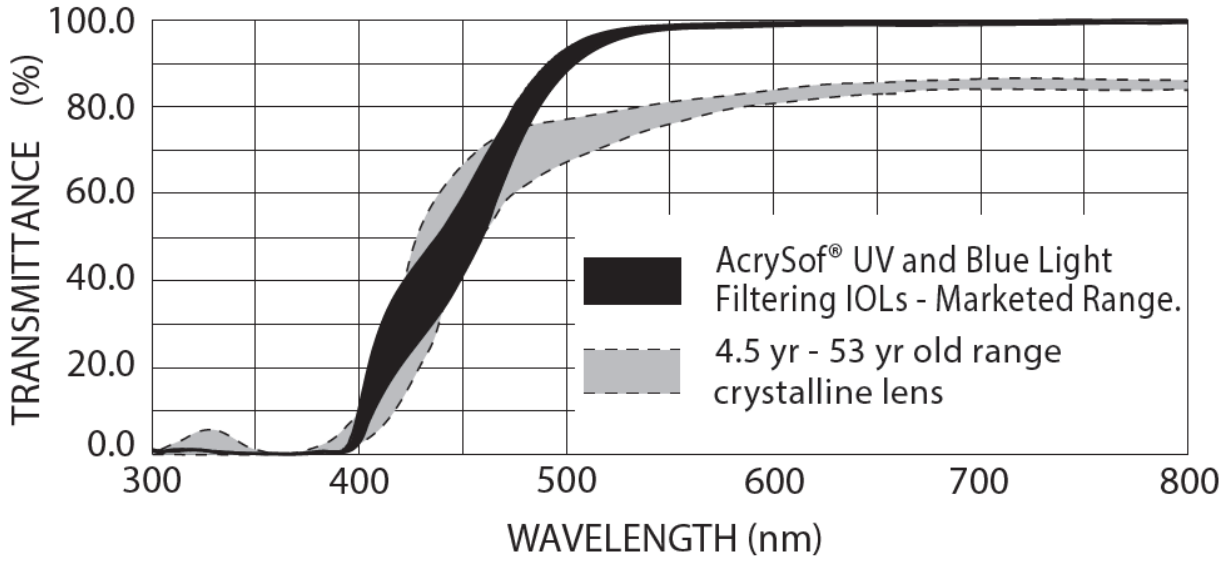
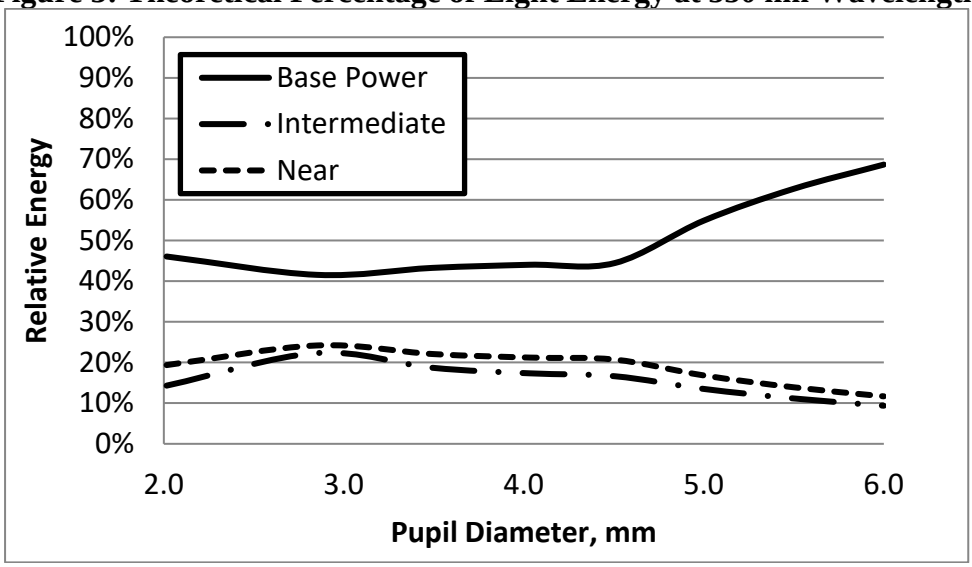


Figure 2: Spectral Transmittance



Human crystalline lens data is from Boettner and Wolter (1962).

Figure 3: Theoretical Percentage of Light Energy at 550 nm Wavelength



The AcrySof® IQ PanOptix® Trifocal IOLs are intended to be positioned in the lens capsule in the posterior chamber of the eye, replacing the human crystalline lens. This position allows the lens to function as a refractive medium in the correction of aphakia. This IOL has a biconvex optic containing an aspheric design and a diffractive structure on the anterior surface. The diffractive structure divides incoming light to provide a range of vision from distance to intermediate to near. This IOL provides an option for clinicians to provide patients an intermediate add power of +2.17 D and a near add power of +3.25 D. Additionally, the AcrySof® IQ PanOptix® Toric Trifocal IOLs have a toric component on the posterior surface with axis marks to denote the flat meridian (plus cylinder axis). Alignment of the toric axis marks with the post-operative steep corneal

meridian allows the lens to correct pre-existing corneal astigmatism. The astigmatic correction at the corneal plane for each model is shown in **Table 2.**

Table 2: Cylinder Power and Corneal Astigmatism Correction Range

	Cylinder Power		Recommend Corneal Astigmatism Range*	
Lens Model	IOL Plane	Corneal Plane*	Lower	Upper
TFNT30	1.50	1.03	0.75	1.28
TFNT40	2.25	1.55	1.29	1.80
TFNT50	3.00	2.06	1.81	2.32
TFNT60	3.75	2.57	2.33	2.82

*Based on an average pseudophakic human eye

An Alcon web-based calculator is used in conjunction with the AcrySof® IQ PanOptix® Trifocal intraocular Toric IOLs to determine the appropriate intraocular alignment and cylinder power for the patient.

With the exception of the optical modifications the AcrySof® IQ PanOptix® Trifocal intraocular and AcrySof® IQ PanOptix® Toric Trifocal intraocular lenses are identical to the respective parent IOLs in material composition.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Patients who undergo cataract extraction presently have several non-surgical and surgical alternatives for restoring functional vision of the aphakic eye. Non-surgical options include special cataract glasses or contact lenses. Surgical options such as monofocal, multifocal, extended depth of focus or accommodative IOLs are also available. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

The AcrySof® IQ PanOptix® Trifocal Intraocular lenses and AcrySof® IQ PanOptix® Toric Trifocal Intraocular lenses are currently commercially available in the European Union, Australia, Canada, and many countries within Asia, South America, and the Middle 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 effects (e.g., complications) associated with the use of the device include the following:

- lens epithelial cell down-growth
- corneal endothelial damage
- infection (endophthalmitis)
- retinal detachment/tear
- vitritis

- cystoid macular edema
- corneal edema
- pupillary block
- cyclitic membrane
- iris prolapse
- hypopyon
- anterior uveitis
- hyphema
- pigment dispersion
- posterior capsule opacification
- transient or persistent glaucoma
- IOL dislocation, tilt, or decentration requiring repositioning
- residual refractive error resulting in secondary intervention
- increased visual symptoms (compared to a monofocal IOL) related to the optical characteristics of the IOL, including bothersome stray-light artifacts such as halo, starbursts, or glare

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

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

IX. SUMMARY OF NONCLINICAL STUDIES

Biocompatibility Testing

The AcrySof® IQ PanOptix® Trifocal (Model TFNT00), and AcrySof® IQ PanOptix® Toric Trifocal Intraocular Lens (Models TFNT30, TFNT40, TFNT50, and TFNT60) are made of AcrySof® Natural IOL material (AL-37884), the same material that was used with other previously approved IOL designs, where the biocompatibility testing performed on AcrySof® Natural IOL material was incorporated by reference to P930014/S007, P930014/S009 and P940020/S050. The biocompatibility testing (see **Table 3**) was performed in accordance with International Standard Organization (ISO) 10993-1 - Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process, - Part 3: Tests for genotoxicity, carcinogenicity and reproductive toxicity, - Part 5: Tests for in vitro cytotoxicity, - Part 6: Tests for local effects after implantation, - Part 10: Tests for irritation and skin sensitization, and - Part 11: Tests for systemic toxicity. All biocompatibility testing were conducted in accordance with the provisions of 21 CFR 58, Good Laboratory Practice for Nonclinical Laboratory Studies.

Table 3: Biocompatibility Testing

Test	Purpose	Acceptance Criteria	Results
MEM Elution w/ L-929 Mouse Fibroblast Cells	Evaluate the potential for cellular toxicity	Non-cytotoxic	Pass
Agarose Overlay (Direct Contact) w/L-929 Mouse Fibroblast	Evaluate the potential for cellular toxicity	Non-cytotoxic	Pass
Cell Growth Inhibition Assay w/L-929 Mouse Fibroblast Cells	Evaluate the potential for cellular toxicity	Non-cytotoxic	Pass
Cell Growth Inhibition Assay w/L-929 Mouse Fibroblast Cells	Evaluate the potential for cellular toxicity	Non-cytotoxic	Pass
Guinea Pig Maximization	Evaluate the potential of sensitization	Non-sensitizing	Pass
Rabbit Muscle Implantation (7, 30 days)	Evaluate the local effects in skeletal muscle tissue	Non-irritant	Pass
Bacterial Reverse Mutation Mutagenicity Test	Evaluate the mutagenic potential of the implant	Non-mutagenic	Pass
Mammalian Erythrocyte Micronucleus test	Evaluate potential to induce micronuclei formation	Non-genotoxic	Pass
In vitro Mouse Lymphoma Assay	Evaluate potential to induce mutations in mouse lymphoma cells	Non-genotoxic	Pass
Ocular Implantation Study in Rabbits (6 months)	Evaluate local effects in ocular tissue	No significant biological local response	Pass

Chemical Characterization

The AcrySof® IQ PanOptix® Trifocal Intraocular Lenses are manufactured from the same AcrySof® Natural IOL material (AL-37884) that was previously used in the AcrySof ReSTOR IOL (approved P040020-S012) as well as several other approved

ALCON IOLs. The material used for the AcrySof IQ PanOptix Trifocal Intraocular Lens has been previously tested to meet the recommendations in ISO 11979-5 Ophthalmic Implants – Intraocular Lenses Part 5 – Biocompatibility, and has passed the tests listed in **Table 4** below.

Table 4: Chemical testing

TEST	PURPOSE	RESULTS
Exhaustive extraction	Soxhlet extraction to recover polymerization residuals, impurities, and additives, quantitative analysis of extracts	Passed
Leachables	Extraction procedure to simulate leachable components that are expected to be released in-vivo	Passed
Insoluble inorganics	Test to verify removal of residual inorganics residues from the manufacturing process	Passed
Hydrolytic stability	Test to verify material does not degrade by hydrolysis	Passed
Photostability	Test to evaluate photostability over 20 years at 300-400 nm	Passed
Nd-YAG laser	Test to evaluate material stability when exposed to Nd-YAG laser treatment, and no leakage of toxic components	Passed

Optical/Mechanical Testing

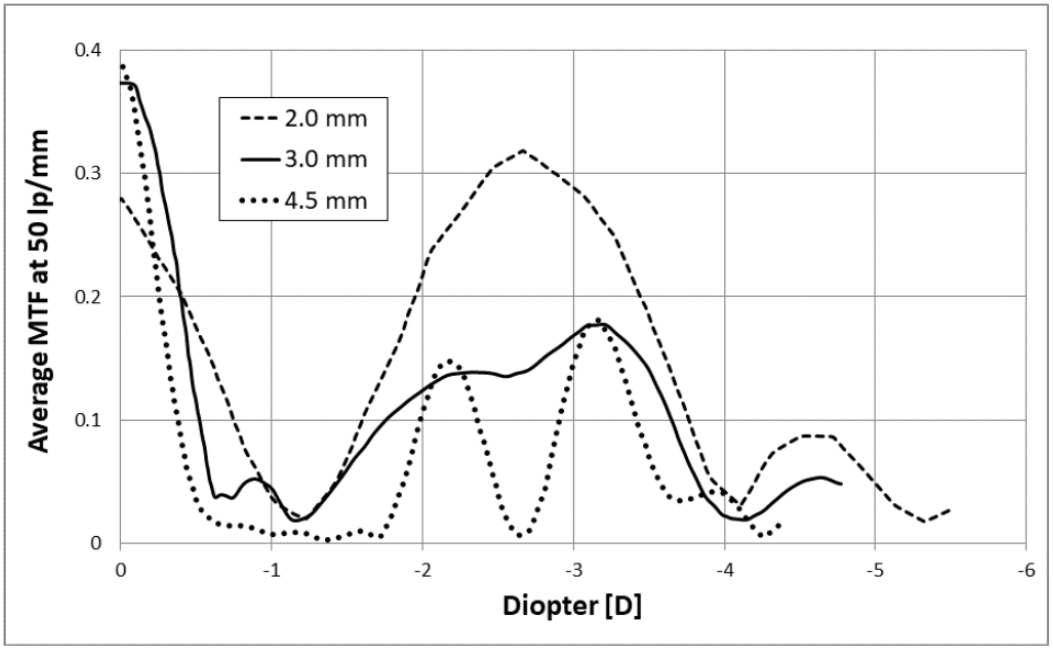
Pre-clinical optical / mechanical tests were performed with the AcrySof® IQ PanOptix® Trifocal Intraocular lenses and were measured in accordance with ISO 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods and ISO 11979-3 Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods. Test results are presented in Table 5.

Table 5: Optical testing

Test	Results
Compression Force	Passed
Axial Displacement in Compression	Passed
Optic Decentration	Passed
Optic Tilt	Passed
Angle of Contact	Passed
Compression Force Decay	Passed
Dynamic Fatigue Durability	Passed
Haptic Strength	Passed
Spectral Transmittance	Passed
Image Quality	Passed
Optical Evaluation after Multiple folds	Passed

The MTF through focus response at 50 lp/mm for a 2.0, 3.0, and 4.5 mm aperture is shown in **Figure 4**.

Figure 4 : MTF Through Focus Response at 50 lp/mm for 2.0, 3.0, and 4.5 mm aperture



AcrySof® IQ PanOptix® Trifocal Intraocular lenses were tested for recovery of properties after simulated surgical manipulation using the Monarch IOL Delivery System in accordance with ISO 11979-2 and ISO 11979-3.

X. SUMMARY OF PRIMARY CLINICAL STUDY(IES)

The applicant performed a clinical study to establish a reasonable assurance of safety

and effectiveness of the AcrySof® IQ PanOptix® Trifocal Intraocular lenses. This study was conducted in the US under IDE G170172. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

The PanOptix Toric IOL is a modification of the currently marketed AcrySof® IQ ReSTOR® Toric +3.0 D Multifocal IOL Model SND1T3, SND1T4, SND1T5, and SND1T6. The ReSTOR IOL was originally approved under P040020, and the ReSTOR Toric IOL was approved under P040020/S049. Although preclinical data/information was leveraged, a clinical study was warranted to assess the change to the optic to establish a reasonable assurance of safety and effectiveness for the new optical design.

