# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

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|---|---|
| Device Generic Name: | Intraocular Lens |
| Device Trade Name: | • TECNIS Synergy™ IOL, Model ZFR00V<br>• TECNIS Synergy™ Toric II IOL, Models ZFW150, ZFW225, ZFW300, ZFW375<br>• TECNIS Synergy™ IOL with TECNIS Simplicity™ Delivery System, Model DFR00V<br>• TECNIS Synergy™ Toric II IOL with TECNIS Simplicity™ Delivery System, Model DFW150, DFW225, DFW300, DFW375 |
| Device Procode: | Multifocal Intraocular (MFK) |
| Applicant's Name and Address: | Johnson & Johnson Surgical Vision, Inc.<br>1700 East Saint Andrew Place<br>Santa Ana, CA 92705 |
| Date(s) of Panel Recommendation: | None |
| Premarket Approval Application (PMA) Number: | P980040/S124 |
| Date of FDA Notice of Approval: | |

The TECNIS Synergy™ multifocal intraocular lens (Daisywheel configuration Model ZFR00V and Simplicity™ preloaded configuration DFW00V) and toric multifocal lenses (Daisywheel configuration ZFW150, ZFW225, ZFW300, and ZFW375; Simplicity™ preloaded configuration DFW150, DFW225, DFW300 and DFW375) are based on the TECNIS multifocal ZM900 and TECNIS Symfony ZXR00 optical parents, the TECNIS Toric 1-Piece ZCT toric parent, and the TECNIS OptiBlue ZV9003 material parent. These were approved under PMAs P080010 (January 9, 2009), P980040/S065 (July 15, 2016), P980040/S039 (April 12, 2013), and P980040/S035 (September 12, 2012), respectively. The optical parents and toric parent devices have the following Indications for Use:

> TECNIS multifocal intraocular lens is indicated for primary implantation for the visual correction of aphakia in adult patients with and without presbyopia in whom

a cataractous lens has been removed by phacoemulsification and who desire near, intermediate, and distance vision with increased spectacle independence. The intraocular lenses are intended to be placed in the capsular bag.

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 Toric 1-piece posterior chamber lenses are indicated for the visual correction of aphakia and pre-existing corneal astigmatism of one diopter or greater in adult patients with or without presbyopia in whom a cataractous lens has been removed by phacoemulsification and who desire improved uncorrected distance vision, reduction in residual refractive cylinder and increased spectacle independence for distance vision. The device is intended to be placed in the capsular bag.

The SSEDs to support the indications are available on the CDRH website and are incorporated by reference here:

- https://www.accessdata.fda.gov/cdrh_docs/pdf8/P080010b.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf/P980040S065B.pdf
- https://www.accessdata.fda.gov/cdrh_docs/pdf/P980040S039b.pdf

The current supplement was submitted to modify the indications and include the TECNIS Synergy™ IOL, Model ZFR00V, TECNIS Synergy™ Toric II IOL, Models ZFW150, ZFW225, ZFW300, ZFW375, the TECNIS Synergy™ IOL with TECNIS Simplicity™ Delivery System, Model DFR00V, and the TECNIS Synergy™ Toric II IOL with TECNIS Simplicity™ Delivery System, Models DFW150, DFW225, DFW300, DFW375.

## II. INDICATIONS FOR USE

**TECNIS Synergy™ IOL, Model ZFR00V**

The TECNIS Synergy™ IOL, Model ZFR00V, 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. Compared to an aspheric monofocal lens, the TECNIS Synergy™ IOL mitigates the effects of presbyopia by providing improved visual acuity at intermediate and near distances to reduce eyeglass

wear, while maintaining comparable distance visual acuity. The lens is intended for capsular bag placement only.

**TECNIS Synergy™ Toric II IOL, Models ZFW150, ZFW225, ZFW300, ZFW375**

The TECNIS Synergy™ Toric II IOL, Models ZFW150, ZFW225, ZFW300, ZFW375, are indicated for primary implantation for the visual correction of aphakia and for the reduction of 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. Compared to an aspheric monofocal lens, the TECNIS Synergy™ Toric II IOLs mitigate the effects of presbyopia by providing improved visual acuity at intermediate and near distances to reduce eyeglass wear while maintaining comparable distance visual acuity. The lens is intended for capsular bag placement only.

**TECNIS Synergy™ IOL with TECNIS Simplicity™ Delivery System, Model DFR00V**

The TECNIS Simplicity™ Delivery System is used to fold and assist in inserting the TECNIS Synergy™ IOL which 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. Compared to an aspheric monofocal lens, the TECNIS Synergy™ IOL mitigates the effects of presbyopia by providing improved visual acuity at intermediate and near distances to reduce eyeglass wear, while maintaining comparable distance visual acuity. The lens is intended for capsular bag placement only.

**TECNIS Synergy™ Toric II IOL with TECNIS Simplicity™ Delivery System, Models DFW150, DFW225, DFW300, DFW375**

The TECNIS Simplicity™ Delivery System is used to fold and assist in inserting the TECNIS Synergy™ Toric II IOLs that are indicated for primary implantation for the visual correction of aphakia and for reduction of 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. Compared to an aspheric monofocal lens, the TECNIS Synergy™ Toric II IOLs mitigate the effects of presbyopia by providing improved visual acuity at intermediate and near distances to reduce eyeglass wear, while maintaining comparable distance visual acuity. The lens is 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 Synergy™ IOLs.

## V. DEVICE DESCRIPTION

The TECNIS Synergy™ IOLs, non-toric lens models ZFR00V/DFR00V and toric lens Models ZFW150/DFW150, ZFW225/DFW225, ZFW300/DFW300, ZFW375/DFW375, are ultraviolet light-absorbing posterior chamber IOLs that provide far vision comparable to an aspheric monofocal IOL and continuous 20/32 or better visual acuity through at least -3.0 D of defocus, which corresponds to distances ranging from approximately 33 cm to infinity. Compared to an aspheric monofocal IOL, the lens provides significantly improved near vision, including in low-light conditions. The lens material blocks UV and violet radiation up to a 10%T cutoff wavelength of 420 nm to 430 nm. In addition, the toric IOLs compensate for corneal astigmatism. TECNIS Synergy™ IOLs are to be positioned in the lens capsule to replace the optical function of the natural crystalline lens. Accommodation will not be restored. **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 anteriorly located cylinder axis marks in the toric-aspheric optic denote the meridian with the lowest power and are to be aligned with the steep corneal meridian. The squared posterior edge of the aspheric and toric-aspheric anterior optic provide a 360-degree barrier and has a frosted design to reduce potential edge glare effects. The TECNIS Synergy™ IOLs share the same one-piece lens platform, the same material, lens geometry, general dimensions, overall manufacturing process, and packaging configuration as their parent lens models, and incorporate a proprietary diffractive technology on the posterior optic that is a combination of the multifocal and extended depth of focus (EDF) technologies derived from the optical parents. The unique design features of the TECNIS Synergy™ IOLs provide far vision comparable to an aspheric monofocal IOL and continuous 20/32 or better vision from 0.0 D through at least -3.0 D of defocus. This corresponds to a distance ranging from optical infinity to 33 cm. The posterior optic of the lens has a diffractive surface derived from a combination of EDF and multifocal technologies and is designed to correct chromatic aberration and provide a range of vision from distance to intermediate to near. The TECNIS Synergy™ IOLs demonstrated pupil-independent lens performance among the pupil sizes tested (>2.5 mm).

The optic is 6.0 mm in diameter and the lens has an overall diameter of 13.0 mm. The toric lenses incorporate perpendicular maximum and minimum radii of curvature and two sets of four (total of eight) axis orientation marks on their anterior optic surfaces that correct astigmatic refractive error when aligned properly with the patient's corneal astigmatism

(predicted postoperative steep corneal meridian). The physical properties of this lens are shown in **Figure 1** and the packaging configurations are shown in **Figure 2**. The implantation systems validated for use with the TECNIS Synergy™ IOLs packaged in the Daisywheel packaging (Models ZFR00V, ZFW150-375) are the UNFOLDER Platinum One Series Implantation system with the 1MTEC30 cartridge, the ONE SERIES Ultra Insertion System (the 1VPR30 Cartridge and the DK7786 or DK7791 inserters) and the UNFOLDER® EMERALD-AR Series Implantation System (with the 1CART30 Cartridge). The TECNIS Synergy™ IOLs packaged with the TECNIS Simplicity™ Delivery System (Models DFR00V, DFW150-375) are preloaded to provide a sterile, single-use, controlled and touch-free disposable system that functions as both the primary packaging and as part of an insertion system for IOL insertion into the eye during cataract surgery.

The conversion table for cylinder powers is provided below:

| IOL Model | Cylinder Power (D) | |
|---|---|---|
| | IOL Plane (Labeled) | Corneal Plane* |
| ZFW150 | 1.50 | 1.03 |
| ZFW225 | 2.25 | 1.54 |
| ZFW300 | 3.00 | 2.06 |
| ZFW375 | 3.75 | 2.57 |

Light Transmittance: UV cut-off at 10% T for a spherical equivalent (SE) +5.0 diopter lens (thinnest), SE +20.0 diopter lens and a SE +34.0 diopter lens (thickest) are shown in **Figure 3**.

The JJSV TECNIS Toric Calculator is a web-based calculator tool that can be used to select the most appropriate TECNIS Synergy™ Toric II IOL that best suits the visual needs of the patient. The TECNIS Toric Calculator is developed and controlled by JJSV's Software Development Procedures.

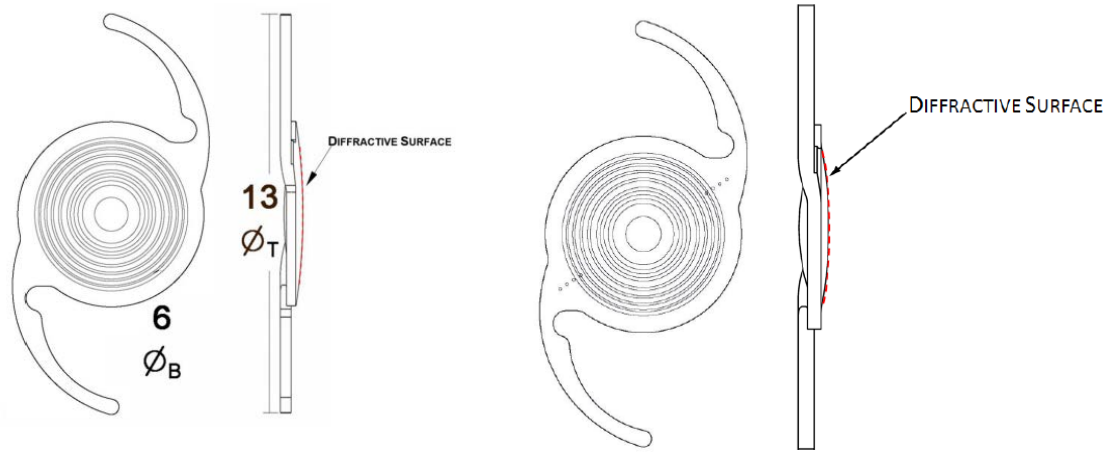
**Table 1**
**Summary of Physical Characteristics**

| Attribute | Non-Toric TECNIS Synergy™ IOL, Model ZFR00V and DFR00V | Toric TECNIS Synergy™ IOL, Model ZFW150-375 and DFW150-375 |
|---|---|---|
| Lens Design | 1-piece acrylic IOL with aspheric anterior surface | 1-piece acrylic IOL with aspheric toric anterior surface |
| Lens Material | Violet-light filtering soft acrylic material with polyethylene glycol surface treatment | |
| Optic diameter | 6.00 mm | |
| Overall Diameter | 13.00 mm | |
| Haptic Style | C-Loop<br>Tumble polished | C-Loop<br>Squared, frosted |
| Haptic angle | No angulation but offset from optic body | |

| Attribute | Non-Toric TECNIS Synergy™ IOL, Model ZFR00V and DFR00V | Toric TECNIS Synergy™ IOL, Model ZFW150-375 and DFW150-375 |
|---|---|---|
| Diopter Power Range | Spherical equivalent: +5.0 D to +34.0 D in 0.5 D increments | Spherical equivalent: +5.0 D to +34.0 D in 0.5 D increments<br><br>Cylinder power:<br>Model ZFW150/DFW150: 1.50D<br>Model ZFW225/DFW225: 2.25D<br>Model ZFW300/DFW300: 3.00D<br>Model ZFW375/DFW375: 3.75D |
| Corneal Plane, approximate (Diopter) | 0.0 | Model ZFW150/DFW150: 1.03D<br>Model ZFW225/DFW225: 1.54D<br>Model ZFW300/DFW300: 2.06D<br>Model ZFW375/DFW375: 2.57D |
| Refractive Index | 1.471 (35°C) | |
| Range of Vision | Through -3.0D | |

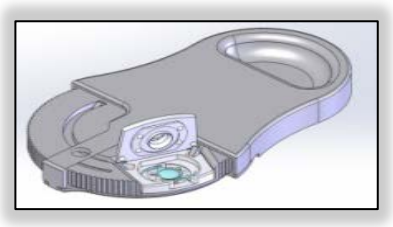
**Figure 1**
**Mechanical Drawings**

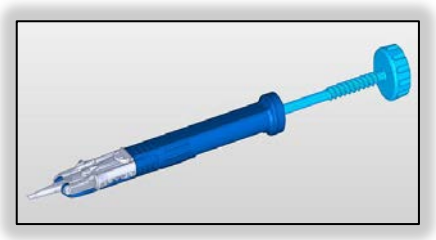
**TECNIS Synergy™ IOLs** **TECNIS Synergy™ Toric II IOLs**



