SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Intraocular Lens
Device Trade Name:	TECNIS® Symfony Extended Range of Vision IOLs - Model ZXR00; Toric Models: ZXT150, ZXT225, ZXT300 and ZXT375
Device Procode:	POE
Applicant's Name and Address:	Abbott Medical Optics Inc. 1700 East Saint Andrew Place Santa Ana, CA 92705

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P980040/S065

Date of FDA Notice of Approval: July 15, 2016

II. INDICATIONS FOR USE

The TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, is indicated for primary implantation 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 an extended depth of focus. Compared to an aspheric monofocal IOL, the lens provides improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model ZXR00 IOL is intended for capsular bag placement only.

The TECNIS® Symfony Toric Extended Range of Vision IOLs, Models ZXT150, ZXT225, ZXT300, and ZXT375, are indicated for primary implantation for the visual correction of aphakia and for reduction of residual refractive astigmatism in adult patients with greater than or equal to 1 diopter of preoperative corneal astigmatism, in whom a cataractous lens has been removed. The lenses mitigate the effects of presbyopia by providing an extended depth of focus. Compared to an aspheric monofocal IOL, the lenses provide improved intermediate and near visual acuity, while maintaining comparable distance visual acuity. The Model Series ZXT IOLs are intended for capsular bag placement only.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the labeling for the TECNIS® Symfony Extended Range of Vision IOLs, Models ZXR00, ZXT150, ZXT225, ZXT300 and ZXT375.

V. DEVICE DESCRIPTION

The TECNIS® Symfony Extended Range of Vision IOLs, non-toric lens model ZXR00 and toric lens models ZXT150, ZXT225, ZXT300, and ZXT375, are ultraviolet light-absorbing posterior chamber IOLs, which are intended to provide a continuous range of vision without compromise in distance vision. In addition, the toric IOLs compensate for corneal astigmatism.

TECNIS® Symfony Extended Range of Vision IOLs are designed to be positioned in the lens capsule to replace the optical function of the natural crystalline lens. **Table 1**, below describes the physical characteristics of the lenses. The biconvex optic incorporates a proprietary wavefront-designed aspheric or toric-aspheric anterior optic, designed to compensate for corneal spherical aberration. The anteriorlylocated, cylinderaxis marks in the toric-aspheric optic denote the meridian with the lowest power and is to be aligned with the steep corneal meridian. The squared posterior edge of the aspheric and toric-aspheric anterior optic is designed to provide a 360-degree barrier and has a frosted design to reduce potential edge glare effects. The posterior optic of the TECNIS® Symfony Extended Range of Vision IOLs has a proprietary achromatic diffractive surface designed to correct chromatic aberration and a echelette feature to extend the range of vision, including far, intermediate, and near, while maintaining the corneal spherical aberration correction. TECNIS® Symfony IOLs are designed to have pupil-independent lens performance in any lighting condition.

TABLE 1
Summary of Physical Characteristics

TECNIS® Symfony Extended Range of Vision IOLs					
Model Numbers	ZXR00	ZXT150	ZXT225	ZXT300	ZXT375
Optic type	Biconvex Aspheric	Biconvex Aspheric Toric			
Optic/Haptic Material *Measured in Water	Hydrophobic SENSAR soft acrylic material with polyethylene glycol surface treatment UV cutoff at 10% Transmittance: 374nm* (5.00 diopter lens) 375nm* (34.00 diopter lens)				
IOL Spherical Equivalent Power (Diopter)	+5.0 D to +34.0 D in +0.50 D increments				
IOL Cylinder Power, Labeled (Diopter)	N/A	1.50 D	2.25 D	3.00 D	3.75 D
Corneal Plane, approximate (Diopter)	0.0	1.03 D	1.54 D	2.06 D	2.57 D
Index of Refraction	1.47 at 35°C				
Haptic Configuration	TRI-FIX design Modified C, integral with optic				
Optic Diameter	6.0 mm				
Overall Length	13.0 mm				
Haptic Angle	No angulation but offset from optic body				

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of aphakia resulting from surgical cataract removal (i.e., for patients who have had a cataractous lens removed) Non-surgical options include eye glasses or contact lenses. Surgical options come in the form of intraocular lenses, which may be monofocal, multifocal, toric or accommodative, depending on the patient's needs, expectations and lifestyle. 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 TECNIS® Symfony Extended Range of Vision IOLs are currently commercially available in Australia, Canada, European Union, India, New Zealand, Singapore, and many other countries in Latin America, the Middle East-Africa region, and Asia Pacific. The lenses have not been withdrawn or recalled from any country for any reason related to safety or 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:

- Infection (endophthalmitis)
- Hypopyon
- IOL dislocation
- Cystoid macular edema
- Corneal edema
- Pupillary block
- Iritis
- Retinal detachment/tear
- Raised IOP requiring treatment
- Tilt and decentration requiring repositioning
- Residual refractive error resulting in secondary intervention.
- Increased visual symptoms (compared to a monofocal IOL) related to the optical characteristics the IOL, including
    - Reduction in contrast sensitivity. This may cause difficulty when driving, e.g., some decrease in visibility distance for detection/identification of road warnings
    - Bothersome stray-light artifacts such as halos, starbursts, or glare.

Secondary surgical interventions include, but are not limited to:

- Lens repositioning (due to decentration, rotation, subluxation, etc.)
- Lens replacement
- Vitreous aspirations or iridectomy for pupillary block
- Wound leak repair
- Retinal detachment repair
- Corneal transplant
- Severe inflammation.

For the specific adverse events that occurred during the TECNIS® Symfony Extended Range of Vision IOL clinical study, please see the *Summary of Primary Clinical Studies* section below.

IX. SUMMARY OF NONCLINICAL STUDIES

Preclinical studies performed on either parent devices or subject devices demonstrate the safety and effectiveness of the TECNIS® Symfony Extended Range of Vision IOLs. The results of these studies are summarized below.

A. Laboratory Studies

Physicochemical Testing

The TECNIS® Symfony Extended Range of Vision IOLs, Models ZXR00, ZXT150, ZXT225, ZXT300, and ZXT375, use the same lens material as the material parent, monofocal analog, and multifocal analog; therefore, physicochemical and biological data for these associated lenses are deemed applicable to the subject devices. All physicochemical reports pertaining to the SENSAR soft acrylic material were previously submitted to FDA in 2007 as part of the 180-Day PMA Supplement for the material parent SENSAR® 1-Piece IOL (P980040/S015). P980040 served as the parent lens for the aforementioned submission to which an SSED is available. The physicochemical characterization of the TECNIS® Symfony IOL material met the requirements of ISO 11979-5, *Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility* and EN ISO 10993-1, *Biological Evaluation of Medical Devices – Part 1: Evaluation and Testing Within a Risk Management Process*. The physicochemical tests are summarized in **Table 2**. All acceptance criteria for physicochemical testing were met.

TABLE 2
Physicochemical Test Summary:
TECNIS® Symfony Extended Range of Vision IOLs,
Indicating Relationship to the SENSAR® AR40e IOL

Physicochemical Tests	Results of Testing
Exhaustive Extraction	Equivalent to Model AR40e approved under P980040
Leachables	Equivalent to Model AR40e approved under P980040
Insoluble Inorganics	No hazardous components identified
Hydrolytic Stability	Stable to 5 years equivalent age
Photostability	Stable to 20 years equivalent age
Nd:YAG Laser	Equivalent to Model AR40e approved under P980040

Note: The SENSAR® AR40e IOL has the OptiEdge design and was approved in the same PMA (P980040) as the SENSAR® AR40 IOL, which has a rounded optic edge design.

B. Animal Studies

Biological Testing

The TECNIS® Symfony Extended Range of Vision IOLs, Models ZXR00, ZXT150, ZXT225, ZXT300, and ZXT375, are made of the same SENSAR soft acrylic material and

have the same manufacturing contact materials previously qualified with the material parent, the SENSAR® 1-Piece IOL, Model AAB00. With the exception of genotoxicity testing, all other biocompatibility tests conducted on Model AAB00 were previously submitted to FDA in 2007 (P980040/S015). The biocompatibility studies were performed in accordance with the requirements in ISO 10993, Biological Evaluation of Medical Devices, and 11979-5 Ophthalmic Implants – Intraocular Lenses – Part 5: Biocompatibility guidelines, to establish a complete profile of the IOL material. The results are summarized in **Table 3**. All acceptance criteria for biocompatibility were met.

TABLE 3
Biocompatibility Test Summary:
TECNIS® Symfony Extended Range of Vision IOL

Biological Tests	Results of Testing
Cytotoxicity: MEM	Non-cytotoxic
Agar Diffusion solid & saline extract	Non-cytotoxic
Percent Inhibition of Cell Growth Method (%ICG)	Non-inhibitory to cell growth
Guinea Pig Maximization a. Saline Extract b. Sesame Oil Extract	 Non-sensitizing Non-sensitizing
Non-ocular Implant Study (Six-Week Subcutaneous Implantation in Rabbits)	Passed
Six-Month Rabbit Intraocular Study	Passed
Genotoxicity Testing (*Salmonella typhimurium* and *Escherichia coli* reverse mutation assay)	Non-genotoxic, non-mutagenic
Genotoxicity Testing (Chromosomal aberration assay in Chinese hamster ovary [CHO] cells)	Non-clastogenic
Genotoxicity Testing (Mouse lymphoma mutagenesis assay ISO 10993-3)	Non-mutagenic under short and long exposure conditions

C. Additional Studies

Dimensional, Optical, and Mechanical Testing

Dimensional, optical, and mechanical tests were conducted on finished, sterilized, TECNIS® Symfony Extended Range of Vision IOLs to verify the conformance to applicable sections of ISO 11979-2, *Ophthalmic Implants-Intraocular Lenses-Part 2: Optical Properties and Test Methods*, and ISO 11979-9, *Ophthalmic Implants-Intraocular Lenses-Part 9: Multifocal Intraocular Lenses*; ISO 11979-3, *Ophthalmic Implants-Intraocular Lenses-Part 3: Mechanical Properties and Test Methods*; and ANSI Z80.30, *American National Standard for Ophthalmics: Toric Intraocular Lenses*. As part of mechanical assessment, folding and insertion testing was also performed to verify recovery of lens properties (e.g., optical, etc.) following simulated insertion. Here, the TECNIS® Symfony Extended Range of Vision IOLs passed all predetermined requirements established in the aforementioned standards where applicable and internal product specifications. **Table 4** summarizes the results of the dimensional, optical and mechanical testing.

