# SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

## I. GENERAL INFORMATION

**Device Generic Name:** Lens, Multifocal Intraocular
Lens, Intraocular, Toric Optics

**Device Trade Name:** enVista Envy™ hydrophobic acrylic intraocular lens (IOL),
enVista Envy™ toric hydrophobic acrylic intraocular lens (IOL)

**Device Procode:** MFK, MJP

**Applicants Name and Address:** Bausch & Lomb Incorporated
1400 North Goodman Street
Rochester, NY 14609

**Date(s) of Panel Recommendation:** None

**Premarket Approval Application (PMA) Number:** P240005

**Date of FDA Notice of Approval:** 10/10/2024

## II. INDICATIONS FOR USE

**enVista Envy™ hydrophobic acrylic intraocular lens**
The enVista Envy hydrophobic acrylic IOL (non-preloaded model: EN / preloaded into shuttle model: EPN) is indicated for primary implantation in the capsular bag of the eye in adult patients for the visual correction of aphakia with less than or equal to 1.0 D preoperative corneal astigmatism following removal of a cataractous lens to mitigate the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity to an aspheric monofocal IOL.

**enVista Envy™ toric hydrophobic acrylic intraocular lens**
The enVista Envy toric hydrophobic acrylic IOL (non-preloaded model: ETN / preloaded into shuttle model: ETPN) is indicated for primary implantation in the capsular bag of the eye in adult patients for the visual correction of aphakia and corneal astigmatism following removal of a cataractous lens to mitigate the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity to an aspheric monofocal IOL.

## III. CONTRAINDICATIONS

There are no known contraindications.

## IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the enVista Envy and enVista Envy toric IOL labeling.

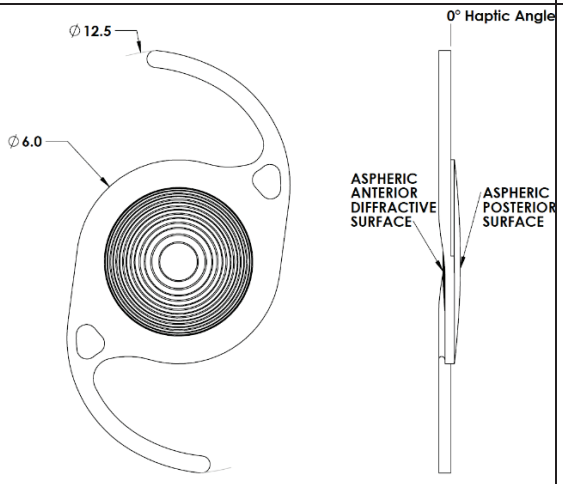
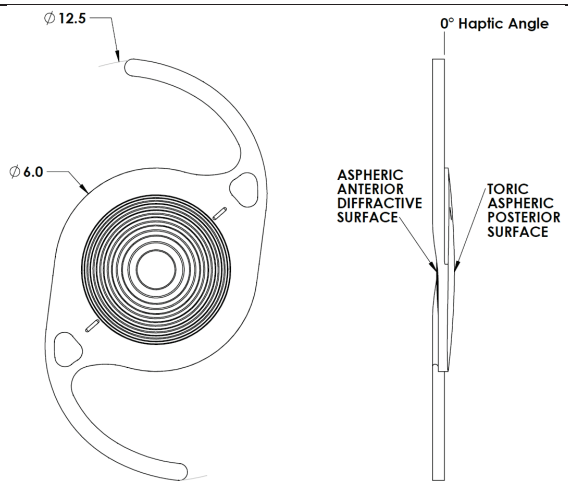
## V. DEVICE DESCRIPTION

The enVista Envy and enVista Envy toric IOLs are one-piece, hydrophobic acrylic, trifocal intraocular lenses intended to replace the natural crystalline lens in adult patients in whom the cataractous lens has been removed. The IOLs have an aspheric apodized diffractive optic on the anterior surface, the posterior surface is aspheric refractive or aspheric refractive toric and is designed to have -0.15 µm of spherical aberration at focus in an EN ISO 11979-2 Model Eye 1 at 5.1mm aperture on the optic surface. The IOLs have near add power of +3.1 diopters and intermediate add power of +1.6 diopters. They have a 12.5 mm overall diameter, a 6.0 mm optic body diameter, and 0° haptic angulation. The haptics are modified C-Loop. The clear optical diameter ranges from 4.5 mm to 5.9 mm across the power range. The posterior side of the lens has a continuous 360° square edge to help prevent Posterior Capsular Opacification.

The IOLs are manufactured using a UV absorbing foldable hydrophobic acrylic material. The design and material of the IOLs allow them to be folded and inserted into the capsular bag through a small incision to minimize the extent of surgically induced astigmatism. The IOLs' unique fenestration holes facilitate intraoperative lens manipulation, allowing for both clockwise and counterclockwise manipulation when positioning the lens in the capsular bag. A representative image of the subject devices is included below.

Key physical properties of the enVista Envy or enVista Envy toric IOLs are identified in **Table 1** and **Figure 1**. The enVista Envy toric IOL has axis markings at the haptic-optic junction to identify the flat meridian of the enVista Envy toric IOL and represent an imaginary line of the plus cylinder axis. The astigmatic correction at the corneal plane for each toric model is also shown in **Table 1** below.