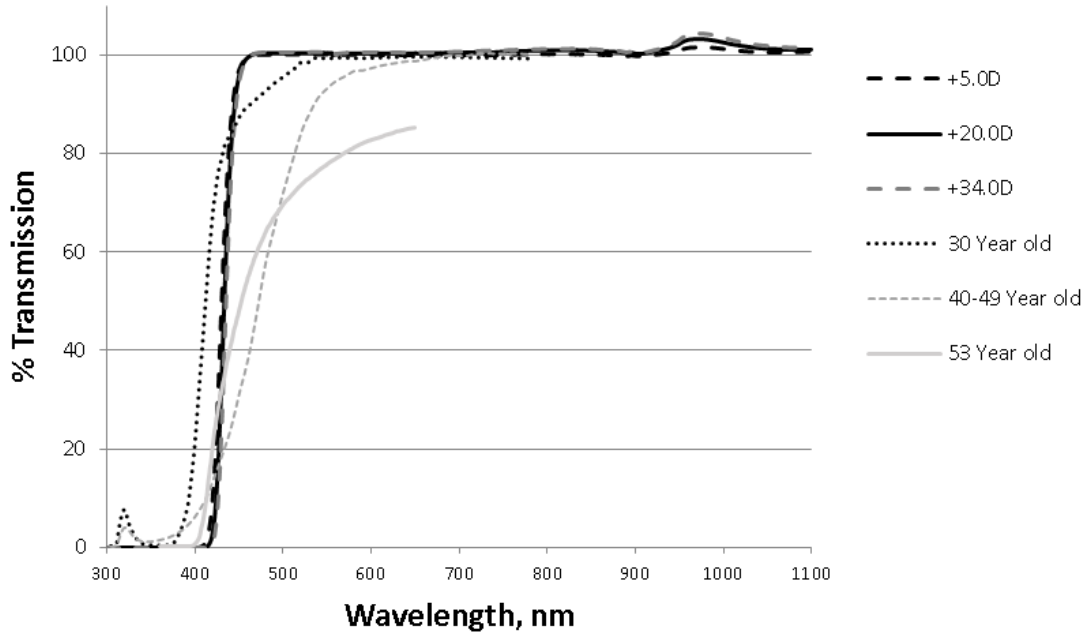
## Figure 2
## Packaging Configurations

**Daisywheel Packaging** **TECNIS Simplicity™ Packaging**





## Figure 3
## Spectral Transmittance Curve




**Legend:**
Spectral transmittance curve of a typical 5-diopter IOL (thinnest). UV(420): UV cut-off at 10%T is 420 nm.
Spectral transmittance curve of a typical 20-diopter IOL. UV(424): UV cut-off at 10%T is 424 nm.
Spectral transmittance curve of a typical 34-diopter IOL (thickest). UV(426): UV cut-off at 10%T is 426 nm.
Spectral transmittance curve of crystalline lenses: 30 year old and 40-49 year old from Artigas, J.M., Felipe, A., Navea, A., Fandino, A., & Artigas, C. Spectral transmission of the human crystalline lens in adult and elderly persons: color and total transmission of visible light. Invest Ophthalmol Vis Sci (2012);53(7):4076-4084. 53 year old from Boettner, E.A., and Wolter J.R. Transmission of the Ocular Media. Investigative Ophthalmology. 1962;1:776-783.

## 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). Nonsurgical options include eyeglasses or contact lenses. Surgical options come in the form of intraocular lenses, which may be monofocal, multifocal, extended depth of focus, 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 Synergy™ IOLs in select models 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 complications generally associated with cataract surgery include, but are not limited to: endophthalmitis/intraocular infection, hypopyon, hyphema, IOL dislocation, persistent cystoid macular edema, pupillary block, retinal detachment/tear, persistent corneal stromal edema, persistent uveitis, persistent raised intraocular pressure (IOP) requiring treatment (e.g., AC tap), retained lens material, or toxic anterior segment syndrome, or any other adverse event that leads to permanent visual impairment or requires surgical or medical intervention to prevent permanent visual impairment.

Adverse events that may be associated with use of the device include: IOL dislocation, tilt or decentration, visual symptoms requiring lens removal, residual refractive error, secondary surgical intervention (including IOL repositioning or removal).

For the specific adverse events that occurred during the TECNIS Synergy™ IOL clinical study, please see the Summary of Primary Clinical Studies section below.

## IX. SUMMARY OF NONCLINICAL STUDIES

Nonclinical studies performed on either parent devices or subject devices demonstrate the safety and effectiveness of the TECNIS Synergy™ IOLs. The results of these studies are summarized below.

### A. Laboratory Studies

Physicochemical Testing

The TECNIS Synergy™ IOLs use the same lens material as the material parent, the TECNIS OptiBlue 3-Piece IOL, Model ZV9003 (P980040/S035); therefore, physicochemical and biological data for these associated lenses are deemed applicable to the subject devices. All physicochemical reports pertaining to the SENSAR violet-light filtering soft acrylic material were previously submitted to FDA in 2006 as part of the 180-Day PMA Supplement for the material parent TECNIS OptiBlue 3 Piece IOL, Model ZV9003 (P980040/S035). P980040 served as the parent lens for the aforementioned submission to which an SSED is available. The physicochemical characterization of the TECNIS Synergy™ 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 Synergy™ IOLs,**
**Indicating Relationship to the SENSAR® AR40e IOL**

| Physicochemical Tests | Results of Testing |
|---|---|
| **Exhaustive Extraction** | Equivalent to SENSAR soft acrylic IOL, Model AR40e (P980040) |
| **Leachables** | Equivalent to SENSAR soft acrylic IOL, Model AR40e (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 SENSAR soft acrylic IOL, Model AR40e (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 Synergy™ IOLs are made of the same soft acrylic violet-filtering material and have the same manufacturing contact materials previously qualified with the material parent, the TECNIS OptiBlue 3-Piece IOL, Model ZV9003 (P980040/S035). All physicochemical reports pertaining to the SENSAR® violet-light filtering soft acrylic material was previously submitted to FDA in 2006 as part of the 180-Day PMA Supplement for the material parent TECNIS OptiBlue 3 Piece IOL, Model ZV9003 (P980040/S035). P980040 served as the parent lens for the aforementioned submission to which an SSED is available. 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 Synergy™ IOL**

| Biological Tests | Results of Testing |
|---|---|
| Cytotoxicity: (MEM)<br>Agar Diffusion Solid Contact & Saline Extract) | Non-cytotoxic |
| Percentage Inhibition of Cell Growth Method | Non-inhibitory to cell growth |
| Guinea Pig Maximization<br>a. Saline Extract<br>b. Sesame Oil Extract | Non-sensitizing |
| Non-Ocular Implant Study<br>(Six-Week Subcutaneous Implantation in Rabbits) | **Passed** |
| Six-Month Rabbit Intraocular Study | **Passed** |
| Genotoxicity Testing<br>*(Salmonella typhimurium* and *Escherichia coli* reverse mutation assay) | Non-genotoxic, non-mutagenic |
| Genotoxicity testing (chromosomal aberration assay in Chinese hamster ovary cells)<br><br>Genotoxicity Testing (Mouse Lymphoma Forward Mutation Assay) | Non-clastogenic<br>Non-mutagenic under short and long exposure conditions |

## C. Additional Studies

Optical/Mechanical Testing

Dimensional, optical, and mechanical tests were conducted on finished, sterilized, TECNIS Synergy™ IOLs to verify the conformance to applicable sections of ISO 11979-2, Ophthalmic Implants-Intraocular Lenses-Part 2: Optical Properties and Test Methods; ISO 11979-3, Ophthalmic Implants-Intraocular Lenses Part 3: Mechanical Properties and Test Methods; ANSI Z80.30, American National Standard for Ophthalmics: Toric Intraocular Lenses; ANSI Z80.35, American National Standard for Ophthalmics: Extended Depth of Focus Intraocular Lenses; and ANSI Z80.12, American National Standard for Ophthalmics: Multifocal 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 Synergy™ 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. Testing for the TECNIS Simplicity™ Delivery System was completed on representative lenses and was focused on optical and mechanical testing on attributes that can be impacted by a change in the storage and delivery of the device; specifically, the recovery of properties following simulated surgical manipulation pertinent to the preloaded IOLs, according to testing requirements from ISO 11979-2 and ISO 11979-3.Here, the lenses met the acceptance criteria and met all predetermined requirements established in the aforementioned standards where applicable and internal product specifications. **Table 5** summarizes the results of the recovery of properties following simulated surgical manipulation for the TECNIS Simplicity™ Delivery System.

**Table 4**
**Dimensional, Optical and Mechanical Test Results**

| Requirements | Results |
|---|---|
| **Optical Requirements** | |
| Diopter power | **Passed** |
| Cylinder Power (TECNIS Synergy™ Toric II IOLs only) | **Passed** |
| Image quality | **Passed** |
| Spectral transmittance | **Passed** |
| Axis Orientation Mark(s) (toric TECNIS Synergy™ IOLs only) | **Passed** |
| **Mechanical and Dimensional Testing** | |
| Overall Diameter | **Passed** |

| Requirements | Results |
|---|---|
| Vault Height | **Passed** |
| Sagitta | **Passed** |
| Clear Optic diameter | **Passed** |
| Optic Body Diameter | **Passed** |
| Axial Displacement in Compression | **Passed** |
| Optic Decentration | **Passed** |
| Optic Tilt | **Passed** |
| Angle of Contact | **Passed** |
| Compression Force and Decay | **Passed** |
| Dynamic Fatigue Durability | **Passed** |
| Surgical Manipulation | **Passed** |
| Surface and Bulk Homogeneity | **Passed** |
| **Recovery of Properties Following Simulated Surgical Manipulation** | |
| Diopter power | **Passed** |
| Cylinder Power (TECNIS Synergy™ Toric II IOLs only) | **Passed** |
| Image quality | **Passed** |
| Axis Orientation Mark(s) (TECNIS Synergy™ Toric II IOLs only) | **Passed** |
| Overall Diameter | **Passed** |
| Sagitta | **Passed** |
| Surface and Bulk Homogeneity | **Passed** |

**Table 5**
**TECNIS Simplicity™ Testing**

| Testing | Results |
|---|---|
| Dimensional Testing of the IOLs | **Passed** |
| Optical Testing of the IOLs (ISO 11979-2) | **Passed** |

| Testing | Results |
|---|---|
| Mechanical Testing of the IOLs (ISO 11979-3) | **Passed** |
| Functional Testing of the IOLs | **Passed** |
| Characterization Testing for IOL Delivery | The lens delivery factors were identified and further characterized to ensure the optimal lens delivery using the TECNIS Simplicity™ Delivery System. |

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 Synergy™ IOLs packaged in the Daisywheel configuration are the same as those of the FDA-approved monofocal IOL, the TECNIS 1-Piece OptiBlue IOL, Model ZCB00V (P980040/S035), as the reference lens models. The TECNIS Synergy™ IOLs in the Daisywheel configuration will be labeled with a 5-year shelf life. Sterilization validations performed for this associated lens model are deemed applicable to the subject lenses and assures a minimum sterility assurance level of $10^{-6}$. A 3-year shelf life was established for the TECNIS Synergy™ IOLs packaged in the TECNIS Simplicity™ Delivery System based on a 3-year shelf life approved by FDA for the TECNIS Simplicity™ Delivery System in P980040/S098. These tests were conducted in accordance with the following standards and United States Pharmacopeia 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
- USP <85>, Bacterial Endotoxins Test
- ISO 11979-6, Ophthalmic Implants – Intraocular Lenses – Part 6: Shelf-life and transport stability.

## X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the TECNIS Synergy™ IOL, Model ZFR00V under IDE #G190057. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

The TECNIS Synergy™ Toric II IOLs (Models ZFW150, ZFW225, ZFW300, ZFW375) involved imposing the toric feature from the toric design parents (P980040/S039): TECNIS Toric 1-Piece IOL, Models ZCT150, ZCT225, ZCT300 and ZCT400. Since the study for TECNIS Synergy™ IOL Model ZFR00V 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, as the only difference is in cylinder powers.

## A. Study Design

Subjects were treated between August 13, 2019 and November 26, 2019. The database for this PMA reflected data collected through June 18, 2020 (6-month visit) and included 272 subjects. There were 15 investigational sites.

The study was a prospective, multicenter, bilateral, comparative, three-way masked (Sponsor, subject, and evaluator), randomized, 6-month clinical investigation of the safety and effectiveness of the TECNIS Synergy™ IOL (study lens) compared to the monofocal TECNIS 1-Piece IOL, Model ZCB00 (control lens). Up to 300 subjects were to be enrolled to achieve approximately 270 bilaterally implanted subjects, resulting in approximately 244 evaluable subjects (122 subjects per IOL group) at 6 months. Each site was to implant a minimum of 20 subjects, and no site was to have implanted more than 25% of the enrollment total.

The statistical analyses were frequentist. The purpose of this study was to evaluate the safety and effectiveness of the investigational TECNIS Synergy™ IOL in comparison to a monofocal control IOL. The 6-month postoperative visit was the key analysis time point for all endpoints. Data for other visits were also included in the final analysis.

The clinical hypotheses were that the investigational TECNIS Synergy™ IOL would provide improved distance corrected near visual acuity (DCNVA), as well as decreased spectacle wear compared to the monofocal control, TECNIS 1-Piece IOL, Model ZCB00. The mean monocular best corrected distance visual acuity (BCDVA) of the investigational TECNIS Synergy™ IOL was to be non-inferior to that of the monofocal control IOL Model ZCB00. Complication and adverse event (AE) rates associated with the investigational TECNIS Synergy™ IOL was to be within the rates for posterior chamber IOLs referenced in ISO 119797:2018.

Study sample sizes were based on the ISO 22979 (Technical Report: Ophthalmic implants — Intraocular lenses — Guidance on assessment of the need for clinical investigation of intraocular lens design modifications) requirements for a Level B modification of a parent lens as well as the requirement for contrast sensitivity testing. The minimum requirements

were 100 evaluable test subjects per IOL group for Level B, and 122 evaluable test subjects per IOL group for contrast sensitivity. The screen failure rate was assumed to be 10%, and the drop-out rate was assumed to be 10%. To achieve approximately 122 evaluable subjects in each IOL group at 6 months postoperative and allowing for screen failures and drop-out, 150 subjects were to be enrolled in each IOL group to achieve approximately 135 bilaterally implanted subjects in each IOL group.

The control was an active alternative treatment [TECNIS 1-Piece IOL, Model ZCB00 (monofocal)], which 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.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the Clinical Investigation of the Safety and Effectiveness of an Investigational Model of the TECNIS Intraocular Lens (Model ZFR00V) study was limited to subjects who met the following inclusion criteria:

- Minimum 22 years of age
- Bilateral cataracts for which posterior chamber IOL implantation had been planned
- Preoperative BCDVA of 20/40 Snellen or worse with or without a glare source
- Potential for postoperative BCDVA of 20/30 Snellen or better
- Normal corneal topography with a predicted postoperative corneal astigmatism of less than 1.00 D in both eyes including posterior corneal astigmatism (PCA)
- Clear intraocular media other than cataract in each eye
- Availability, willingness, and sufficient cognitive awareness to comply with examination procedures and study visits
- Signed informed consent and HIPAA authorization or equivalent documentation necessary to comply with applicable privacy laws pertaining to medical treatment in the governing countries

Subjects were not permitted to enroll in the Clinical Investigation of the Safety and Effectiveness of an Investigational Model of the TECNIS Intraocular Lens (Model ZFR00V) study if they, or either eye, met any of the following exclusion criteria:

- Prior corneal refractive (laser-assisted in situ keratomileusis, laser-assisted sub-epithelial keratectomy, radial keratotomy, photorefractive keratectomy, etc.) or intraocular surgery, including prophylactic peripheral iridotomies and peripheral laser

retinal repairs, or recent ocular trauma or ocular surgery that was not resolved/stable or may have affected visual outcomes or increased risk to the subject.