TABLE 4
Dimensional, Optical and Mechanical Test Requirements Summary:
TECNIS® Symfony Extended Range of Vision IOLs

Preclinical Testing Requirement	Acceptance Criteria Based on What Standard?	Result
Optical Requirements		
Dioptric Power (D)	$0 \le D \le 15$: ±0.3D $15 < D \le 25$: ±0.4D $25 < D \le 30$: ±0.5 D $30 < D$: ±1.0D	Passed
Cylinder Power [C] (toric TECNIS® Symfony IOLs only)	$0 < C \le 2.5$: ±0.3D $2.5 < C \le 4.5$: ±0.4D $4.5 < C$: ±0.5D	Passed
Image Quality	Greater or equal to 0.43 or 70% of maximal theoretical MTF value	Passed
Axis Orientation Mark(s) (toric TECNIS® Symfony IOLs only)	Combined angular errors of the cylindrical axis mark and any deviation from orthogonality between the meridians of highest and lowest dioptric power within ±5°	Passed

Preclinical Testing Requirement	Acceptance Criteria Based on What Standard?	Result
Spectral Transmittance	% T > 90% at 600nm % T=10% at ~380nm	Passed
Mechanical Requirements		
Overall Diameter	13.00 ± 0.20mm	Passed
Vault Height	± 0.25mm from nominal	Passed
Sagitta	0.64 ± 0.35 mm	Passed
Clear Optic Diameter	>4.50mm	Passed
Optic Body Diameter	± 0.10mm	Passed
Axial Displacement in Compression	0.11 mm ± 0.062mm	Passed
Optic Decentration	Mean + 2SD= 0.076mm < 0.60mm (10% clear optic)	Passed
Optic Tilt	Mean + 2SD = 2.98° < 5°	Passed
Angle of Contact	42° ± 1.0°	Passed
Compression Force and Decay	0.39 mN ± 0.05	Passed
Dynamic Fatigue Durability	No breakage or damage after 250,000 cycles of haptic compression	Passed
Surgical Manipulation	The IOL manufacturer shall provide evidence that the loops of an IOL design are capable of withstanding surgical manipulations without failure.	Passed
Surface and Bulk Homogeneity	The IOL shall be essentially free from defects	Passed
Recovery of Properties Following Simulated Surgical Manipulation		
Dioptric Power	0 ≤ D ≤ 15: ±0.3D 15 < D ≤ 25: ±0.4D 25 < D ≤ 30: ±0.5 D 30 < D: ±1.0D	Passed
Cylinder Power (toric TECNIS® Symfony IOLs only)	0 < C ≤ 2.5: ±0.3D 2.5 < C ≤ 4.5: ±0.4D 4.5 < C: ±0.5D	Passed

Preclinical Testing Requirement	Acceptance Criteria Based on What Standard?	Result
Axis Orientation Mark(s) (toric TECNIS® Symfony IOLs only)	Combined angular errors of the cylindrical axis mark and any deviation from orthogonality between the meridians of highest and lowest dioptric power within ±5°	Passed
Image Quality	Greater or equal to 0.43 or 70% of maximal theoretical MTF value	Passed
Overall Diameter	13.00 ± 0.20mm	Passed
Sagitta	0.64 ± 0.35 mm	Passed
Surface and Bulk Homogeneity	The IOL shall be essentially free from defects	Passed

Microbiology, Sterilization, and Shelf Life Adoption / Testing

The lens material and platform, geometry, dimensions, manufacturing method, materials and equipment, sterilization method, and packaging materials and configuration of the TECNIS® Symfony Extended Range of Vision IOLs are the same as those of its monofocal analog, the TECNIS® 1-Piece IOL, Model ZCB00 (P980040/S015). Therefore, stability, packaging integrity, and transport stability data supporting this reference lens model was used to support the subject lenses. The TECNIS® Symfony Extended Range of Vision IOLs will be labeled with a 5-year shelf life.

The lens material/product configuration, packaging configuration, and load density used for the TECNIS® Symfony Extended Range of Vision IOLs are the same as those used for the approved and validated reference monofocal lens. Sterilization validations performed for this associated lens model are deemed applicable to the subject lenses. The ethylene oxide sterilization cycle was validated for the monofocal analog and assures a minimum sterility assurance level of 10^{-6}. The TECNIS® Symfony Extended Range of Vision IOLs were successfully adopted into this validated cycle per the appropriate standard operating procedures and passed all acceptance criteria for bioburden, bacterial endotoxin, and sterilant residual levels.

These tests were conducted in accordance with the following standards and United States Pharmacopoeial chapters:

- ANSI/AAMI/ISO 11135-1, *Sterilization of Healthcare Products – Ethylene Oxide – Part 1: Requirements for Development, Validation, and Routine Control of a Sterilization Process*
- ISO 10993-7, *Biological evaluation of medical devices – Part 7: Ethylene oxide sterilization residuals*
- 34/29 USP 2011, *Bacterial Endotoxin Testing*
- ISO 11979-6, *Ophthalmic Implants – Intraocular Lenses – Part 6: Shelf-life and transport stability*

The results of the sterilization, packaging, shelf life and transport stability studies are summarized in **Table 5**.

TABLE 5
Microbiology, Sterilization, and Shelf Life Testing / Adoption:
TECNIS® Symfony Extended Range of Vision IOLs

Test	Results
Lens material/product configuration	Same
Packaging material and configuration	Same
Sterilization load configuration and density	Same
Shelf life	5 years
Package integrity	Equivalent
Transport stability	Equivalent
Bioburden	Passed
Bacterial Endotoxin	Passed
Ethylene Oxide Residuals	Passed

Toric Calculator Software Validation

A software validation was performed for the TECNIS® Symfony Toric Calculator according to FDA's guidance documents, *Guidance for the Content of Premarket Submissions for Software Contained in Medical Devices*, dated May 11, 2005, *General Principles of Software Validation: Final Guidance for Industry and FDA Staff*, dated January 11, 2002, and *Content of Premarket Submissions for Management of Cybersecurity in Medical devices – Guidance for Industry and Food and Drug Administration Staff*, dated October 2, 2014. The TECNIS® Symfony Toric Calculator was developed using an appropriate software development program. The hazard analysis addressed all identified hazards applicable to both patient and user. These procedures help assure that the TECNIS® Symfony Toric Calculator will operate in a manner described in the specifications when used according to its instructions for use.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

Data from a recent clinical study of the TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00 (non-toric), and data from other relevant prior clinical studies are included to support the safety and effectiveness of the TECNIS Symfony IOLs, Model ZXR00, and TECNIS Symfony Toric IOLs, Models ZXT150, ZXT225, ZXT300, and ZXT375.

As stated above in the nonclinical section, the applicant leveraged data/information from various parent lenses. The TECNIS Multifocal IOL (Model ZM900) approved under P980040 served as the optical parent whereby the posterior optic design of the TECNIS® Symfony Extended Range of Vision IOLs (non-toric and toric) was derived from that of the TECNIS Multifocal IOL. The SENSAR 1-Piece IOL, Model AAB00 which was approved under P980040/S015 served as the material and mechanical parent to support the safety and effectiveness of the 1-piece platform and SENSAR acrylic material used for the TECNIS® Symfony Extended Range of Vision IOLs (non-toric and toric models). Although preclinical data/information was leveraged, a clinical study was warranted to assess the change to the optic to support the extended depth of focus claim.

The toric toric models (ZXT150, ZXT225, ZXT300, and ZXT375) involved imposing the toric feature from the toric design parents (P980040/S039: TECNIS Toric 1-Piece IOLs (Models ZCT150, ZCT225, ZCT300 and ZCT400Model ZCT400) onto the anterior optic surface of the TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00 (non-toric). Since the study for Model ZXR00 established safety and the applicant has approved toric parent IOLs, additional clinical data was not warranted as the only difference is in cylinder powers.

A. Study Design

Subjects were treated between August 2014 and June 2015. The database for this Panel-Track PMA Supplement reflected data collected through June 2015 and included 299 implanted subjects. There were 15 investigative sites in the U.S.

The clinical study of the TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, was a prospective, 6-month, multicenter, bilateral, randomized, subject/evaluator-masked clinical investigation designed to evaluate at least 135 subjects bilaterally implanted with the Symfony IOL, and 135 subjects bilaterally implanted with the monofocal TECNIS® 1-Piece IOL, Model ZCB00. The monofocal control IOL is a legally-marketed alternative with similar indications for use, except that it does not provide an extended depth of focus and is not intended to provide improved vision at intermediate and near distances.

Statistical analyses were frequentist. For the key effectiveness analyses the hypothesis tests were to demonstrate superiority over the control group. In addition, an independent Data Safety Monitoring Board (DSMB), comprised of two ophthalmologists, one statistician, and one facilitator, was used to monitor all safety endpoints.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the TECNIS® Symfony Extended Range of Vision IOL clinical study was limited to subjects who met the following inclusion criteria:

- Age 22 years or greater
- Bilateral cataracts for which phacoemulsification extraction and posterior IOL implantation were planned for both eyes
- Preoperative best corrected distance visual acuity (BCDVA) of 20/40 Snellen or worse with or without a glare source
- Potential for postoperative BCDVA of 20/30 Snellen or better
- Preoperative corneal astigmatism of 1.00 D or less in both eyes

Subjects were not permitted to enroll in the TECNIS® Symfony Extended Range of Vision IOL clinical study if they met any of the following exclusion criteria:

- Requiring an intraocular lens power outside the available range of +16.0 D to +28.0 D
- Use of systemic or ocular medications that may affect vision or likely to impact pupil dilation or iris structure
- Acute, chronic, or uncontrolled systemic or ocular disease or any illness that, in the opinion of the investigator, would increase the operative risk or confound the outcome(s) of the study (e.g., poorly-controlled diabetes)
- History of ocular trauma, prior refractive or other ocular surgery or subjects expected to require retinal laser treatment or other surgical intervention
- Presence of ocular pathology other than cataract such as:
  - Corneal abnormalities (including irregular astigmatism)
  - Pupil abnormalities
  - Strabismus or any inability to focus, or fixate for prolonged periods of time
  - Capsule or zonule abnormalities
  - Glaucomatous changes
  - Intraocular inflammation
  - Known pathology that may affect visual acuity and/or is predicted to cause future acuity losses to a level of 20/30 or worse (e.g., macular degeneration)
- Inability to achieve keratometric stability for contact lens wearers
- Desire for monovision correction

2. Follow-up Schedule

All subjects were evaluated according to the follow-up schedule below:

TABLE 6
Clinical Study Visit Schedule

Visit	Exam	Eyes Evaluated	Visit Window
1	Preoperative Exam	Both Eyes	Within 45 days prior to 1st surgery
2	Operative	1st Eye	0-45 days following preoperative exam
3	Postop 1 (1 day)	1st Eye	1-2 days postoperative
4	Postop 2 (1 week)*	1st Eye	7-14 days postoperative
5	Operative	2nd Eye	Within 1 month after 1st eye surgery
6	Postop 1 (1 day)	2nd Eye	1-2 days postoperative
7	Postop 2 (1 week)	2nd Eye	7-14 days postoperative
8	Postop 3 (1 month)	Both Eyes	30-60 days postop from 2nd eye surgery
9	Postop 4 (6 months)	Both Eyes	120-180 days postop from 2nd eye surgery

* Postop 2 for the first eye was to be completed prior to surgery on the second eye.

Preoperative study procedures included informed consent, ocular history, potential visual acuity, uncorrected and best corrected distance visual acuity, slit-lamp and fundus examinations and determination of the subject meeting all inclusion/exclusion criteria. Following determination of the first study eye, subjects were randomized and underwent cataract surgery and IOL implantation; all eyes were targeted for emmetropia. Subject and testing evaluators were masked throughout the study as to which lens type each subject received.

Postoperative study procedures included uncorrected and best corrected distance visual acuity, uncorrected and distance corrected intermediate visual acuity at 66 cm, uncorrected, distance corrected and best corrected (with add) near visual acuity at 40 cm, defocus testing (sub-study), contrast sensitivity, keratometry, intraocular pressure, pupil size, slit-lamp and fundus examinations, assessment of spontaneously-reported optical visual symptoms, subject questionnaires (spectacle wear, directed optical visual symptoms, etc.), and assessment of complications and adverse events. Adverse events and complications were recorded at all visits.