The PanOptix Toric IOL models (TFNT30, TFNT40, TFNT50, TFNT60) involved imposing the toric feature from the toric design parents (P980040/S049: ReSTOR Toric IOL Models SND1T3, SND1T4, SND1T5, SND1T6) onto the posterior surface of the PanOptix Toric IOL models. Since the study for PanOptix IOL Model TFNT00 established safety and the applicant has approved toric parent IOLs, additional clinical data was not required to support safety and effectiveness of the toric models, because the only difference is in cylinder powers.

A. Study Design

Subjects were treated between November 2017 and September 2018. The database for this Panel Track PMA Supplement reflected data collected through September 2018 and included 243 implanted subjects. There were 12 investigational sites in the U.S.

A prospective, 6-month, multicenter, bilateral, non-randomized, vision-assessor masked, parallel-group study was designed to evaluate bilateral implantation of a total of 250 subjects (125 bilaterally implanted subjects in each arm). This study was designed to evaluate the effectiveness and safety of AcrySof® IQ PanOptix® Trifocal Intraocular lenses in providing a range of vision (distance, intermediate, and near) as compared to a standard monofocal IOL, the AcrySof Monofocal IOL Model SN60AT. The monofocal control IOL is a legally-marketed alternative with similar indications for use, except that it is not intended to provide improved vision at intermediate and near distances.

Statistical analyses were frequentist. For the key effectiveness analyses, two hypothesis tests were to demonstrate superiority over the control group with respect to distance-corrected intermediate (DCIVA) and near visual acuity (DCNVA). An additional non-inferiority hypothesis was used to demonstrate non-inferiority of the test group compared to the control group with respect to best-corrected distance visual acuity (BCDVA).

A total of 250 subjects were planned for bilateral implantation in a 1:1 ratio, in order to ensure that at least 226 eligible subjects (113 in each arm) completed the study.

This sample size assumed a dropout rate of 10%, and was based on the following assumptions (Table 6):

Table 6: Sample Size Calculations

	Margin	Expected Difference	SD	Type I error sided	Power
Non-Inferiority					
BCDVA (4 m)	0.1	0.0	0.18	5%	99%
Superiority					
DCNVA (40 cm)		0.1	0.18	2.5%	98%
DCIVA (66 cm)		0.1	0.18	2.5%	98%
Spectacle need		20%		2.5%	83%

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the AcrySof® IQ PanOptix® Trifocal Intraocular lens study was limited to patients who met the following inclusion criteria in both eyes:

   1. Adults, 22 years of age or older at the time of surgery, diagnosed with bilateral cataracts with planned cataract removal by phacoemulsification with a clear cornea incision
   2. Able to comprehend and willing to sign informed consent and complete all required postoperative follow-up procedures
   3. Best Corrected Distance Visual Acuity (BCDVA) projected to be 0.2 logMAR (Minimum Angle of Resolution) or better
   4. Calculated lens power within the available range
   5. Preoperative keratometric astigmatism of less than 1.0 D in both operative eyes
   6. Clear intraocular media other than cataract in both eyes

   Subjects were not permitted to enroll in the AcrySof® IQ PanOptix® Trifocal Intraocular lens study if they met any of the following exclusion criteria:

   1. Clinically significant corneal abnormalities including corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), irregularity (including irregularity due to dry eye syndrome), inflammation or edema per the Investigator's expert medical opinion. *Note*: conditions including, but not limited to: keratitis, keratoconjunctivitis, keratouveitis, keratopathy, or keratectasia should be excluded.
   2. Previous corneal transplant;
   3. Previous refractive surgery or refractive surgery procedures (including, but not limited to LASIK, astigmatic keratotomy, and limbal relaxing incisions)
   4. History of or current retinal conditions or predisposition to retinal conditions, previous history of, or a predisposition to, retinal detachment

or presence of diabetic retinopathy that the Investigator judges could confound outcomes. Note: Conditions including but not limited to background of diabetic retinopathy, diabetic macular edema or proliferative diabetic retinopathy, macular degeneration).
5. Amblyopia
6. Rubella, congenital, traumatic, or complicated cataracts
7. Extremely shallow anterior chamber not due to swollen lens
8. History of or current anterior or posterior segment inflammation of any etiology, or any disease producing an inflammatory reaction in the eye (eg, iritis or uveitis)
9. Iris neovascularization
10. Glaucoma (uncontrolled or controlled with medication)
11. Optic nerve atrophy
12. Subjects with diagnosed degenerative eye disorders (e.g. macular degeneration or other retinal disorders)
13. Pregnancy or lactation
14. Any subject currently participating in another investigational drug or device study
15. Subjects who may reasonably be expected to require a SSI at any time during the study (other than YAG capsulotomy)
16. Subjects who are expected to require retinal laser treatment
17. Any disease or pathology, other than cataract, that (in the expert opinion of the Investigator) is expected to reduce the potential postoperative BCDVA to a level worse than 0.30 logMAR. *Note*: Conditions including, but not limited to the following: amblyopia, clinically severe corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), diabetic retinopathy, extremely shallow anterior chamber, not due to swollen cataract, microphthalmos, previous retinal detachment, previous corneal transplant, recurrent severe anterior or posterior segment inflammation of unknown etiology, iris neovascularization, uncontrolled glaucoma, aniridia, or optic nerve atrophy, or diagnosis of pseudoexfoliation.
18. An additional exclusion criterion for the Astigmatic Blur Sub-study only is oblique post-operative residual astigmatism (axis between 30 to 60 degrees or 120 to 150 degrees).

The following were intraoperative criteria for not implanting the device:

1. Any other additional procedures during the phacoemulsification and IOL implant due to intraoperative complications that require further intervention (including but not limited to posterior capture rupture, with vitreous loss, zonular dehiscence that may make the IOL implant less stable, etc.)
2. Excessive iris mobility
3. Mechanical or surgical manipulation required to enlarge the pupil prior to or at IOL implantation
4. Zonular or capsule rupture
5. Significant anterior chamber bleeding

6. Unrecognized (pre-existing but discovered during surgery) ocular conditions or complications in which the IOL stability could be compromised, including zonular weakness
7. Bag-sulcus, sulcus-sulcus or unknown placement of the haptics
8. Any other capsulorhexis other than circular continuous capsulorhexis (eg, no anterior radial inconsistencies in the capsulorhexis such as anterior capsular tears or any areas of 'can-opener' capsulotomy)

2. Follow-up Schedule
The follow-up visit schedule is presented in Table 7. Specific examinations and scheduled clinical assessments are presented in Table 8.

Table 7: **Study Design**

Time From Implantation	**First Eye**	**Second Eye**
-30 to 0 days pre-operatively	Visit 0 (monocular [First and Second eye] and binocular)	
Operative (IOL implantation)	Visit 00	Visit 00A*
1 - 2 days post-operatively	Visit 1 (monocular)	Visit 1A (monocular)
7 - 14 days post-operatively	Visit 2 (monocular)	Visit 2A (monocular)
30 - 60 days post-operatively	Visit 3 (monocular)	Visit 3A (monocular)
120 - 180 days post-operatively (after Second eye implantation)	Visit 4A^ (monocular [First and Second eye] and binocular)	

*NOTE: IOL implantation in the second eye is intended to occur between 7 and 30 days after IOL implantation in the first eye.
^NOTE: Visit 4A will be completed in 2 parts that should be completed within 2 weeks (14 day) timeframe.

Table 8: Schedule of Visits

	Visit 0	Visit 00	Visit 1	Visit 2	Visit 3	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A		USV
										Part 1	Part 2	
Procedure/ Assessment	**Screen (Day -30to 0)**	**Implant 1**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Implant 2**	**Day 1-2**	**Day 7-14**	**Day 30-60**	**Day 120-180** (From 2nd)		**NA**
Informed Consent	X											
Demographics	X											
Medical History	X											
Concomitant Medications	X	X	X	X	X	X	X	X	X	X	X	X
Inclusion/Exclusion	X	X				X						
Corneal Topography	X											
Biometry (Keratometry, Axial length, Anterior Chamber depth with corneal thickness, lens thickness)	X										X	
Predicted Residual Refractive Error	X											
Urine Pregnancy Test	X											
Administer Treatment(s)		X				X						
Device Deficiencies		X	X	X	X	X	X	X	X	X	X	X
Adverse Events (Both Volunteered and Elicited)	X	X	X	X	X	X	X	X	X	X	X	X
Manifest refraction	X			X	X			X	X	X	X	
Photopic and Mesopic Pupil Size at Distance	X									X		
Photopic and Mesopic Pupil Size at Near (40cm)										X		
Photopic Uncorrected Distance Visual Acuity (4m)				X	X			X	X		X, Xb	
Photopic Best Corrected Distance Visual Acuity (4m)	X			X	X			X	X	X, Xb		
Photopic Distance Corrected Intermediate Visual Acuity (66 cm)					X				X	X, Xb		
Photopic Uncorrected Intermediate Visual Acuity (66 cm)					X				X		X, Xb	
Photopic Uncorrected Near Visual Acuity (40cm)					X				X		X, Xb	

	Visit 0	Visit 00	Visit 1	Visit 2	Visit 3	Visit 00A	Visit 1A	Visit 2A	Visit 3A	Visit 4A		USV
										Part 1	Part 2	
Photopic Uncorrected Distance Visual Acuity (4m)				X	X			X	X		X, Xb	
Photopic Best Corrected Distance Visual Acuity (4m)	X			X	X			X	X	X, Xb		
Photopic Distance Corrected Intermediate Visual Acuity (66 cm)					X				X	X, Xb		
Photopic Uncorrected Intermediate Visual Acuity (66 cm)					X				X		X, Xb	
Photopic Uncorrected Near Visual Acuity (40cm)					X				X		X, Xb	
Mesopic Distance Corrected Near Visual Acuity (40 cm)										X, Xb		
Photopic Distance Corrected Near Visual Acuity (40 cm)					X				X	X, Xb		
Distance Contrast Sensitivity – photopic without glare										Xb		
Distance Contrast Sensitivity – photopic without glare										Xb		
Distance Contrast Sensitivity – mesopic with glare										Xb		
Distance Contrast Sensitivity – mesopic without glare										Xb		
Binocular defocus curve											Xb	
Mesopic distance corrected LCVA (10%) at 4 m										Xb		
Photopic distance corrected LCVA (10%) at 4 m										Xb		
Photopic distance corrected LCVA (10%) at 66 cm										Xb		
Photopic distance corrected LCVA (10%) at 40 cm										Xb		
QUVID questionnaire for visual disturbances)†	Xb								Xb	Xb		Xb
IOLSAT questionnaire for spectacle need	Xb								Xb	Xb		
Astigmatic Blur test^											X, Xb	
Operative Eye		X				X						
Surgical Problems		X				X						
Other Procedures at Surgery		X				X						

Incision Site		X				X						
Final Incision Size		X				X						
Lens Information		X				X						
IOL Damage		X				X						
Slit Lamp Examination	X		X	X	X		X	X	X		X	X
Fundus Visualization					X				X		X	
Dilated Fundus Examination	X				X				X		X	X
IOL Observations			X	X	X		X	X	X		X	X
Secondary Surgical Interventions			X	X	X		X	X	X		X	X
Subjective Posterior Capsule Opacification			X	X	X		X	X	X		X	X
Posterior Capsulotomy			X	X	X		X	X	X		X	X
Lens decentration and tilt			X		X			X	X		X	X
Intraocular pressure	X		X	X	X		X	X	X		X	X

Xb - Binocular testing is performed on the study group subjects who are implanted bilaterally with the MIOL and on the control group subjects who are implanted bilaterally with the control IOL. The questionnaires will be completed in all subjects.

^This sub-study is conducted for approximately 30 subjects per arm at the selected sites.

†QUVID is administered prior to all Secondary Surgical Interventions.

3. Clinical Endpoints

With regards to safety:

- The primary safety co-endpints were:
  - Estimate the cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL for first operative eye up to Month 6. (No specific success criteria were pre-specified.)
  - Evaluate the mean binocular distance contrast sensitivity with and without glare for photopic and mesopic conditions at 6 months. (No specific success criteria were pre-specified.)
- The secondary safety endpoint was to estimate the rates of severe and most bothersome (separately) visual disturbances as reported by the subjects using a questionnaire (QUVID). (No specific success criteria were pre-specified.)
- The third safety endpoint was to evaluate the cumulative and persistent rates of adverse events in first operative eyes in comparison to ISO 11979-7:2014 SPE historical control grid rates. Success criteria for each type of event was a rate not statistically greater than the control rate.
- Other safety endpoints included:
  - Binocular Mesopic Low Contrast (10%) Visual Acuity at Distance
  - Intraocular Pressure (IOP)
  - Slit Lamp Examination
  - IOL Observations
  - IOL Position Change
  - Subjective Posterior Capsule Opacification
  - Posterior Capsulotomy
  - Fundus Visualization

- Rates of all visual disturbances as reported using the QUIVD Questionnaire

With regards to effectiveness:

- The primary effectiveness co-endpoints were:
  - Mean photopic monocular best corrected distance visual acuity (4 m, BCDVA) for the first operative eye at Month 6. The success criteria was statistical non-inferiority of BCDVA compared to the control.The non-inferiority margin was set at 0.10 logMAR.
  - Mean photopic monocular distance corrected visual acuity at near (40 cm, DCNVA) for the first operative eye at Month 6. The success criteria was statistical superiority of DCNVA compared to the control. The superiority margin was set at 0.0 logMAR.
- The first secondary effectiveness endpoint was mean photopic monocular distance corrected visual acuity at intermediate (66 cm, DCIVA) for the first operative eye at Month 6. The success criteria was statistical superiority of DCIVA compared to the control. The superiority margin was set at 0.0 logMAR.
- The second secondary effectiveness endpoint was the proportion of subjects who respond "Never" to Question 1 of the IOLSAT questionnaire ("Overall, in the past 7 days, how often did you need to wear eyeglasses to see?") at Month 6. The success criteria was statistical superiority compared to the control.
- Other effectiveness endpoints included:
  - Astigmatic Blur sub-study: monocular (first operative eye) and binocular photopic visual acuity at distance, intermediate and near with monocular and binocular astigmatic blur at Month 6
  - Mean binocular photopic low contrast visual acuity (10%) at distance, intermediate and near at Month 6
  - Mean corrected binocular visual acuity by level of defocus at Month 6
  - Mean corrected binocular photopic visual acuity for each distance (best corrected distance visual acuity, distance corrected visual acuity at intermediate and distance corrected visual acuity at near)
  - Mean uncorrected monocular (first operative eyes and second operative eyes) and binocular photopic visual acuity for each distance (uncorrected distance visual acuity, uncorrected visual acuity at intermediate and uncorrected visual acuity at near)
  - Cumulative categorical monocular (first operative eyes and second operative eyes) and binocular visual acuity for each distance and condition (photopic best corrected distance visual acuity, photopic distance corrected visual acuity at intermediate, photopic and mesopic distance corrected visual acuity at near, photopic uncorrected distance visual acuity, photopic uncorrected visual acuity at intermediate and photopic uncorrected visual acuity at near)

All of these clinical endpoints were evaluated at 6 months postoperatively. Because the PanOptix IOL and PanOptix Toric IOL are modifications of approved IOLs,

conclusions regarding device safety and effectiveness are also substantiated by the results of the studies of the parent IOLs.