- Corneal abnormalities such as stromal, epithelial, or endothelial dystrophies (e.g., any observed guttata) that were predicted to cause visual acuity losses to a level worse than 20/30 Snellen during the study
- Inability to achieve keratometric stability for contact lens wearers
- Subjects with diagnosed degenerative visual disorders (e.g., macular degeneration or other retinal disorders) that were predicted to cause visual acuity losses to a level of 20/30 Snellen or worse during the study
- Subjects with conditions associated with increased risk of zonular rupture, including capsular or zonular abnormalities that may have led to IOL decentration or tilt, such as pseudoexfoliation, trauma, or posterior capsule defects
- Use of systemic or ocular medications that may, in the opinion of the Investigator, have confounded the outcome or increased the risk to the subject (e.g., poor dilation or a lack of adequate iris structure to perform standard cataract surgery)
- Acute, chronic, or uncontrolled systemic or ocular disease or illness that, in the opinion of the Investigator, would have increased the operative risk or confounded the outcome(s) of the study (e.g., poorly controlled diabetes, immunocompromised, connective tissue disease, suspected glaucoma, glaucomatous changes in the fundus or visual field, ocular inflammation, etc.).
- Any known ocular disease or pathology that, in the opinion of the Investigator, may have affected visual acuity, may have required surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, uncontrolled glaucoma, etc.), may have been expected to require retinal laser treatment or other surgical intervention during the course of the study (macular degeneration, cystoid macular edema, diabetic retinopathy, etc.).
- Subject was pregnant, planned to become pregnant, was lactating, or had another condition associated with the fluctuation of hormones that could have led to refractive changes
- Concurrent participation or participation within 60 days prior to preoperative visit in any other clinical trial

2. Follow-up Schedule

All subjects were scheduled to return for follow-up examinations as described in **Table 6**.

**Table 6**
**Clinical Study Visit Schedule**

| VISIT | EYES EVALUATED | EXAM | VISIT WINDOW |
|---|---|---|---|
| 1 | Both Eyes | Preoperative Exam | Within 60 days prior to 1st surgery |
| 2 | First Eye | Operative | 0-60 days after preoperative exam |
| 3 | First Eye | 1 day | 1-2 days postoperative |
| 4 | First Eye | 1 week[a] | 7-14 days postoperative |
| 5 | Second Eye | Operative[a] | No more than 30 days after 1st eye surgery |
| 6 | Second Eye | 1 day | 1-2 days postoperative |
| 7 | Second Eye | 1 week | 7-14 days postoperative |
| 8 | Both Eyes | 1 month | 30 - 60 days postoperative from 2nd eye surgery[b] |
| 9 | Both Eyes | 6 months | 120 - 180 days postoperative from 2nd eye surgery[b] |

Shaded rows indicate study visits where both eyes are evaluated at the same visit
[a] The 1-week exam for the first eye should have been completed prior to implanting the second eye.
[b] If for any reason the second eye was not implanted, the first eye was to be examined for the 1-month study visit 37 to 67 days following the first-eye surgery and for the 6-month study visit 127 to 210 days following the first-eye surgery.

Preoperatively and postoperatively, the objective parameters measured during the study are presented in **Table 7**. Adverse events and complications were recorded at all visits. The key timepoints are shown in the tables summarizing safety and effectiveness (Section 3. Clinical Endpoints). Visual acuity testing included uncorrected distance visual acuity (UCDVA), best-corrected distance visual acuity (BCDVA), uncorrected intermediate visual acuity (UCIVA), distance-corrected intermediate visual acuity (DCIVA), uncorrected near visual acuity (UCNVA), and distance-corrected near visual acuity (DCNVA).

**Table 7**
**Clinical Study Visit Schedule**

| Examination (shaded lines indicate masked testing) | Preop | Op | 1 day | 1 week | 1 month | 6 months |
|---|---|---|---|---|---|---|
| Informed consent, ocular history, inclusion/exclusion criteria, potential visual acuity, targeted refraction, IOL | X | | | | | |
| Lens power/serial number (masked), operative procedures | | X | | | | |
| Manifest refraction (Snellen preop; ETDRS postop) | X | | | X | X | X |
| UCDVA – photopic, monocular | | | X | X | X | X |
| UCDVA – photopic, binocular | | | | | X | X |
| BCDVA – photopic, monocular (Snellen preop; ETDRS | X | | | X | X | X |
| BCDVA – photopic binocular | | | | | X | X |
| UCIVA – photopic, binocular at 66 cm | | | | | X | X |
| DCIVA – photopic, monocular at 66 cm | | | | | | X |
| UCNVA – photopic, binocular at 40 cm | | | | | X | X |
| DCNVA – photopic, monocular at 40 cm | | | | | X | X |
| DCNVA – photopic, binocular at 40 cm | | | | | X | X |
| DCNVA – photopic, monocular at 33 cm | | | | | | X |
| Defocus – distance-corrected, monocular (first eye) | | | | | | X |
| Defocus – distance-corrected, binocular | | | | | X | |
| Contrast sensitivity – monocular (first eye) | | | | | | X |
| Contrast sensitivity - binocular | | | | | X | |
| DCNVA – mesopic, monocular at 40 cm | | | | | | X |
| DCNVA – mesopic, binocular at 40 cm | | | | | | X |
| Pupil size | | | | | | X |
| Keratometry | X | | | | | X |
| Intraocular pressure | X | | X | X | X | X |
| Biomicroscopic slit-lamp exam[a] | X | | X | X | X | X |
| Fundus exam with fundus visualization | X | | | | | X |
| Adverse event assessment | | X | X | X | X | X |
| Ocular medications | X | X | X | X | X | X |
| Ocular/visual symptoms (non-directed) | X | | X | X | X | X |
| Subject questionnaires | X | | | | X | X |

[a] Includes determination of medical and lens findings/complications.

3. Clinical Endpoints

With regard to safety, the primary and co-primary safety endpoints and success criteria were:

- The rate of secondary surgical interventions (SSIs) related to optical properties of the lens in first eyes of the TECNIS Synergy™ group was analyzed using descriptive statistics and compared to that of the control group.

- All safety and performance endpoint (SPE) AEs, including total SSI, reported among first eyes of the TECNIS Synergy™ group were compared to ISO SPE rates. The success criterion is that the AE rate in the test group is not statistically significantly higher than the ISO SPE rate (ISO 11979-7:2018 safety and performance endpoint rates).

- All other non-SPE AEs were analyzed using descriptive statistics comparing the two IOL groups.

- Rate of monocular BCDVA 20/40 or better among first eyes in the TECNIS Synergy™ group was compared to the ISO SPE rate.

In addition, the secondary safety endpoint was the monocular (first eyes) best-corrected distance contrast sensitivity for the TECNIS Synergy™ group were compared to control (mesopic with and without glare at 1.5, 3.0, 6.0, and 12.0 cpd and photopic with glare at 3.0, 6.0, 12.0, and 18.0 cpd).

With regard to effectiveness, the primary effectiveness endpoint was monocular photopic DCNVA at 40 cm. Success criteria were a statistically significant improvement in mean monocular photopic DCNVA for first eyes in the TECNIS Synergy™ group vs. first eyes in the control group and a mean DCNVA for the TECNIS Synergy™ group of at least 0.2 logarithm of the minimum angle of resolution (LogMAR).

The secondary effectiveness endpoints included statistically and clinically significant improvements in mean LogMAR distance corrected intermediate visual acuity (DCIVA) at 66 cm and DCNVA at 33 cm for first eyes in the TECNIS Synergy™ group vs. the control, with a mean of at least 0.2 LogMAR. Other secondary effectiveness endpoints included non-inferior (within 0.1 LogMAR) monocular photopic BCDVA for first eyes in the TECNIS Synergy™ group vs. the control, monocular distance-corrected defocus curve for first eyes in the TECNIS Synergy™ group demonstrating 0.2 LogMAR or better from 0.0 D to -2.5 D of defocus, and a statistically significant difference in the proportion of Synergy™ compared to control subjects who reported wearing glasses “None of the time” for all four conditions (distance, intermediate, near, and overall vision), as determined from the Patient Reported Spectacle Independence Questionnaire. In addition, clinical significance was determined by:

1) At least 50% of subjects in the Synergy™ group who reported wearing glasses "None of the time" for all four conditions (distance, intermediate, near, and overall vision), and

2) The proportion of subjects in the Synergy™ group who reported wearing glasses or contacts "None of the time" for all four conditions was at least 25 percentage points higher than that for the control group.

## B. Accountability of PMA Cohort

At the time of database lock, of 297 patients enrolled in the PMA study, (89.9% (267/297) patients are available for analysis at the completion of the study at the 6-month post-operative visit.

Of the 272 subjects implanted, 135 were in the Synergy™ group, and 137 were in the control group; all 272 subjects were bilaterally implanted with the same IOL model in both eyes in the PMA study. At the time of database lock, 97.0% (131/135) of Synergy™ first eyes (**Table 8**), and 95.6% (131/137) of control first eyes (**Table 9**) were available for analysis at the 6-month final study exam.

**Table 8**
**Accountability**
**First Eyes – TECNIS Synergy™**
**N = 135**

| | 1 Day | | 1 Week | | 1 Month | | 6 Months | |
|---|---|---|---|---|---|---|---|---|
| **Subject status** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| **Available for Analysis** | 135 | 100.0 | 135 | 100.0 | 135 | 100.0 | 131 | 97.0 |
| **Missing Subjects** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 4 | 3.0 |
| o Discontinued | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.7 |
| o Missed visit | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| o Not seen but accounted for | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 2 | 1.5 |
| o Lost-to-follow-up | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.7 |
| **Active** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Percent Accountability** | - | 100.0 | - | 100.0 | - | 100.0 | - | 97.8 |

**Table 9**
**Accountability**
**First Eyes – TECNIS monofocal**
**N = 137**

| | 1 Day | | 1 Week | | 1 Month | | 6 Months | |
|---|---|---|---|---|---|---|---|---|
| **Subject status** | **n** | **%** | **n** | **%** | **n** | **%** | **n** | **%** |
| **Available for Analysis** | 137 | 100.0 | 137 | 100.0 | 136 | 99.3 | 131 | 95.6 |
| **Missing Subjects** | 0 | 0.0 | 0 | 0.0 | 1 | 0.7 | 6 | 4.4 |
| o Discontinued | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| o Missed visit | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| o Not seen but accounted for | 0 | 0.0 | 0 | 0.0 | 1[b] | 0.7 | 5 | 3.6 |
| o Lost-to-follow-up | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 1 | 0.7 |
| **Active** | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| **Percent Accountability** | - | 100.0 | - | 100.0 | - | 99.3 | - | 95.6 |

## 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 US.

**Table 10** presents demographic information for Synergy™ and control subjects. The mean age was 68.5 years (standard deviation (SD) 7.1) in the Synergy™ group and 68.5 years (SD 7.7) in the control group. Female subjects comprised more than half of both the Synergy™ group (69.6%; 94/135) and the control group (65.7%; 90/137). No statistically significant differences were found for age, sex, race, ethnicity, or iris color between the two IOL groups.

**Table 11** presents the preoperative parameters for Synergy™ and control subjects. The differences in the means between IOL groups were very small for preoperative intended mean refractive spherical equivalent (MRSE) (difference of 0.036 D first eyes and 0.068 D second eyes), preoperative keratometric cylinder (difference of -0.019 D first eyes and -0.030 D second eyes), and the IOL power implanted (difference of 0.361 D first eyes and 0.361 D second eyes).

**Table 10**
**Demographics**
**Synergy™ and Control Subjects**

| | | **TECNIS Synergy™** | **TECNIS monofocal** | **P-Value** |
|---|---|---|---|---|
| Age (years) | N | 135 | 137 | 0.9940[a] |
| | Mean | 68.5 | 68.5 | |

| | | TECNIS Synergy™ | | TECNIS monofocal | | P-Value |
|---|---|---|---|---|---|---|
| | SD | 7.1 | | 7.7 | | |
| | Median | 70 | | 69 | | |
| | Min | 48 | | 46 | | |
| | Max | 85 | | 92 | | |
| | Not Reported | 0 | | 0 | | |
| | | **n** | **%** | **n** | **%** | |
| Age Group | <60 | 17 | (12.6%) | 17 | (12.4%) | |
| | 60 to 69 | 50 | (37.0%) | 57 | (41.6%) | |
| | 70 to 79 | 62 | (45.9%) | 56 | (40.9%) | |
| | ≥80 | 6 | (4.4%) | 7 | (5.1%) | |
| | Total n | 135 | - | 137 | - | |
| | Not Reported | 0 | - | 0 | - | |
| Sex | Male | 41 | (30.4%) | 47 | (34.3%) | 0.5185[b] |
| | Female | 94 | (69.6%) | 90 | (65.7%) | |
| | Total n | 135 | - | 137 | - | |
| | Not Reported | 0 | - | 0 | - | |
| Race | Asian (including Indian) | 3 | (2.2%) | 1 | (0.7%) | 0.6200[b] |
| | Black | 15 | (11.1%) | 19 | (13.9%) | |
| | Native Hawaiian/Pacific Islander | 1 | (0.7%) | 0 | (0.0%) | |
| | Caucasian | 114 | (84.4%) | 116 | (84.7%) | |
| | Other Race | 2 | (1.5%) | 1 | (0.7%) | |
| | Total n | 135 | - | 137 | - | |
| | Not Reported | 0 | - | 0 | - | |
| Ethnicity | Hispanic/Latino | 8 | (5.9%) | 7 | (5.1%) | 0.7969[b] |
| | Not Hispanic/Latino | 127 | (94.1%) | 130 | (94.9%) | |
| | Total n | 135 | - | 137 | - | |
| | Not Reported | 0 | - | 0 | - | |
| Iris Color | Blue/Gray | 42 | (31.1%) | 37 | (27.0%) | 0.6008[b] |
| | Brown/Black | 54 | (40.0%) | 63 | (46.0%) | |
| | Green/Hazel | 39 | (28.9%) | 37 | (27.0%) | |
| | Total n | 135 | - | 137 | - | |
| | Not Reported | 0 | - | 0 | - | |

%=n/Total n
[a] P-value from two-sided two sample t-test
[b] P-value from two-sided Fisher's exact test

**Table 11**
**Mean Intended MRSE and Preoperative Keratometric Cylinder**
**First Eyes – TECNIS Synergy™ (N=135) and TECNIS monofocal (N=137)**

| Variable | IOL | n | Mean | Standard Deviation | Median | Minimum | Maximum |
|---|---|---|---|---|---|---|---|
| Intended MRSE (D) | ZFR00V | 135 | -0.009 | 0.097 | -0.010 | -0.24 | 0.19 |
| | Control | 137 | -0.045 | 0.114 | -0.050 | -0.35 | 0.22 |
| | Difference | - | 0.036 | 0.106 | - | - | - |
| Keratometric Cylinder (D) | ZFR00V | 135 | 0.473 | 0.247 | 0.460 | 0.00 | 1.13 |
| | Control | 137 | 0.492 | 0.241 | 0.470 | 0.00 | 1.31 |
| | Difference | - | -0.019 | 0.244 | - | - | - |

## D. Safety and Effectiveness Results

### 1. Safety Results

The analysis of safety was based on the safety cohort of 135 subjects with Synergy™ bilaterally and 137 subjects with control bilaterally and available for the 6-month evaluation.