The key time points are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

With regards to safety:

- The primary co-endpoints were the rates of serious adverse events vs. the historical control safety and performance endpoints (SPE) rates in ISO 11979-7 (2006).
    - Success criterion for each type of event was a rate not statistically greater for the Symfony than the historical control rate.
- A secondary endpoint was monocular (primary eye) best corrected distance contrast sensitivity under mesopic conditions with and without glare at 12 cycles per degree (cpd). (This was related to a potential claim of non-inferiority compared to monofocal control.)
    - Success criterion was statistical non-inferiority, based upon a non-inferiority margin of 0.15 log units.

- Other safety endpoints included:
    - Mean monocular (primary eye) BCDVA compared to the monofocal control IOL.
        - Success criterion was statistical non-inferiority for Symfony compared to the control, with a non-inferiority margin of 1 line (logMAR).
    - Visual symptoms via patient-reported outcomes (PRO) instrument.
        - Success criterion: no specific criterion
    - Other contrast sensitivity outcomes under mesopic, mesopic with glare and photopic with glare conditions
        - Success criterion: no specific criterion

With regards to effectiveness:

- The primary effectiveness co-endpoints were monocular (primary eye) uncorrected intermediate visual acuity (UCIVA) and distance corrected intermediate visual acuity (DCIVA) under photopic conditions at 66 cm.
    - For each of these, the success criteria were statistical superiority of the mean Symfony acuity compared to the control; plus the proportion of Symfony eyes achieving at least 20/25 had to be at least 50%, and at least 25% higher than the control.

- Secondary endpoints were:

    - Mean monocular (primary eye) diopters of depth of focus from optical infinity. (Sub-study of eyes achieving at least BCDVA of 20/25 consistently.)
        - Success criteria were statistical superiority over the control, plus a mean difference of ≥ 0.50 D.
    - The proportion of subjects who reported wearing glasses or contacts ”none of the time” or “a little of the time” for overall spectacle wear via binocular questionnaire response,
        - Success criteria were at least 50% of Symfony eyes achieving this outcome, and the proportion had to be at least 25% higher than the control.
    - Monocular (primary eye) distance corrected near visual acuity (DCNVA) at 40 cm.

        - Success criteria were statistical superiority of the mean Symfony acuity compared to the control; plus the proportion of Symfony eyes achieving at least 20/40 had to be at least 50%, and at least 25% higher than the control.

- Another endpoint was tolerance to residual refractive error as assessed by mean monocular (primary eye) uncorrected distance visual acuity (UCDVA) for eyes with ≥0.50 D of absolute residual manifest refraction spherical equivalent (MRSE).
    - Success criterion was statistical demonstration of superiority of Symfony over the control.

All clinical endpoints were evaluated at 6 months postoperatively. Because the TECNIS® Symfony IOL is a modification of approved IOLs, conclusions regarding device effectiveness and safety are also substantiated from the results of the studies of the parent IOLs.

The primary and secondary study endpoints were analyzed in three population groups: safety (all implanted eyes), intent-to-treat with data imputation for missing values (ITT; included all implanted eyes and all subjects not necessarily implanted), and per-protocol (subjects/eyes without any protocol deviations). Safety endpoints and all "other" endpoints were primarily analyzed using only the safety population. For consistency, results presented in this summary are predominantly from the safety population, unless otherwise indicated.

4. Statistical Methods

The TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, was compared to the monofocal control IOL (monofocal TECNIS 1-Piece IOL, Model ZCB00) for most safety and effectiveness endpoints. The primary analysis group consists of first eyes implanted or binocular data as appropriate; second-eye and all-eye outcomes are considered supportive. One-sided, two-sample t-tests with an alpha level of 0.025 were used for the primary endpoints of monocular UCIVA and DCIVA and the secondary endpoints of monocular mean diopters of defocus and monocular DCNVA. A logistic regression for imputed data or Fisher's Exact test (for no data imputation) with a one-sided alpha of 0.025 was used for binocular overall spectacle wear. Nonparametric statistics with a lower limit of a 90% confidence interval were used for the contrast sensitivity endpoint. Hierarchical methods were used to adjust for multiple statistical comparisons for these endpoints. The ITT population was the primary analysis population used for the primary and secondary study endpoints with missing data imputed using multiple imputation methods.

Complications and adverse events, as well as the proportion of first eyes achieving 20/40 or better BCDVA, were compared to ISO SPE rates for the Symfony lens group using an Exact test based on the binomial distribution. Monocular, first-eye, mean BCDVA and contrast sensitivity for the Symfony lens group were compared to the control lens group and analyzed using non-inferiority methods.

The sample size was justified based on the primary study endpoints of monocular UCIVA and DCIVA, and the requirements for contrast sensitivity testing. With at least 135 evaluable

subjects in each lens group, this study had greater than 90% power to detect a 0.7 lines or greater difference in mean visual acuity between the Symfony and control lens groups for UCIVA and DCIVA.

B. Accountability of PMA Cohort

At the time of database lock, of 324 patients enrolled (consented) in the PMA study, 299 (of approximately 300 intended per protocol) were implanted with a study lens in at least one operative eye across 15 U.S. investigative sites. Of 299 subjects implanted, 148 were in the Symfony group and 151 were in the monofocal group. Only one monofocal subject was not implanted bilaterally due to illness and subsequent death. A total of 147 Symfony and 148 monofocal control subjects (total N=295) were available for analysis at the completion of the study, the 6-month postoperative visit.

Subject accountability is presented in **Table 7** for Symfony and **Table 8** for monofocal control first eyes (subjects). Subject compliance was excellent at 6 months for an overall percent accountability of 98.7% (295/299). Only four subjects (1.3%; 4/299) were unavailable at 6 months; two were discontinued due to death and two were lost-to-follow-up due to reasons unrelated to vision.

TABLE 7
Symfony First Eyes Accountability (N=148)

	1 Day		1 Week		1 Month		6 Months	
Subject Status	**n**	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Available for Analysis	**148**	**100**	**148**	**100**	**148**	**100**	**147**	**99.3**
--In Interval (included in analysis)	148	100	145	98.0	140	94.6	146	98.6
--Out of Interval (included in analysis)	0	0.0	3	2.0	8	5.4	1	0.7
Missing Subjects	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**1**	**0.7**
--Discontinued	0	0.0	0	0.0	0	0.0	0	0.0
--Missed visit	0	0.0	0	0.0	0	0.0	0	0.0
--Not seen but accounted for	0	0.0	0	0.0	0	0.0	0	0.0
--Lost-to-follow-up	0	0.0	0	0.0	0	0.0	1[a]	0.7
Active	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0
--In interval or Past interval (form not yet received)	0	0.0	0	0.0	0	0.0	0	0.0

[a] One subject was unable to be contacted.

TABLE 8
Monofocal First Eyes Accountability (N=151)

Subject Status	1 Day		1 Week		1 Month		6 Months	
	n	**%**	**n**	**%**	**n**	**%**	**n**	**%**
Available for Analysis	**151**	**100**	**150**	**99.3**	**150**	**99.3**	**148**	**98.0**
--In Interval (included in analysis)	151	100	148	98.0	147	97.4	148	98.0
--Out of Interval (included in analysis)	0	0.0	2	1.3	3	2.0	0	0.0
Missing Subjects	**0**	**0.0**	**1**	**0.7**	**1**	**0.7**	**3**	**2.0**
--Discontinued	0	0.0	0	0.0	1[b]	0.7	2[b,c]	1.3
--Missed visit	0	0.0	1[b]	0.7	0	0.0	0	0.0
--Not seen but accounted for	0	0.0	0	0.0	0	0.0	0	0.0
--Lost-to-follow-up	0	0.0	0	0.0	0	0.0	1[a]	0.7
Active	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**	**0**	**0.0**
--Active (not yet in visit interval)	0	0.0	0	0.0	0	0.0	0	0.0
--In interval or Past interval (form not yet received)	0	0.0	0	0.0	0	0.0	0	0.0

[a] One subject was lost-to-follow-up due to illness (Parkinson's Disease).
[b] One subject died due to cancer approximately 1 month following the first-eye implant; the second eye was not implanted.
[c] One subject died due to stroke following the 1-month visit.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a randomized, prospective, multicenter clinical study performed in the U.S.

Table 9 presents the demographic data for the Symfony group vs. the monofocal control group. Subject demographics were similar between the Symfony and monofocal control groups. The mean age was 68.0 years for both lens groups, females represented more than half of both lens groups and most subjects in both lens groups were White.

TABLE 9
Demographics

		Symfony N=148		Monofocal N=151	
Age (years)	N	148		151	
	Mean	68.0		67.9	
	Std	7.5		7.9	
	Median	68		69	
	Min	46		47	
	Max	86		88	
	Not Reported	0		0	
Age Group	<60	15	(10.1%)	24	(15.9%)
	60–69	70	(47.3%)	61	(40.4%)
	70–79	52	(35.1%)	56	(37.1%)
	≥80	11	(7.4%)	10	(6.6%)
	Not Reported	0	-	0	-
Sex	Male	57	(38.5%)	65	(43.0%)
	Female	91	(61.5%)	86	(57.0%)
	Not Reported	0	-	0	-
Race	African American	4	(2.7%)	16	(10.6%)
	American Indian/ Alaska Native	0	(0.0%)	2	(1.3%)
	Asian	1	(0.7%)	3	(2.0%)
	White	143	(96.6%)	130	(86.1%)
	Not Reported	0	-	0	-
Ethnicity	Hispanic/Latino	5	(3.4%)	4	(2.6%)
	Not Hispanic/Latino	143	(96.6%)	147	(97.4%)
	Not Reported	0	-	0	-
Iris Color	Blue/Gray	47	(31.8%)	47	(31.1%)
	Brown/Black	63	(42.6%)	63	(41.7%)
	Green/Hazel	38	(25.7%)	41	(27.2%)
	Not Reported	0	-	0	-

%=n/N(Total) excluding not reported
[a] P value from 2-sided 2-sample t-test
[b] P value from 2-sided Fisher's exact test

Table 10 presents key ocular baseline parameters of target spherical equivalent and preoperative keratometric cylinder.

Table 10
Mean Target Spherical Equivalent and Preop Keratometric Cylinder

	IOL	N	Mean	Std. Dev.	Median	Min.	Max.
Target Spherical Equivalent (D)	Symfony	148	-0.203	0.148	-0.200	-0.76	0.21
	Monofocal	151	-0.192	0.152	-0.190	-0.49	0.32
	Difference	-	-0.012	-	-	-	-
Keratometric Cylinder (D)	Symfony	148	0.505	0.248	0.490	0.00	1.00
	Monofocal	151	0.532	0.221	0.500	0.00	1.00
	Difference	-	-0.026	-	-	-	-

[a] 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 299 implanted subjects: 148 Symfony subjects (148 bilaterally implanted) and 151 monofocal subjects (150 bilaterally implanted).

Adverse Events that occurred in the PMA clinical study

Overall, 2.7% (4/148) of Symfony subjects experienced serious adverse events during the study and none (0%; 0/148) experienced device-related or unanticipated events. The incidence rates of cumulative serious adverse events for Symfony eyes are presented in **Table 11**. The incidence rates for the Symfony IOL compared favorably to the specified ISO SPE rates, as the observed rates for Symfony were within or not statistically significantly higher than the specified ISO SPE rates (primary safety endpoint). In addition, there were no secondary surgical interventions related to the optical properties of the Symfony IOL. Secondary surgical intervention events for the Symfony IOL are specified in **Table 12**.