## Table 1: Physical properties of the IOLs

| Characteristic | enVista Envy IOL | enVista Envy toric IOL | | | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| Optical Type and Powers | Single-piece, aspheric apodized diffractive / +6.0 to +34.0 Diopters (+6.0 to +9.0 in 1.0 Diopter increments, +10.0 to +34.0 in 0.5 Diopter increments) / Intermediate 1.6 Diopters / Near 3.1 Diopters | Single-piece, aspheric apodized diffractive / +6.0 to +34.0 Diopters in 0.5 Diopter increments (SE – Spherical Equivalent) / Intermediate 1.6 Diopters / Near 3.1 Diopters | | | | | | | |
| Optical Body Diameter | 6.0 mm | 6.0 mm | | | | | | | |
| Overall Diameter | 12.5 mm | 12.5 mm | | | | | | | |
| Haptic Angle | 0° | 0° | | | | | | | |
| Image |  Dimensions are in mm |  Dimensions are in mm | | | | | | | |
| Lens Material | UV absorbing foldable hydrophobic acrylic (hydroxyethyl methacrylate (HEMA)-polyethylene glycol phenyl ether acrylate (poly(EG)PEA)-styrene copolymer, crosslinked with ethylene glycol dimethacrylate) | UV absorbing foldable hydrophobic acrylic (hydroxyethyl methacrylate (HEMA)-polyethylene glycol phenyl ether acrylate (poly(EG)PEA)-styrene copolymer, crosslinked with ethylene glycol dimethacrylate) | | | | | | | |
| Index of Refraction | 1.53 @ 35°C | 1.53 @ 35°C | | | | | | | |
| Spectral Transmittance | Ultraviolet: UV (389) 10% transmittance for +20.0 Diopter IOL. See **Figure 1** | Ultraviolet: UV (389) 10% transmittance for +20.0 Diopter IOL. See **Figure 1** | | | | | | | |
| Cylinder Powers (CYL) – IOL Plane | Not Applicable | 1.25 D | 1.50 D | 2.00 D | 2.50 D | 3.00 D | 3.50 D | 4.25 D | 5.00 D | 5.75 D |
| Cylinder Powers (CYL) – Corneal Plane* | Not Applicable | 0.88 D | 1.05 D | 1.40 D | 1.75 D | 2.10 D | 2.45 D | 2.98 D | 3.50 D | 4.03 D |

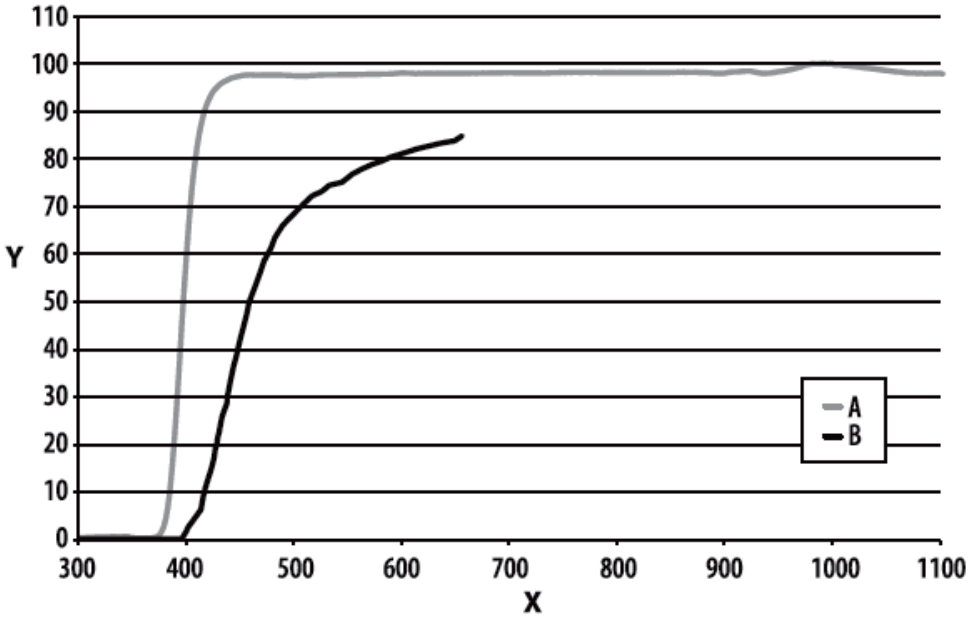
*Based on an average pseudophakic human eye

The IOLs are sold standalone and require use of a legally marketed inserter/injector and viscoelastics. The inserters are used for folding and delivering enVista IOL models into the eye during cataract surgery. Compatible inserters include the INJ100 Inserter and the Bausch and Lomb Injector System™ (B.L.I.S.) Reusable Inserter. The B.L.I.S. and INJ100 IOL Inserters have been marketed in the United States for over eight years. The enVista Preloaded

IOLs are individually "preloaded" into a shuttle assembly that is placed into a plastic vial with BBS solution and then sealed with a foil lid.

enVista Envy IOLs were investigated under IDE G180015 as described in Section X below.

**Figure 1: enVista Envy Spectral Transmittance**




A = + 20 Diopter enVista IOL and B = 53-Year-Old Human Lens. NOTE: Light transmittance values for an IOL material may vary slightly depending on the method of measurement.
X value = Wavelength (nm) and Y value = % Transmittance; chart compares the transmittance curve of an enVista IOL to a 53-Year-Old Human Lens. Human crystalline lens data is from Boettner and Wolter (1962).