The primary safety endpoints were evaluated in the all implanted data set with the exception of contrast sensitivity, which was evaluated in the best case data set. Adverse events were evaluated in the safety data set (all eyes with IOL contact). Effectiveness endpoints were evaluated in the all implanted data set.

B. Accountability of PMA Cohort

At the time of database lock, of 250 subjects enrolled in the PMA study, 243 subjects were successfully implanted, and 99.2% (241) subjects were available for analysis at the completion of the study, the 6 month post-operative visit (Table 9).

Of the 250 enrolled subjects, seven subjects were considered screen failures for not meeting the study eligibility criteria. A total of 243 subjects were implanted, of whom 241 completed the study. A total of 129 subjects (256 eyes) were implanted with the test device (127 bilaterally, 2 unilaterally). The two unilaterally implanted TFNT00 subjects discontinued from participation prior to second eye implantation. All attempted TFNT00 implantations were successful. A total of 114 subjects (225 eyes) were implanted with the control device (111 bilaterally, 3 unilaterally). Three subjects in the control arm were unilaterally implanted with the control device: 2 subjects had intraoperative complications during second eye surgery and did not receive a study device; the third subject had complications after first eye implantation and was not subsequently implanted with study device in second eye.

Table 9: Subject Disposition (All Enrolled subjects)

Subject Disposition	TFNT00 n (%)	SN60AT n (%)	Overall n (%)
Total Enrolled			250
Discontinued prior to Attempted Implantation			7
Screen Failure			7
Attempted Implantation (N)	129[1]	114[2]	243
Successful Implantation	129 (100.0)	114 (100.0)	243 (100.0)
Completed Study	127 (98.4)	114 (100.0)	241 (99.2)
Discontinued after Attempted Implantation	2 (1.6)	0 (0.0)	2 (0.8)

All percentages are based on the number of subjects with attempted implantation in each treatment group or overall.
[1] Two subjects were unilaterally implanted
[2] Three subjects were unilaterally implanted
% = (n/N)*100

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a non-randomized, prospective, multicenter clinical study of intraocular lenses performed in the US.

The study population demographics and baseline parameters are reported in the Tables 10 and 11. The demographic and baseline characteristics were similar between the two groups.

Table 10: Demographic Statistics (All Implanted Analysis set)

Parameter	TFNT00 (N=129)	SN60AT (N=114)	Overall (N=243)
Age (Years), n (%)			
< 65	45 (34.9)	22 (19.3)	67 (27.6)
≥ 65	84 (65.1)	92 (80.7)	176 (72.4)
Mean (SD)	65.8 (7.31)	69.0 (6.46)	67.3 (7.09)
Median	66.0	69.0	68.0
(Min, Max)	(44, 81)	(48, 86)	(44, 86)
Sex, n(%)			
Female	85 (65.9)	79 (69.3)	164 (67.5)
Male	44 (34.1)	35 (30.7)	79 (32.5)
Race, n(%)			
White	113 (87.6)	96 (84.2)	209 (86.0)
Black or African American	8 (6.2)	11 (9.6)	19 (7.8)
American Indian or Alaska Native	0 (0.0)	0 (0.0)	0 (0.0)
Asian	7 (5.4)	1 (0.9)	8 (3.3)
Native Hawaiian or Other Pacific Islander	0 (0.0)	2 (1.8)	2 (0.8)
Other	1 (0.8)	4 (3.5)	5 (2.1)
Ethnicity, n(%)			
Hispanic or Latino	4 (3.1)	7 (6.1)	11 (4.5)
Not Hispanic or Latino	124(96.1)	106 (93.0)	230 (94.7)
Not Reported	1 (0.8)	1 (0.9)	2 (0.8)

% = (n/N)*100

Table 11: Baseline Characteristics, First Eye (All-Implanted Analysis Set)

	TFNT00 (N = 129)	**SN60AT (N = 114)**	**Overall (N = 243)**
Mesopic Pupil Size (mm) n	129	114	243
Mean (SD)	4.98 (1.07)	4.97 (1.04)	4.98 (1.06)
Median	5.0	5.0	5.0
(Min, Max)	(2.0, 8.0)	(2.5, 8.5)	(2.0, 8.5)
Photopic Pupil Size (mm) n	129	114	243
Mean (SD)	4.14 (0.93)	4.10 (0.89)	4.12 (0.91)
Median	4.0	4.0	4.0
(Min, Max)	(1.5, 6.5)	(2.0, 6.5)	(1.5, 6.5)

% = (n/N)*100

Table 12 presents key ocular baseline parameters of target spherical equivalent and preoperative keratometric cylinder.

Table 12: Group Comparison for Baseline Characteristics, First Eye Target Residual Refractive Error and Keratometric Cylinder (All-Implanted Analysis Set)

Parameter	Statistic	TFNT00 (N = 129)	SN60AT (N = 114)	TFNT00 - SN60AT
TRRE (D)	n	129	114	
	Mean (SD)	-0.015 (0.104)	-0.020 (0.174)	0.005
	Median	-0.01	0.00	
	(Min, Max)	(-0.29, 0.16)	(-0.54, 0.75)	
	SE	0.0092	0.0163	0.0182
	95% CI	(-0.034, 0.003)	(-0.052, 0.012)	(-0.032, 0.042)
	p-value			0.8073
Keratometric Cylinder (D)	n	129	114	
	Mean (SD)	0.484 (0.270)	0.544 (0.267)	-0.060
	Median	0.48	0.56	
	(Min, Max)	(0.00, 0.99)	(0.00, 1.00)	
	SE	0.0238	0.0250	0.0345
	95% CI	(0.437, 0.531)	(0.494, 0.593)	(-0.128, 0.008)
	p-value			0.0858

TFNT00 = AcrySof PanOptix IOL Model TFNT00
SN60AT = AcrySof Monofocal IOL Model SN60AT
TRRE = Raw value of Target Residual Refractive Error
Keratometric Cylinder (D) = abs(K1-K2)
N = Number of eyes in each treatment group, n = Number of eyes with data
SD = Standard Deviation, SE = Standard Error, CI = Confidence Interval
p-value = p-value from two sided two sample t-test

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the safety cohort of 243 implanted subjects: 129 PanOptix subjects (127 bilaterally implanted) and 114 monofocal subjects (111 bilaterally implanted).

The first co-primary safety objective was to estimate the cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL for the first operative eye up to Month 6. One SSI related to the optical properties of the IOLs was reported in the clinical study. The second co-primary safety objective was to evaluate the mean binocular contrast sensitivity with and without glare for photopic and mesopic conditions at Month 6. The mean log contrast sensitivity values for the PanOptix IOL were slightly worse than control at higher spatial frequencies, however the differences were not clinically meaningful.

The secondary safety objective was to estimate the rates of severe and most bothersome visual disturbances as reported by the subjects using a questionnaire at Month 6. Visual disturbances of starbursts, halos, and glare were the most frequently

rated “severe” symptoms in the TFNT00 group. Starbursts, halos, and glare were also rated as the most bothersome symptoms by subjects in the TFNT00 group; however, less than 5% of subjects rated these symptoms as “bothered very much” at Month 6.

The third safety objective was to evaluate rates of cumulative and persistent adverse events in first operative eyes at Month 6 in comparison to ISO 11979-7 Safety and Performance Endpoints grid (SPE rates). All SPE rates for TFNT00 were below the SPE threshold as set forth by ISO 11979-7:2014.

Adverse effects that occurred in the PMA clinical study:

The ocular adverse events (serious and non-serious) for both the study and control lens, first eye, are presented in **Table 13**. Posterior Capsular Opacification was the most frequently reported adverse event in the first operative eyes of the TFNT00 group, followed by increased IOP, dry eye, and vitreous detachment, which occurred at a similar rate between the two groups. All other adverse events in the first eyes were reported at a rate of < 2% in both groups. Results for the second eyes were similar to first eyes (**Table 14**).

Table 13 Ocular Adverse Events (Serious and Non-Serious Combined), First Eye (Safety Analysis Set)

	TFNT00 (N = 129)			SN60AT (N = 114)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**	**n (%)**	**2-sided 95% CI**	**E**
Posterior capsule opacification	17 (13.2)	(7.87, 20.26)	17	4 (3.5)	(0.96, 8.74)	4
Intraocular pressure increased	6 (4.7)	(1.73, 9.85)	6	6 (5.3)	(1.96, 11.10)	6
Dry eye	5 (3.9)	(1.27, 8.81)	5	3 (2.6)	(0.55, 7.50)	3
Vitreous detachment	4 (3.1)	(0.85, 7.75)	4	3 (2.6)	(0.55, 7.50)	3
Photophobia	0 (0.0)	(0.00, 2.82)	0	2 (1.8)	(0.21, 6.19)	3
Excessive eye blinking	2 (1.6)	(0.19, 5.49)	2	0 (0.0)	(0.00, 3.18)	0
Eye irritation	0 (0.0)	(0.00, 2.82)	0	2 (1.8)	(0.21, 6.19)	2
Eye pain	1 (0.8)	(0.02, 4.24)	1	1 (0.9)	(0.02, 4.79)	1
Lens extraction	1 (0.8)	(0.02, 4.24)	1	1 (0.9)	(0.02, 4.79)	1
Ocular discomfort	1 (0.8)	(0.02, 4.24)	1	1 (0.9)	(0.02, 4.79)	1
Vitreous floaters	0 (0.0)	(0.00, 2.82)	0	2 (1.8)	(0.21, 6.19)	2
Intra-ocular injection	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	3
Age-related macular degeneration	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Blepharochalasis	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Blepharospasm	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Chalazion	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Conjunctival hyperaemia	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Conjunctivitis	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0

Preferred Term	TFNT00 (N = 129) n (%)	TFNT00 (N = 129) 2-sided 95% CI	TFNT00 (N = 129) E	SN60AT (N = 114) n (%)	SN60AT (N = 114) 2-sided 95% CI	SN60AT (N = 114) E
Device dislocation	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Diplopia	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Eye inflammation	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Face injury	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Foreign body sensation in eyes	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Glare	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Halo vision	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Iridocyclitis	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Iritis	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Lacrimation increased	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Meibomian gland dysfunction	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Muscle twitching	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Ocular rosacea	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Ophthalmic herpes zoster	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Pain	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Photopsia	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Post procedural inflammation	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Posterior capsule rupture	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Punctate keratitis	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Retinal tear	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Retinopathy hypertensive	0 (0.0)	(0.00, 2.82)	0	1 (0.9)	(0.02, 4.79)	1
Vision blurred	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0
Vitreous degeneration	1 (0.8)	(0.02, 4.24)	1	0 (0.0)	(0.00, 3.18)	0

TFNT00 = AcrySof PanOptix IOL Model TFNT00
SN60AT = AcrySof Monofocal IOL Model SN60AT
If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE
Events are counted each time in the event (E) column
N= Number of eyes in each treatment group, n= Number of eyes with event
E= Number of events, CI= Confidence Interval
Percentages are calculated as (n/N) * 100, Adverse events are coded using MedDRA version 20.0

Table 14 Ocular Adverse Events (Serious and Non-Serious Combined), Second Eye (Safety Analysis Set)

	TFNT00 (N = 127)			SN60AT (N = 111)		
Preferred Term	**n (%)**	**2-sided 95% CI**	**E**	**n (%)**	**2-sided 95% CI**	**E**
Posterior capsule opacification	19 (15.0)	(9.25, 22.37)	19	5 (4.5)	(1.48, 10.20)	5
Iritis	3 (2.4)	(0.49, 6.75)	4	2 (1.8)	(0.22, 6.36)	2
Vitreous detachment	4 (3.1)	(0.86, 7.87)	4	1 (0.9)	(0.02, 4.92)	1
Dry eye	2 (1.6)	(0.19, 5.57)	2	2 (1.8)	(0.22, 6.36)	2
Intraocular pressure increased	3 (2.4)	(0.49, 6.75)	3	1 (0.9)	(0.02, 4.92)	1
Vitreous floaters	0 (0.0)	(0.00, 2.86)	0	3 (2.7)	(0.56, 7.70)	3
Corneal abrasion	0 (0.0)	(0.00, 2.86)	0	2 (1.8)	(0.22, 6.36)	2
Eye pain	2 (1.6)	(0.19, 5.57)	2	0 (0.0)	(0.00, 3.27)	0
Ocular discomfort	1 (0.8)	(0.02, 4.31)	1	1 (0.9)	(0.02, 4.92)	1
Vitreous degeneration	2 (1.6)	(0.19, 5.57)	2	0 (0.0)	(0.00, 3.27)	0
Intra-ocular injection	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	3
Chalazion	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	2
Device dislocation	1 (0.8)	(0.02, 4.31)	2	0 (0.0)	(0.00, 3.27)	0
Punctate keratitis	1 (0.8)	(0.02, 4.31)	2	0 (0.0)	(0.00, 3.27)	0
Age-related macular degeneration	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Blepharochalasis	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Cataract operation complication	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Conjunctival haemorrhage	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Conjunctivitis	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Corneal erosion	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Cystoid macular oedema	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Diplopia	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Excessive eye blinking	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Eye irritation	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Foreign body in eye	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Foreign body sensation in eyes	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Glare	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Halo vision	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Hordeolum	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1

Preferred Term	TFNT00 (N = 127) n (%)	TFNT00 (N = 127) 2-sided 95% CI	TFNT00 (N = 127) E	SN60AT (N = 111) n (%)	SN60AT (N = 111) 2-sided 95% CI	SN60AT (N = 111) E
Intraocular lens repositioning	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Iris transillumination defect	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Lacrimation increased	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Meibomian gland dysfunction	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Muscle twitching	0 (0.0)	(0.00, 2.86)	0	1 (0.9)	(0.02, 4.92)	1
Ocular rosacea	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Post procedural inflammation	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Vision blurred	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Vitrectomy	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Vitreous prolapse	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0

TFNT00 = AcrySof PanOptix IOL Model TFNT00
SN60AT = AcrySof Monofocal IOL Model SN60AT
If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE
Events are counted each time in the event (E) column
N= Number of eyes in each treatment group, n= Number of eyes with event
E= Number of events, CI= Confidence Interval
Percentages are calculated as (n/N) * 100, Adverse events are coded using MedDRA version 20.0

Secondary Surgical Interventions Due to Optical Properties of the IOL

One of the co-primary safety endpoints was to estimate the cumulative rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL for the first operative eye up to Month 6. One SSI related to the optical properties of the IOLs was reported in the clinical study as shown in Table 15. In the first eye for a PanOptix IOL subject, there was an explant of the IOL due to subjective complaints of dissatisfaction with the level of vision.