The incidence rates of persistent serious adverse events at 6 months for Symfony eyes also compared favorably to the ISO SPE (safety and performance endpoint) rates (**Table 13**). There were no persistent medical complications/adverse events present at 6 months for Symfony first eyes. There was one case of cystoid macular edema (0.7%; 1/147) for Symfony second eyes at 6 months, however, this rate was not statistically significantly higher than the ISO SPE rate of 0.5% (p=0.5238). As there were no other persistent medical complications/adverse events at 6 months, all other persistent event rates for Symfony eyes were below the ISO SPE persistent rates (corneal edema 0.3%; iritis 0.3%; and, raised IOP requiring treatment 0.4%).

The safety of the device for the correction of aphakia was not based on this sample alone, but rather on all available data for the device (and parent IOLs) to date. The safety data

from this study were for confirmatory purposes. The adverse events and complications observed in this study were typical for similar types of IOLs.

TABLE 11
Serious Adverse Events for Symfony Eyes

Cumulative Medical Complications/ Adverse Events	ISO SPE Rate	First Eyes N=148		Second Eyes N=148		All Eyes N=296	
		n	%	n	%	n	%
Cystoid macular edema	3	1	0.7	1	0.7	2	0.7
Hypopyon	0.3	0	0	1[b]	0.7[b]	1[f]	0.3[f]
Endophthalmitis	0.1	0	0	1[c]	0.7[c]	1[g]	0.3[g]
Lens dislocated from posterior chamber	0.1	0	0	0	0	0	0
Pupillary block	0.1	0	0	0	0	0	0
Retinal detachment	0.3	0	0	0	0	0	0
Eyes with secondary surgical intervention	0.8	0	0	2[d]	1.4[e]	2	0.7
-- Device related	NA	0	0	0	0	0	0
-- Not device related	NA	0	0	2[d]	1.4	2	0.7
Other:							
- Pupillary capture	NA	0	0.0	1	0.7	1	0.3

[a] Per ISO 11979-7: 2006/Amd. 1:2012 (E) ophthalmic Implants – Intraocular Lenses (Part 7): The SPE rate is the safety and performance endpoint.

[b] Incidence rate for "Hypopyon-Second Eye" is not statistically significantly higher than ISO SPE rate (p = 0.3590) using 1-sided exact test.

[c] Incidence rate for "Endophthalmitis-Second Eye" is not statistically significantly higher than ISO SPE rate (p = 0.1376) using 1-sided exact test.

[d] Treatment injections for endophthalmitis (Subject 1314) and CME (Subject 1425).

[e] Incidence rate for secondary surgical interventions is not statistically significantly higher than ISO SPE rate (p = 0.3318) using 1-sided exact test.

[f] Incidence rate for "Hypopyon--All Eyes" (0.34)is not statistically significantly higher than ISO SPE rate (p = 0.5891) using 1-sided exact test.

[g] Incidence rate for "Endophthalmitis-All Eyes" is not statistically significantly higher than ISO SPE rate (p = 0.2563) using 1-sided exact test.

TABLE 12
Secondary Surgical Interventions for Symfony Eyes

Secondary Surgical Interventions[a]: Not Device-Related	First Eyes N=148		Second Eyes N=148		All Eyes N=296	
	n	%	n	%	n	%
Treatment injections for medical complications:	0	0	2	1.4	2	0.7
- Cystoid macular edema	0	0	1	0.7	1	0.3
- Endophthalmitis (with AC tap)	0	0	1	0.7	1	0.3

%=n/N(Total)

[a] All SSIs were treatments for SAEs; there were no SSIs as the original event.

Rates of serious adverse events were similar to those seen in other IOL studies. There is no reason to believe that the adverse events rates for the Symfony lens differ substantially from those of the relevant parent IOLs from which the Symfony is an optical modification.

TABLE 13
6-Month Persistent Serious Adverse Events for the Symfony IOL Group

Persistent Medical Complications/ Adverse Events	ISO SPE Rate[a]	First Eyes N=148		Second Eyes N=148		All Eyes N=296	
		n	%	n	%	n	%
Corneal edema	0.3	0	0	0	0	0	0
Cystoid macular edema	0.5	0	0.0	1	0.7[b]	1	0.3
Iritis	0.3	0	0	0	0	0	0
Raised IOP requiring treatment	0.4	0	0	0	0	0	0
Other:							
- Pupillary capture	NA	0	0.0	1	0.7	1	0.3

[a] Per ISO 11979-7: 2006/Amd. 1:2012 (E) ophthalmic Implants – Intraocular Lenses (Part 7): The SPE rate is the safety and performance endpoint.

[b] Incidence rate for "Cystoid Macular Edema-Second Eye" is not statistically significantly higher than ISO SPE rate (p = 0.5238) using 1-sided exact test.

Contrast Sensitivity

Monocular best corrected distance contrast sensitivity testing was performed using the Vector Vision ETDRS light box and contrast sensitivity charts under three lighting conditions: mesopic with glare, mesopic without glare, and photopic with glare. Hypothesis tests were conducted using the Hodges-Lehmann method, using a pre-assigned score for subjects who could not see the reference pattern. This may introduce potential bias, which would tend to cause underestimation of the difference in contrast sensitivity between the arms. An alternative analysis method that avoids this bias

is a simple comparison of the medians of the two arms. Median contrast scores for the Symfony IOL group were reduced compared to the monofocal control group under each lighting condition and spatial frequency (**Table 14**), particularly at the higher spatial frequencies. In addition, the secondary study endpoint hypothesis test for median contrast sensitivity at the 12 cpd spatial frequency under mesopic conditions with and without glare failed to demonstrate non-inferiority, as the lower 90% confidence intervals (CI) of the median differences were below the criterion of -0.15 log units (-0.165 log units under mesopic without glare conditions and -0.265 log units under mesopic with glare conditions; ITT population). Differences between Symfony and control medians at 12 cpd were -0.170 log units under mesopic without glare conditions and -0.320 log units under mesopic with glare conditions. No statistically significant difference in contrast sensitivity across pupil size groups was observed; however, the sample size may not have been sufficient to detect differences for subgroup analyses.

TABLE 14
Monocular Best Corrected Distance Contrast Sensitivity at 6 Months

			Mesopic Without Glare			Mesopic With Glare			Photopic With Glare		
				Subjects who did not see the reference pattern			Subjects who did not see the reference pattern			Subjects who did not see the reference pattern	
Spatial Frequency	**Lens Model**	**N**	**Median[a]**	**n**	**%**	**Median[a]**	**n**	**%**	**Median[a]**	**n**	**%**
1.5 cpd	Symfony	146	1.520	0	0.0	1.520	0	0.0	Not tested		
	Control	147	1.595	1	0.7	1.520	1	0.7	Not tested		
	Difference		-0.075			0.00			Not tested		
3.0 cpd	Symfony	146	1.415	0	0.0	1.445	1	0.7	1.560	0	0.0
	Control	147	1.490	3	2.0	1.490	3	2.0	1.705	1	0.7
	Difference		-0.075			-0.045			-0.145		
6.0 cpd	Symfony	146	1.380	16	11.0	1.380	19	13.0	1.700	4	2.7
	Control	147	1.540	6	4.1	1.550	7	4.8	1.840	5	3.4
	Difference		-0.160			-0.170			-0.140		
12.0 cpd	Symfony	146	0.910	38	26.0	0.760	44	30.1	1.325	12	8.2
	Control	147	1.080	23	15.6	1.080	28	19.0	1.540	9	6.1
	Difference		-0.170			-0.320			-0.215		
18.0 cpd	Symfony	146	Not tested			Not tested			0.885	14	9.6
	Control	147	Not tested			Not tested			1.100	8	5.4
	Difference		Not tested			Not tested			-0.215		

cpd = Cycles per degree
[a] In log units.

Distance High-Contrast Photopic Visual Acuity

Distance visual acuities were tested using 100% Early Treatment Diabetic Retinopathy Study (ETDRS) charts at 4.0 meters under photopic conditions (85 cd/m^2).

Table 15 presents mean monocular distance visual acuities at 6 months for Symfony and monofocal control first eyes. Mean UCDVA and BCDVA outcomes were comparable between IOL groups at 20/25 and 20/20, respectively. Comparison of mean monocular BCDVA to the control lens was one of the key safety endpoints. Non-inferiority testing showed the lower limit of the 90% confidence interval (CI) of the mean difference in BCDVA between IOL groups to be less than 1.0 line (LogMAR -0.036; -0.4 lines) between groups, indicating that the Symfony IOL is non-inferior to the control lens in providing best corrected distance visual acuity. It was hypothesized that Symfony-implanted subjects would have greater "tolerance to refractive error." This was evaluated by trying to demonstrate that for eyes with residual manifest spherical equivalent ≥0.50 D at 6 months, the Symfony arm had statistically superior UCDVA compared to the control. Results did not confirm that Symfony eyes had greater "tolerance to refractive error."

TABLE 15
Monocular and Binocular Distance Visual Acuity at 6 Months

		Monocular				Binocular			
Distance Visual Acuity	**Lens Group**	**N**	**Mean LogMAR**	**Snellen Line Equivalent**	**Std. Dev. LogMAR**	**N**	**Mean LogMAR**	**Snellen Line Equivalent**	**Std. Dev. LogMAR**
Uncorrected	Symfony	147	0.114	20/25	0.142	147	0.034	20/20	0.106
	Control	148	0.088	20/25	0.149	148	0.013	20/20	0.118
	Difference			**-0.3 lines**				**-0.2 lines**	
Best	Symfony	147	-0.021	20/20	0.082	147	-0.045	20/20	0.077
Corrected	Control	148	-0.040	20/20	0.093	148	-0.075	20/16	0.081
	Difference		**-0.020**[a]	**-0.2 lines**				**-0.3 lines**	

[a] 90% Confidence Interval around mean difference: [-0.036; -0.003]

Table 16 presents the distribution of monocular distance visual acuity results for Symfony and monofocal control first eyes at 6 months. As all eyes were best -case, the proportion of first eyes achieving monocular best corrected distance visual acuity (BCDVA) of 20/40 or better for the Symfony lens group (100.0%) was above the ISO Safety and Performance Endpoint (SPE) rates for overall (92.5%) and best-case (96.7%) BCDVA 20/40 or better. The distribution of binocular distance visual acuity results for Symfony and monofocal control subjects at 6 months are presented in **Table 17**.

TABLE 16
Monocular Distance Visual Acuity at 6 Months

Visual Acuity LogMAR (Snellen)	Symfony N=147				Monofocal Control N=148			
	Uncorrected		Best Corrected		Uncorrected		Best Corrected	
	n	%	n	%	n	%	n	%
0.0 (20/20) or better	57	38.8	123	83.7	70	47.3	131	88.5
0.1 (20/25) or better	96	65.3	144	98.0	106	71.6	143	96.6
0.2 (20/32) or better	129	87.8	147	100.0	126	85.1	146	98.6
0.3 (20/40) or better	**142**	**96.6**	**147**	**100.0**	**139**	**93.9**	**148**	**100.0**
0.4-0.6 (20/50-20/80)	4	2.7	0	0.0	9	6.1	0	0.0
0.7 (20/100) or worse	1	0.7	0	0.0	0	0.0	0	0.0

TABLE 17
Binocular Distance Visual Acuity at 6 Months

Visual Acuity LogMAR (Snellen)	Symfony N=147				Monofocal Control N=148			
	Uncorrected		Best Corrected		Uncorrected		Best Corrected	
	n	%	n	%	n	%	n	%
0.0 (20/20) or better	92	62.6	137	93.2	106	71.6	141	95.3
0.1 (20/25) or better	134	91.2	145	98.6	125	84.5	146	98.6
0.2 (20/32) or better	143	97.3	147	100.0	142	95.9	148	100.0
0.3 (20/40) or better	**147**	**99.3**	**147**	**100.0**	**148**	**100.0**	**148**	**100.0**
0.4-0.6 (20/50-20/80)	1	0.7	0	0.0	0	0.0	0	0.0
0.7 (20/100) or worse	0	0.0	0	0.0	0	0.0	0	0.0

Note that low contrast acuties were not evaluated in this study.