The first co-primary safety endpoint was the rate of secondary surgical interventions (SSIs) related to the optical properties of the IOL in first operative eyes. One SSI related to the optical properties of the IOL was reported in the clinical study among all implanted eyes in the Synergy™ group. The second co-primary safety endpoint was the rates of cumulative and persistent adverse events in first operative eyes at 6 Months in comparison to ISO 11979-7 Safety and Performance Endpoints grid (SPE rates). All SPE rates for the Synergy™ group at 6 months were below those specified in ISO 11979-7:2018 (12-month rates).

The third co-primary safety endpoint was the rate of all non-SPE adverse events in the study. The fourth co-primary safety endpoint was met, where the rate of monocular BCDVA 20/40 or better among first eyes was better than the rate specified in ISO 11979-7:2018.

Secondary safety endpoints included assessments of monocular and binocular contrast sensitivity with and without glare for photopic and mesopic conditions. Log contrast sensitivity was measured to be lower for the Synergy™ group than control at higher spatial frequencies, however the differences were not clinically meaningful.

The key safety outcomes for this study are presented below in **Tables 12 to 16** (adverse effects) and **Figures 4-9** (contrast sensitivity).

**Adverse effects that occurred in the PMA clinical study:**

During the study, reports of serious adverse events (SAEs) and serious adverse device effects (SADEs) were low for both lens groups. None of the events reported were unanticipated. One Synergy™ subject had lens decentration (1/135, 0.7%) in both eyes.

**Table 12** presents the incidence of serious and non-serious medical findings/adverse events at 6-months for all Synergy™ and monofocal control eyes.

Among first and second eyes with the TECNIS Synergy™ IOL, ocular AEs occurring at 6 months with a rate of 2% or more were: posterior capsule opacification (116/263; 44.1%), posterior vitreous detachment (76/263; 28.9%), dermatochalasis (56/263; 21.3%), dry eye/superficial punctate keratopathy/epithelial erosion/tear film insufficiency (50/263; 19.0%), blepharitis/meibomianitis (40/263; 15.2%), posterior capsular striae/wrinkles (16/263; 6.1%), pinguecula (14/263; 5.3%), periorbital fat herniation (14/263; 5.3%), and ptosis (6/263; 2.3%).

Among first and second eyes with the control IOL, ocular AEs occurring at 6 months with a rate of 2% or more were: posterior capsule opacification (106/262; 40.5%), posterior vitreous detachment (76/262; 29.0%), dermatochalasis (49/262, 18.7%), dry eye/superficial punctate keratopathy/epithelial erosion/tear film insufficiency (46/262; 17.6%), blepharitis/meibomianitis (48/262; 18.3%), pinguecula (15/262; 5.7%), posterior capsular striae/wrinkles (10/262; 3.8%), periorbital fat herniation (10/262; 3.8%), arcus (9/262; 3.4%), and corneal scar (6/262; 2.3%).

**Table 12**
**Medical Findings/Adverse Events at 6 Months**
**TECNIS Synergy™ and TECNIS Monofocal**
**Pooled (First and Second) Eyes**
**Safety Population**

| | TECNIS Synergy N=263 | | TECNIS Monofocal N=262 | |
|---|---|---|---|---|
| **Medical Findings** | **n** | **%** | **n** | **%** |
| Posterior capsule opacification (any) | 116 | 44.1 | 106 | 40.5 |
| Posterior vitreous detachment | 76 | 28.9 | 76 | 29.0 |
| Dermatochalasis | 56 | 21.3 | 49 | 18.7 |
| Dry eye/superficial punctate keratopathy/ epithelial erosion/tear film insufficiency | 50 | 19.0 | 46 | 17.6 |
| Blepharitis/meibomianitis | 40 | 15.2 | 48 | 18.3 |
| Posterior capsular striae/wrinkles (any) | 16 | 6.1 | 10 | 3.8 |
| Periorbital fat herniation | 14 | 5.3 | 10 | 3.8 |

| | TECNIS Synergy N=263 | | TECNIS Monofocal N=262 | |
|---|---|---|---|---|
| **Medical Findings** | **n** | **%** | **n** | **%** |
| Pinguecula | 14 | 5.3 | 15 | 5.7 |
| Ptosis | 6 | 2.3 | 4 | 1.5 |
| Chorioretinal atrophy | 5 | 1.9 | 5 | 1.9 |
| Congenital optic nerve anomaly | 5 | 1.9 | 0 | 0.0 |
| Epiretinal membrane | 5 | 1.9 | 1 | 0.4 |
| Corneal dystrophy | 4 | 1.5 | 4 | 1.5 |
| Drusen | 4 | 1.5 | 5 | 1.9 |
| Eye nevus | 4 | 1.5 | 1 | 0.4 |
| Guttata | 4 | 1.5 | 2 | 0.8 |
| Corneal scar | 3 | 1.1 | 6 | 2.3 |
| Optic nerve cup/disc ratio increased | 3 | 1.1 | 0 | 0.0 |
| Pterygium | 3 | 1.1 | 2 | 0.8 |
| Retinal degeneration | 3 | 1.1 | 0 | 0.0 |
| Retinal pigment epithelium (RPE) changes | 3 | 1.1 | 2 | 0.8 |
| Arcus | 2 | 0.8 | 9 | 3.4 |
| Conjunctival hyperemia/injection | 2 | 0.8 | 0 | 0.0 |
| Conjunctivitis | 2 | 0.8 | 0 | 0.0 |
| Conjunctivochalasis | 2 | 0.8 | 0 | 0.0 |
| Corneal disorder | 2 | 0.8 | 0 | 0.0 |
| Corneal pigmentation[b] | 2 | 0.8 | 2 | 0.8 |
| Heterophoria | 2 | 0.8 | 0 | 0.0 |
| Macular degeneration | 2 | 0.8 | 0 | 0.0 |
| Optic nerve cupping | 2 | 0.8 | 0 | 0.0 |
| Optic nerve hypoplasia | 2 | 0.8 | 0 | 0.0 |
| Telangiectasia | 2 | 0.8 | 0 | 0.0 |
| Anterior chamber cells (if any) | 1 | 0.4 | 4 | 1.5 |
| Chorioretinal scar | 1 | 0.4 | 1 | 0.4 |
| Corneal opacity | 1 | 0.4 | 1 | 0.4 |
| Eyelid cyst | 1 | 0.4 | 2 | 0.8 |
| Lagophthalmos | 1 | 0.4 | 0 | 0.0 |
| Macular hole | 1 | 0.4 | 0 | 0.0 |
| Retinal anomaly congenital | 1 | 0.4 | 1 | 0.4 |
| Retinal scar | 1 | 0.4 | 0 | 0.0 |
| Vitreous degeneration | 1 | 0.4 | 0 | 0.0 |
| Anterior chamber flare (if any) | 0 | 0.0 | 3 | 1.1 |
| Cornea verticillata | 0 | 0.0 | 2 | 0.8 |
| Corneal edema (if any)[b] | 0 | 0.0 | 2 | 0.8 |

| | TECNIS Synergy N=263 | | TECNIS Monofocal N=262 | |
|---|---|---|---|---|
| **Medical Findings** | **n** | **%** | **n** | **%** |
| Iris transillumination defect[b] | 0 | 0.0 | 2 | 0.8 |
| Madarosis | 0 | 0.0 | 2 | 0.8 |
| Presumed ocular histoplasmosis syndrome | 0 | 0.0 | 2 | 0.8 |
| Retinal hemorrhage | 0 | 0.0 | 2 | 0.8 |
| Elevated IOP/ocular hypertension[b] | 0 | 0.0 | 1 | 0.4 |
| Hyalosis asteroid | 0 | 0.0 | 1 | 0.4 |
| Retinal exudates | 0 | 0.0 | 1 | 0.4 |
| Retinal tear[b] | 0 | 0.0 | 1 | 0.4 |
| Strabismus | 0 | 0.0 | 1 | 0.4 |
| Other | 0 | 0.0 | 2[a] | 0.8[a] |

[a] Other includes orbital fat prolapse and negative dysphotopsia.
[b] As defined by AAO IOL Task Force (Masket *et al*., 2016).

The incidence rates of persistent (**Table 13**) and cumulative (**Table 14**) adverse events for all implanted Synergy™ eyes were compared to the ISO SPE (safety and performance endpoint) rates. There were no persistent medical findings/adverse events per the ISO SPE at 6 months in the Synergy™ group. The rate of cumulative medical findings/adverse events reported in Synergy™ group were not statistically significantly higher than the specified ISO SPE rates.

All SSIs during the study are presented by IOL group in **Table 15**. Five SAEs/SADEs required SSIs for treatment: one first eye (0.7%, 1/135 for Synergy™ vs. 0%, 0/137 for control) and four second eyes (2.2%, 3/135 for Synergy™ vs. 0.7%, 1/137 for control). There was one (0.7%, 1/135) SSI related to optical properties of the lens in the Synergy™ group.

**Table 13**
**6-Month Persistent Adverse Events vs. ISO 11979-7 SPE 12-Month Rates**
**TECNIS Synergy™**

| Persistent Medical Complication/Adverse Event | ISO SPE Rate | First Eyes N=131 | | Second Eyes N=132 | |
|---|---|---|---|---|---|
| | % | n | % | n | % |
| Corneal edema | 0.3 | 0 | 0.0 | 0 | 0.0 |
| Cystoid macular edema | 0.5 | 0 | 0.0 | 0 | 0.0 |
| Iritis | 0.3 | 0 | 0.0 | 0 | 0.0 |
| Raised IOP requiring treatment | 0.4 | 0 | 0.0 | 0 | 0.0 |

**Table 14**
**6-Month Cumulative Adverse Events vs. ISO 11979-7 SPE 12-Month Rates**
**TECNIS Synergy™**

| Cumulative Medical Complication/ Adverse Event | ISO SPE Rate | First Eyes N=135 | | Second Eyes N=135 | |
|---|---|---|---|---|---|
| | % | n | % | n | % |
| Cystoid macular edema | 3.0 | 1 | 0.7 | 1 | 0.7 |
| Hypopyon[a] | 0.3 | 0 | 0.0 | 1 | 0.7* |
| Endophthalmitis | 0.1 | 0 | 0.0 | 0 | 0.0 |
| 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 | 1 | 0.7 | 3 | 2.2* |
| -- Device related | - | 1 | 0.7 | 1 | 0.7 |
| -- Not device related | - | 0 | 0.0 | 2 | 1.5* |

% = (n/N) *100
* Rate is not statistically significantly higher than ISO SPE rate (p>0.05).
[a]Associated with a single report of toxic anterior segment syndrome (TASS), which occurred in same eye.

**Table 15**
**Secondary Surgical Interventions by IOL Group**

| | TECNIS Synergy™ | | | | TECNIS monofocal | | | |
|---|---|---|---|---|---|---|---|---|
| | First Eyes N=135 | | Second Eyes N=135 | | First Eyes N=137 | | Second Eyes N=137 | |
| | n | % | n | % | n | % | n | % |
| **Secondary Surgical Interventions (SSIs)** | | | | | | | | |

| | TECNIS Synergy™ | | | | TECNIS monofocal | | | |
|---|---|---|---|---|---|---|---|---|
| | First Eyes N=135 | | Second Eyes N=135 | | First Eyes N=137 | | Second Eyes N=137 | |
| | n | % | n | % | n | % | n | % |
| -- Lens Removal | 1[a] | 0.7 | 0 | 0.0 | 0 | 0.0 | 0 | 0.0 |
| -- Aspiration (Removal) of Lens Fragments | 0 | 0.0 | 1[b] | 0.7 | 0 | 0.0 | 0 | 0.0 |
| -- Retinal Repair | 0 | 0.0 | 1[c] | 0.7 | 0 | 0.0 | 1[e] | 0.7 |
| -- Treatment Injection | 0 | 0.0 | 1[d] | 0.7 | 0 | 0.0 | 0 | 0.0 |
| **TOTAL Eyes with SSIs** | **1** | **0.7** | **3** | **2.2** | **0** | **0.0** | **1** | **0.7** |

% = (n/N) *100

[a]SSI related to visual symptoms (optical properties of the lens). The second eye lens for same subject was removed after study exit for similar reason.

[b]Due to retained lens material

[c]Due to macular hole

[d]Due to hypopyon and TASS in same eye

[e]Due to retinal detachment/tear

### Contrast Sensitivity

Monocular best-corrected distance contrast sensitivity was evaluated under three lighting conditions: mesopic without glare, mesopic with glare, and photopic with glare. The secondary safety endpoint was a comparison of the median monocular and binocular contrast sensitivity measurements at all spatial frequencies and all lighting conditions at 6 months. In all conditions, contrast sensitivity was measured to be generally lower for the Synergy™ group than the control group (**Figures 4, 5, and 6**), especially under extremely high glare conditions. Glare setting used for testing was high enough to reduce the mesopic contrast sensitivity in both lens groups by at least 0.2 log units with a greater impact on mesopic contrast sensitivity for the Synergy™ group (up to 0.448 log) than the control group (up to 0.392 log). However, lower contrast sensitivity measurements were not found to be associated with clinically significant impact to patient reported vision quality. In addition, median binocular contrast sensitivity measurements at all spatial frequencies and all lighting conditions at 1 month are presented in **Figures 7, 8,** and **9**.