## VI. ALTERNATIVE PRACTICES AND PROCEDURES

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

## VII. MARKETING HISTORY

The enVista Envy and enVista Envy toric IOLs are currently commercially available in Canada. The lenses have not been withdrawn from any country for any reason related to safety or effectiveness.

## VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Below is a list of the potential adverse effects (e.g., complications) associated with the use of the device include the following:

- lens epithelial cell down-growth
- corneal endothelial damage
- infection (endophthalmitis)
- retinal detachment/tear
- vitritis
- cystoid macular edema
- corneal edema
- pupillary block
- cyclitic membrane
- iris prolapse
- hypopyon
- anterior uveitis
- hyphema
- pigment dispersion
- posterior capsule opacification
- transient or persistent glaucoma
- IOL dislocation, tilt, or decentration requiring repositioning
- residual refractive error resulting in secondary intervention
- increased visual disturbances (compared to a monofocal IOL) related to the optical characteristics of the IOL, including bothersome stray-light artifacts such as halo, starbursts, or glare

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

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

## IX. SUMMARY OF NON-CLINICAL STUDIES

### Biocompatibility Testing

The enVista Envy and enVista Envy toric IOLs are made of the same material that was used with previously approved enVista IOLs (P910056/S051). Biocompatibility testing (see **Table 2**) was performed to support P910056/S051 in accordance with all relevant ISO Standards ISO 11979-5 and ISO 10993-1), as well as the United States Food and Drug Administration. Use of International Standards ISO 10993-1, "Biological evaluation of medical devices – Part 1: Evaluation and testing within a risk management process".

All tests to evaluate the biocompatibility were conducted in accordance with provisions of 21 CFR 58, Good Laboratory Practice (GLP) for Nonclinical Laboratory Studies.

**Table 2: Biocompatibility assessment of the enVista Envy and enVista Envy toric IOLs**

| Test (ISO Standard) | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Cytotoxicity - MEM elution (ISO 10993-5, ISO 11979-5) | Evaluates the potential for cellular toxicity | Non-cytotoxic | Pass |
| Cytotoxicity – Agar Diffusion (ISO 10993-5, ISO 11979-5) | Evaluates the potential for cellular toxicity | Non-cytotoxic | Pass |
| Sensitization - Guinea Pig Maximization (ISO 10993-10, ISO 11979-5) | Evaluates the potential for sensitization | Non-sensitizer | Pass |
| Irritation – Rabbit Intracameral (intraocular) Irritation (ISO 10993-23) | Evaluates the potential for irritation | Non-irritant | Pass |
| Rabbit Intramuscular Implantation – 12-week Study with Histopathology (ISO 10993-6, ISO 11979-5) | Evaluate the potential local tissue response | Good tissue tolerability | Pass |
| Acute Systemic Toxicity in Mice (ISO 10993-11) | Evaluates the potential for systemic toxicity | Non-toxic | Pass |
| Genotoxicity - Bacterial Reverse Mutation Test (Ames Test) (ISO 10993-3, ISO 11979-5) | Evaluates the potential for mutagenic changes | Non-mutagenic | Pass |
| Genotoxicity - In vitro chromosome aberration test (ISO 10993-3, ISO 11979-5) | Evaluates the clastogenic (large scale genetic damage) potential of the implant in Chinese hamster ovary cells | Non-clastogenic | Pass |
| Ocular Implantation – 12-Month Ocular Implantation (ISO 10993-6, ISO 11979-5) | Evaluate the potential local tissue response | Good tissue tolerability | Pass |

**Physiochemical Tests**

The enVista Envy and enVista Envy toric IOLs are made of the same material that was used for previously approved enVista IOLs (P910056/S051). Chemical Characterization (**Table 3**) was performed to support P910056/S051 in accordance with the recommendations in ISO 11979-5 Ophthalmic Implants – Intraocular Lenses Part 5 – Biocompatibility. New leachable and particulate testing was performed on sterile, finished enVista Envy IOLs (preloaded in shuttle) at baseline and after shelf-life conditioning.

**Table 3: Physiochemical tests of the enVista Envy and enVista Envy toric IOLs**

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Exhaustive Extraction (ISO 11979-5, ISO 10993-18) | Soxhlet extraction to recover polymerization residuals, impurities, and additives, quantitative analysis of extracts | Extraction profile is similar to previous enVista IOL material (e.g., no higher concentration of UV absorber compounds).<br><br>New IOL materials passes biocompatibility and toxicology assessment. | Pass |
| Leachables (ISO 11979-5, ISO 10993-18) | Extraction procedure to simulate leachable components that are expected to be released in-vivo | New IOL material passes biocompatibility and toxicology assessment. | Pass |
| Insoluble Inorganics (ISO 11979-5) | Test to verify removal of residual inorganics residues from the manufacturing process | Residual profile and concentrations are similar to previous enVista material. | Pass |
| Hydrostatic Stability (ISO 11979-5) | Test to verify material does not degrade by hydrolysis | New material is stable under exaggerated hydrolytic conditions equivalent to 5 years real time exposure. | Pass |
| Photostability (ISO 11979-5) | Test to evaluate photostability over 20 years | No significant difference in physical appearance, spectral transmittance, or dioptric power. | Pass |
| Nd:YAG Laser (ISO 11979-5) | Test to evaluate material stability when exposed to Nd-YAG laser treatment, and no leakage of toxic components | No significant difference in physical appearance, spectral transmittance, or dioptric power. | Pass |

**Optical and Mechanical Testing**

Pre-clinical optical / mechanical tests were performed with the enVista Envy and enVista Envy toric IOLs and were measured in accordance with ISO 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods and ISO 11979-3 Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods. Test results are presented in **Table 4**.