Optical/Visual Symptoms

The most commonly reported directed symptoms at 6 months based on a questionnaire (**Table 18**) were halos, starbursts, and glare for both IOL groups; halos and starbursts were reported with increased bother in the Symfony group compared with the monofocal group.

TABLE 18
Experience/Bother with Visual Symptoms over the Past 7 Days at 6 Months (Directed Reports)

		Symfony N=147		Monofocal N=148	
		n	**%**	**n**	**%**
Halos	None	60	40.8	105	70.9
	Bother a little bit	46	31.3	24	16.2
	Bother somewhat	18	12.2	13	8.8
	Bother quite a bit	13	8.8	2	1.4
	Very bothered	10	6.8	4	2.7
Starbursts	None	62	42.2	110	74.3
	Bother a little bit	42	28.6	18	12.2
	Bother somewhat	18	12.2	12	8.1
	Bother quite a bit	13	8.8	2	1.4
	Very bothered	12	8.2	6	4.1
Glare[b]	None	62	42.8	85	57.4
	Bother a little bit	53	36.6	35	23.6
	Bother somewhat	12	8.3	18	12.2
	Bother quite a bit	10	6.9	5	3.4
	Very bothered	8	5.5	5	3.4
Streaks of Light[b]	None	122	84.7	126	85.1
	Bother a little bit	11	7.6	10	6.8
	Bother somewhat	5	3.5	7	4.7
	Bother quite a bit	2	1.4	1	0.7
	Very bothered	4	2.8	4	2.7
Occlusions (Shadows)[b]	None	139	95.2	140	94.6
	Bother a little bit	4	2.7	4	2.7
	Bother somewhat	1	0.7	2	1.4
	Bother quite a bit	0	0.0	0	0.0
	Very bothered	2	1.4	2	1.4
Sensitivity to Light[b]	None	65	44.5	75	50.7
	Bother a little bit	53	36.3	38	25.7
	Bother somewhat	15	10.3	18	12.2
	Bother quite a bit	9	6.2	6	4.1
	Very bothered	4	2.7	11	7.4
Poor Low Light Vision[b]	None	60	41.1	60	40.5
	Bother a little bit	64	43.8	56	37.8
	Bother somewhat	13	8.9	21	14.2

		Symfony N=147		Monofocal N=148	
		n	**%**	**n**	**%**
	Bother quite a bit	7	4.8	8	5.4
	Very bothered	2	1.4	3	2.0

%=n/N (total) excluding not reported

[a] None includes "did not experience symptom" and "experienced symptom but not bothered".

[b] "Not Reported" - Two Symfony subjects did not respond to the glare question, three Symfony subjects did not respond to the streaks of light question, and one Symfony subject did not respond to the occlusion question, to the sensitivity to light question and to the poor low light vision question.

Optical/visual symptoms spontaneously reported by subjects to investigators (non-directed reports) are noted in **Table 19.** Note that symptoms rates based upon reports directly to investigators are generally not considered as reliable as those collected using questionnaires. The rates reported to physicians are typically lower than the rates reported by patients on a questionnaire specifically asking about their experience (directed reports; **Table 18**).

TABLE 19
Spontaneous (Non-Directed[a]) Reports of Ocular Symptoms at 6 Months

Ocular Symptoms	Symfony N=147		Control N=148	
	n	%	n	%
Image Quality				
Blurred vision	25	17.0	35	23.6
Overall	6	4.1	8	5.4
Distance	9	6.1	3	2.0
Intermediate	1	0.7	2	1.4
Near	13	8.8	26	17.6
Optical/Visual				
Halos	24	16.3	2	1.4
Mild	9	6.1	1	0.7
Moderate	11	7.5	0	0.0
Severe	4	2.7	1	0.7
Night Glare	4	2.7	0	0.0
Mild	1	0.7	0	0.0
Moderate	3	2.0	0	0.0
Severe	0	0.0	0	0.0
Starbursts	13	8.8	2	1.4
Mild	6	4.1	1	0.7
Moderate	5	3.4	1	0.7
Severe	2	1.4	0	0.0
Night vision difficulty (overall)	4	2.7	0	0.0
Sensation Dryness	12	8.2	16	10.8

%=n/N (Total)

Note: Includes reports of optical/visual symptoms common to traditional multifocal IOLs (halos, night glare, starbursts, and night vision difficulties) as well as any findings reported with an incidence of 10% or more at 6 months.

[a] Non-directed, spontaneously-reported subject responses were obtained from the open-ended question “Are you having any difficulties with your eyes or vision?”.

The rates of subjects expressing some desire to have lenses removed or replaced due to visual symptoms or other problems with vision are shown in **Table 20**.

TABLE 20
Would Want to Have Lens(es) Removed and Replaced due to Visual Symptoms or Other Problems with Vision at 6 Months

		Symfony N=147		Monofocal N=148	
		n	**%**	**n**	**%**
Lens removed and replaced	Yes	5[a]	3.4	13[a]	8.8
	No	119	81.0	108	73.0
	NA[b]	23	15.6	27	18.2

%=n/N(Total) excluding not reported.

[a] One Symfony subject (0.7%; 1/147) and one monofocal subject (0.7%; 1/148) indicated a desire to have the lenses removed/replaced and the investigator determined the subject reason(s) to be related to optical lens design, i.e., a potential secondary surgical intervention.

[b] NA = NOT APPLICABLE, did not experience any visual symptoms

Based upon the safety analyses provided for this study, and the safety results of the parent IOLs, of which the Symfony is only an optical modification, FDA review finds that there is reasonable assurance of device safety.

2. Effectiveness Results

The analysis of effectiveness was based on 147 evaluable subjects for Symfony and 148 evaluable subjects for the control group at the 6-month time point. Key effectiveness outcomes are presented in **Tables 21 to 29** and **Figures 2 to 5**.

Intermediate High-Contrast Photopic Visual Acuities

Intermediate visual acuities were tested using 100% ETDRS near charts at a fixed test distance of 66 cm, with and without distance correction, under photopic (85 cd/m^2) lighting conditions.

The primary effectiveness endpoints of improved monocular, uncorrected and distance corrected intermediate visual acuity (UCIVA and DCIVA) at 66 cm were achieved for the Symfony IOL. As shown in **Table 21**, there were statistically significant improvements (**p<0.0001**; ITT population) in mean UCIVA and DCIVA at 6 months in favor of the Symfony lens with improvements of 1.7 and 2.4 lines, respectively. Additionally, as shown in **Table 22**, there were clinically significant improvements in favor of the Symfony IOL with 76.9% (113/147) and 70.1% (103/147) of Symfony eyes achieving UCIVA and DCIVA of 20/25 or better, respectively, compared to 33.8% (50/148) and 13.5% (20/148) of monofocal eyes. These intermediate visual acuity results demonstrate the effectiveness of the Symfony IOL to provide improved intermediate vision compared to the monofocal control lens. Binocular distribution results are presented in **Table 23.**

TABLE 21
Mean Monocular and Binocular Uncorrected and Distance Corrected Intermediate Visual Acuity at 66 cm at 6 Months

		Monocular				Binocular			
Visual Acuity[a]	Lens Group	N	Mean LogMAR	Snellen Line Equiv.	Line Change vs. Control	N	Mean LogMAR	Snellen Line Equiv.	Line Change vs. Control
Uncorrected	Symfony	147	0.087[a]	20/25	1.7 lines	147	0.002	20/20	1.3 lines
	Control	148	0.256[a]	20/40		148	0.134	20/25	
Distance Corrected	Symfony	147	0.104[a]	20/25	2.4 lines	147	0.032	20/20	1.9 lines
	Control	148	0.342[a]	20/40		148	0.227	20/32	

[a] The primary study endpoints are uncorrected and distance corrected intermediate VA for first eyes. Symfony had significantly better mean UCIVA and DCIVA compared to Control with **p<0.0001** (from one-sided two-sample t-test).

TABLE 22
Monocular Uncorrected and Distance Corrected Intermediate Visual Acuity at 66 cm at 6 Months

Monocular Intermediate Visual Acuity LogMAR (Snellen)	Symfony				Monofocal Control			
	Uncorrected N=147		Distance Corrected N=147		Uncorrected N=148		Distance Corrected N=148	
	N	%	n	%	n	%	n	%
0.0 (20/20) or better	60	40.8	51	34.7	19	12.8	7	4.7
0.1 (20/25) or better	**113**	**76.9**	**103**	**70.1**	**50**	**33.8**	**20**	**13.5**
0.2 (20/32) or better	136	92.5	133	90.5	81	54.7	47	31.8
0.3 (20/40) or better	145	98.6	143	97.3	103	69.6	79	53.4
0.4-0.6 (20/50-20/80)	2	1.4	4	2.7	45	30.4	63	42.6
0.7 (20/100) or worse	0	0.0	0	0.0	0	0.0	6	4.1

TABLE 23
Binocular Uncorrected and Distance Corrected Intermediate Visual Acuity at 66 cm at 6 Months

Binocular Visual Acuity	Symfony		Control	
	Uncorrected	Distance Corrected	Uncorrected	Distance Corrected
20/20 or better	74.8%	61.9%	31.1%	8.1%
20/25 or better	**96.6%**	**92.5%**	**60.1%**	**35.1%**
20/32 or better	100.0%	100.0%	83.1%	62.8%
20/40 or better	100.0%	100.0%	91.9%	79.7%
20/50-20/80	0.0%	0.0%	8.1%	20.3%
20/100 or worse	0.0%	0.0%	0.0%	0.0%
Total	**147**	**147**	**148**	**148**

Binocular UCIVA and DCIVA results are presented in **Tables 24 and 25**. Mean binocular results improved by 1-2 lines over monocular testing, although the differences between groups remained comparable (**Table 26**). The proportions of subjects achieving 20/25 or better binocularly were higher for the Symfony IOL vs. control IOL for binocular UCIVA and DCIVA (**Table 24**).

All statements apply only to high-contrast photopic visual acuities, as low-contrast intermediate visual acuities were not assessed in this study.

Table 24
Mean Binocular Uncorrected and Distance Corrected Intermediate Visual Acuity at 66 cm at 6 Months

Binocular Intermediate Visual Acuity	IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.
Uncorrected	Symfony	147	0.002	20/20	0.085
	Monofocal	148	0.134	20/25	0.142
	Difference		**0.132**	**1.3 lines**	-
Distance	Symfony	147	0.032	20/20	0.086
Corrected	Monofocal	148	0.227	20/32	0.140
	Difference		**0.195**	**1.9 lines**	-

Near High-Contrast Photopic Visual Acuities

Near visual acuities were tested using 100% ETDRS near charts at a fixed test distance of 40 cm, with and without distance correction, under photopic (85 cd/m2) lighting conditions.