Table 15: Secondary Surgical Interventions Due to Optical Properties of the IOL, First Eye (Safety Analysis Set)

Statistic	TFNT00 (N = 129)	SN60AT (N = 114)	TFNT00-SN60AT
n	1	0	1
%	0.8	0.0	0.8
95% CI	(0.02, 4.24)	(0.00, 3.18)	(-11.79, 13.32)

Percentages are calculated as (n/N) * 100, CI = Confidence Interval (exact)
n and % for the treatment difference column are based on observed differences between the groups

The incidences of cumulative adverse events for the PanOptix IOL and the control Monofocal IOL as compared to the ISO 11979-7:2014 historical grid (SPE) rates are provided in **Tables 16** and **17**. If the same event occurred multiple times in an eye, only the first occurrence is counted in the table below. All SPE rates for TFNT00 were below the SPE threshold as set forth by ISO 11979-7:2014. The results of adverse events analyses based on the consensus definitions as set forth by American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) are shown in **Tables 18** and **19**.

Table 16: Cumulative and Persistent Serious Adverse Events and SPE Rates for TFNT00, First Eye (Safety Analysis Set)

	TFNT00			
	(N = 129) n %	**2-sided 95% CI**	**1-sided 95% Lower CL**	**SPE %**
Cumulative Serious Adverse Events				
Cystoid macular oedema	0 (0.0)	(0.00, 2.82)	0.00	3.0
Hypopyon	0 (0.0)	(0.00, 2.82)	0.00	0.3
Endophthalmitis	0 (0.0)	(0.00, 2.82)	0.00	0.1
Lens dislocated from posterior chamber	0 (0.0)	(0.00, 2.82)	0.00	0.1
Pupillary block	0 (0.0)	(0.00, 2.82)	0.00	0.1
Retinal detachment	0 (0.0)	(0.00, 2.82)	0.00	0.3
Secondary surgical intervention	1 (0.8)	(0.02, 4.24)	0.04	0.8
Other				
Retinal tear	1 (0.8)	(0.02, 4.24)	0.04	N/A
Persistent Serious Adverse Events				
Corneal stroma oedema	0 (0.0)	(0.00, 2.82)	0.00	0.3
Cystoid macular oedema	0 (0.0)	(0.00, 2.82)	0.00	0.5
Iritis	0 (0.0)	(0.00, 2.82)	0.00	0.3
Raised IOP requiring treatment	0 (0.0)	(0.00, 2.82)	0.00	0.4

% = (n/N)*100

The single secondary surgical intervention that occurred with the first eye for TFNT00 was an explant of the IOL due to subjective complaints of dissatisfaction with the level of vision. This SSI was determined to be related to the optical properties of the IOL.

Table 17: Cumulative and Persistent Serious Adverse Events and SPE Rates for TFNT00, Second Eye (Safety Analysis Set)

	TFNT00			
	(N = 127) n %	2-sided 95% CI	1-sided 95% Lower CL	SPE %
Cumulative Serious Adverse Events				
Cystoid macular oedema	1 (0.8)	(0.02, 4.31)	0.04	3.0
Hypopyon	0 (0.0)	(0.00, 2.86)	0.00	0.3
Endophthalmitis	0 (0.0)	(0.00, 2.86)	0.00	0.1
Lens dislocated from posterior chamber	0 (0.0)	(0.00, 2.86)	0.00	0.1
Pupillary block	0 (0.0)	(0.00, 2.86)	0.00	0.1
Retinal detachment	0 (0.0)	(0.00, 2.86)	0.00	0.3
Secondary surgical intervention	2 (1.6)	(0.19, 5.57)	0.28	0.8
Other				
Device dislocation	1 (0.8)	(0.02, 4.31)	0.04	N/A
Vitreous prolapse	1 (0.8)	(0.02, 4.31)	0.04	N/A
Persistent Serious Adverse Events				
Corneal stroma oedema	0 (0.0)	(0.00, 2.86)	0.00	0.3
Cystoid macular oedema	0 (0.0)	(0.00, 2.86)	0.00	0.5
Iritis	0 (0.0)	(0.00, 2.86)	0.00	0.3
Raised IOP requiring treatment	0 (0.0)	(0.00, 2.86)	0.00	0.4

% = (n/N)*100

The first secondary surgical intervention that occurred with the second eye for TFNT00 was a vitrectomy performed due to a vitreous prolapse. The second secondary surgical intervention that occurred with the second eye for TFNT00 was a lens repositioning procedure due to a tilted/displaced IOL. These SSIs occurred in different subjects and neither were determined to be related to the optical properties of the IOL.

Table 18: Supportive Characterization of Ocular Adverse Events based on a Modified Version of AAO Consensus (Masket, 2017), First Eye (Safety Analysis Set)

	PanOptix® IOL (N = 129)			Monofocal IOL (N = 114)		
Adverse Event	**n (%)**	**2-sided 95% CI**	**E**	**n (%)**	**2-sided 95% CI**	**E**
Chronic anterior uveitis	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Clinically significant cystoid macular edema	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Visually significant corneal edema	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Endophthalmitis	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Mechanical pupillary block	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Increased IOP	5 (3.9)	(1.27, 8.81)	5	2 (1.8)	(0.21, 6.19)	2
Rhegmatogenous RD	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Toxic anterior segment syndrome	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Secondary IOL intervention - Exchange	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Secondary IOL intervention - Removal	1 (0.8)	(0.02, 4.24)	1	1 (0.9)	(0.02, 4.79)	1
Secondary IOL intervention - Reposition	0 (0.0)	(0.00, 2.82)	0	0 (0.0)	(0.00, 3.18)	0
Percentage calculated as (n / N) * 100						

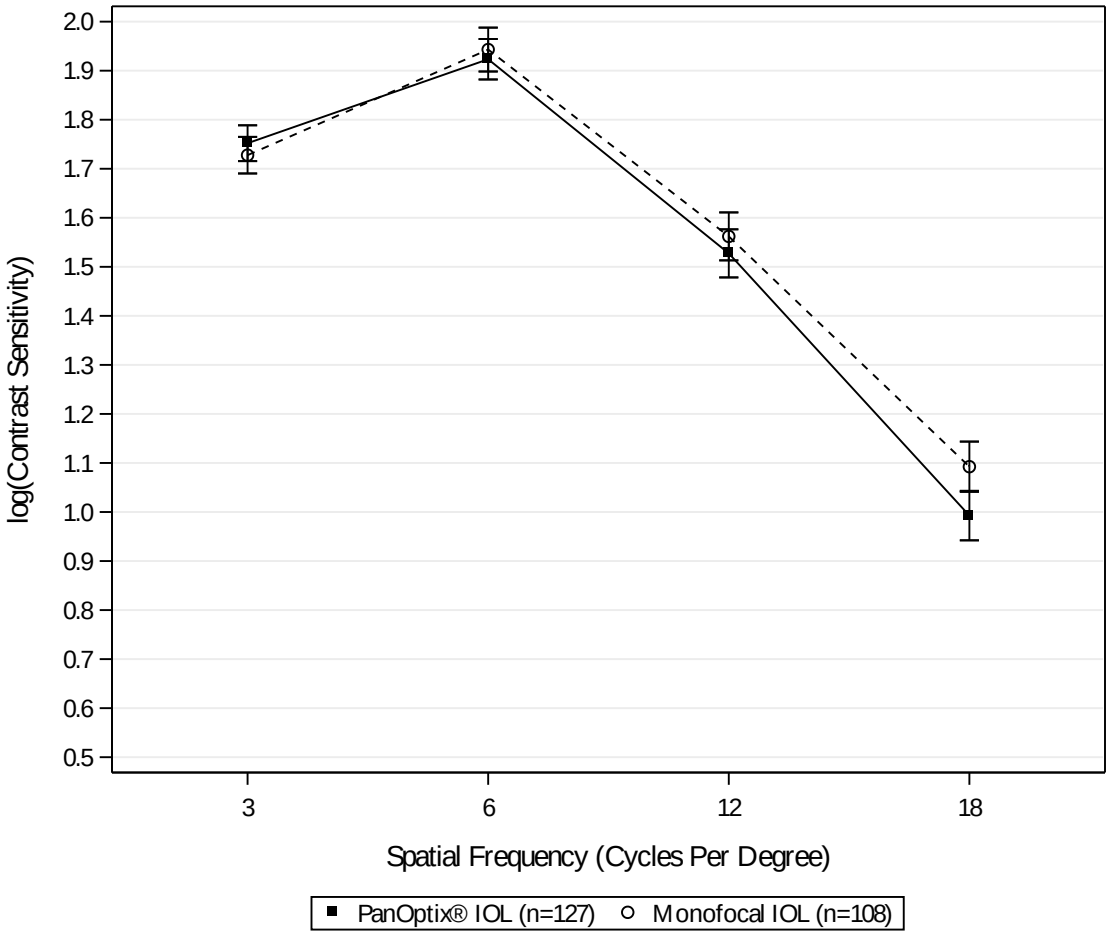
Table 19: Supportive Characterization of Ocular Adverse Events based on a Modified Version of AAO Consensus (Masket, 2017), Second Eye (Safety Analysis Set)

	PanOptix® IOL (N = 127)			Monofocal IOL (N = 111)		
Adverse Event	**n (%)**	**2-sided 95% CI**	**E**	**n (%)**	**2-sided 95% CI**	**E**
Chronic anterior uveitis	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Clinically significant cystoid macular edema	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Visually significant corneal edema	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Endophthalmitis	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Mechanical pupillary block	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Increased IOP	3 (2.4)	(0.49, 6.75)	4	1 (0.9)	(0.02, 4.92)	1
Rhegmatogenous RD	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Toxic anterior segment syndrome	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Secondary IOL intervention - Exchange	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Secondary IOL intervention - Removal	0 (0.0)	(0.00, 2.86)	0	0 (0.0)	(0.00, 3.27)	0
Secondary IOL intervention - Reposition	1 (0.8)	(0.02, 4.31)	1	0 (0.0)	(0.00, 3.27)	0
Percentage calculated as (n / N) * 100						

Contrast Sensitivity

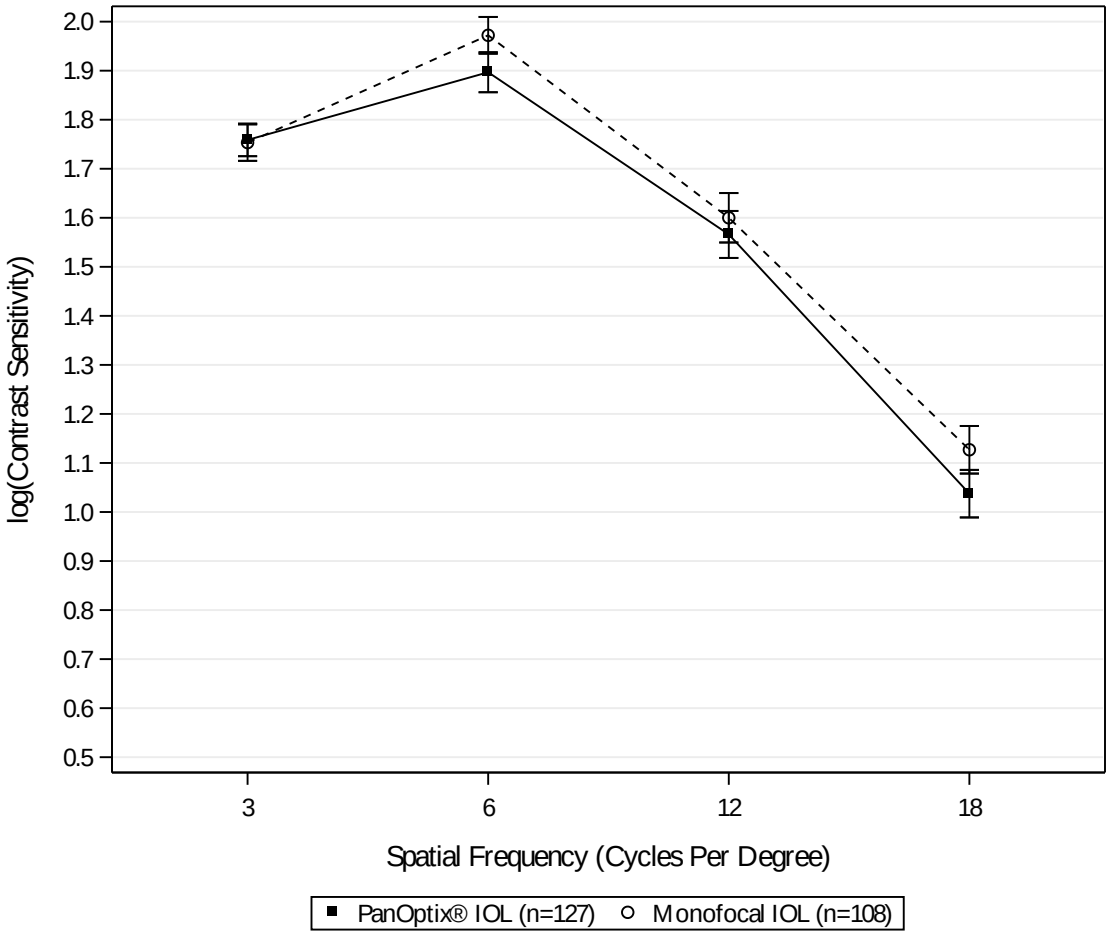
Binocular best corrected distance contrast sensitivity was performed using a backlit sine wave grating chart system (CSV1000, VectorVision, Greenville, OH) at 6 months under four conditions: photopic without glare, photopic with glare, mesopic without glare, and mesopic with glare. Chart luminances were 85 cd/m^2 for photopic conditions and 3 cd/m^2 for mesopic conditions. This analysis uses the best-case cohort. The mean and 95% confidence intervals results are shown in **Figures 5 to 8**. The binocular contrast sensitivity results were slightly reduced for the PanOptix IOL compared to the monofocal control IOL, however these differences were not clinically meaningful. It was noted that monocular contrast sensitivity was not performed in this study. Monocular contrast sensitivity is a more accurate assessment of individual IOL performance compared to binocular contrast sensitivity, and results for monocular contrast sensitivity would be expected to be reduced compared to binocular contrast sensitivity results.