**Figure 2**
**Monocular Best-Corrected Distance Contrast Sensitivity at 6 Months**
**Mesopic Without Glare**
**Medians with 5th and 95th Percentile Error Bars**

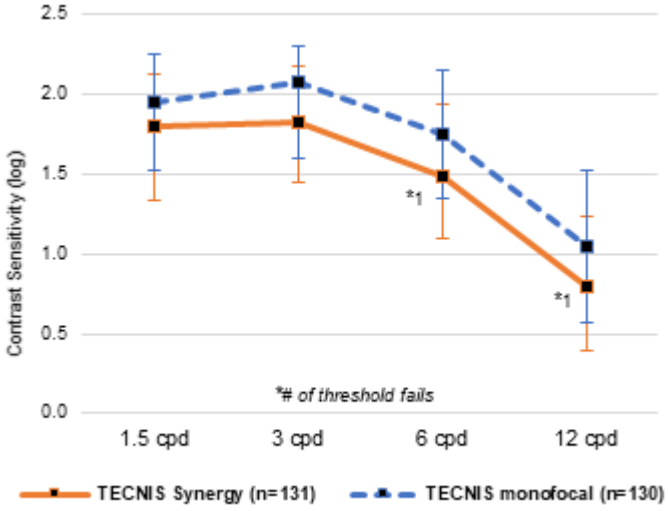



**Figure 3**
**Monocular Best-Corrected Distance Contrast Sensitivity at 6 Months**
**Mesopic With Glare**
**Medians with 5th and 95th Percentile Error Bars**

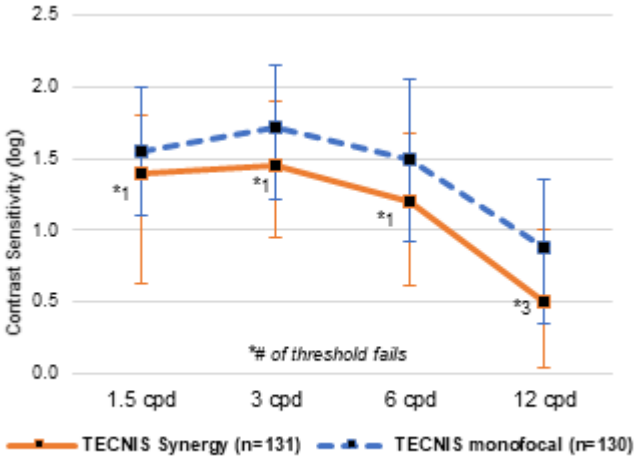


**Figure 4**
**Monocular Best-Corrected Distance Contrast Sensitivity at 6 Months**
**Photopic With Glare**
**Medians with 5th and 95th Percentile Error Bars**

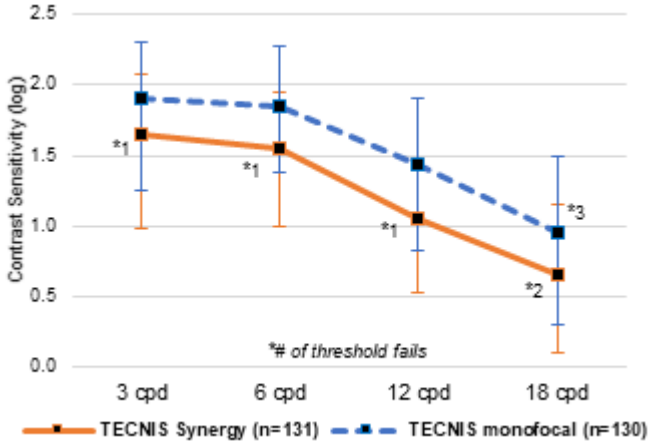



**Figure 5**
**Binocular Best-Corrected Distance Contrast Sensitivity at 1 Month**
**Mesopic without Glare**
**Medians with 5th and 95th Percentile Error Bars**

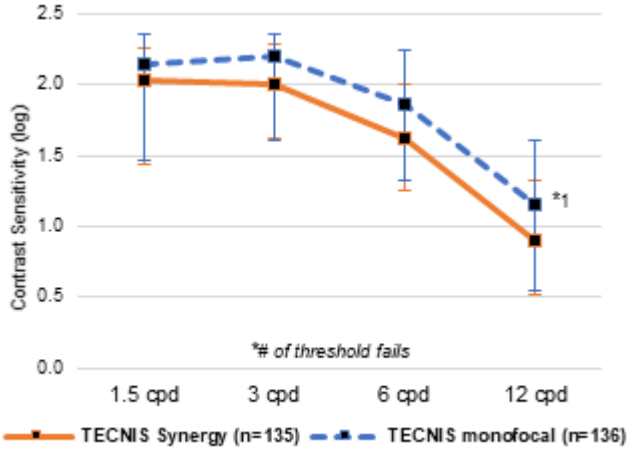


**Figure 6**
**Binocular Best-Corrected Distance Contrast Sensitivity at 1 Month**
**Mesopic with Glare**
**Medians with 5th and 95th Percentile Error Bars**

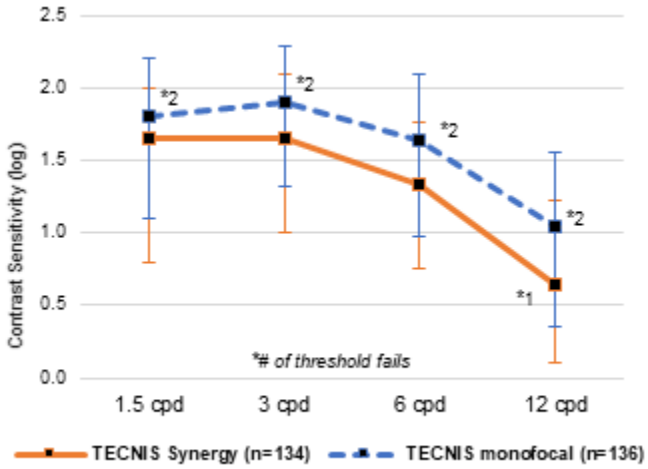
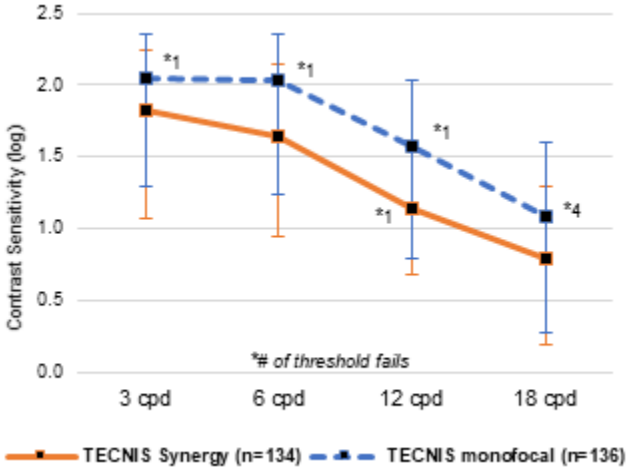



**Figure 7**
**Binocular Best-Corrected Distance Contrast Sensitivity at 1 Month**
**Photopic with Glare**
**Medians with 5th and 95th Percentile Error Bars**




## Optical/Visual Symptoms

Optical/visual symptoms that were spontaneously reported by subjects (non-directed) and questionnaire-directed reports of experience/bother/difficulty with visual problems (directed) were evaluated. Non-directed reports of optical/visual symptoms included halos, night glare, and starbursts, of which there were few reports of severe symptoms for both Synergy and control groups (**Table 16**). As shown in the responses to the directed questionnaire (**Table 17**), reports of

bothersome visual disturbances were generally acceptable for the Synergy group at 6 months. The highest rate of the most bothersome reports ("extremely bothersome") of optical/visual symptoms at 6 months was for starbursts, at 5.3% (7/131) for Synergy and 0.0% (0/131) for the control.

Bother or difficulty with a visual symptom that interfered with a daily activity for more than 3 months and was considered by the investigator to be at least possibly related to the IOL was considered an Adverse Device Effect. There were eleven such events from 8.1% (11/135) of Synergy™ subjects and none for control subjects; one resulted in lens removal.

**Table 16**
**Spontaneous (Non-directed[a]) Reports of Optical/Visual Symptoms (First Eyes) at 6 Months**

| | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | **n** | **%** | **n** | **%** |
| Halos[b] | 30 | 22.9 | 5 | 3.8 |
| o Mild | 8 | 6.1 | 3 | 2.3 |
| o Moderate | 17 | 13.0 | 2 | 1.5 |
| o Severe | 5 | 3.8 | 0 | 0.0 |
| Night Glare[b] | 11 | 8.4 | 2 | 1.5 |
| o Mild | 1 | 0.8 | 0 | 0.0 |
| o Moderate | 7 | 5.3 | 2 | 1.5 |
| o Severe | 3 | 2.3 | 0 | 0.0 |
| Starbursts[b] | 13 | 9.9 | 2 | 1.5 |
| o Mild | 3 | 2.3 | 2 | 1.5 |
| o Moderate | 5 | 3.8 | 0 | 0.0 |
| o Severe | 5 | 3.8 | 0 | 0.0 |
| Photophobia | 2 | 1.5 | 3 | 2.3 |
| Day glare | 2 | 1.5 | 1 | 0.8 |
| Night vision difficulty | 6 | 4.6 | 1 | 0.8 |

% = (n/N)*100
Subjects may report multiple symptoms.
[a]Responses to the question, "Are you having any difficulties with your eyes or vision?"
[b]Severity collected in follow-up response

**Table 17**
**Experience/Bother With Visual Symptoms at 6 Months (Directed Questionnaire)**

| | | TECNIS Synergy™ N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|---|
| | | **n** | **%** | **n** | **%** |
| **Halos** | Did not experience or NR | 24 | 18.3 | 79 | 60.3 |
| | Not at all bothered | 19 | 14.5 | 23 | 17.6 |
| | Slightly bothered | 40 | 30.5 | 22 | 16.8 |
| | Moderately bothered | 30 | 22.9 | 6 | 4.6 |
| | Very bothered | 13 | 9.9 | 1 | 0.8 |
| | Extremely bothered | 5 | 3.8 | 0 | 0.0 |
| **Starbursts** | Did not experience or NR | 46 | 35.1 | 102 | 77.9 |
| | Not at all bothered | 18 | 13.7 | 17 | 13.0 |
| | Slightly bothered | 27 | 20.6 | 4 | 3.1 |
| | Moderately bothered | 25 | 19.1 | 6 | 4.6 |
| | Very bothered | 8 | 6.1 | 2 | 1.5 |
| | Extremely bothered | 7 | 5.3 | 0 | 0.0 |
| **Multiple or Double Vision** | Did not experience or NR | 113 | 86.3 | 116 | 88.5 |
| | Not at all bothered | 2 | 1.5 | 5 | 3.8 |
| | Slightly bothered | 10 | 7.6 | 4 | 3.1 |
| | Moderately bothered | 2 | 1.5 | 5 | 3.8 |
| | Very bothered | 2 | 1.5 | 1 | 0.8 |
| | Extremely bothered | 2 | 1.5 | 0 | 0.0 |
| **Sensitivity to Light** | Did not experience or NR | 63 | 48.1 | 71 | 54.2 |
| | Not at all bothered | 13 | 9.9 | 9 | 6.9 |
| | Slightly bothered | 30 | 22.9 | 32 | 24.4 |
| | Moderately bothered | 19 | 14.5 | 11 | 8.4 |
| | Very bothered | 5 | 3.8 | 6 | 4.6 |
| | Extremely bothered | 1 | 0.8 | 2 | 1.5 |
| **Glare Related to Scattered Light** | Did not experience or NR | 69 | 52.7 | 110 | 84.0 |
| | Not at all bothered | 9 | 6.9 | 4 | 3.1 |
| | Slightly bothered | 23 | 17.6 | 12 | 9.2 |
| | Moderately bothered | 19 | 14.5 | 3 | 2.3 |
| | Very bothered | 5 | 3.8 | 2 | 1.5 |
| | Extremely bothered | 6 | 4.6 | 0 | 0.0 |
| **Occlusions** | Did not experience or NR | 127 | 96.9 | 128 | 97.7 |
| | Not at all bothered | 1 | 0.8 | 1 | 0.8 |
| | Slightly bothered | 1 | 0.8 | 2 | 1.5 |
| | Moderately bothered | 0 | 0.0 | 0 | 0.0 |

| | | TECNIS Synergy™ N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|---|
| | | **n** | **%** | **n** | **%** |
| | Very bothered | 2 | 1.5 | 0 | 0.0 |
| | Extremely bothered | 0 | 0.0 | 0 | 0.0 |
| **Poor Low Light Vision** | Did not experience or NR | 79 | 60.3 | 80 | 61.1 |
| | Not at all bothered | 9 | 6.9 | 6 | 4.6 |
| | Slightly bothered | 25 | 19.1 | 34 | 26.0 |
| | Moderately bothered | 15 | 11.5 | 6 | 4.6 |
| | Very bothered | 3 | 2.3 | 4 | 3.1 |
| | Extremely bothered | 0 | 0.0 | 1 | 0.8 |

% = (n/N)*100
NR = Not Reported

2. Effectiveness Results

Effectiveness analyses were based on the modified intent-to-treat (mITT) cohort of 135 subjects with bilateral Synergy™ lenses and 137 subjects with bilateral control lenses who were available for the 6-month evaluation. For determination of endpoint criteria, statistical significance was assessed using the mITT population, and clinical significance was assessed using the safety population. The key effectiveness outcomes for this study are presented below in **Tables 18, 21, 22, and 25**, and in **Figures 10 to 15**.

**Near Visual Acuity at 40 cm**

The primary study endpoint of monocular photopic distance-corrected near visual acuity (DCNVA) at 40 cm was achieved, demonstrating the effectiveness of the TECNIS Synergy™ IOL in providing substantially improved near vision at 40 cm compared to an aspheric monofocal. The results of monocular (first eye) photopic (85 cd/$m^2$) DCNVA testing at 40 cm at 6 months for both the Synergy™ and control groups are presented in **Table 17**. There was a statistically significant improvement ($p<0.0001$) in mean monocular distance corrected near visual acuity at 6 months in favor of the Synergy™ group (0.104 LogMAR), with an improvement of 4.2 lines, or 0.42 LogMAR over the control group.