**Table 4: Optical and Mechanical Test Results**

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Surface and Bulk Homogeneity (Pre and Post Folding) | To ensure IOL is free of surface and bulk defects | ISO 11979-3:2012 Section 4.12 | Pass |
| Dioptric Power and Image Quality (Pre and Post Folding) | To assess conformance to optical power and image quality tolerances | ISO 11979-2:2014 Sections 4.2.1, 4.2.2, 4.2.3, 4.3 | Pass |
| Dimensions (Pre and Post Folding) | To assess conformance to dimensional tolerances | ISO 11979-3:2012 Section 4.2 | Pass |
| Recovery of Properties | To assess the ability of the IOL to return to optical, dimensional, and cosmetic specifications after simulated surgical manipulation | ISO 11979-3:2012 Section 5 | Pass |
| Axial Displacement | To characterize the axial displacement in compression | ISO 11979-3:2012 Section 4.5 | Pass |
| Optic Decentration | To assess optic decentration under compression | ISO 11979-3:2012 Section 4.6 | Pass |
| Optic Tilt | To assess optic tilt under compression | ISO 11979-3:2012 Section 4.7 | Pass |
| Mechanical Characterization (Compression Force, Force Decay, Angle of Contact) | To characterize the mechanical properties of the IOL | Must match criteria for a Level A modification described in ISO/TR 22979 when compared to enVista MX60 design verification test results. | Pass |
| Dynamic Fatigue | To assess the ability of the haptics to withstand cyclic compressive loading | ISO 11979-3:2012 Section 4.10 | Pass |
| Surgical Manipulation (Haptic Pull Test) | To assess the force required to separate the haptic from the optic | ISO 11979-3:2012 Section 4.11 | Pass |
| Spectral Transmittance | To characterize the spectral transmittance of the IOL | ISO 11979-2:2014 Section 4.4.2 | Pass |
| Glistening Testing | To characterize glistenings performance of the IOL | No glistenings observed | Pass |

**Sterilization and Stability Evaluation**

Sterilization evaluation, shelf-life and transport stability testing, and bacterial endotoxin testing were performed to support the enVista Envy and Envy toric IOLs. The results are summarized in **Table 5**.

**Table 5: Sterilization Evaluation Results**

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Gamma radiation sterilization validation (VDmax25 method) (ISO 11137-1 & ISO 11137-2) | Substantiate a 25 kGy dose for routine sterilization of product, and demonstrate process can achieve a Sterility Assurance Level (SAL) of $10^{-6}$, based upon the average product bioburden. | Successful performance of verification dose experiment (i.e., ≤ 1 positive test of sterility result [growth of microorganisms on solid, or in liquid, microbial growth media]) to demonstrate process can achieve an SAL ≤ $10^{-6}$, based upon the average product bioburden. | Pass |
| Transport stability (ISO 11979-6, ISO 11607-1, ASTM F2096, ASTM F1886) | Confirm that the sterile barrier packaging can maintain device sterility throughout anticipated transport conditions. Testing includes visual inspection, whole package integrity, and seal integrity assessments after transport conditioning (e.g., ISTA 3A sequence). | Meets lens cosmetics and functional delivery requirements. Meets sterile barrier packaging visual inspection, whole package integrity & seal integrity requirements. For visual inspection, no channels, voids, punctures, or breaches observed, and labels are legible. For whole package integrity assessed by bubble leak testing of the Tyvek pouch packaging, no leaks are observed. For seal integrity, assessed by leak testing of the vial packaging, no leaks are observed. | Pass |
| Shelf-life stability (ISO 11979-6 & ISO 11607-1) | Confirm that device performance is maintained throughout claimed shelf-life. | Meets optical, mechanical, chemical and biological testing requirements | Pass |
| Package Integrity (ISO 11979-6, ISO 11607-1, ASTM F2096, ASTM F1886) | Confirm that the primary sterile barrier packaging can maintain device sterility throughout claimed shelf life. Testing includes visual inspection, whole package integrity, and seal integrity assessments after aging (both accelerated aging and real-time aging conditions). | Meets sterile barrier packaging visual inspection, whole package integrity & seal integrity requirements. For visual inspection, no channels, voids, punctures, or breaches observed, and labels are legible. For whole package integrity assessed by bubble leak testing of the Tyvek pouch packaging, no leaks are observed. For seal integrity, assessed by leak testing of the vial packaging, no leaks are observed. | Pass |
| Bacterial Endotoxin Testing (ANSI/AAMI ST72, USP<85>, FDA Guidance on Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices) | Confirms Endotoxin present on product is below the permanent intraocular device limit to confirm product is non-pyrogenic. | ≤ 0.2 Endotoxin Units (EU)/device | Pass |

**Inserter Validations**

The objective of the inserter validations was to document that the enVista Envy and Envy toric IOLs can be successfully delivered using the compatible INJ100 and B.L.I.S (with BLIS-X1) inserters. Testing was performed to demonstrate that the enVista Envy and Envy toric IOLs can be successfully delivered across the entire range of IOLs using Amvisc, Amvisc Plus, or OcuCoat viscoelastics. Test results are presented in **Table 6**.