Figure 5: Mean Binocular Photopic Contrast Sensitivity without Glare (log units) with 2-sided 95% confidence interval at 6 Months (Best-Case Analysis Set)



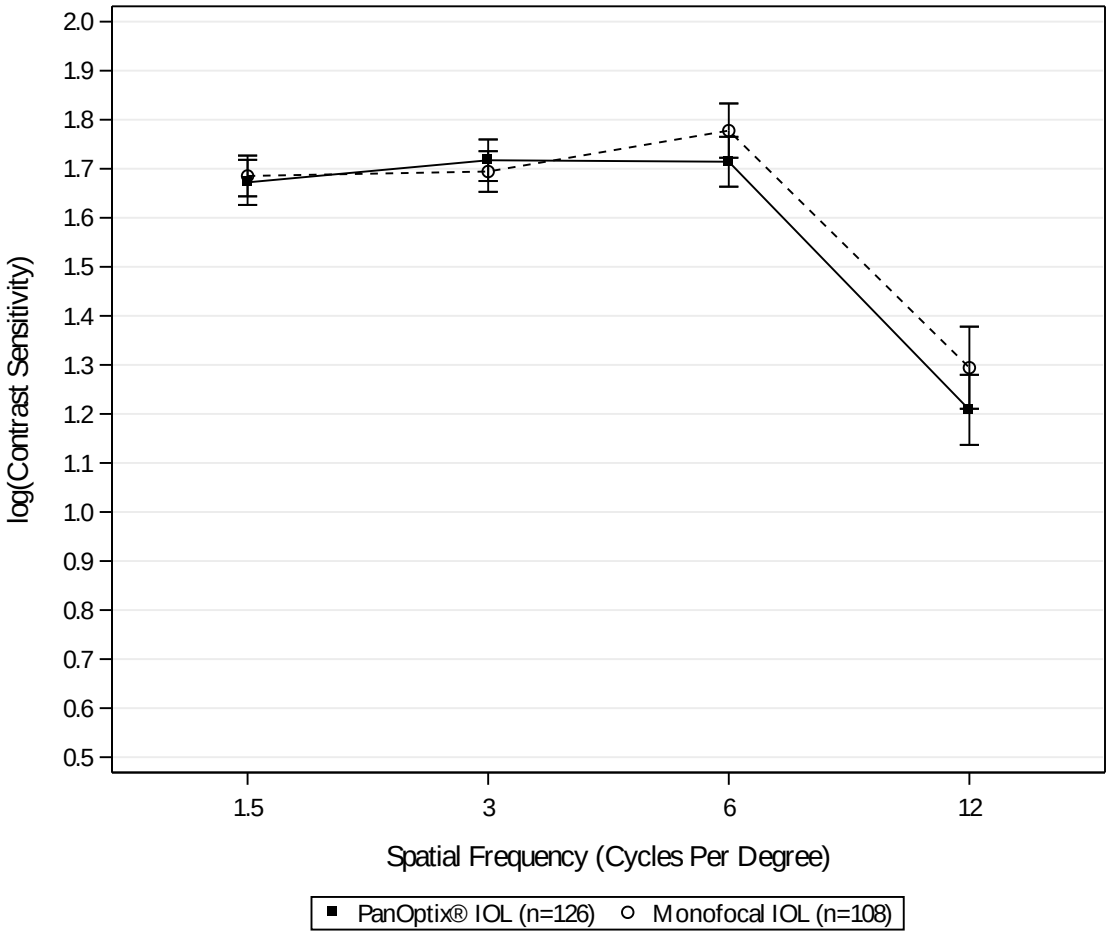
n = Number of subjects with contrast sensitivity test

Figure 6: Mean Binocular Photopic Contrast Sensitivity with Glare (log units) with 2-sided 95% confidence interval at 6 Months (Best-Case Analysis Set)



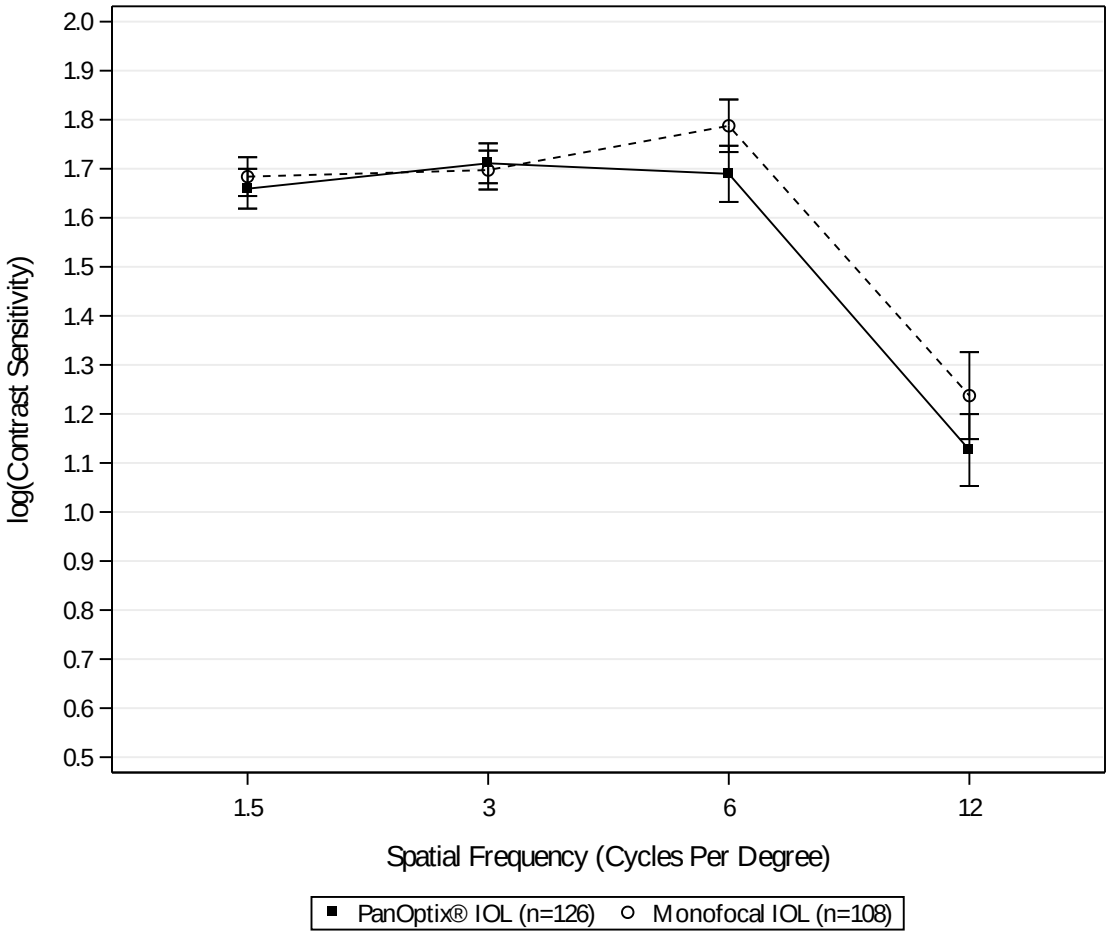
n = Number of subjects with contrast sensitivity test

Figure 7: Mean Binocular Mesopic Contrast Sensitivity without Glare (log units) with 2-sided 95% confidence interval at 6 Months (Best-Case Analysis Set)



n = Number of subjects with contrast sensitivity test

Figure 8: Mean Binocular Mesopic Contrast Sensitivity with Glare (log units) with 2-sided 95% confidence interval at 6 Months (Best-Case Analysis Set)



n = Number of subjects with contrast sensitivity test

Low Contrast Visual Acuity

Binocular low contrast visual acuity assessments were performed using a 10% low contrast visual acuity chart. Testing was completed under photopic conditions at 4 m, 66 cm, and 40 cm and under mesopic conditions at 4 m. Subjects were corrected for the 4 m distance for acuity measurements at all three distances. Low contrast VA assessments reduced the percentage of subjects achieving 0.3 logMAR or better compared to high contrast VA assessments for both groups. The PanOptix® IOL group was impacted largely at intermediate and near distances while the control Monofocal IOL group was impacted largely at the intermediate distance. Differences in distance VA mean values between the 2 groups for all assessments were not clinically significant (all means within 1 line). The 2-line improvement of PanOptix® IOL over control Monofocal IOL, observed for the high contrast DCIVA assessment, reduced to a 1-line improvement in low contrast conditions. The near 4-line improvement of PanOptix® IOL over control Monofocal IOL for high contrast DCNVA was reduced to a 3-line difference in low contrast conditions.

Visual Disturbances

A Patient Reported Outcome Measure instrument was developed and validated for use in this clinical study to assess visual disturbances. Subjects were first asked if they experienced a particular visual disturbance. If the subject responded affirmatively, he or she was asked to rate the severity, frequency, and bothersomeness. A single subject may report multiple symptoms.

As demonstrated in **Table 20** reports of visual disturbances were similar between the PanOptix® IOL and the control Monofocal IOL groups at 6 months. The highest rate of most bothersome reports ("Bothered Very Much") of visual disturbances/distortions at 6 months was for starbursts at 4.8% for the PanOptix® Trifocal IOL and 0.9% for the control Monofocal IOL. As demonstrated in **Table 21**, starbursts and halos were perceived by subjects with a higher rate of severity (moderate to severe) than all other reported symptoms, and at a higher rate in the PanOptix® IOL group; however, the majority of subjects reported these symptoms as "not bothered at all" to "bothered somewhat" as shown in **Table 20**.

Table 20: Visual Disturbance Bothersomeness, Safety Analysis Set

	PanOptix® IOL N=129						Monofocal IOL N=114					
		Bothered						Bothered				
Visual Disturbance	**n**	**Not experienced or Not bothered at all %**	**A Little bit %**	**Some-what %**	**Quite a bit %**	**Very much %**	**n**	**Not experienced or Not bothered at all %**	**A Little bit %**	**Some-what %**	**Quite a bit %**	**Very much %**
Glare	126	54.8	18.3	18.3	7.1	1.6	111	69.4	15.3	8.1	6.3	0.9
Halos	127	51.2	21.3	16.5	8.7	2.4	110	83.6	10.9	3.6	0.9	0.9
Starbursts	125	55.2	16.8	16.0	7.2	4.8	109	79.8	10.1	8.3	0.9	0.9
Hazy vision	125	86.4	6.4	6.4	0.8	0.0	110	89.1	5.5	3.6	0.9	0.9
Blurred vision	127	81.1	10.2	6.3	2.4	0.0	111	86.5	4.5	3.6	3.6	1.8
Double vision	125	96.0	2.4	1.6	0.0	0.0	110	98.2	0.0	1.8	0.0	0.0
Dark Area*	127	89.8	7.1	3.1	0.0	0.0	111	92.8	3.6	2.7	0.9	0.0

Percentage calculated as (n / N) * 100
*Dark Area corresponds to negative dysphotopsia

Table 21: Visual Disturbance Severity, Safety Analysis Set

	PanOptix® IOL N=129						Monofocal IOL N=114					
		Severity						Severity				
Visual Disturbance	**n**	**None %**	**A Little %**	**Mild %**	**Moderate %**	**Severe %**	**n**	**None %**	**A Little %**	**Mild %**	**Moderate %**	**Severe %**
Glare	126	49.2	7.9	21.4	18.3	3.2	111	67.6	3.6	13.5	13.5	1.8
Halos	127	36.2	9.4	18.9	22.8	12.6	110	77.3	7.3	8.2	6.4	0.9
Starbursts	125	44.0	2.4	10.4	27.2	16.0	109	73.4	8.3	9.2	7.3	1.8
Hazy vision	125	84.0	4.0	6.4	5.6	0.0	110	88.2	1.8	8.2	1.8	0.0
Blurred vision	127	80.3	10.2	8.7	0.8	0.0	111	82.0	6.3	9.0	2.7	0.0
Double vision	125	96.0	4.0	0.0	0.0	0.0	110	98.2	0.9	0.9	0.0	0.0
Dark Area*	127	89.8	3.9	3.9	2.4	0.0	111	88.3	6.3	3.6	1.8	0.0

Percentage calculated as (n / N) * 100
*Dark Area corresponds to negative dysphotopsia

Fundus Visualization

There was no reported difficulty in fundus visualization at any postoperative visits for the first or second eyes in the study.

Device Failures

One device failure of the IOL incorrectly folded into the inserter occurred with the TFNT00 lens in the study. This device failure did not lead to a complication or an AE for the eye.

Patient Satisfaction

A Patient Reported Outcome Measure instrument was developed for use in this clinical study to assess descriptive patient satisfaction results following implantation with the IOL. **Table 22** provides the results.

Table 22: IOLSAT: Satisfaction with Your Vision (Collected at 6 Months) (All-Implanted Analysis Set)

		PanOptix® IOL (N = 129)	Monofocal IOL (N = 114)
Question	**Response**	**n (%)**	**n (%)**
In the past 7 days, how satisfied were you with your vision?	Total	127	110
	Very Dissatisfied	2 (1.6)	0 (0.0)
	Dissatisfied	2 (1.6)	3 (2.7)
	Neither Satisfied nor Dissatisfied	2 (1.6)	7 (6.4)
	Satisfied	27 (21.3)	34 (30.9)
	Very Satisfied	94 (74.0)	66 (60.0)
Given your vision today, if you had to do it all over, would you have the same lenses implanted again?	Total	127	111
	No	1 (0.8)	14 (12.6)
	Yes	126 (99.2)	97 (87.4)
Given your vision today, would you recommend the lenses you had implanted to your family or friends?	Total	127	110
	No	2 (1.6)	5 (4.5)
	Yes	125 (98.4)	105 (95.5)
Percentage calculated as (n / Total) * 100			

2. Effectiveness Results

The analyses of effectiveness were based on the 240 evaluable subjects at the 6-month time point. Key effectiveness outcomes are presented in Tables 23-26.

The co-primary effectiveness objectives were to demonstrate statistical non-inferiority in mean photopic monocular BCDVA (non-inferiority margin of 0.1 logMAR) and to demonstrate statistical superiority of mean photopic monocular DCNVA for the first operative eyes at Month 6. With respsect to BCDVA, non-inferiority of TFNT00 to SN60AT was demonstrated as the 95% upper confidence limit of the difference of the least squared means (0.04 logMAR) was less than the margin of 0.1 logMAR. The second co-primary effectiveness objective was also met because results demonstrated a statistically significant difference in population means for DCNVA of 0.42 logMAR in favor of TFNT00. The secondary effectiveness objectives were to demonstrate statistical superiority of mean photopic monocular DCIVA for first operative eyes at Month 6 and the superiority of TFNT00 compared to the concurrent control SN60AT in proportion of subjects who respond “Never” to Q1 of the IOLSAT questionnaire (Overall, in the past 7 days, how often did you need to wear eyeglasses to see?) at Month 6. A statistically significant difference in population means for DCIVA of 0.26 logMAR was observed in favor of TFNT00. Superiority of TFNT00 to SN60AT in proportion of subjects who respond “Never”

was demonstrated, based on the 71.2% statistically significant difference in proportions, in favor of TFNT00.

All eyes with successful IOL implantation and at least one post-operative visit were considered evaluable for the All Implanted analyses. All eyes successfully implanted that had at least one postoperative visit and had no preoperative ocular pathology or macular degeneration at any time were evaluable for Best Case analyses. The Best Case data set was the primary data set for contrast sensitivity and binocular defocus analyses. The analyses for the astigmatic blur sub-study were performed on the "Astigmatic Blur Sub-Study Set (ABS)", which included a subset of the best case data set. All eyes with attempted IOL implantation (successful or aborted after contact with the eye) were considered evaluable for the safety analyses. The Safety Analysis Set (SAS) was the primary set for all safety analyses except contrast sensitivity. The tables below summarize the information for the pre-specified endpoints of the clinical study.