**Table 18**
**Mean Near Visual Acuity at 40 cm at 6 Months**

| Near (40 cm) Visual Acuity | Lens Group | Monocular N | Monocular n | Monocular Mean LogMAR | Monocular Snellen Equiv. | Monocular Line Change vs. Control[a] | Binocular N | Binocular n | Binocular Mean LogMAR | Binocular Snellen Equiv. | Binocular Line Change vs. Control[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Uncorrected | TECNIS Synergy | Not tested | | | | | 131 | 131 | 0.060 | 20/23 | 3.3 lines |
| | TECNIS monofocal | | | | | | 131 | 130 | 0.393 | 20/49 | |
| Distance Corrected | TECNIS Synergy | 131 | 131 | 0.104 | 20/25 | 4.2 lines[b] | 131 | 131 | 0.047 | 20/22 | 3.6 lines |
| | TECNIS monofocal | 131 | 130 | 0.522 | 20/67 | | 131 | 130 | 0.403 | 20/51 | |
| Mesopic Distance Corrected | TECNIS Synergy | 131 | 131 | 0.315 | 20/41 | 3.4 lines | 131 | 131 | 0.244 | 20/35 | 3.5 lines |
| | TECNIS monofocal | 131 | 130 | 0.654 | 20/90 | | 131 | 130 | 0.591 | 20/78 | |

[a] Line difference (control minus Synergy) is converted directly from LogMAR difference.
[b] Synergy met the primary study endpoint of significantly better mean DCNVA than control ($p<0.0001$, one-sided two-sample t-test) and a mean DCNVA of 0.104 LogMAR (Safety population).

Monocular near (40 cm) visual acuity distributions for both lens groups are presented in **Tables 19A and 19B**; binocular near (40 cm) visual acuity distributions are presented in **Tables 20A and 20B**. Near (40 cm) visual acuity results demonstrate the effectiveness of the Synergy lens in providing improved near vision compared to the monofocal control lens.

**Table 19A**
**Distribution of Monocular Distance-Corrected Near Visual Acuity at 40 cm at 6 Months**

| Monocular Snellen Visual Acuity | TECNIS Synergy N=131 n | TECNIS Synergy N=131 % | TECNIS monofocal N=131 n | TECNIS monofocal N=131 % |
|---|---|---|---|---|
| $20/20^{-2}$ or better | 44 | 33.6% | 2 | 1.5% |
| $20/25^{-2}$ or better | 92 | 70.2% | 7 | 5.4% |
| $20/32^{-2}$ or better | 119 | 90.8% | 10 | 7.7% |
| $20/40^{-2}$ or better | 124 | 94.7% | 25 | 19.2% |
| Worse than $20/40^{-2}$ | 7 | 5.3% | 105 | 80.8% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Table 19B**
**Distribution of Monocular Distance-Corrected Near Visual Acuity at 40 cm at 6 Months**

| Monocular LogMAR Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 0.00 LogMAR or better | 33 | 25.2% | 0 | 0.0% |
| 0.10 LogMAR or better | 76 | 58.0% | 6 | 4.6% |
| 0.20 LogMAR or better | 110 | 84.0% | 9 | 6.9% |
| 0.30 LogMAR or better | 123 | 93.9% | 19 | 14.6% |
| Worse than 0.30 LogMAR | 8 | 6.1% | 111 | 85.4% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Table 20A**
**Distribution of Binocular Uncorrected Near Visual Acuity at 40 cm at 6 Months**

| Binocular Snellen Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| $20/20^{-2}$ or better | 61 | 46.6% | 0 | 0.0% |
| $20/25^{-2}$ or better | 114 | 87.0% | 158 | 6.2% |
| $20/32^{-2}$ or better | 122 | 93.1% | 25 | 19.2% |
| $20/40^{-2}$ or better | 127 | 96.9% | 57 | 43.8% |
| Worse than $20/40^{-2}$ | 4 | 3.1% | 73 | 56.2% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Table 20B**
**Distribution of Binocular Uncorrected Near Visual Acuity at 40 cm at 6 Months**

| Binocular LogMAR Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 0.00 LogMAR or better | 43 | 32.8% | 0 | 0.0% |
| 0.10 LogMAR or better | 101 | 77.1% | 2 | 1.5% |
| 0.20 LogMAR or better | 120 | 91.6% | 14 | 10.8% |
| 0.30 LogMAR or better | 126 | 96.2% | 42 | 32.3% |
| Worse than 0.30 LogMAR | 5 | 3.8% | 88 | 67.7% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Near Visual Acuity at 33 cm**

The secondary study endpoint of monocular DCNVA at 33 cm was achieved, demonstrating that the TECNIS Synergy™ IOL provides substantially improved near vision at 33 cm compared to an aspheric monofocal. The results of near visual acuity testing at 33 cm under photopic (85 cd/$m^2$) lighting conditions at 6 months for both Synergy™ and control groups are presented in **Table 21**. There was a statistically significant improvement ($p<0.0001$) in mean monocular DCNVA at 33 cm at 6 months in favor of the Synergy™ group (mean 0.154 LogMAR), with an improvement of 4.5 lines, or 0.455 LogMAR over the control group.

**Table 21**
**Mean Monocular Near Visual Acuity at 33 cm at 6 Months**

| Lens Group | N | n | Mean LogMAR | Snellen Equivalent | Line Change vs. Control[a] |
|---|---|---|---|---|---|
| TECNIS Synergy | 131 | 131 | 0.154 | 20/29 | 4.5 lines[b] |
| TECNIS monofocal | 131 | 130 | 0.608 | 20/81 | |

[a] Line difference (control minus Synergy) is converted directly from LogMAR difference.
[b] Synergy met the secondary study endpoint of significantly better mean DCNVA at 33 cm than control ($p<0.0001$, one-sided two-sample t-test) and a mean DCNVA of 0.154 LogMAR (Safety population).

## Intermediate Visual Acuity

The secondary effectiveness study endpoint of monocular, photopic DCIVA at 66 cm was achieved, demonstrating that the TECNIS Synergy™ IOL provides substantially improved intermediate vision compared to an aspheric monofocal. The results of intermediate visual acuity testing at 66 cm under photopic (85 cd/m$^2$) lighting conditions at 6 months for both Synergy™ and control IOL groups are presented in **Table 22**. There was a statistically significant improvement ($p<0.0001$) in mean monocular DCIVA at 6 months in favor of the Synergy™ lens (0.060 LogMAR), with an improvement of 2.8 lines, or 0.275 LogMAR over the control group.

**Table 22**
**Mean Intermediate Visual Acuity at 66 cm at 6 Months**

| Intermediate Visual Acuity | Lens Group | Monocular | | | | | Binocular | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| | | N | n | Mean LogMAR | Snellen Equiv. | Line Change vs. Control[a] | N | n | Mean LogMAR | Snellen Equiv. | Line Change vs. Control[a] |
| Uncorrected | TECNIS Synergy | Not Tested | | | | | 131 | 131 | 0.022 | 20/21 | 1.8 lines |
| | TECNIS monofocal | | | | | | 131 | 130 | 0.199 | 20/32 | |
| Distance Corrected | TECNIS Synergy | 131 | 131 | 0.060 | 20/23 | 2.8 lines[b] | Not Tested | | | | |
| | TECNIS monofocal | 131 | 130 | 0.335 | 20/43 | | | | | | |

[a] Line difference (control minus Synergy) is converted directly from LogMAR difference.
[b] Synergy met the secondary study endpoint of significantly better mean DCIVA than control ($p<0.0001$, one-sided two-sample t-test) and a mean DCIVA of 0.060 LogMAR (Safety population).

Monocular intermediate visual acuity distributions for both lens groups are presented in **Tables 23A and 23B**; binocular intermediate visual acuity distributions are presented in **Tables 24A and 24B**. Overall, the intermediate visual acuity results demonstrate the effectiveness of the Synergy lens to provide improved intermediate vision compared to the monofocal control lens.

**Table 23A**
**Distribution of Monocular Distance-Corrected Intermediate Visual Acuity at 66 cm at 6 Months**

| Monocular Snellen Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 20/20$^{-2}$ or better | 72 | 55.0% | 8 | 6.2% |
| 20/25$^{-2}$ or better | 105 | 80.2% | 17 | 13.1% |
| 20/32$^{-2}$ or better | 125 | 95.4% | 37 | 28.5% |
| 20/40$^{-2}$ or better | 129 | 98.5% | 68 | 52.3% |
| Worse than 20/40$^{-2}$ | 2 | 1.5% | 62 | 47.7% |
| **Total n** | **131** | | **130** | |

Monocular UCIVA was not tested
%=(n/Total n) * 100

**Table 23B**
**Distribution of Monocular Distance-Corrected Intermediate Visual Acuity at 66 cm at 6 Months**

| Monocular LogMAR Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 0.00 LogMAR or better | 47 | 35.9% | 4 | 3.1% |
| 0.10 LogMAR or better | 97 | 74.0% | 10 | 7.7% |
| 0.20 LogMAR or better | 117 | 89.3% | 24 | 18.5% |
| 0.30 LogMAR or better | 127 | 96.9% | 55 | 42.3% |
| Worse than 0.30 LogMAR | 4 | 3.1% | 75 | 57.7% |
| **Total n** | **131** | | **130** | |

Monocular UCIVA was not tested
%=(n/Total n) * 100

**Table 24A**
**Distribution of Binocular Uncorrected Intermediate Visual Acuity at 66 cm at 6 Months**

| Binocular Snellen Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 20/20$^{-2}$ or better | 84 | 64.1% | 18 | 13.8% |
| 20/25$^{-2}$ or better | 117 | 89.3% | 44 | 33.8% |
| 20/32$^{-2}$ or better | 130 | 99.2% | 96 | 73.8% |
| 20/40$^{-2}$ or better | 131 | 100.0% | 114 | 87.7% |
| Worse than 20/40$^{-2}$ | 0 | 0.0% | 16 | 12.3% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Table 24B**
**Distribution of Binocular Uncorrected Intermediate Visual Acuity at 66 cm at 6 Months**

| Binocular LogMAR Visual Acuity | TECNIS Synergy N=131 | | TECNIS monofocal N=131 | |
|---|---|---|---|---|
| | n | % | n | % |
| 0.00 LogMAR or better | 64 | 48.9% | 8 | 6.2% |
| 0.10 LogMAR or better | 107 | 81.7% | 31 | 23.8% |
| 0.20 LogMAR or better | 127 | 96.9% | 78 | 60.0% |
| 0.30 LogMAR or better | 131 | 100.0% | 106 | 81.5% |
| Worse than 0.30 LogMAR | 0 | 0.0% | 24 | 18.5% |
| **Total n** | **131** | | **130** | |

%=(n/Total n) * 100

**Distance (Far) Visual Acuity**

The secondary effectiveness endpoint of BCDVA was achieved, demonstrating the TECNIS Synergy™ IOL to provide BCDVA that is non-inferior to that of an aspheric monofocal. The results of best-corrected distance visual acuity testing at 4.0 m under photopic (85 cd/m$^2$) lighting conditions at 6 months for Synergy™ and control first eyes are presented in **Table 25**. Monocular BCDVA was comparable between the Synergy™ and control IOL groups, with mean Snellen equivalents of 20/19 and 20/18, respectively. The lower limit of the two-sided 95% confidence

interval (CI) of the mean difference in BCDVA between IOL groups was greater than the non-inferiority margin.

**Table 25**
**Mean Distance (Far) Visual Acuity at 6 Months**

| Distance Visual Acuity | Lens Group | Monocular N | Monocular n | Monocular Mean LogMAR | Monocular Snellen Equiv. | Monocular Line Change vs. Control[a] | Binocular N | Binocular n | Binocular Mean LogMAR | Binocular Snellen Equiv. | Binocular Line Change vs. Control[a] |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Uncorrected | TECNIS Synergy | 131 | 131 | 0.090 | 20/25 | **-0.4 lines** | 131 | 131 | 0.023 | 20/21 | **-0.5 lines** |
| | TECNIS monofocal | 131 | 130 | 0.052 | 20/23 | | 131 | 130 | -0.028 | 20/19 | |
| Best Corrected | TECNIS Synergy | 131 | 131 | -0.014 | 20/19 | **-0.3 lines**[b] | 131 | 131 | -0.056 | 20/18 | **-0.3 lines** |
| | TECNIS monofocal | 131 | 130 | -0.045 | 20/18 | | 131 | 130 | -0.086 | 20/16 | |

[a] Line difference (control minus Synergy) is converted directly from LogMAR difference.
[b] Synergy met the secondary study endpoint for statistically non-inferiority to the control (Safety population).

The distributions of monocular distance visual acuity for Synergy and control first eyes at 6 months are presented in **Tables 26A and 26B**. The proportion of Synergy first eyes achieving monocular best-corrected distance visual acuity (BCDVA) of 20/40 or better (100.0%) was above the ISO Safety and Performance Endpoint (SPE) rates for BCDVA. The distributions of binocular distance visual acuity for Synergy and control subjects at 6 months are presented in **Tables 27A and 27B**.