**Table 6: Inserter Validation Results**

| Test | Purpose | Acceptance Criteria | Results |
|---|---|---|---|
| Surface and Bulk Homogeneity (Post-Delivery) | To assess conformance to dimensional tolerances and free of surface defects | ISO 11979-3:2012 Section 5 > ISO 11979-3:2012 Section 4.12 | Pass |
| Dioptric Power and Image Quality (Post-Delivery) | To assess accuracy of optical power and image quality of the IOL | ISO 11979-3:2012 Section 5 > ISO 11979-2:2014 | Pass |
| Lens Dimensions (Post-Delivery) | To assess conformance to dimensional tolerances | ISO 11979-3:2012 Section 5> ISO 11979-3:2012 Section 4.2 | Pass |
| Recovery of Properties (Post-Delivery) | To assess the ability of the IOL to withstand simulated surgical implantation without damage | ISO 11979-3:2012 Section 5 | Pass |
| Insertion Device Cosmetic Inspection (Post-Delivery) | To assess the ability of the insertion device to withstand simulated surgical implantation without damage | No damage to the insertion device during the delivery (i.e. split tips) when viewed at 10x magnification | Pass |
| Delivery Outcome (Post-Delivery) | To assess the ability of the insertion device to deliver the IOL | IOL cannot flip over upon delivery, IOL must exit inserter upon completion of delivery, and folding and/or delivery process shall not cause IOL cosmetic defects | Pass |

## X. SUMMARY OF CLINICAL STUDIES

### Overview of Clinical Studies

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of implantation with the enVista Envy IOL for the visual correction of aphakia with less than or equal to 1.0 D preoperative corneal astigmatism following removal of a cataractous lens to mitigate the effects of presbyopia by providing improved intermediate and near visual acuity, while maintaining comparable distance visual acuity to an aspheric monofocal IOL, in the US under IDE #G180015.

The toric model of the enVista Envy IOL combines the optical designs of the enVista Envy trifocal IOL and the posterior surface toric feature of the parent enVista monofocal toric IOL (model MX60T). The applicant previously performed a clinical study to establish a reasonable assurance of safety and effectiveness of implantation with the enVista monofocal toric IOL for visual correction of aphakia and corneal astigmatism following removal of a cataractous lens in the US under IDE #G120193. The study data support a significant dioptric reduction in refractive cylinder and reduction in absolute cylinder, rotational stability of the lens, and UDVA following implantation of the enVista monofocal toric IOL. The enVista monofocal toric IOL received marketing approval from the Agency on June 8, 2018, under Panel-Track Supplement, P910056/S027.

Since the enVista toric monofocal IOL (model MX60T) has received marketing approval, the enVista toric monofocal IOL (model MX60T) clinical study established the safety profile of toric device, and the materials used to manufacture the enVista Envy IOL received marketing approval from the Agency under 180-Day Supplement, P910056/S051 (on August, 21, 2023), additional clinical data were not required to support the safety and effectiveness of the enVista Envy IOL toric model.

The summary of the enVista Envy trifocal IOL clinical study is presented below.

### A. STUDY DESIGN

Subjects were treated between 2018 and 2023. The database for this PMA reflected data collected through 2023 and included 501 subjects. There were 23 investigational sites in the United States.

This was a prospective, multicenter, randomized, active-controlled binocularly implanted study of the enVista one-piece hydrophobic acrylic trifocal IOL in subjects undergoing cataract extraction compared to the enVista one-piece hydrophobic acrylic monofocal IOL. Subjects scheduled to undergo cataract surgery by phacoemulsification and implantation of bilateral IOLs were screened for eligibility through extensive inclusion exclusion criteria, and with extensive preoperative assessments with both eyes of each subject included in the study after having met eligibility criteria at the Preoperative Visit. At the time of the first surgery,

subjects were enrolled and randomly assigned by an Interactive Response Technology system in a 2:1 ratio to either the test - enVista trifocal IOL or the control- enVista monofocal IOL, respectively. The monofocal control IOL is a legally marketed alternative with similar indications for use, except that it is not intended to provide improved vision at intermediate and near distances.

All subjects underwent bilateral implantation of the enVista trifocal IOL or the enVista monofocal IOL and were followed up through post-operative scheduled visits through Postoperative Visit # 5 (11-14 Months) with ophthalmic examinations and standardized pre-, peri-, and postoperative care under the supervision of the Physician/ Investigator.

The sample size, which assumed a dropout rate of up to 10%, was based on the assumptions shown in **Table 7** and on the requirements of ISO 11979-7.

**Table 7: Sample Size Assumptions**

| | Margin | Expected Difference | SD | Type I error (1-sided) | Power |
|---|---|---|---|---|---|
| **Non-inferiority** | | | | | |
| **SSI Proportion** | 0.034 | 0.005-0.001 | N/A | 5% | 99% |
| **BCDVA** | 0.10 | 0.00 | 0.15 | 5% | 99% |
| **Superiority** | | | | | |
| **DCNVA** | | -0.10 | 0.15 | 2.5% | 99% |
| **DCIVA** | | -0.10 | 0.15 | 2.5% | 99% |

Abbreviations: BCDVA = Best Corrected Distance Visual Acuity; DCIVA = Distance-Corrected Intermediate Visual Acuity; DCNVA = Distance-Corrected Near Visual Acuity; N/A = Not Applicable; SD = Standard Deviation; SSI = Secondary surgical interventions.