Monocular Visual Acuity

Visual Acuity was assessed using a computerized test system (CTS, M&S Technologies, Niles, IOL). The first co-primary effectiveness endpoint was statistical non-inferiority of mean photopic monocular BCDVA with a noninferiority margin of 0.1 logMAR. Noninferiority of the PanOptix Trifocal IOL to the monofocal IOL was demonstrated as the 95% upper confidence limit of the difference of least squared means (0.04 logMAR) was less than the margin of 0.1 logMAR for the first operative eyes at Month 6. The other co-primary effectiveness endpoint was statistical superiority of mean photopic monocular DCNVA. A statistically significant difference in population means of 0.42 logMAR was observed in favor of TFNT00 for the first operative eyes at Month 6.

The secondary effectiveness objective was statistical superiority of mean photopic monocular DCIVA. A statistically significant difference in population means of 0.26 logMAR was observed in favor of TFNT00 for the first operative eye at Month 6.

Tables 23 – 26 summarize the monocular visual acuity (VA) endpoint analysis and results for subjects who completed the Form 4A (4-6 months after second eye implantation) visit. The applicant's use of a logMAR-to-Snellen conversion of 0.04 logMAR = 20/20 Snellen acuity was consistent with the previously approved labeling of the parent IOL.

Table 23: Comparison of Mean Photopic Monocular Distance Corrected Visual Acuity (logMAR) in First Eyes Using Least Square Estimates, All Implanted

		PanOptix® IOL (N=129)	Monofocal IOL (N=114)	Difference (95%UCL)
4 m	**n**	127	113	
	Mean	-0.014	-0.039	0.024
	SE	0.008	0.009	0.010
	Snellen line approximate equivalent	20/20	20/20	--
	95% UCL	--	--	0.041
66 cm	**n**	127	113	
	Mean	0.070	0.327	-0.257
	SE	0.011	0.011	0.015
	Snellen line approximate equivalent	20/25	20/40	--
	95% CI	--	--	(-0.287, -0.227)
40 cm	**N**	127	113	
	Mean	0.105	0.529	-0.424
	SE	0.012	0.013	0.017
	Snellen line approximate equivalent	20/25	20/63	--
	95% CI	--	--	(-0.458, -0.390)

Difference = PanOptix® IOL – Monofocal IOL
Estimates were based on the repeated measure analysis of covariance
UCL = Upper confidence limit; SE = Standard error; CI = Confidence interval

Table 24A:

Cumulative Monocular Photopic Distance (4 m) Snellen Visual Acuity by Lens Model, First Eye, All Implanted

				$20/20^{-2}$ or better	**$20/25^{-2}$ or better**	**$20/32^{-2}$ or better**	**$20/40^{-2}$ or better**	**Worse than $20/40^{-2}$**
		N	**Total**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Uncorrected	**PanOptix® IOL**	129	127	57 (44.9)	92 (72.4)	118 (92.9)	124 (97.6)	3 (2.4)
	Monofocal IOL	114	113	57 (50.4)	95 (84.1)	107 (94.7)	112 (99.1)	1 (0.9)
Best Corrected	**PanOptix® IOL**	129	127	104 (81.9)	124 (97.6)	125 (98.4)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	113	100 (88.5)	112 (99.1)	113 (100.0)	113 (100.0)	0 (0.0)

Percentage calculated as (n / Total) * 100
Snellen VA was converted from logMAR VA. A Snellen notation of $20/20^{-2}$ or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

Table 24B:

Cumulative Monocular Photopic Distance (4 m) LogMAR Visual Acuity by Lens Model, First Eye, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	PanOptix® IOL	129	127	39 (30.7)	87 (68.5)	114 (89.8)	124 (97.6)	3 (2.4)
	Monofocal IOL	114	113	42 (37.2)	82 (72.6)	103 (91.2)	108 (95.6)	5 (4.4)
Best Corrected	PanOptix® IOL	129	127	85 (66.9)	121 (95.3)	125 (98.4)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	113	85 (75.2)	111 (98.2)	113 (100.0)	113 (100.0)	0 (0.0)

Percentage calculated as (n / Total) * 100

Table 25A:

Cumulative Monocular Photopic Intermediate (66 cm) Snellen Visual Acuity by Lens Model, First Eye, All Implanted

				20/20^{-2} or better	20/25^{-2} or better	20/32^{-2} or better	20/40^{-2} or better	Worse than 20/40^{-2}
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	PanOptix® IOL	129	127	47 (37.0)	90 (70.9)	113 (89.0)	123 (96.9)	4 (3.1)
	Monofocal IOL	114	113	13 (11.5)	32 (28.3)	64 (56.6)	82 (72.)6	31 (27.4)
Distance Corrected	PanOptix® IOL	129	127	63 (49.6)	103 (81.1)	119 (93.7)	126 (99.2)	1 (0.8)
	Monofocal IOL	114	113	0 (0.0)	8 (7.1)	39 (34.5)	67 (59.3)	46 (40.7)

Percentage calculated as (n / Total) * 100
Snellen VA was converted from logMAR VA. A Snellen notation of 20/20^{-2} or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

Table 25B:

Cumulative Photopic Monocular Photopic Intermediate (66 cm) LogMAR Visual Acuity by Lens Model, First Eye, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	PanOptix® IOL	129	127	21 (16.5)	70 (55.1)	102 (80.3)	119 (93.7)	8 (6.3)
	Monofocal IOL	114	113	7 (6.2)	21 (18.6)	50 (44.2)	74 (65.5)	39 (34.5)
Distance Corrected	PanOptix® IOL	129	127	40 (31.5)	89 (70.1)	115 (90.6)	124 (97.6)	3 (2.4)
	Monofocal IOL	114	113	0 (0.0)	3 (2.7)	30 (26.5)	49 (43.4)	64 (56.6)

Percentage calculated as (n / Total) * 100

Table 26A:

Cumulative Monocular Near (40 cm) Snellen Visual Acuity by Lens Model, First Eye, All Implanted

				20/20^{-2} or better	20/25^{-2} or better	20/32^{-2} or better	20/40^{-2} or better	Worse than 20/40^{-2}
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected Photopic	PanOptix® IOL	129	127	32 (25.2)	83 (65.4)	112 (88.2)	121 (95.3)	6 (4.7)
	Monofocal IOL	114	113	0 (0.0)	2 (1.8)	16 (14.2)	34 (30.1)	79 (69.9)
Distance Corrected Photopic	PanOptix® IOL	129	127	34 (26.8)	96 (75.6)	120 (94.5)	125 (98.4)	2 (1.6)
	Monofocal IOL	114	113	0 (0.0)	0 (0.0)	3 (2.7)	21 (18.6)	92 (81.4)
Distance Corrected Mesopic	PanOptix® IOL	129	127	3 (2.4)	20 (15.7)	54 (42.5)	97 (76.4)	30 (23.6)
	Monofocal IOL	114	113	0 (0.0)	1 (0.9)	5 (4.4)	8 (7.1)	105 (92.9)

			20/20^{-2} or better	20/25^{-2} or better	20/32^{-2} or better	20/40^{-2} or better	Worse than 20/40^{-2}
	N	**Total**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Percentage calculated as (n / Total) * 100 Snellen VA was converted from logMAR VA. A Snellen notation of 20/20^{-2} or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.							

Table 26B:

Cumulative Monocular Near (40 cm) LogMAR Visual Acuity by Lens Model, First Eye, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	**Total**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Uncorrected Photopic	**PanOptix® IOL**	129	127	15 (11.8)	62 (48.8)	104 (81.9)	119 (93.7)	8 (6.3)
	Monofocal IOL	114	113	0 (0.0)	1 (0.9)	11 (9.7)	28 (24.8)	85 (75.2)
Distance Corrected Photopic	**PanOptix® IOL**	129	127	13 (10.2)	78 (61.4)	117 (92.1)	124 (97.6)	3 (2.4)
	Monofocal IOL	114	113	0 (0.0)	0 (0.0)	2 (1.8)	16 (14.2)	97 (85.8)
Distance Corrected Mesopic	**PanOptix® IOL**	129	127	2 (1.6)	10 (7.9)	38 (29.9)	87 (68.5)	40 (31.5)
	Monofocal IOL	114	113	0 (0.0)	1 (0.9)	5 (4.4)	6 (5.3)	107 (94.7)
Percentage calculated as (n / Total) * 100								

Binocular Visual Acuity

There were clinically relevant differences in mean photopic binocular Distance Corrected Visual Acuity (DCVA) at 40 cm and 66 cm for subjects implanted with the PanOptix® IOL compared with subjects implanted with the control Monofocal IOL. The following is a summary of photopic binocular visual acuity (VA) results for subjects who completed the Form 4A (6 months after second eye implantation) visit. The data are presented in **Tables 27 – 31** below.

Table 27: Overall Comparison of Mean (±SD) Photopic Binocular Distance-Corrected Visual Acuity (logMAR), All Implanted

	Near VA @ 40 cm		Intermediate VA @ 66 cm		Distance VA	
Model	**logMAR**	**Snellen Line Approximate Equivalent**	**logMAR**	**Snellen Line Approximate Equivalent**	**logMAR**	**Snellen Line Approximate Equivalent**
PanOptix® IOL	0.050 (0.070)	20/25	-0.007 (0.079)	20/20	-0.062 (0.066)	20/16
Monofocal IOL	0.406 (0.148)	20/50	0.230 (0.124)	20/32	-0.086 (0.063)	20/16

Table 28A:

Cumulative Binocular Near (40 cm) Snellen Visual Acuity by Lens Model, All Implanted

				$20/20^{-2}$ or better	**$20/25^{-2}$ or better**	**$20/32^{-2}$ or better**	**$20/40^{-2}$ or better**	**Worse than $20/40^{-2}$**
		N	**Total**	**n (%)**	**n (%)**	**n (%)**	**n (%)**	**n (%)**
Uncorrected Photopic	**PanOptix® IOL**	129	127	63 (49.6)	117 (92.1)	125 (98.4)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	1 (0.9)	10 (9.0)	38 (34.2)	67 (60.4)	44 (39.6)
Distance Corrected Photopic	**PanOptix® IOL**	129	127	60 (47.2)	122 (96.1)	127 (100.0)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	0 (0.0)	0 (0.0)	18 (16.2)	44 (39.6)	67 (60.4)
Distance Corrected Mesopic	**PanOptix® IOL**	129	127	5 (3.9)	33 (26.0)	85 (66.9)	119 (93.7)	8 (6.3)
	Monofocal IOL	114	111	0 (0.0)	2 (1.8)	6 (5.4)	12 (10.8)	99 (89.2)

Percentage calculated as (n / Total) * 100
Snellen VA was converted from logMAR VA. A Snellen notation of $20/20^{-2}$ or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

Table 28B:

Cumulative Binocular Near (40 cm) LogMAR Visual Acuity by Lens Model, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected Photopic	**PanOptix® IOL**	129	127	40 (31.5)	106 (83.5)	123 (96.9)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	0 (0.0)	6 (5.4)	24 (21.6)	56 (50.5)	55 (49.5)
Distance Corrected Photopic	**PanOptix® IOL**	129	127	32 (25.2)	105 (82.7)	127 (100.0)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	0 (0.0)	0 (0.0)	11 (9.9)	30 (27.0)	81 (73.0)
Distance Corrected Mesopic	**PanOptix® IOL**	129	127	4 (3.1)	16 (12.6)	63 (49.6)	111 (87.4)	16 (12.6)
	Monofocal IOL	114	111	0 (0.0)	0 (0.0)	5 (4.5)	9 (8.1)	102 (91.9)

Percentage calculated as (n / Total) * 100

Table 29A:

Cumulative Binocular Photopic Intermediate (66 cm) Snellen Visual Acuity by Lens Model, All Implanted

				20/20^{-2} or better	20/25^{-2} or better	20/32^{-2} or better	20/40^{-2} or better	Worse than 20/40^{-2}
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	PanOptix® IOL	129	127	93 (73.2)	119 (93.7)	124 (97.6)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	25 (22.5)	56 (50.5)	85 (76.6)	102 (91.9)	9 (8.1)
Distance Corrected	PanOptix® IOL	129	127	104 (81.9)	124 (97.6)	127 (100.0)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	6 (5.4)	29 (26.1)	71 (64.0)	92 (82.9)	19 (17.1)

Percentage calculated as (n / Total) * 100
Snellen VA was converted from logMAR VA. A Snellen notation of 20/20^{-2} or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

Table 29B:

Cumulative Binocular Photopic Intermediate (66 cm) LogMAR Visual Acuity by Lens Model, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	PanOptix® IOL	129	127	69 (54.3)	109 (85.8)	123 (96.9)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	16 (14.4)	50 (45.0)	75 (67.6)	96 (86.5)	15 (13.5)
Distance Corrected	PanOptix® IOL	129	127	80 (63.0)	118 (92.9)	126 (99.2)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	3 (2.7)	15 (13.5)	54 (48.6)	85 (76.6)	26 (23.4)

Percentage calculated as (n / Total) * 100

Table 30A:

Cumulative Binocular Photopic Distance (4 m) Snellen Visual Acuity by Lens Model, All Implanted

				20/20^{-2} or better	20/25^{-2} or better	20/32^{-2} or better	20/40^{-2} or better	Worse than 20/40^{-2}
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	**PanOptix® IOL**	129	127	93 (73.2)	117 (92.1)	126 (99.2)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	87 (78.4)	105 (94.6)	110 (99.1)	111 (100.0)	0 (0.0)
Best Corrected	**PanOptix® IOL**	129	127	123 (96.9)	127 (100.0)	127 (100.0)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	109 (98.2)	111 (100.0)	111 (100.0)	111 (100.0)	0 (0.0)

Percentage calculated as (n / Total) * 100
Snellen VA was converted from logMAR VA. A Snellen notation of 20/20^{-2} or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.

Table 30B:

Cumulative Binocular Photopic Distance (4 m) LogMAR Visual Acuity of by Lens Model, All Implanted

				0.00 logMAR or better	0.10 logMAR or better	0.20 logMAR or better	0.30 logMAR or better	Worse than 0.30 logMAR
		N	Total	n (%)	n (%)	n (%)	n (%)	n (%)
Uncorrected	**PanOptix® IOL**	129	127	82 (64.6)	109 (85.8)	123 (96.9)	126 (99.2)	1 (0.8)
	Monofocal IOL	114	111	76 (68.5)	102 (91.9)	107 (96.4)	110 (99.1)	1 (0.9)
Best Corrected	**PanOptix® IOL**	129	127	111 (87.4)	126 (99.2)	127 (100.0)	127 (100.0)	0 (0.0)
	Monofocal IOL	114	111	104 (93.7)	111 (100.0)	111 (100.0)	111 (100.0)	0 (0.0)

Percentage calculated as (n / Total) * 100

Table 31A shows the proportion of subjects achieving each Snellen level or better uncorrected binocular visual acuity for all distances (distance – 4 m, intermediate – 66 cm, near – 40 cm). 95.3% of the PanOptix® IOL subjects achieved 20/32 at all distances while Table **31B** shows the logMAR visual acuity.