The secondary effectiveness endpoint of improved monocular, distance corrected near visual acuity (DCNVA) at 40 cm was achieved for the Symfony IOL. As shown in **Table 25**, there was a statistically significant improvement (**$p<0.0001$**; ITT population) in mean monocular DCNVA at 6 months in favor of the Symfony lens with an improvement of 2.2 lines. Additionally, as shown in **Table 27**, there were clinically significant improvements in favor of the Symfony IOL with 61.9% (91/147) of Symfony eyes achieving DCNVA of 20/40 or better compared to 16.2% (24/148) of monofocal eyes. Monocular uncorrected distance visual acuity results (UCNVA) were comparable to DCNVA results. These near visual acuity results demonstrate the effectiveness of the Symfony IOL to provide substantial near vision improvement compared to the monofocal control lens. **Table 26**, shows the mean binocular uncorrected and distance corrected near visual acuity at 40 cm at 6 months

Table 25
Mean Monocular Uncorrected and Distance Corrected Near Visual Acuity at 40 cm at 6 Months

Monocular Near Visual Acuity	IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.
Uncorrected	Symfony	147	0.241	20/32	0.142
	Monofocal	148	0.459	20/63	0.183
	Difference		**0.218**	**2.2 lines**	-
Distance Corrected	Symfony	147	0.323[a]	20/40	0.146
	Monofocal	148	0.544[a]	20/63	0.175
	Difference		**0.221[a]**	**2.2 lines**	-

[a] Statistically significant improvement, **p<0.0001** (1-sided 2-sample t-test) 90% Confidence Interval around mean difference [0.184; 0.258].

TABLE 26
Mean Binocular Uncorrected and Distance Corrected Near Visual Acuity at 40 cm at 6 Months

		Binocular			
Visual Acuity	Lens Group	N	Mean LogMAR	Snellen Line Equiv.	Line Change vs. Control
Uncorrected	Symfony	147	0.146	20/25	1.8 lines
	Control	148	0.328	20/40	
Distance Corrected	Symfony	147	0.229	20/32	2.0 lines
	Control	148	0.426	20/50	

TABLE 27
Monocular Uncorrected and Distance Corrected Near Visual Acuity at 40 cm at 6 Months

Monocular Near Visual Acuity LogMAR (Snellen)	Symfony				Monofocal Control			
	Uncorrected N=147		Distance Corrected N=147		Uncorrected N=148		Distance Corrected N=148	
	N	%	n	%	n	%	n	%
0.0 (20/20) or better	14	9.5	5	3.4	0	0.0	0	0.0
0.1 (20/25) or better	42	28.6	16	10.9	1	2.7	1	0.7
0.2 (20/32) or better	82	55.8	49	33.3	26	17.6	5	3.4
0.3 (20/40) or better	**119**	**81.0**	**91**	**61.9**	**46**	**31.1**	**24**	**16.2**
0.4-0.6 (20/50-20/80)	28	19.0	54	36.7	80	54.1	83	56.1
0.7 (20/100) or worse	0	0	2	1.4	22	14.9	41	27.7

Binocular UCNVA and DCNVA results are presented in **Tables 28 and 29**. Mean binocular results improved by 1 - 2 lines over monocular testing, although the differences

between groups remained comparable (**Table 28**). The proportions of subjects achieving 20/40 or better binocularly were higher for the Symfony IOL vs. control IOL for binocular UCNVA and DCNVA, respectively (**Table 29**).

All statements apply only to high-contrast photopic visual acuities, as low-contrast near visual acuities were not assessed in this study.

Table 28
Mean Binocular Uncorrected and Distance Corrected Near Visual Acuity at 40 cm at 6 Months

Binocular Near Visual Acuity	IOL	N	Mean LogMAR	Snellen Line Equivalent	Std. Dev.
Uncorrected	Symfony	147	0.146	20/25	0.112
	Monofocal	148	0.328	20/40	0.167
	Difference		**0.181**	**1.8**	-
Distance Corrected	Symfony	147	0.229	20/32	0.114
	Monofocal	148	0.426	20/50	0.159
	Difference		**0.197**	**2.0 lines**	-

TABLE 29
Binocular Uncorrected and Distance Corrected Near Visual Acuity at 40 cm at 6 Months

Binocular Near Visual Acuity LogMAR (Snellen)	Symfony				Monofocal Control			
	Uncorrected N=147		Distance Corrected N=147		Uncorrected N=148		Distance Corrected N=148	
	N	%	n	%	n	%	n	%
0.0 (20/20) or better	32	21.8	12	8.2	7	4.7	2	1.4
0.1 (20/25) or better	81	55.1	35	12.8	19	12.8	7	4.7
0.2 (20/32) or better	124	84.4	77	52.4	50	33.8	19	12.8
0.3 (20/40) or better	**141**	**95.9**	**133**	**90.5**	**93**	**62.8**	**51**	**34.5**
0.4-0.6 (20/50-20/80)	6	4.1	14	9.5	48	32.4	87	58.8
0.7 (20/100) or worse	0	0.0	0	0.0	7	4.8	10	6.8

Defocus Testing

Defocus curve testing was performed on a subset of subjects from each lens group at 8 sites at the 6-month study exam to evaluate monocular and binocular best corrected distance visual acuity defocus curves and any effects of pupil size. Defocus testing was performed using the electronic Freiburg Visual Acuity and Contrast Test (FrACT). Mean monocular defocus range for which acuity was 20/32 or better was a secondary study endpoint; the primary analysis group included eyes that achieved BCDVA of 20/25 or better using both ETDRS and FrACT. Monocular results were also analyzed for three pupil size ranges: ≤2.5 mm; >2.5 mm and <4.0 mm; and ≥4.0 mm. The defocus secondary effectiveness endpoint was met, with >0.5 D of increased range of focus

(**p<0.0001**; ITT population) of 20/32 or better visual acuity for Symfony subjects vs. monofocal control subjects.

Figures 1 and 2 present the monocular defocus curve for the Symfony and monofocal control groups with mean values and error bars for confidence intervals and standard deviations, respectively, while **Figure 3** represents the binocular defocus curves for the Symfony and monofocal groups (with mean values and error bars for confidence intervals). **Figure 4** presents monocular defocus curves by pupil size for the Symfony group. Mean monocular visual acuities were 20/32 or better for the Symfony group through intermediate defocus values of -1.5 D (66 cm); mean binocular acuities were 20/32 or better for the Symfony group through -2.0 D (50 cm). Both the monocular and binocular defocus curves demonstrate that visual acuity monotonically decreased while maintaining a 1-2 line acuity difference over the monofocal group through 4.0 D of defocus. Visual inspection of the defocus curves yielded an improvement in the range of defocus with visual acuity of 20/32 or better in favor of the Symfony IOL by approximately 1 D. When monocular results were analyzed by pupil size, no appreciable pupil size effect was observed. Because visual acuity improves in monofocal subjects with pupil sizes ≤ 2.5 mm, the improvements in depth of focus between Symfony and monofocal groups are less pronounced in this subset of subjects. Some individual eyes showed drops in acuity below 20/32 between far and intermediate/near distances that are believed to be related to measurement noise when using the FrACT automated test system used in the study.

FIGURE 1
Monocular Defocus Curves at 6 Months
Symfony and Monofocal Control
(with 95% Confidence Intervals)

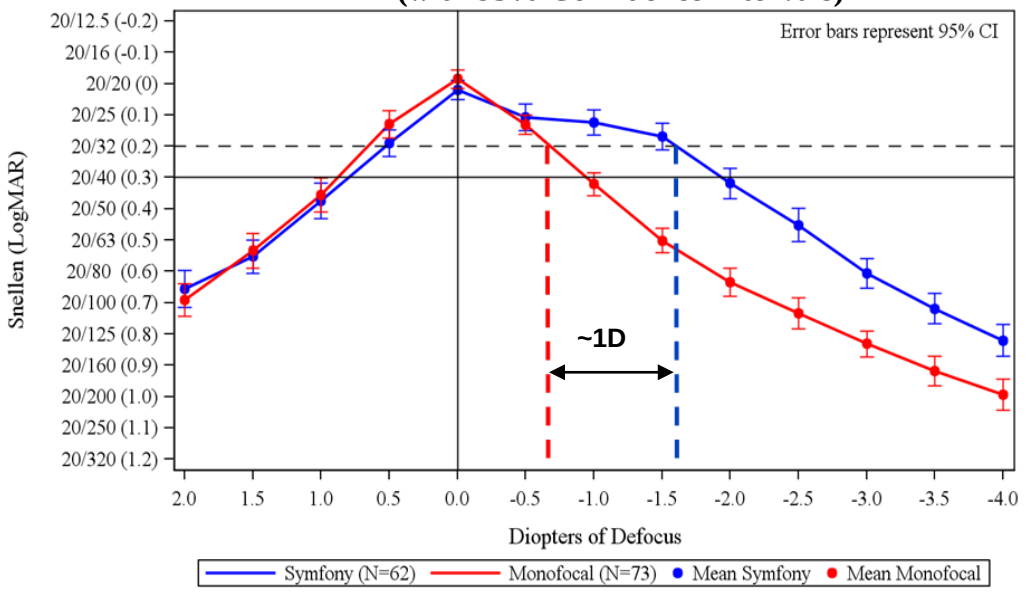


FIGURE 2
Monocular Defocus Curves at 6 Months
Symfony and Monofocal Control
(with Error Bars Representing 1 Standard Deviation)