Study enrollment occurred in 3 phases covering Phase 1/ pilot, Phase II and Phase III. Enrolled subjects who met eligibility criteria were seen at 11 or 12 visits, including a preoperative visit, 2 operative visits (1 for each eye), and 8 mandatory postoperative visits (3 for each eye and 2 for both eyes), as well as an additional 1 postoperative visit only for those subjects who consented at participating sites (Day 2 to 30 after otherwise last visit/Postoperative Visit 5) for the Trial Frame Astigmatism Sub-Study.

The subject was considered enrolled in the study at the time of randomization at the first Operative Visit (Visit 00A). Randomization followed the completion of uncomplicated cataract extraction in the first eye. Only subjects who were randomized but did not have the lens inserted into the eye could be replaced. For those eligible subjects who consented to participate in the Trial Frame Astigmatism Simulation Sub-Study, a Postoperative Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5) was conducted as the final visit to complete the study.

1. **Clinical Inclusion and Exclusion Criteria**

Enrollment in the enVista Envy Trifocal Intraocular lens study was limited to patients

who met the following inclusion criteria in both eyes:

1. Subjects must be 22 years of age or older on the date the Informed Consent Form (ICF) is signed.
2. Subjects must have the capability to understand and provide written informed consent on the Institutional Review Board (IRB)/Independent Ethics Committee (IEC) approved Informed Consent Form (ICF) and authorization as appropriate for local privacy regulations.
3. Subjects must have a BCDVA equal to or worse than 20/40 in each eye, with or without a glare source, due to a clinically significant cataract (cortical, nuclear, subcapsular, or combination) that is considered amenable to treatment with standard phacoemulsification cataract extraction and capsular IOL implantation.
4. Subjects must have a BCDVA projected to be better than 20/32 after IOL implantation in each eye, as determined by the medical judgment of the Investigator or measured by potential acuity meter (PAM) testing, if necessary.
5. Subjects must have clear intraocular media other than the cataract in both eyes.
6. Contact lens wearers must demonstrate a stable refraction (within ±0.50 D for both sphere and cylinder) in both eyes, as determined by manifest refraction on two consecutive examination dates after discontinuation of contact lens wear.
7. Subjects must require an IOL power from +16.0 diopter (D) to +24.0 D in both eyes.
8. Subjects must be willing and able to comply with all treatment and follow-up study visits and procedures, and to undergo second eye surgery within 7-30 days of the first eye surgery.

Subjects were not permitted to enroll in the enVista Envy Trifocal Intraocular lens study if they met any of the following exclusion criteria:

1. Subjects who have used an investigational drug or device within 30 days prior to entry into this study and/or will participate in another investigation during the period of study participation.
2. Subjects who have any corneal pathology (e.g., significant scarring, guttata, inflammation, edema, dystrophy, etc.) in either eye.
3. Subjects who have significant anterior segment pathology that might increase intraoperative risk or compromise IOL stability (e.g., pseudoexfoliation syndrome, synechiae, iris atrophy, traumatic cataract, lens subluxation, traumatic zonulolysis, zonular dialysis, evident zonular weakness or dehiscence, hypermature or brunescent cataract, etc.) in either eye.
4. Subjects who have uncontrolled glaucoma in either eye.
5. Subjects who have previous retinal detachment or clinically significant retinal pathology involving the macula in either eye.
6. Subjects who have proliferative or non-proliferative diabetic retinopathy in either eye.

7. Subjects who have a congenital ocular anomaly (e.g., aniridia, congenital cataract) in either eye.
8. Subjects using any systemic or topical drug known to interfere with visual performance, pupil dilation, or iris structure within 30 days of enrollment or during the study.
9. Subjects who have a history of chronic or recurrent inflammatory eye disease (e.g., iritis, scleritis, iridocyclitis, or rubeosis iridis) in either eye.
10. Subjects who have a visual disorder, other than cataracts, that could potentially cause future acuity losses to a level of 20/100 or worse in either eye.
11. Subjects who have had previous intraocular or corneal surgery in either eye, with the exception of laser trabeculoplasty.
12. Subjects with any preoperative infectious conjunctivitis, keratitis, or uveitis in either eye.
13. Subjects who have a preoperative corneal astigmatism > 1.0 D in either eye, irregular astigmatism, or skewed radial axis (note: corneal incisions intended specifically to reduce astigmatism are not allowed during the study).
14. Subjects who cannot achieve a minimum pharmacologic pupil dilation of 5.0 mm in both eyes.
15. Subjects who may be expected to require a combined or other secondary surgical procedure in either eye.
16. Subjects who during the first cataract extraction experience an anterior or posterior capsule tear or rupture, zonular dialysis, significant iris trauma, or other complications that may cause untoward effects in the judgment of the Investigator.
17. Females of childbearing potential (those who are not surgically sterilized or at least 12 months postmenopausal) are excluded from enrollment in the study if they are currently pregnant or plan to become pregnant during the study. Females of childbearing potential must be willing to practice effective contraception for the duration of the study.
18. Subjects with any other serious ocular pathology or underlying systemic medical condition (e.g., uncontrolled diabetes) or circumstance that, based on the Investigator's judgment, poses a concern for the subjects' safety or could confound the results of the study.
19. Subjects who have current or previous usage of an alpha-1-selective adrenoceptor blocking agent or an antagonist of alpha 1A adrenoceptor (e.g., Flomax® (tamsulosin HCl), Terazosin, or Cardura).