Table 31A: Proportion of Subjects Achieving Snellen VA Thresholds for the Near, Intermediate, and Distance Uncorrected Photopic Binocular Visual Acuity, All Implanted

Snellen Category	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)
Total	127	111
$20/20^{-2}$ or better	50 (39.4)	1 (0.9)
$20/25^{-2}$ or better	106 (83.5)	9 (8.1)
$20/32^{-2}$ or better	121 (95.3)	37 (33.3)
$20/40^{-2}$ or better	127 (100.0)	66 (59.5)
Worse than $20/40^{-2}$	0 (0.0)	45 (40.5)
Percentage calculated as (n / Total) * 100 Snellen VA was converted from logMAR VA. A Snellen notation of $20/20^{-2}$ or better indicates a logMAR VA of 0.04 or better, which means 3 or more of the 5 ETDRS chart letters in the line were identified correctly.		

Table 31B: Proportion of Subjects Achieving LogMAR VA Thresholds for the Near, Intermediate, and Distance Uncorrected Photopic Binocular Visual Acuity, All Implanted

Snellen Category	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)
Total	127	111
0.00 logMAR or better	25 (19.7)	0 (0.0)
0.10 logMAR or better	89 (70.1)	4 (3.6)
0.20 logMAR or better	117 (92.1)	23 (20.7)
0.30 logMAR or better	126 (99.2)	55 (49.5)
Worse than 0.30 logMAR	1 (0.8)	56 (50.5)
Percentage calculated as (n / Total) * 100		

Binocular Defocus Curves

Binocular defocus curves were obtained at 6 months for the PanOptix IOL and the Monofocal IOL and are shown in **Figure 9** with 95% confidence intervals error bars and in **Figure 10** with error bars representing 1 Standard Deviation. Vertical lines indicate the distance (optical infinity), intermediate, and near visual acuity testing distance. Binocular defocus curves obtained at 6 months stratified by post-operative (6 months) pupil size are presented in **Figures 11** and **12** for the PanOptix IOL and the Monofocal IOL, respectively.

Data were obtained from best-case subjects in each arm using a computerized visual acuity test system (CTS, M&S Technologies, Niles, IL). The curves display two peaks and one peak respectively that demonstrate the PanOptix IOL versus Monofocal IOL performance. The main peak, or single peak for the Monofocal IOL,

is at the zero defocus baseline position, which corresponds to optical infinity. For the PanOptix IOL, an additional peak demonstrates the improved performance compared to a monofocal IOL. The PanOptix IOL provided mean performance of 0.1 logMAR or better vision (depth of focus) from -2.5 D to 0.00 D, corresponding to a range of distances from approximately 40 cm to infinity.

Figure 9: Mean Binocular Defocus Curves with 95% Confidence Limits by Lens Model at 6 Months, Best-Case

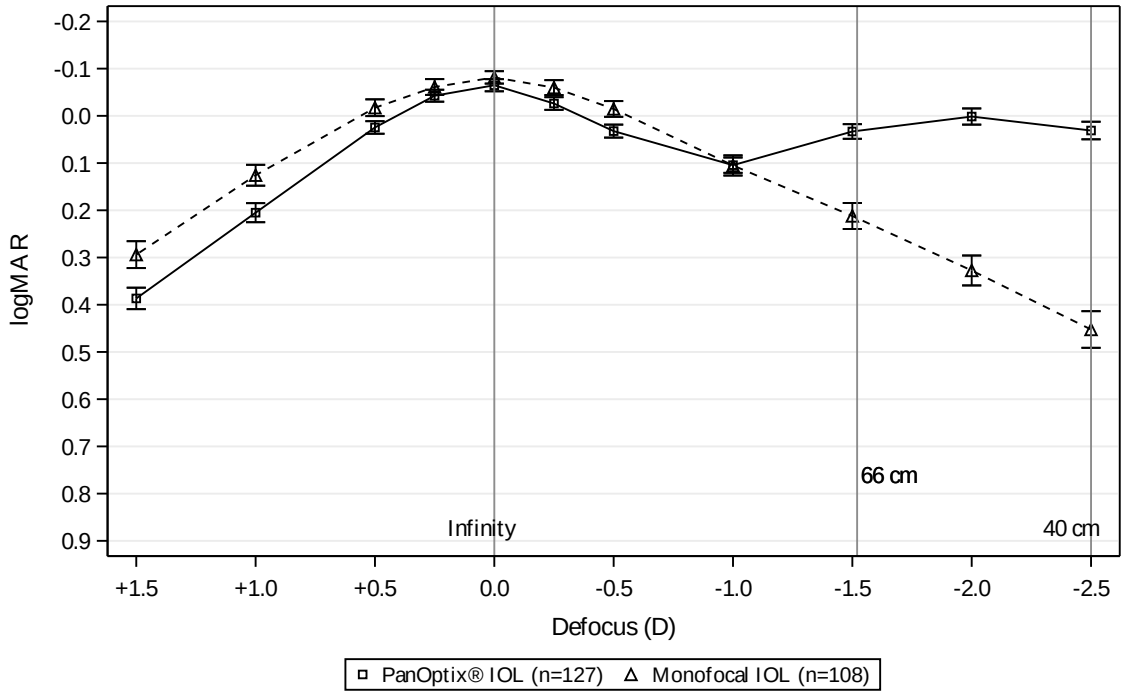


Figure 10: Mean Binocular Defocus Curves with ±1 Standard Deviations by Lens Model at 6 Months, Best-Case

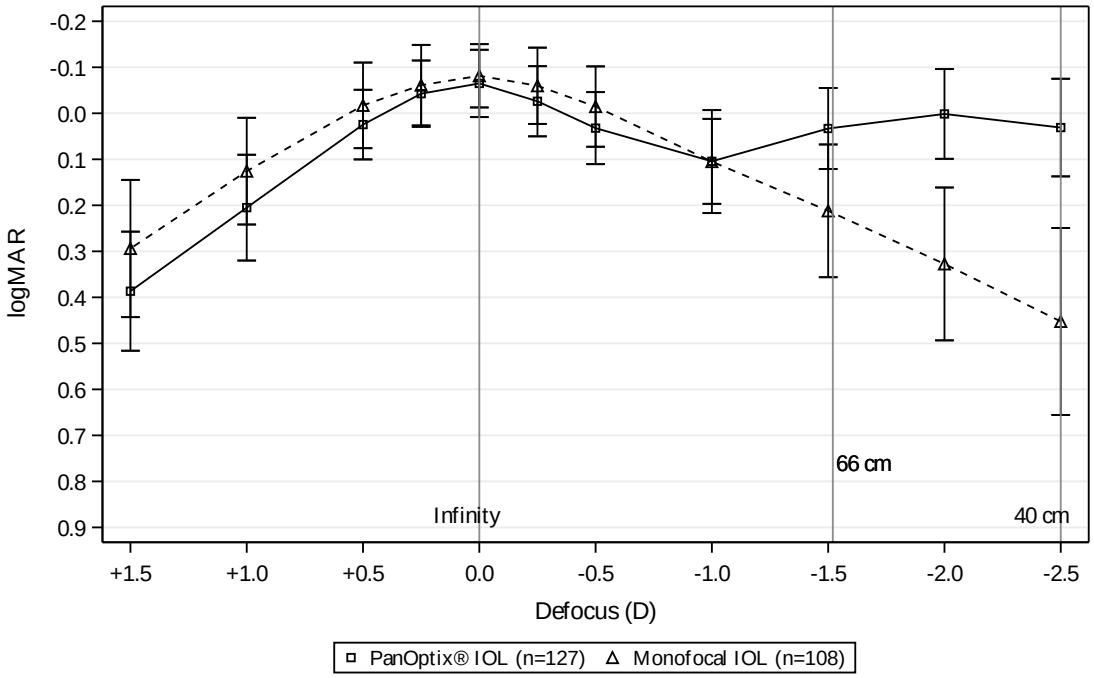


Figure 11: Mean Binocular Defocus Curves (logMAR) by Post-operative Pupil Size Category at 6 Months, Best-Case

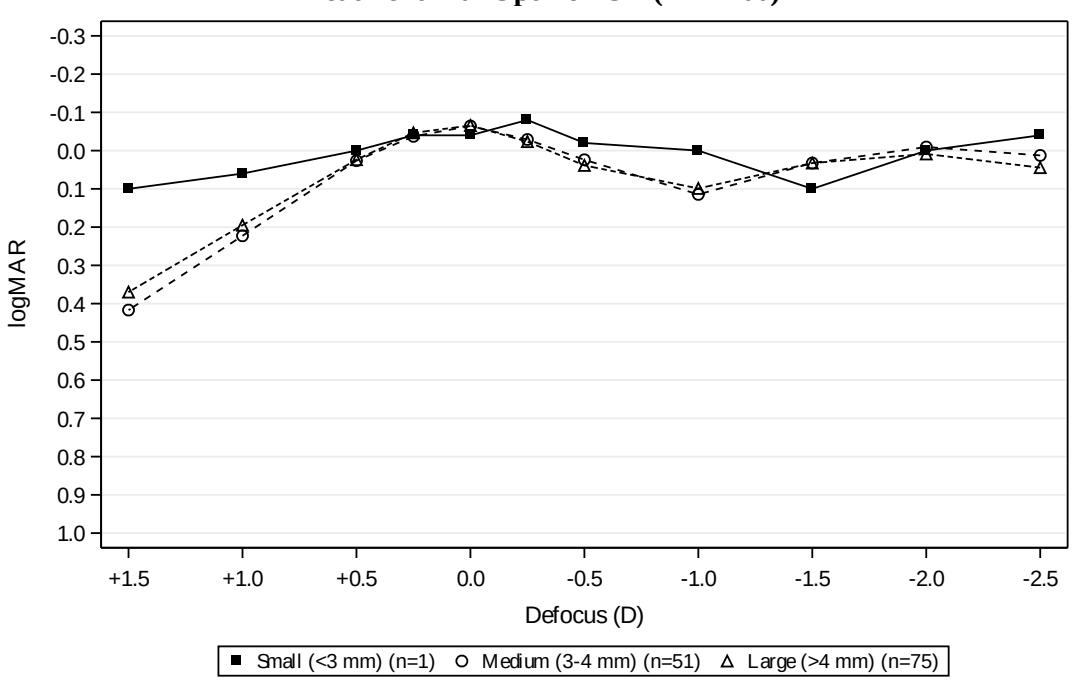
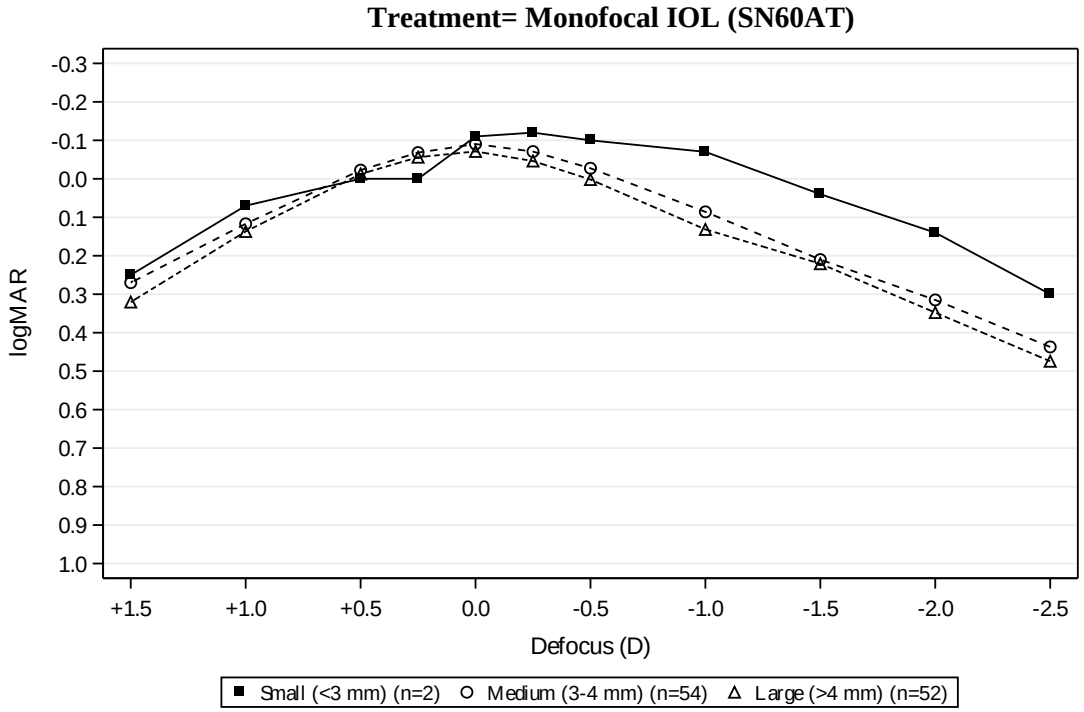


Figure 12: Mean Binocular Defocus Curves (logMAR) by Post-operative Pupil Size Category at 6 Months, Best-Case



Astigmatic Blur Sub-Study

To assess the potential effect of residual astigmatism on visual performance, four different residual astigmatism conditions (1.0 D and 1.5 D of mixed astigmatism, with and against the rule) were added to each subject's distance correction and visual acuity tested at 4 m, 66 cm, and 40 cm. Testing was planned for 30 best-case subjects for both the test and control groups across five clinical sites. Subjects were excluded from the sub-study if they had oblique post-operative residual astigmatism (axis between 30 to 60 degrees or 120 to 150 degrees). Baseline characteristics for these subjects are shown in **Table 32** below.