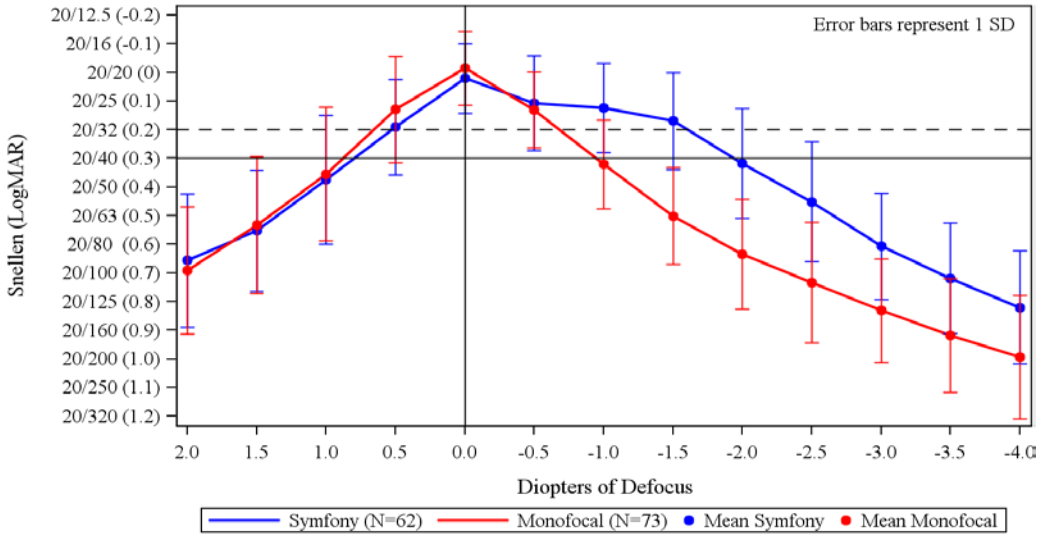


FIGURE 3
Binocular Defocus Curves at 6 Months
Symfony and Monofocal Control

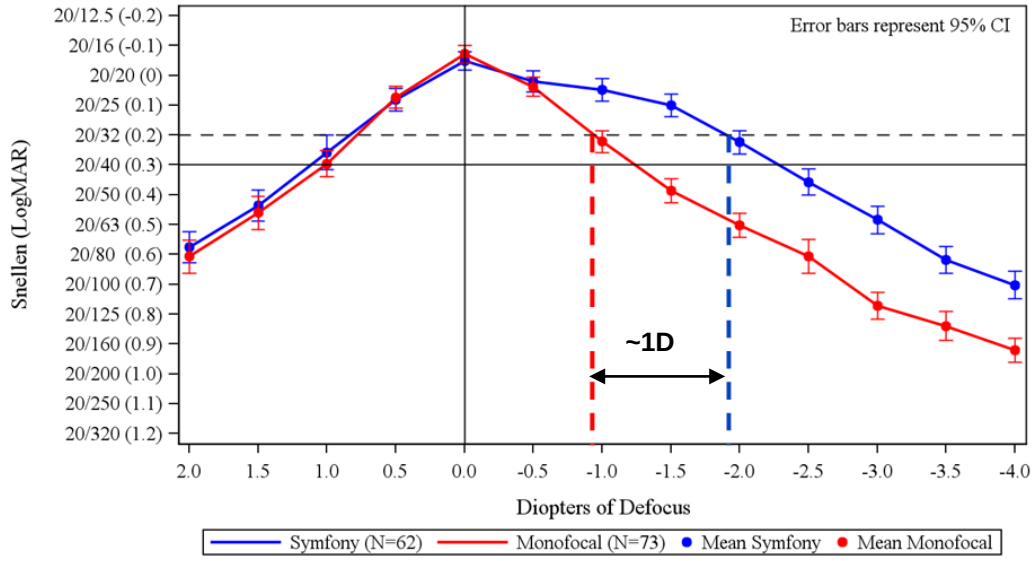
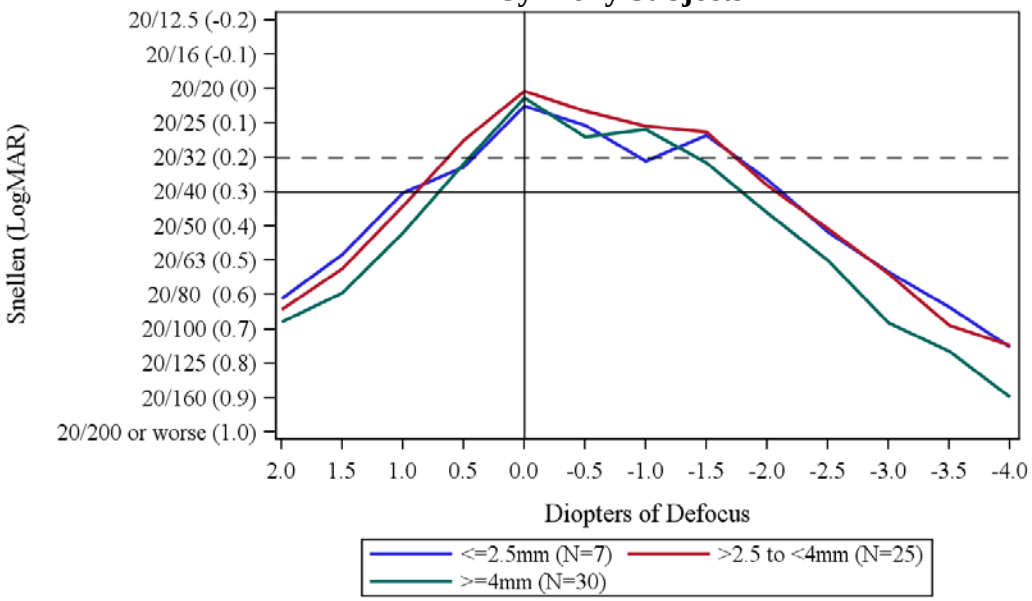


FIGURE 4
Monocular Defocus Curve at 6 Months By Pupil Size
Symfony Subjects

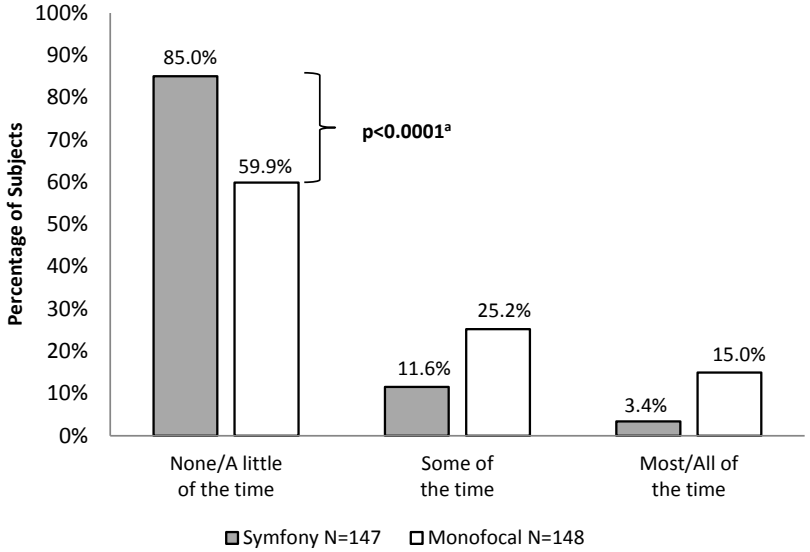


Overall Spectacle Wear

Spectacle wear and other related items were assessed using a self-reported, binocular subjective questionnaire: the Patient Reported Spectacle Independence Questionnaire (PRSIQ). This questionnaire was developed and evaluated following the US FDA guidance document "Patient-Reported Outcomes Measures: Use in Medical Product Development to Support Labeling Claims," dated December 2009. Although the questionnaire was not determined to be a psychometrically valid assessment of the concept of spectacle independence, data showed that the Symfony IOL achieved the secondary effectiveness endpoint of reduced overall spectacle wear compared to the control monofocal IOL.

The spectacle wear secondary effectiveness endpoint is based on the proportion of subjects who reported wearing glasses or contacts "none of the time" or "a little of the time" for overall vision, collected from a single question in the PRSIQ. **Figure 5** presents the frequency of overall spectacle wear for bilaterally implanted subjects at 6 months. There was a statistically significantly higher ($p<0.0001$; modified ITT population) proportion of subjects in the Symfony group compared to the monofocal group who reported wearing glasses "none of the time" or "a little of the time" (secondary effectiveness endpoint). Clinical significance was achieved with 85% (125/147) of Symfony subjects vs. 59.9% (88/148) of control subjects reporting wearing glasses "none of the time" or "a little of the time" for overall vision. Additionally, 62.6% (92/147) of Symfony subjects vs. 32.0% (47/148) of monofocal subjects indicated wearing glasses or contacts "none of the time" for overall vision.

FIGURE 5
Overall Spectacle Wear at 6 Months



[a] "None of the time" and "A little of the time" combined; 1-sided Fisher's exact test.

FDA review found the analyses on the key effectiveness endpoint as providing valid scientific evidence concerning the effectiveness of the device in providing improved intermediate and near visual acuity, while maintaining comparable distance high contrast visual acuity.

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes: age, sex, ethnicity, iris color and race. No statistically significant differences were found for age, sex, ethnicity or iris color. Although, there was a statistically significant difference with respect to race, with more non-White subjects in the monofocal control group than in the Symfony group, primary and secondary effectiveness endpoints were not significantly different among races. As expected, best corrected distance visual acuity was related to age, with younger subjects having a larger proportion of eyes at 20/20 or better. Outcomes for intermediate visual acuity, near visual acuity, depth of focus, and contrast sensitivity were consistent across demographic population and among study sites.

4. 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 18 investigators of which none were full-time or part-time employees of the sponsor and 4 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0 investigators
- Significant payments of other sorts: 4 investigators
- Proprietary interest in the product tested held by the investigator: 0 investigators
- Significant equity interest held by investigator in sponsor of covered study: 0 investigators.

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

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

. Two feasibility studies comparing the non-toric TECNIS® Symfony IOL to a monofocal control were conducted. No issues regarding device safety or lack of effectiveness were raised by the results from these studies.

Please note that **Tables 17-38** in the labeling are incorporated by reference from previous approvals. As a result, these tables were not repeated within this SSED. Below identifies which tables are associated with each submission:

Tables 17-26: P980040/S039
Tables 27-35: P080010
Tables 36-38: P980040/S015

P980040/S015 was a 180-day supplement; therefore, for convenience these tables are provided below and referenced as Tables 29-31. Here, a total of 123 subjects were enrolled and implanted with the SENSAR 1-Piece IOL, Model AAB00. In the study population, 56.9% of subjects were female and 43.1% were male; 93.5% were Caucasian, 4.1% were Black and 2.4% were Asian. The best corrected distance visual acuity results for the "best case" subjects at 1 year postoperatively are provided in **Table 30**. In addition the results compared to the FDA Grid values (historical control) are presented in **Table 31**. All the associated adverse events for this study is included in **Table 32**.

TABLE 30
Best Corrected Distance Visual Acuity (Snellen Equivalent) at 1 Year
Best Case Subjects[a] (N = 110)

Age Group	N	20/20 or Better		20/25 to 20/40		20/50 to 20/100		20/125 or Worse	
		n	%	N	%	n	%	n	%
< 60	11	11	100.0	0	0.0	0	0.0	0	0.0
60-69	35	29	82.9	6	17.1	0	0.0	0	0.0
70-79	46	39	84.8	7	15.2	0	0.0	0	0.0
≥ 80	18	14	77.8	4	22.2	0	0.0	0	0.0
TOTAL[b]	**110**	**93**	**84.5**	**17**	**15.5**	**0**	**0.0**	**0**	**0.0**

[a] Excludes subjects with macular degeneration at any time during the study.

[b] Includes three subjects who experienced a Nd:YAG posterior capsulotomy.

TABLE 31
Best Corrected Distance Visual Acuity (Snellen Equivalent) at 1 Year
Best Case Subjects[a] (N = 110) vs. FDA Grid

Age Group	TOTAL		VISUAL ACUITY 20/40 OR BETTER		FDA GRID
	N	%	N	%	%
< 60	11	10.0	11	100.0	98.5
60 – 69	35	31.8	35	100.0	96.5
70 – 79	46	41.8	46	100.0	97.5
> 80	18	16.4	18	100.0	94.8
TOTAL[b]	**110**	**100.0**	**110**	**100.0**	**96.7**

[a] Excludes subjects with macular degeneration at any time during the study.

[b] Includes three subjects who experienced a Nd:YAG posterior capsulotomy.

TABLE 32
Adverse Events Model AAB00
All Subjects (N = 123)

ADVERSE EVENTS	Cumulative		Persistent at 1 Year		FDA Grid	
	N	%	N	%	Cumulative %	Per %
Persistent Corneal Edema	-	-	0	0.0	-	0.3
Cystoid Macular Edema (CME)	4	3.3[a]	1	0.9[b]	3.0	0.5
Endophthalmitis	0	0.0	-	-	0.1	-
Hyphema	0	0.0	-	-	2.2	-
Hypopyon	0	0.0	-	-	0.3	-
Persistent Iritis	-	-	0	0.0	-	0.3
Secondary Surgical Intervention – Pars Plana Vitrectomy with Membrane Peel	1	0.8	-	-	0.8	-
Lens Dislocation	0	0.0	-	-	0.1	-
Pupillary Block	0	0.0	-	-	0.1	-
Retinal Detachment	0	0.0	-	-	0.3	-
Persistent Raised IOP Requiring Treatment	-	-	0	0.0	-	0.4
Lens Exchange						
–Torn Haptic related to improper loading technique	1	0.8	-	-	-	-

[a] This rate is not statistically significantly higher than the FDA Grid cumulative rate for posterior chamber IOLs of 3.0% (p=0.5060).
[b] This rate is not statistically significantly higher than the FDA Grid rate for posterior chamber IOLs of 0.5% (p=0.4437).

Overall, the safety and effectiveness outcomes from prior clinical studies support the safety and effectiveness of the TECNIS® Symfony Extended Range of Vision IOLs.