The following were intraoperative criteria for not implanting the device:

- Capsulorhexis tear, iris damage, posterior capsular rupture, vitreous prolapse, or zonular weakness or dehiscence
- Zonular rupture
- Evident zonular weakness or dehiscence
- Posterior capsule rupture

- Vitreous loss
- Significant detachment of Descemet's membrane
- Wound burn or damage
- Anterior chamber bleeding
- Iris incarceration or damage
- Corneal endothelial touch
- Unsuccessful/incomplete phacoemulsification
- Posterior capsule plaque
- Optic and/or haptic damage/amputation

## 2. Follow-up Schedule

The follow-up visit schedule is presented in **Table 8**. Specific examinations and scheduled clinical assessments are presented in **Table 9**.

**Table 8: Follow up Schedule**

| Visit Name | Eyes Evaluated | Visit Window |
|---|---|---|
| Preoperative Visit 0A/B | Both Eyes | Day -30 to -5 |
| Operative Visit 00A | 1st Eye | Day 0 |
| Post-Operative Visit 1A | 1st Eye | Day 1 to 2 post Visit 00A |
| Post-Operative Visit 2A | 1st Eye | Day 7 to 14 post Visit 00A |
| Post-Operative Visit 3A | 1st Eye | Day 30 to 60 post Visit 00A |
| Operative Visit 00B | 2nd Eye | Day 7 to 30 post Visit 00A |
| Post-Operative Visit 1B | 2nd Eye | Day 1 to 2 post Visit 00B |
| Post-Operative Visit 2B | 2nd Eye | Day 7 to 14 post Visit 00B |
| Post-Operative Visit 3B | 2nd Eye | Day 30 to 60 post Visit 00B |
| Post-Operative Visit 4 | Both Eyes | Day 120 to 180 post Visit 00B |
| Post-Operative Visit 5 | Both Eyes | Day 330 to 420 post Visit 00B |
| Post-Operative Visit 6 | Both Eyes | Day 2 to 30 post Visit 5 |

## Table 9: Schedule of Clinical Assessments

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| Informed Consent | X | | | | | | | | | | X[o] | |
| Demographics | X | | | | | | | | | | | |
| Ocular and Non-Ocular Medical History | X | | | | | | | | | | | |
| Inclusion/Exclusion | X | X[b] | | | | X[b] | | | | | | X[p] |
| Subject Questionnaires[c] | X | | | | | | | | | X | | |
| Potential Visual Acuity | X | | | | | | | | | | | |
| Corneal Topography | X | | | | | | | | | | | |
| Targeted Refraction / IOL Power Calculation / Axial Length Determination/Anterior Chamber Depth | X | | | | | | | | | | | |
| Chord length μ | X | | | | | | | | | X | X | |
| Keratometry | X | | | | X | | | | X | X | X | |
| Manifest Refraction (ETDRS) | X | | | X | X | | | X[d] | X[d] | X | X | |
| Randomization | | X | | | | | | | | | | |
| Operative Procedures | | X | | | | X | | | | | | |
| Photopic Pupil Size | X | | | | | | | | X[d] | X | | |
| Mesopic Pupil Size | X | | | | | | | | | X | | |
| UCDVA – photopic, monocular (ETDRS) | X | | X | X | X | | X | X | X | X | X | |
| UCDVA- photopic, binocular (ETDRS) | | | | | | | | X | X | X | X | |

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| BCDVA – photopic, monocular (ETDRS) | X | | | X | X | | | X | X | X | X | |
| BCDVA – photopic, binocular (ETDRS) | | | | | | | | X | X | X | X | |
| UCNVA[e,f] – photopic, monocular | | | | | X | | | | X | X | X | |
| UCNVA[e,f] – photopic, binocular | | | | | | | | | X | X | X | |
| DCNVA[e]– photopic, monocular | | | | | X[g] | | X | X | [f] X | [f] | [f] | |
| DCNVA[e,f] – photopic, binocular | | | | | | | | | | X | X | |
| DCNVA[e,f] – mesopic, monocular | | | | | X | | | | X | X | X | |
| DCNVA[e,f] – mesopic, binocular | | | | | | | | | | X | X | |
| UCIVA[h,i] – photopic, monocular | | | | | X | | | | X | X | X | |
| UCIVA[h,i] – photopic, binocular | | | | | | | | | X | X | X | |
| DCIVA[h] – photopic, monocular | | | | | X[j] | | | | X[i] | X[i] | X[i] | |
| DCIVA[h,i] – photopic, binocular | | | | | | | | | | X | X | |
| DCIVA[h,i] – mesopic, monocular | | | | | X | | | | X | X | X | |
| DCIVA[h,i] – mesopic, binocular | | | | | | | | | | X | X | |
| Binocular best-corrected distance contrast sensitivity testing (photopic with glare at 3, 6, 12 and 18 cpd)[k] | | | | | | | | | | X | X[l] | |

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| Binocular best-corrected distance contrast sensitivity (mesopic with and without glare at 1.5, 3, 6, and 12 cpd)[k] | | | | | | | | | | X | X[l] | |
| Binocular BCDVA Defocus Curves[k] | | | | | | | | | | X | | |
| Intraocular Pressure | X | | X | X | X | | X | X | X | X | X | |
| Slit-Lamp Exam[m] | X | | X | X | X | | X | X | X | X | X | |
| Dilated Fundus Exam | X | | | | X | | | | X | X | X[n] | |
| OCT Imaging[k] | | | | | | | | | | X | | |
| Trial Frame Astigmatism Simulation sub-study (assessments below) | | | | | | | | | | | | X |
| BCDVA photopic monocular (no additional sphere, cylinder or axis) | | | | | | | | | | | | X |
| BCDVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 180°) | | | | | | | | | | | | X |
| BCDVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| BCDVA photopic, monocular (simulated astigmatism 1.50 D plus cylinder, 180°) | | | | | | | | | | | | X |