Table 32: Baseline Characteristics, First Eye, Astigmatic Blur Sub-Study Set

	PanOptix® IOL (N = 38)	Monofocal IOL (N = 33)	Overall (N = 71)
Age (Years), n (%)			
< 65	**13 (34.2)**	**7 (21.2)**	**20 (28.2)**
≥ 65	**25 (65.8)**	**26 (78.8)**	**51 (71.8)**
Mean (SD)	**64.5 (8.02)**	**69.1 (6.77)**	**66.6 (7.77)**
Median	**66.5**	**68.0**	**67.0**
(Min, Max)	**(44, 79)**	**(58, 84)**	**(44, 84)**
Sex, n (%)			
Female	**27 (71.1)**	**21 (63.6)**	**48 (67.6)**
Male	**11 (28.9)**	**12 (36.4)**	**23 (32.4)**
Race, n (%)			
White	**32 (84.2)**	**30 (90.9)**	**62 (87.3)**
Black or African American	**4 (10.5)**	**3 (9.1)**	**7 (9.9)**
American Indian or Alaska Native	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Asian	**2 (5.3)**	**0 (0.0)**	**2 (2.8)**
Native Hawaiian or Other Pacific Islander	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Other	**0 (0.0)**	**0 (0.0)**	**0 (0.0)**
Mesopic Pupil Size (mm)			
n	**38**	**33**	**71**
Mean (SD)	**4.67 (1.22)**	**4.70 (1.05)**	**4.68 (1.13)**
Median	**5.0**	**4.5**	**5.0**
(Min, Max)	**(2.0, 7.5)**	**(2.5, 7.0)**	**(2.0, 7.5)**
Photopic Pupil Size (mm)			
n	**38**	**33**	**71**
Mean (SD)	**4.28 (0.76)**	**3.94 (0.85)**	**4.12 (0.82)**
Median	**4.0**	**4.0**	**4.0**
(Min, Max)	**(3.0, 6.0)**	**(2.0, 5.5)**	**(2.0, 6.0)**
Absolute Refractive Cylinder (D)			
n	**38**	**33**	**71**
Mean (SD)	**0.171 (0.329)**	**0.235 (0.306)**	**0.201 (0.318)**
Median	**0.00**	**0.00**	**0.00**
(Min, Max)	**(0.00, 1.50)**	**(0.00, 1.00)**	**(0.00, 1.50)**

Percentage calculated as (n / N) * 100
N = Number of eyes in each treatment group
n = Number of eyes at visit
SD = Standard Deviation
Baseline = Preoperative
Absolute refractive cylinder collected at 6-months

A within-subject analysis of the mean paired differences in *distance* VA before and after inducing blur, showed a maximum of 0.28 logMAR mean reduction and 0.22 logMAR mean reduction for the PanOptix® IOL and Monofocal Control subjects respectively, indicating a less than 1 line difference between the two groups, regardless of the orientation of astigmatism or cylinder magnitude.

A within-subject analysis of the mean paired differences in *near* VA before and after inducing blur, showed minimal impact of induced astigmatism on monocular and binocular near VA for the PanOptix® IOL subjects, with a maximum of 0.12 logMAR mean reduction, irrespective of the orientation of astigmatism or cylinder magnitude.

A within-subject analysis of the mean paired differences in *intermediate* VA before and after inducing blur, also showed minimal impact of induced astigmatism on monocular and binocular intermediate VA for the PanOptix® IOL subjects, with a maximum of 0.14 logMAR mean reduction, irrespective of the orientation of astigmatism or cylinder magnitude. Under simulated astigmatic blur conditions, the resultant mean intermediate and mean near visual acuity remained better than 0.23 logMAR for the PanOptix® IOL group.

The results of the astigmatic blur sub-study demonstrated small differences in visual acuity after blur induction. However, subjects that have significant toric lens misalignment from the intended position, or errors in the estimated postoperative astigmatism, are still likely to achieve poorer results with respect to uncorrected visual acuities (far, intermediate, and near), rates of spectacle wear, and rates of secondary surgical interventions (to correct axial misalignment).

Need for Eyeglasses/Contact Lenses

A Patient Reported Outcome Measure instrument was developed and validated for use in this clinical study to assess need for eyeglass/contact lens following implantation with the IOL. **Table 33** provides the proportions of subjects who responded "never" to Question 1 (Q1) "Overall, in the past 7 days, how often did you need to wear eyeglasses to see?" In the study, PanOptix® IOL was shown to be superior in the proportion of subjects who responded "never" compared to the Monofocal IOL control subjects (80.5% to 8.2%).

Table 33
Proportion of Subjects Who Respond "Never" to Q1 of the IOLSAT Questionnaire at 6 Months, All Implanted

	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)	Difference	
			%	(95% CI)
Total	123	110		
Never	99 (80.5)	9 (8.2)	71.2	(61.87, 80.46)
Percentage calculated as (n / Total) * 100 Difference = PanOptix® IOL – Monofocal IOL				

	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)	Difference	
			%	(95% CI)
Treatment 1 - Treatment 2 estimate based on Mantel-Haenszel common difference in proportions stratified by site CI = Confidence Interval for the common difference, Response scored per user manual				

Additionally, the need for eyeglasses or contact lenses was evaluated using the IOLSAT questionnaire at three specific distances by all subjects. The responses are shown in **Tables 34** to **36**.

Table 34 provides the proportions for each response to Question 2 (Q2) "In the past 7 days, how often did you need to wear eyeglasses to see **'up close'** (for example, reading a book)?"

Table 34: Proportion of Subject Responses to Q2 of the IOLSAT Questionnaire at 6 Months (All-Implanted Analysis Set)

	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)
Total	122	110
Never	102 (83.6)	9 (8.2)
Rarely	10 (8.2)	4 (3.6)
Sometimes	7 (5.7)	18 (16.4)
Most of the time	2 (1.6)	35 (31.8)
All the time	1 (0.8)	44 (40.0)
Percentage calculated as (n / Total) * 100		

Table 35 provides the proportions for each response to Question 3 (Q3) "In the past 7 days, how often did you need to wear eyeglasses to see **'at arm's length'** (for example, using an ATM or seeing the dashboard of a car)?"

Table 35: Proportion of Subject Responses to Q3 of the IOLSAT Questionnaire at 6 Months (All-Implanted Analysis Set)

	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)
Total	122	110
Never	115 (94.3)	45 (40.9)
Rarely	6 (4.9)	29 (26.4)
Sometimes	0 (0.0)	20 (18.2)
Most of the time	1 (0.8)	12 (10.9)
All the time	0 (0.0)	4 (3.6)
Percentage calculated as (n / Total) * 100		

Table 36 provides the proportions for each response to Question 4 (Q4) "In the past 7 days, how often did you need to wear eyeglasses to see **'far away'** (for example, seeing street signs)?"

Table 36: Proportion of Subject Responses to Q4 of the IOLSAT Questionnaire at 6 Months (All-Implanted Analysis Set)

	PanOptix® IOL (N = 129) n (%)	Monofocal IOL (N = 114) n (%)
Total	122	110
Never	117 (95.9)	93 (84.5)
Rarely	2 (1.6)	5 (4.5)
Sometimes	1 (0.8)	8 (7.3)
Most of the time	1 (0.8)	2 (1.8)
All the time	1 (0.8)	2 (1.8)
Percentage calculated as (n / Total) * 100		

3. Subgroup Analyses
   A subgroup analysis of the co-primary effectiveness endpoints (BCDVA at 4 m, DCNVA at 40 cm) and the first secondary endpoint (DCIVA at 66 cm) was completed by age category, site, ocular AEs, and preoperative pathology. Although age category and site were found to have significant interaction effect with the treatment group regarding DCNVA and DCIVA, the differences were found to be only quantitative, but not qualitative. The results indicated no impact of presence of AEs or preoperative ocular pathology on the primary or secondary endpoint results.

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 12 investigators of which none were full-time or part-time employees of the sponsor and 6 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
- Significant payment of other sorts: 6
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

The applicant has adequately disclosed the financial interest/arrangements with clinical investigators. Statistical analyses were conducted by FDA to determine whether the financial interests/arrangements had any impact on the clinical study outcome. The information provided does not raise any questions about the reliability of the data.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Two relevant studies were conducted on the parent models that were part of prior FDA approvals:

1. Comparing AcrySof® IQ ReSTOR® Multifocal IOL (Models MA60D3 and SA60D3) with AcrySof® monofocal IOL model MA60BM. Models MA60D3 and SA60D3 were approved under PMA P040020 on March 21, 2005).

2. Comparing AcrySof® IQ ReSTOR® 3.0 D Toric Multifocal IOL (Models SND1T3, SND1T4, SND1T5, and SND1T6) with AcrySof® IQ ReSTOR (+4.0 D Add) Multifocal IOL Model SA60D3. Models SND1T3, SND1T4, SND1T5, and SND1T6 were approved under P040020/S049 on December 22, 2016.

No issues regarding device safety or lack of effectiveness were raised by the results from these studies.

Additional data are incorporated in the product labeling by reference to the parent lenses, the AcrySof® IQ ReSTOR® Multifocal IOL (Models MA60D3 and SA60D3) and the AcrySof® IQ ReSTOR® 3.0 D Toric Multifocal IOL (Models SND1T3, SND1T4, SND1T5, and SND1T6). Additional tables describing sign identification and hazard detection distances were incorporated from PMA P040020. Additional tables describing visual acuities, lens axis orientation and rotation, and adverse events were incorporated from PMA P040020/S049.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The overall effectiveness of the AcrySof® IQ PanOptix® Trifocal, Model TFNT00, was demonstrated based on the 6-month results of the IDE clinical investigation. In addition, the effectiveness of the toric models (Models TFNT30, TFNT40, TFNT50, TFNT60) in providing reduced postoperative refractive astigmatism is supported by the clinical data provided for the toric parent IOL in P040020/S049, which has the same toric surface and mechanical/material design (differing only in the diffractive pattern of the optical design).

The first co-primary effectiveness endpoint (non-inferiority of mean monocular BCDVA) was met. The second co-primary effectiveness endpoint (superiority of DCNVA) was met with both a statistically significant and clinically meaningful difference between the PanOptix and monofocal control arms of approximately 4 logMAR lines of vision. The first secondary effectiveness endpoint (superiority of mean monocular DCIVA) was also met with a statistically significant and clinically meaningful difference between arms of approximately 2.5 logMAR lines. The second secondary effectiveness endpoint was related to a patient-reported outcome measure assessment of overall need for eyeglasses. Although the analysis of this endpoint appeared to support statistical success, it was determined that the proposed analysis of the patient-reported outcome measure was appropriate to support an indications for use claim regarding need for eyeglasses.

Overall, this study has demonstrated effectiveness of the AcrySof® IQ PanOptix® Trifocal IOL to provide improved intermediate and near visual acuity compared to a monofocal IOL with a reduced need for eyeglasses, while maintaining comparable distance visual acuity.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as a primary clinical study conducted to support PMA approval as described above. In addition, the clinical data from the U.S. studies for the parent IOLs, AcrySof IQ ReSTOR +3.0 D Multifocal IOL Model SN6AD1 (P040020/S012) and AcrySof IQ ReSTOR +3.0 D Toric IOL Model SND1T3-T6 (P040020/S049), provided data that

are relevant to PanOptix device safety. These studies of the parent IOLs included 1 year of follow-up on at least 300 subjects.

The AcrySof® IQ PanOptix® Trifocal Intraocular lenses 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 (P930014/S009, Model SB30EL). The results of prior nonclinical laboratory testing and animal studies on the AcrySof acrylic material and the one-piece lens design support safety of this lens model. The results of biocompatibility testing, dimensional, optical and mechanical testing, and chemical testing demonstrated conformance to applicable sections of ISO 10993-1, ISO 10993-3, ISO 10993-5, ISO 10993-6, ISO 10993-10, ISO 10993-12, ISO 10993-18, ISO 11979-2, ISO 11979-3, ISO 11979-5, ISO 11979-9, ANSI Z80.12, and ANSI Z80.30 and internal product specifications.

The 6-month results of the IDE clinical investigation of the AcrySof® IQ PanOptix® Trifocal, Model TNFT00, provide reasonable assurance of the safety of this lens model. The incidence of adverse events in the study was 3.1% (4/129 subjects) for PanOptix subjects and 2.0% (2/114 subjects) for control subjects with regards to serious adverse events. No subjects in either group experienced unanticipated adverse events. The observed persistent and cumulative complication/adverse event rates for the AcrySof® IQ PanOptix® Trifocal were not statistically higher than the specified ISO SPE (safety performance endpoint) rates.

The binocular contrast sensitivity results were slightly reduced for the PanOptix IOL compared to the monofocal control IOL. However, the differences were not clinically meaningful. Visual disturbances of starbursts, halos, and glare were the most frequently rated "severe" symptoms in the TFNT00 group. Starbursts, halos, and glare were also rated as the most bothersome symptoms by subjects in the TFNT00 group; however, less than 5% of subjects rated these symptoms as "bothered very much" at Month 6.

C. Benefit-Risk Determination

The probable benefits and risks of the AcrySof® IQ PanOptix® Trifocal Intraocular lenses, Models TFNT00, TFNT30, TFNT40, TFNT50, TFNT60), are based on data collected in a clinical study conducted to support PMA approval and other clinical studies, as described above. This study has demonstrated statistically significant and clinically meaningful results in favor of the PanOptix IOL regarding preservation of BCDVA, and improvement in DCNVA and DCIVA, compared to a monofocal control. Medical adverse events and complications (e.g., risks of infection, inflammation, corneal edema, etc.) were similar to those associated with most other intraocular lenses. Contrast sensitivity and device explants due to optical properties are the main additional safety concerns for multifocal IOLs, including trifocal IOLs, compared to monofocal IOLs (the most commonly used alternative treatment).

Adverse event rates, including SSIs, were not clinically concerning for the PanOptix IOL.

Additional factors to be considered in determining probable risks and benefits for the AcrySof® IQ PanOptix® Trifocal Intraocular lenses included:

- There was a low uncertainty in the quality of the study design, study conduct, and the study results.
- Potential issues related to contrast sensitivity and subjective visual symptoms are mitigated by labeling which informs users of these risks and quantifies them.
- Patient Perspectives: This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information above, the data support that for the visual correction of aphakia in patients for whom a cataract lens has been removed, and for mitigating the effects of presbyopia in these patients by providing improved intermediate and near visual acuity while maintaining comparable distance visual acuity with a reduced need for eyeglasses, compared to a monofocal IOL, the probable benefits of the Acrysof® IQ PanOptix® Trifocal IOL Model (TFNT00) outweigh the probable risks. Similarly, the data support that for the visual correction of aphakia and the reduction of residual refractive astigmatism, in adult patients in whom a cataractous lens has been removed, and for mitigating the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity with a reduced need for eyeglasses, compared to a monofocal IOL, the probable benefits of the toric models of the Acrysof® IQ PanOptix® Trifocal IOL outweigh the probable risks.

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 indications for use. Key effectiveness endpoints related to near, intermediate, and distance visual acuity were met, demonstrating the ability of the AcrySof® IQ PanOptix® Trifocal IOL to provide clinically meaningful improvements in intermediate visual acuity and near visual acuity, compared to an aspheric monofocal IOL. Adverse events were compared favorably to grid rates established in an FDA-recognized international standard. Differences between the PanOptix IOL and monofocal IOL with respect to contrast sensitivity were not clinically meaningful.

XIV. CDRH DECISION

CDRH issued an approval order on 8/26/2019.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

International Standard Organization 10993, Biological Evaluation of Medical Devices

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

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

International Standard Organization 11979-3 Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods

International Standard Organization 11979-7 -Intraocular Lenses – Part 7: Clinical Investigations

Masket S, Rorer E, Stark W, Holladay JT, MacRae S, Tarver ME, et al. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. Ophthalmology. 2017 Jan;124(1):142-144.