**Table 26A**
**Distribution of Monocular Distance (Far) Visual Acuity at 6 Months**

| Monocular Snellen Visual Acuity | TECNIS Synergy Uncorrected N=131 n | TECNIS Synergy Uncorrected N=131 % | TECNIS Synergy Best Corrected N=131 n | TECNIS Synergy Best Corrected N=131 % | TECNIS monofocal Uncorrected N=131 n | TECNIS monofocal Uncorrected N=131 % | TECNIS monofocal Best Corrected N=131 n | TECNIS monofocal Best Corrected N=131 % |
|---|---|---|---|---|---|---|---|---|
| $20/20^{-2}$ or better | 50 | 38.2% | 105 | 80.2% | 72 | 55.4% | 115 | 88.5% |
| $20/25^{-2}$ or better | 93 | 71.0% | 127 | 96.9% | 107 | 82.3% | 126 | 96.9% |
| $20/32^{-2}$ or better | 115 | 87.8% | 130 | 99.2% | 121 | 93.1% | 130 | 100.0% |
| $20/40^{-2}$ or better | 128 | 97.7% | 131 | 100.0% | 126 | 96.9% | 130 | 100.0% |
| Worse than $20/40^{-2}$ | 3 | 2.3% | 0 | 0.0% | 4 | 3.1% | 0 | 0.0% |
| **Total n** | **131** | | **131** | | **130** | | **130** | |

%=(n/Total n) * 100

## Table 26B
## Distribution of Monocular Distance (Far) Visual Acuity at 6 Months

| Monocular LogMAR Visual Acuity | TECNIS Synergy | | | | TECNIS monofocal | | | |
|---|---|---|---|---|---|---|---|---|
| | Uncorrected N=131 | | Best Corrected N=131 | | Uncorrected N=131 | | Best Corrected N=131 | |
| | n | % | n | % | n | % | n | % |
| 0.00 LogMAR or better | 33 | 25.2% | 88 | 67.2% | 55 | 42.3% | 102 | 78.5% |
| 0.10 LogMAR or better | 76 | 58.0% | 122 | 93.1% | 92 | 70.8% | 121 | 93.1% |
| 0.20 LogMAR or better | 106 | 80.9% | 130 | 99.2% | 116 | 89.2% | 129 | 99.2% |
| 0.30 LogMAR or better | 126 | 96.2% | 131 | 100.0% | 124 | 95.4% | 130 | 100.0% |
| Worse than 0.30 LogMAR | 5 | 3.8% | 0 | 0.0% | 6 | 4.6% | 0 | 0.0% |
| **Total n** | **131** | | **131** | | **130** | | **130** | |

%=(n/Total n) * 100

## Table 27A
## Distribution of Binocular Distance (Far) Visual Acuity at 6 Months

| Binocular Snellen Visual Acuity | TECNIS Synergy | | | | TECNIS monofocal | | | |
|---|---|---|---|---|---|---|---|---|
| | Uncorrected N=131 | | Best Corrected N=131 | | Uncorrected N=131 | | Best Corrected N=131 | |
| | n | % | n | % | n | % | n | % |
| $20/20^{-2}$ or better | 88 | 67.2% | 118 | 90.1% | 105 | 80.8% | 119 | 91.5% |
| $20/25^{-2}$ or better | 113 | 86.3% | 130 | 99.2% | 123 | 94.6% | 129 | 99.2% |
| $20/32^{-2}$ or better | 127 | 96.9% | 130 | 99.2% | 127 | 97.7% | 130 | 100.0% |
| $20/40^{-2}$ or better | 129 | 98.5% | 131 | 100.0% | 129 | 99.2% | 130 | 100.0% |
| Worse than $20/40^{-2}$ | 2 | 1.5% | 0 | 0.0% | 1 | 0.8% | 0 | 0.0% |
| **Total n** | **131** | | **131** | | **130** | | **130** | |

%=(n/Total n) * 100

## Table 27B
## Distribution of Binocular Distance (Far) Visual Acuity at 6 Months

| Binocular LogMAR Visual Acuity | TECNIS Synergy | | | | TECNIS monofocal | | | |
|---|---|---|---|---|---|---|---|---|
| | Uncorrected N=131 | | Best Corrected N=131 | | Uncorrected N=131 | | Best Corrected N=131 | |
| | n | % | n | % | n | % | n | % |
| 0.00 LogMAR or better | 67 | 51.1% | 108 | 82.4% | 88 | 67.7% | 116 | 89.2% |
| 0.10 LogMAR or better | 105 | 80.2% | 130 | 99.2% | 118 | 90.8% | 128 | 98.5% |
| 0.20 LogMAR or better | 123 | 93.9% | 130 | 99.2% | 126 | 96.9% | 130 | 100.0% |
| 0.30 LogMAR or better | 129 | 98.5% | 131 | 100.0% | 128 | 98.5% | 130 | 100.0% |
| Worse than 0.30 LogMAR | 2 | 1.5% | 0 | 0.0% | 2 | 1.5% | 0 | 0.0% |
| **Total n** | **131** | | **131** | | **130** | | **130** | |

%=(n/Total n) * 100

### Defocus Curve

The secondary effectiveness study endpoint of monocular distance-corrected depth of focus at 6 months was achieved. The mean monocular defocus range at 0.2 LogMAR for each lens group at 6 months are presented in **Figure 10**. The TECNIS Synergy™ IOL achieved at least 0.2 LogMAR

VA from 0.0 D to -2.5 D of defocus and sustained it beyond -3.0 D of defocus, which corresponds to a range of distances from approximately 33 cm to infinity.

**Figure 11** presents monocular defocus curves for the Synergy™ group by pupil size. The curves for medium and large pupils are essentially indistinguishable with 0.2 LogMAR visual acuity sustained to beyond -3.0 D. It should be noted that there were no eyes in the small pupil size category for the Synergy™ group. Therefore, the TECNIS Synergy™ IOLs demonstrated pupil-independent lens performance between 0 and -3.0 D of defocus among the pupil sizes available (>2.5 mm).

Monocular defocus curves for the Synergy™ and control groups are presented by small, medium, and large pupil sizes in **Figures 12 and 13**, respectively. The range of defocus for medium and large pupils in the Synergy™ group are greater than that for the control group by approximately 2.5 D and 2.0 D, respectively.

**Figure 14** presents the binocular defocus curves for the Synergy™ and control groups at 1 month. The binocular defocus curves show results similar to the monocular 6-month defocus results, with a difference favoring the Synergy™ group, with approximately 2.5 D more defocus range (at 0.2 LogMAR) than the control group.

**Figure 8**
**Mean Monocular Distance-Corrected Defocus Curve at 6 Months**
**TECNIS Synergy™ (N=131) and TECNIS monofocal (N=131)**

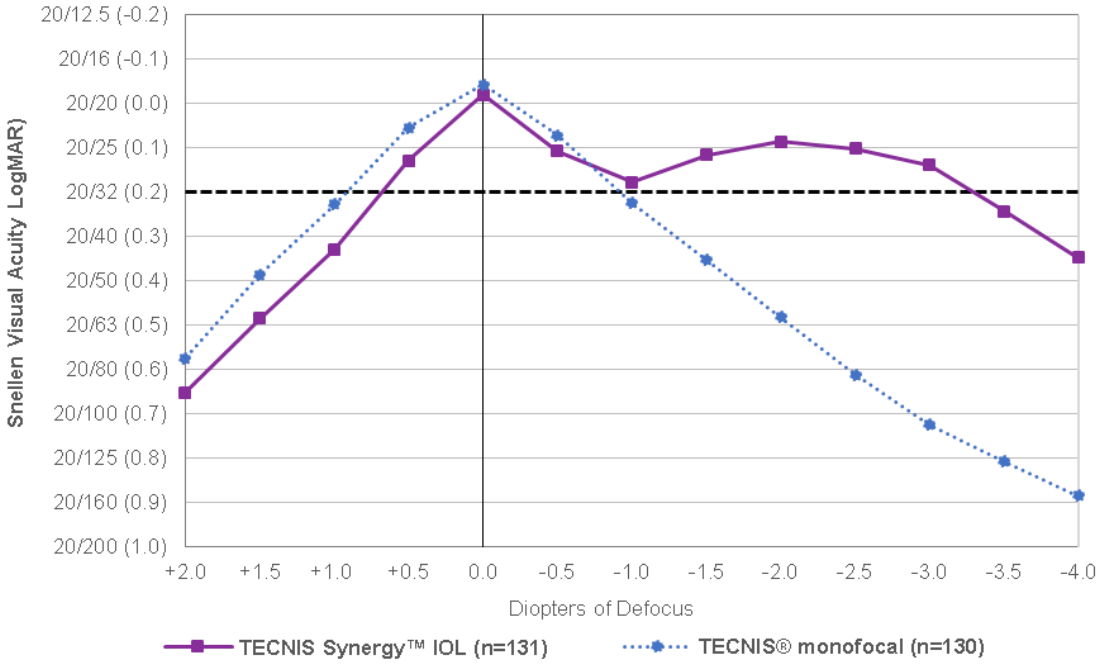



**Figure 9**
**Mean Monocular Distance-Corrected Defocus Curve By Pupil Size at 6 Months**
**TECNIS Synergy™**

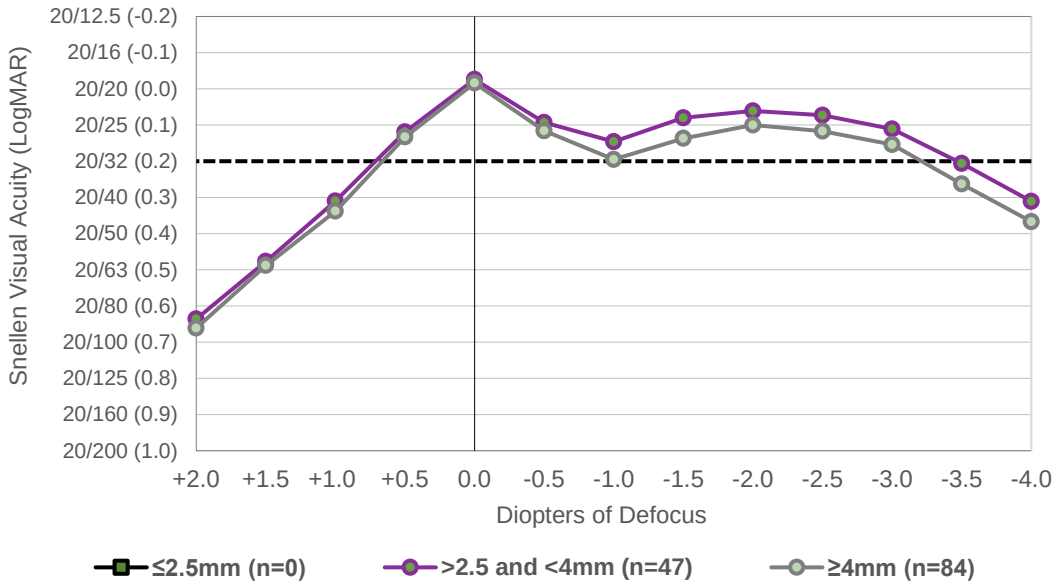


**Figure 10**
**Mean Monocular Distance-Corrected Defocus Curve for Medium Pupils (>2.5 and <4 mm) at 6 Months**
**TECNIS Synergy™ and TECNIS monofocal**

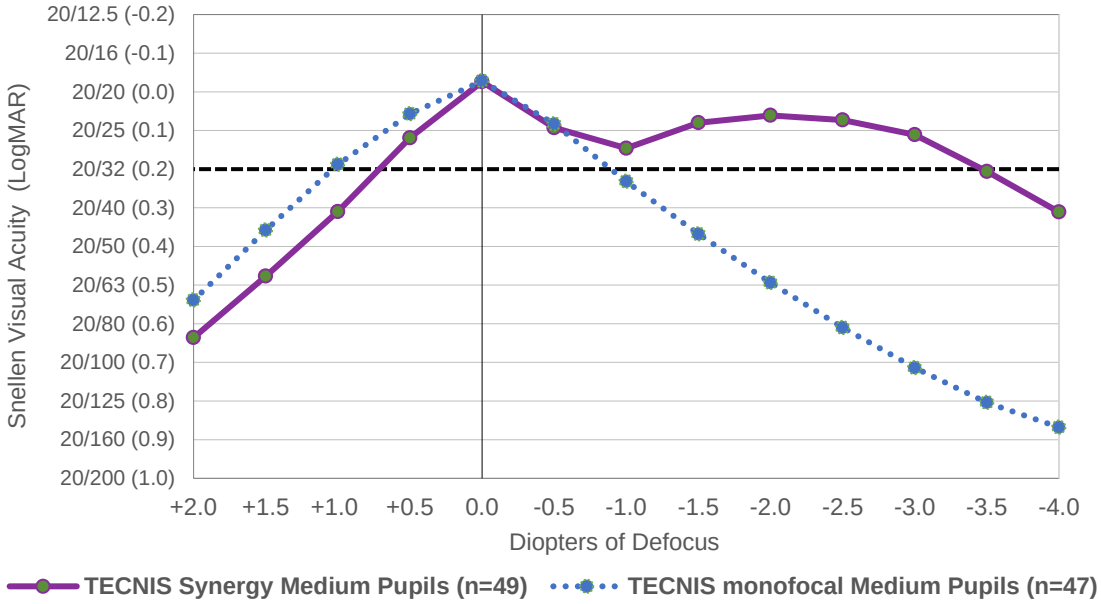



**Figure 11**
**Mean Monocular Distance-Corrected Defocus Curve for Large Pupils (≥4 mm) at 6 Months**
**TECNIS Synergy™ and TECNIS monofocal**

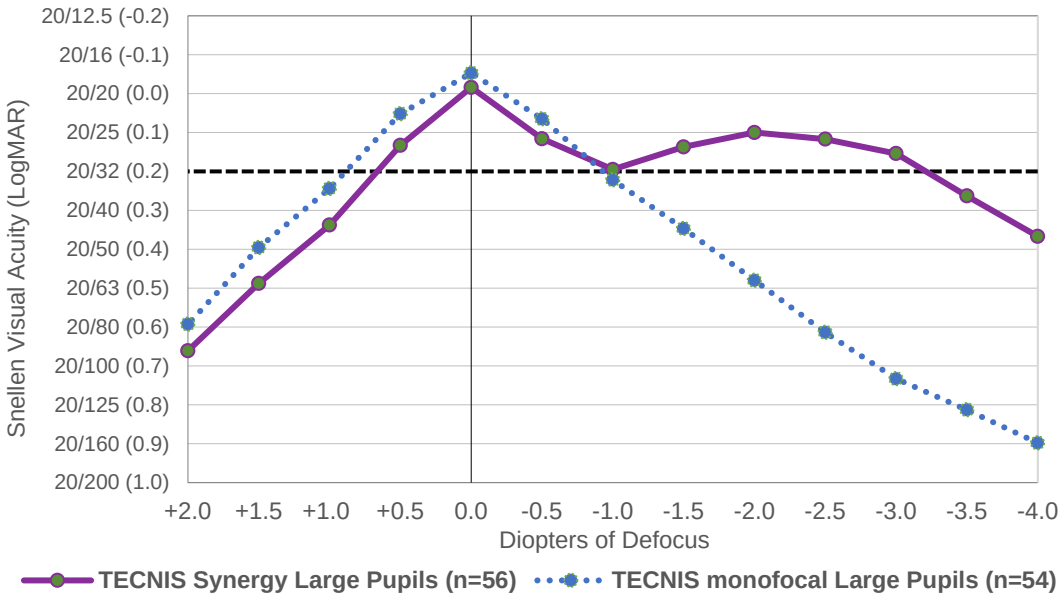
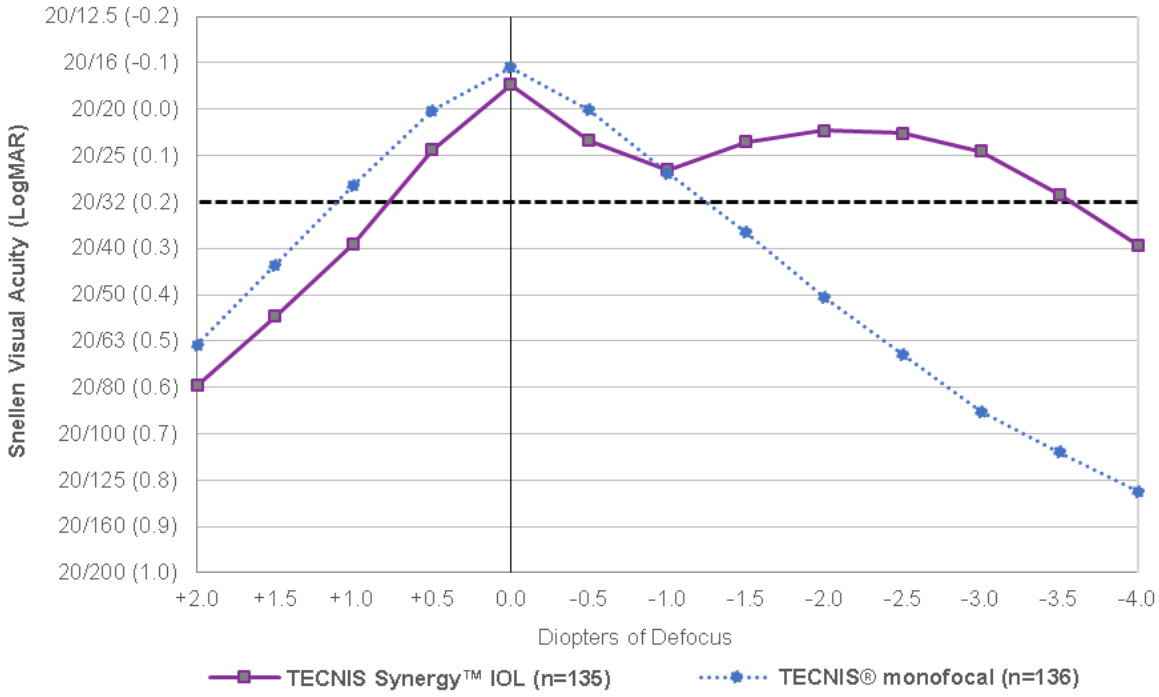