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The overall effectiveness of the TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, was demonstrated based on the 6-month results of the IDE clinical investigation. In addition, the effectiveness of the toric models (Models ZXT150, ZXT225, ZXT300, and ZXT375) in providing reduced postoperative refractive astigmatism is supported by the clinical data provided for the toric parent IOL in P980040-S039, which has the same toric surface and mechanical/material design (differing only in not having an extended depth of focus optical design).

The primary effectiveness endpoints, improvements in monocular uncorrected and distance corrected intermediate visual acuity (UCIVA and DCIVA) at 66 cm compared

to control, were achieved by the TECNIS® Symfony IOL. There were statistically significant improvements ($p<0.0001$) of 1.7 lines in mean UCIVA and 2.4 lines in mean DCIVA in favor of the TECNIS® Symfony IOL compared to the monofocal IOL. Additionally, there were clinically significant improvements in favor of the Symfony IOL with 76.9% (113/147) and 70.1%, (103/147) of Symfony eyes achieving UCIVA and DCIVA of 20/25 or better, respectively, compared to 33.8% (50/148) and 13.5% (20/148) of monofocal eyes.

The secondary endpoint of mean range of monocular defocus was achieved with a statistically significantly ($p<0.0001$) greater mean range visual acuity of 20/32 or better for the TECNIS® Symfony IOL compared to the monofocal IOL. Graphical analyses yielded a difference between IOL groups of approximately 1 D of improved defocus range with visual acuity of 20/32 or better. The secondary endpoint of monocular distance corrected near visual acuity (DCNVA) was also achieved with a statistically significant improvement ($p<0.0001$) in mean monocular DCNVA at 40 cm in favor of the TECNIS® Symfony IOL with 2.2 lines of improvement in near visual acuity. There was also a clinically significant improvement in DCNVA as 61.9% (91/147) of Symfony eyes achieved 20/40 or better DCNVA compared to 16.2% (24/148) of control eyes.

Overall, the effectiveness of the TECNIS® Symfony Extended Range of Vision IOL was demonstrated in the clinical IDE investigation with the ability of the IOL to increase depth of focus, providing improved uncorrected and distance corrected intermediate and near vision compared to a monofocal IOL.

B. Safety Conclusions

The safety profile of the TECNIS® Symfony Extended Range of Vision IOL is based on nonclinical laboratory studies as well as a primary clinical study conducted to support PMA approval. In addition, the clinical data from the U.S. studies for the TECNIS® Multifocal IOL Model ZM900 (G030191, P080010 – the multifocal optical parent lens) and the SENSAR 1-Piece IOL, Model AAB00 (G050183, P980040/S015 – the material/mechanical parent lens) provided data that are highly relevant to Symfony device safety. These studies of the parent IOLs included 1 year of patient follow-up on at least 300 subjects.

The TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, is made of the same FDA-approved surface-treated SENSAR soft acrylic material as its material parent, the SENSAR 1-Piece IOL, Model AAB00 (P980040/S015), and its monofocal analog, the TECNIS® 1-Piece IOL, Model ZCB00 (P980040/S015), which has a long history of safe clinical use. The results of prior nonclinical laboratory testing and animal studies on the SENSAR acrylic material and the one-piece lens design support safety of this lens model. The results of dimensional, optical and mechanical testing, and folding/recovery properties of the TECNIS® Symfony IOL demonstrated conformance to applicable sections of ISO 11979-2 and ISO 11979-9, ISO 11979-3, ANSI Z80.30, and internal product specifications.

The 6-month results of the IDE clinical investigation of the TECNIS® Symfony Extended Range of Vision IOL, Model ZXR00, provide reasonable assurance of the safety of this lens model. The incidence of adverse events in the study was 2.7% (4/148) of TECNIS® Symfony patients and 6.0% (9/151) of monofocal control subjects experienced serious adverse events and no subjects (0%; 0/299) experienced unanticipated events. The observed persistent and cumulative complication/adverse event rates for the TECNIS® Symfony IOL were not statistically higher than the specified ISO SPE (safety performance endpoint) rates.

The study failed to provide evidence to support the sponsor's proposed claim that the monocular mesopic contrast sensitivity (at the 12 cpd spatial frequency – tested with and without glare) for Symfony IOL-implanted subjects is non-inferior to that of monofocal IOL-implanted subjects. In general, contrast sensitivity for Symfony-implanted eyes was lower than that for monofocal-implanted eyes. Best corrected distance visual acuity results at 6 months for the TECNIS® Symfony IOL were clinically comparable and statistically non-inferior to those for the monofocal control group. When asked in the PRSVQ questionnaire, increased rates of bothersome visual symptoms due to halos, starbursts and glare were reported by TECNIS® Symfony subjects compared to monofocal subjects.

C. Benefit-Risk Determination

The probable benefits of the TECNIS® Symfony Extended Range of Vision IOLs, Models ZXR00, ZXT150, ZXT225, ZXT300, and ZXT375, are based on data collected in a clinical study conducted to support PMA approval and other clinical studies, as described above. The benefits of the subject devices are summarized as follows:

a. As do all intraocular lenses, these provide a lifelong benefit of optically replacing the crystalline lens for adult patients in whom a cataractous lens has been removed. This is a defined and predictable patient group with a non-life-threatening, well-characterized condition (aphakia).
b. Compared to an aspheric monofocal IOL, these Symfony lens models provide improved intermediate and near visual acuity, while maintaining comparable distance visual acuity.
c. For patients with preoperative corneal astigmatism greater than 1 diopter, the toric models provide reduction in residual refractive astigmatism, compared to a monofocal IOL.

Additional factors to be considered in determining probable risks and benefits for the TECNIS® Symfony Extended Range of Vision IOLs, Models ZXR00, ZXT150, ZXT225, ZXT300, and ZXT375, include:

a. The results of the clinical study can be considered generalizable to the intended market or target patient population.

b. Clinical data were collected using a study design that included randomized treatment and masking of subjects and evaluators.
c. Medical adverse events and complications (e.g., risks of infection, inflammation, corneal edema, etc.) are similar to those associated with most other intraocular lenses.

d. The risks associated with the optical design providing an extended depth of focus include reduced contrast sensitivity and visual symptoms related to stay light, such as glare, halos and starbursts. Some of these may make some tasks such as driving, more difficult under certain circumstances. These issues are mitigated by labeling which informs users of these risks and quantifies them.

e. 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 related to cataract surgery, in adult patients with less than 1 diopter of pre-existing corneal astigmatism, and for mitigating the effects of presbyopia in these patients by providing an extended depth of focus, the probable benefits of the Model ZXR00 TECNIS® Symfony IOL outweigh the probable risks. Similarly, the data support that for the visual correction of aphakia related to cataract surgery, in adult patients with greater than or equal to 1 diopter of preoperative corneal astigmatism, and for the reduction of residual refractive astigmatism, and for mitigating the effects of presbyopia in these patients by providing an extended depth of focus, the probable benefits of the toric models of the TECNIS® Symfony IOL outweigh the probable risks.

D. Overall Conclusions

The data in this premarket application support the reasonable assurance of safety and effectiveness of the subject devices when used in accordance with the Indications for Use and the labelled Directions for Use. All effectiveness endpoints related to depth of focus, intermediate and near vision were met, demonstrating the ability of the TECNIS® Symfony IOL to provide an extended depth of focus, with clinically significant 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. Contrast sensitivity losses were observed as compared to monofocal IOLs, while best corrected distance high contrast visual acuity was comparable

XIV. CDRH DECISION

CDRH issued an approval order on July 15, 2016. The final conditions of approval cited in the approval order are described below.

The TECNIS® Symfony Toric New-Enrollment Study is a study designed to evaluate the rate of visual symptoms and distortions experienced with the TECNIS® Symfony Toric Intraocular Lenses (IOLs) with greater than 2.0 D of cylinder correction at the corneal plane (Models ZXT300 and ZXT375, "higher-cylinder group") in comparison to the rate of visual symptoms and distortions experienced with the TECNIS® Symfony Toric IOL with approximately 1.0 D of cylinder correction at the corneal plane (Model ZXT150, "lower-cylinder group"). The study is intended to ensure the safety of the approved devices and will be conducted in three phases.

Phase One:
Phase one of the study is comprised of the development of the *Patient Reported Visual Symptoms Questionnaire* (PRVSQ) and further development of the existing *Patient Reported Visual Distortions Questionnaire* (PRVDQ). Using an iterative process, the questionnaires will be modified and evaluated through patient interviews; final versions will undergo cognitive debriefing processes for further qualitative assessment.

Results of the development work for both questionnaires will be submitted to and must be accepted by the FDA prior to the initiation of Phase two.

Phase Two:
Phase two involves the quantitative assessment and validation of the aforementioned questionnaires. The design of the validation studies will be submitted to FDA for review and approval prior to initiation. If the PRVDQ is modified, the validation will involve the assessment of visual distortions with and without induced astigmatism (similar to the processes performed under P980040/S039 and P980040/S044). For the PRVSQ, quantitative evaluation will be performed using an existing population of multifocal and monofocal patients to assess the ability of the questionnaire to discriminate known differences between populations, as well as the repeatability of responses.

The results of this validation work will be submitted to the FDA for review and approval prior to the initiation of Phase three. Additionally, if determined to be necessary based on the results from phases one and two, a protocol revision for Phase three will also be submitted and must be approved by the FDA prior to Phase three initiation.

Phase Three:
Phase three, or the Post-Approval Study Phase, consists of a prospective, multicenter (up to 50 sites), bilateral, non-randomized, open-label comparative clinical study of TECNIS Symfony Toric patients in the higher-cylinder group (models ZXT300 and ZXT375) in comparison to patients in the lower-cylinder group (model ZXT150).

The primary endpoint is the rate of bothersome visual symptoms at six months postoperatively, defined as the percentage of patients that either have a 'severe' visual *distortion*:

- Lines that slant, tilt, split, or separate
- Flat surfaces appearing curved

- Objects appearing further away or closer than they actually are
- Objects appearing to have a different size or shape
- Physical discomfort related to vision

or a visual *symptom* that 'extremely bothered' them and impacted daily activity (determined by a 'yes' response to the question 'Is there anything you have a lot of difficulty with, or do not do, because of {the symptom}'):

- Halos
- Glare
- Starbursts

The study hypothesis associated with this endpoint is that the rate of bothersome visual symptoms for the higher-cylinder group will be less than eight percentage points above the rate of bothersome visual symptoms for the lower-cylinder group.

Results for bothersome visual symptoms will be evaluated using a non-inferiority approach with a non-inferiority margin of eight percentage points. The upper limit of the 95% confidence interval of the difference in bothersome visual symptom rates (lower-cylinder group subtracted from higher-cylinder group) will be used to evaluate the primary endpoint.

Other endpoints to be collected in this study include:

1. Ratings of individual items included on the PRVDQ
2. The rates of 'very bothersome' glare, halos, and starbursts.
3. Rates of IOL repositioning procedures (secondary surgical intervention) due to IOL misalignment
4. The rate of explants related to visual symptoms for both the higher and lower-cylinder groups
5. The rates of other adverse events

Based on the study hypothesis, 298 adult patients in the higher-cylinder group and 298 adult patients in the lower-cylinder group will need to be enrolled to ensure that 240 patients in each group are available at 6 months postoperatively; the sample size allows for an anticipated screen failure rate of 15% and an overall attrition rate of 5%. The 240 subjects in each group will provide over 90% power to evaluate the rate of bothersome visual symptoms for the higher-cylinder group as being non-inferior to the lower-cylinder group.

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.