**Figure 12**
**Mean Binocular Distance-Corrected Depth of Focus Curve at 1 Month Bilateral TECNIS Synergy™ (N=135) and TECNIS monofocal (N=136)**



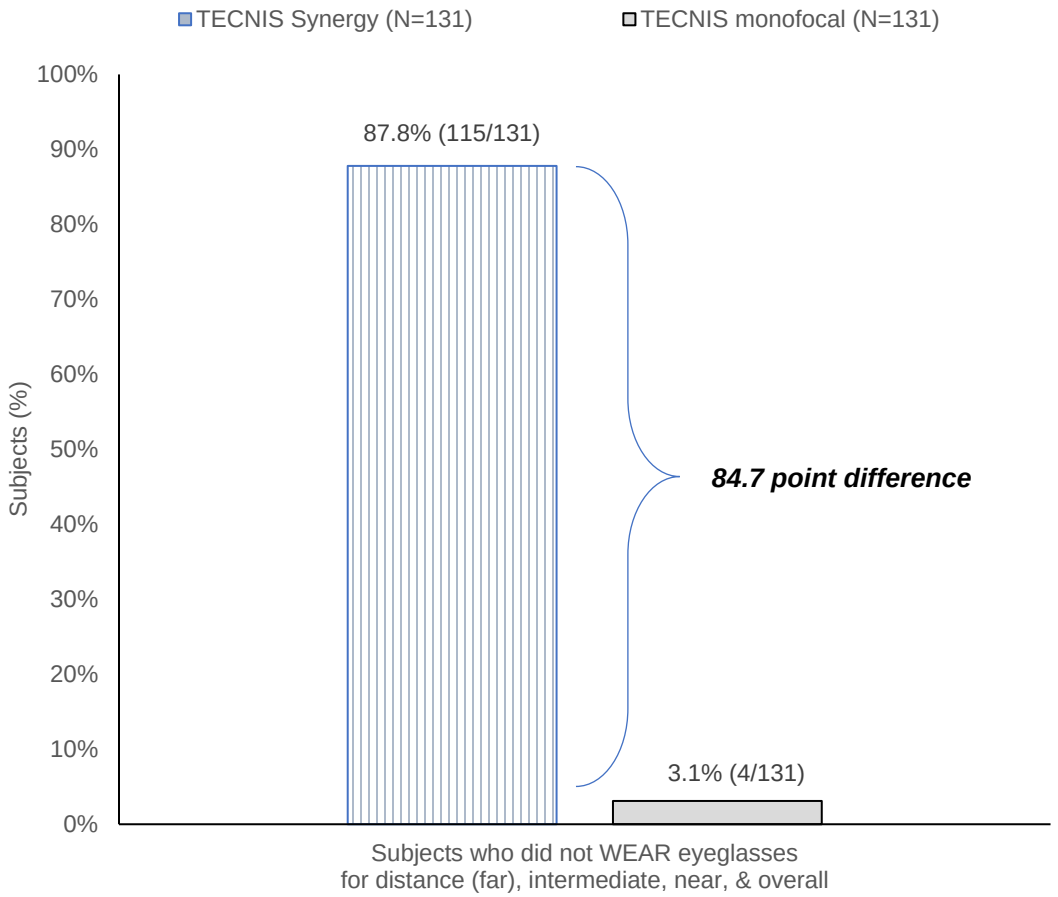

## Patient Reported Spectacle Independence Questionnaire Results

The secondary effectiveness endpoint regarding spectacle wear was achieved, based on the responses to the Patient Reported Spectacle Independence Questionnaire (PRSIQ), which was developed and evaluated following the US FDA guidance document "Patient-Reported Outcomes Measures: Use in Medical Product Development to Support Labeling Claims" (2009). The endpoint was based on the proportion of subjects who reported wearing glasses or contacts "none of the time" under all four conditions: distance, intermediate, near, and overall vision at 6 months, and results are shown in **Figure 15**. There was a statistically significantly greater ($p<0.0001$) proportion of subjects in the Synergy™ group (87.8%; 115/131) who reported wearing glasses "none of the time" in all four conditions (distance, intermediate, near, and overall vision) compared to the control group (3.1%; 4/131), which was a 84.7 percentage point difference.

Subjects who responded positively to multiple questions from the PRSIQ regarding eyeglass need and wear, and straining to see without glasses at distance, intermediate, near, and overall, at 6 months were also tabulated for each lens group. A greater proportion of

positive responses were observed for the Synergy™ group, where 55.7% (73/131) of subjects reported reduced eyeglass need and wear without straining to see without eyeglasses with the Synergy™ IOL, compared to 2.3% (3/131) with the control.

**Figure 13**
**Patient Reported Spectacle Independence Questionnaire[a] Results at 6 months**




*Each subject reported "None of the time" for all four conditions.*

3. Subgroup Analyses

A subgroup analysis for the primary effectiveness endpoint (DCNVA at 40 cm) and all secondary effectiveness endpoints (DCIVA at 66 cm, BCDVA at 4 m, DCNVA at 33 cm, defocus curve and spectacle wear) was done by stratifying the results by the following preoperative characteristics: site, age group (<60, 60-69, 70-79 and >=80), sex and race. The results of DCNVA, DCIVA, defocus curve and spectacle wear endpoints when

stratifying by preoperative characteristics all uniformly show improvement of ZFR00V group over the control group. For BCDVA, the result shows that ZFR00V is no worse than 1 line compared to control when stratifying by all preoperative characteristics.

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 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

One feasibility study comparing the TECNIS Synergy™ IOL [Non violet-light filtering SENSAR equivalent (Model ZFR00) of TECNIS Synergy™ IOL] to a multifocal control (Model ZLB00) conducted. No issues regarding device safety or lack of effectiveness were raised by the results from these studies.

Primary clinical study outcomes for the parent lenses are provided in the TECNIS Synergy™ labeling in Tables 16-43; these tables are incorporated by reference from previous approvals. As a result, these tables were not repeated within this SSED. Below identify which tables are associated with each submission:

- Tables 16-25: TECNIS Toric 1-Piece IOLs, Models ZCT150, ZCT225, ZCT300 and ZCT400 (P980040/S039)
- Tables 26-30: TECNIS Symfony® Extended Range of Vision IOL, Model ZXR00 (P980040/S065)
- Tables 31-34: TECNIS Multifocal IOL, Model ZM900 (P080010)
- Tables 35 to 42: TECNIS 3-Piece OptiBlue™ IOL, Model ZV9003 (P980040/S035)
- Tables 43: SENSAR® 1-Piece IOL, Model AAB00

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

No Panel meeting.

## XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

The overall effectiveness of the TECNIS Synergy™ IOL, Model ZFR00V, was demonstrated based on the 6-month results of the IDE clinical investigation. In addition, the effectiveness of the toric models (Models ZFW150, ZFW225, ZFW300, and ZFW375) in providing reduced postoperative refractive astigmatism is supported by the clinical data provided for the monofocal toric parent IOL in P980040/S039, which has the same toric surface and mechanical design. The primary effectiveness endpoint, statistically and clinically significant improvements in monocular distance-corrected near visual acuity (DCNVA) at 40 cm compared to control, was achieved by the TECNIS Synergy™ IOL (mean 0.104 LogMAR), with an improvement of 4.2 lines in mean DCNVA compared to the monofocal IOL.

The secondary effectiveness endpoints of mean distance-corrected intermediate visual acuity at 66 cm and near visual acuity at 33 cm were also met with statistical and clinical significance, where the TECNIS Synergy™ group showed a 2.8-line improvement in DCIVA (mean 0.060 LogMAR) and a 4.5-line improvement in DCNVA at 33 cm (mean 0.154 LogMAR) over the control. The secondary endpoint for best-corrected distance (far) visual acuity was also met, where the TECNIS Synergy™ group was non-inferior to the control (lower two-sided 95% CI of the mean difference was greater than the non-inferiority margin) in BCDVA.

The secondary effectiveness endpoint for monocular distance-corrected defocus for the TECNIS Synergy™ IOL was achieved with a range of 0.2 LogMAR or better visual acuity that spanned from 0.0 to beyond -3.0 D of defocus, which was approximately 2.5 D more than the control.

The secondary endpoint of spectacle wear was achieved with a statistically and clinically significant improvements in the proportion of subjects in the TECNIS Synergy™ group (15/131, 87.8%) who responded "None of the time" to wearing glasses for far, intermediate, near and overall vision compared to the control (4/131, 3.1%).

## B. Safety Conclusions

The safety profile of the TECNIS Synergy™ IOL is based on nonclinical laboratory studies as well as a primary clinical study conducted to support PMA approval in G190057. In addition, the clinical data from previous U.S. studies for the TECNIS Multifocal IOL, Model ZM900 (G030191, P080010 – the multifocal optical parent lens, TECNIS Symfony Extended Range Of Vision IOL Model ZXR00 (G140094, P980040/S065 – the EDF optical parent lens), the SENSAR 1-piece IOL, Model AAB00 (G050183, P980040/S015 – the mechanical parent lens) and the TECNIS OptiBlue 3 Piece IOL, Model ZV9003 (G060212, P980040/S035 – the material parent) provided data that are relevant to the TECNIS Synergy™ IOL device safety. These studies of the parent IOLs included patient follow-up up to 1 (one) year of up to least 300 subjects. The TECNIS Synergy™ IOL, Model ZFR00V, made of the same FDA-approved surface-treated SENSAR violet-light filtering soft acrylic material as its material parent, and has a design that is derived from proven material, mechanical and optical parents that have a long history of safe clinical use. The results of prior nonclinical laboratory testing, animal studies on the SENSAR violet-light filtering acrylic material and the one-piece lens design support safety of this lens model. In addition, the results of dimensional, optical cosmetic and folding/recovery properties of the TECNIS Synergy™ 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 Synergy™ IOL, Model ZFR00V, provide reasonable assurance of the safety of this lens model. There were no unanticipated adverse events. One secondary surgical intervention related to the optical properties of the lens occurred during the study, and the second eye lens of the same subject was removed after the study exit for similar reason. The rates of cumulative and persistent adverse events in first eyes, including secondary surgical interventions and BCDVA of 20/40 or better, were below or not statistically higher than the ISO 11979-7 Safety and Performance Endpoint (SPE) rates and the rate of all non-SPE adverse events were comparable to that of the control. Monocular contrast sensitivity without and with glare for photopic and mesopic conditions were lower for the TECNIS Synergy™ group than control under the glare conditions evaluated in this study; these differences did not appear to be clinically meaningful.

Reports of optical/visual symptoms that were rated as extremely bothersome were higher in the TECNIS Synergy™ group, including halos (5/131, 3.8%), glare (6/131, 4.6%), and starbursts (7/131, 5.3%), which were higher than reported the rates in the control group. Taken together, the clinical evidence demonstrates a reasonable assurance of safety for the TECNIS Synergy™ IOL when used as indicated.

## C. Benefit-Risk Determination

The probable benefits of the TECNIS Synergy™ IOLs, Models ZFR00V, ZFW150, ZFW225, ZFW300, and ZFW375, 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 with 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 lens models provide improved intermediate and near visual acuity, while distance visual acuity is comparable. 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 Synergy™ IOLs, Models ZFR00V, ZFW150, ZFW225, ZFW300, and ZFW375, include:

a. Clinical data were collected using a study design that included randomized treatment and masking of subjects and evaluators.

b. Medical adverse events and complications (e.g., risks of infection, inflammation, corneal edema, etc.) are similar to those associated with most other intraocular lenses.

c. The risks associated with the optical design include reduced contrast sensitivity (compared to monofocal) and visual symptoms related to stray 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.

1. Patient Perspective

   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA 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 a range of vision (far to intermediate to near), to reduce eyeglass wear compared to an aspheric monofocal lens, the probable benefits of the TECNIS Synergy™ 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 refractive astigmatism, and for mitigating the effects of presbyopia in these patients by providing improved vision to reduce eyeglass wear compared to an aspheric monofocal lens, the probable benefits of the toric models of the TECNIS Synergy™ 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 were met with clinically significant improvements in visual acuity at far, intermediate, and near, defocus, and spectacle wear, demonstrating the ability of the TECNIS Synergy™ IOL to provide improved vision, to reduce eyeglass wear compared to an aspheric monofocal lens. All safety endpoints were also met, and adverse event rates were either lower than or not statistically higher than grid rates established in an FDA-recognized international standard.

## XIV. CDRH DECISION

CDRH issued an approval order on [date of approval order].

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

International Standards Organization 22979 Ophthalmic implants – Intraocular lenses – Guidance on assessment of the need for clinical investigation of intraocular lens design modifications

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.