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| BCDVA photopic, monocular (simulated astigmatism 1.5 D plus cylinder, 90°) | | | | | | | | | | | | X |
| BCDVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 180°) | | | | | | | | | | | | X |
| BCDVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| DCIVA photopic monocular (no additional sphere, cylinder or axis) | | | | | | | | | | | | X |
| DCIVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 180°) | | | | | | | | | | | | X |
| DCIVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| DCIVA photopic, monocular (simulated astigmatism 1.5 D plus cylinder, 180°) | | | | | | | | | | | | X |
| DCIVA photopic, monocular (simulated astigmatism 1.5 D plus cylinder, 90°) | | | | | | | | | | | | X |

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| DCIVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 180°) | | | | | | | | | | | | X |
| DCIVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| DCNVA photopic monocular (no additional sphere, cylinder or axis) | | | | | | | | | | | | X |
| DCNVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 180°) | | | | | | | | | | | | X |
| DCNVA photopic, monocular (simulated astigmatism 2.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| DCNVA photopic, monocular (simulated astigmatism 1.5 D plus cylinder, 180°) | | | | | | | | | | | | X |
| DCNVA photopic, monocular (simulated astigmatism 1.5 D plus cylinder, 90°) | | | | | | | | | | | | X |
| DCNVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 180°) | | | | | | | | | | | | X |

| Examination | Pre-Op 0A/B (Both Eyes) | Operative 00A (1st Eye) | Post-Op 1A (1st Eye) | Post-Op 2A[a] (1st Eye) | Post-Op 3A (1st Eye) | Operative 00B (2nd Eye) | Post-Op 1B (2nd Eye) | Post-Op 2B (2nd Eye) | Post-Op 3B (2nd Eye) | Post-Op 4 (Both Eyes) | Post-Op 5 (Both Eyes) | For sub-study only: Post-Op 6 (Both eyes) |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Day -30 to -5 | Day 0 | Day 1 to 2 | Day 7 to 14 | Day 30 to 60 | Day 7 to 30 | Day 1 to 2 Post Visit 00B | Day 7 to 14 Post Visit 00B | Day 30 to 60 Post Visit 00B | Day 120 to 180 Post Visit 00B | Day 330 to 420 Post Visit 00B | Day 2- 30 post Visit 5 |
| DCNVA photopic, monocular (simulated astigmatism 1.0 D plus cylinder, 90°) | | | | | | | | | | | | X |
| Posterior capsulotomy assessment | | | X | X | X | | X | X | X | X | X | |
| Adverse Events | X | X | X | X | X | X | X | X | X | X | X | X |
| Concomitant Medications | X | X | X | X | X | X | X | X | X | X | X | X |

ETDRS=Early Treatment Diabetic Retinopathy Study visual acuity testing charts, UCDVA=Uncorrected Distance Visual Acuity, BCDVA=Best Corrected Distance Visual Acuity, UCNVA=Uncorrected Near Visual Acuity, DCNVA=Distance Corrected Near Visual Acuity, UCIVA=Uncorrected Intermediate Visual Acuity, DCIVA=Distance Corrected Intermediate Visual Acuity, OCT=Optical Coherence Tomography, D=Diopter

[a] Must occur before Operative Visit 00B

[b] Review of inclusion/exclusion criteria prior to surgery

[c] To additionally be completed at any post-operative Unscheduled Visit and prior to unscheduled study exit (e.g., IOL explanation).

[d] Completed for both eyes

[e] Distance for Phase II and Phase III subjects of 40 cm

[f] Phase I/Pilot: Distance of 40 cm

[g] Phase I/Pilot: Distance of 30 cm, 35cm, and 40 cm

[h] Distances for Phase II and Phase III subjects of 60 cm and 66 cm

[i] Phase I/Pilot: Distance of 66 cm

[j] Phase I/Pilot: Distance of 56 cm, 66 cm, and 76cm

[k] Conducted on a subset of subjects

[l] Done only if subject has posterior capsulotomy after Visit 4; if subject is scheduled for posterior capsulotomy during Visit 4, testing is deferred to Visit 5

[m] Includes determination of medical and lens findings/complications, including decentration, tilt and PCO (note: lens findings/complications, including decentration, tilt and PCO evaluated post-operatively only).

[n] If clinically indicated

[0] Subjects must consent to participate in the Visit 6 Trial Frame Astigmatism Simulation sub-study. New subjects who are enrolled in the study once protocol amendment 6 is instituted will consent to the Trial Frames Astigmatism Simulation sub-study at the Pre-Op Visit, if they so choose, but at a point no later than Visit 5. Existing subjects who are in the study at the time protocol amendment 6 is instituted must provide their consent to participate in the Trial Frame Astigmatism Simulation sub-study no later than Visit 5.

[p] Specific to Visit 6, overall study eligibility will be confirmed as well as criteria for participation in the Trial Frame Astigmatism Simulation sub-study

## 3. Clinical Endpoints

With regards to safety:

Co-primary Safety Endpoints

- The incidence of all serious adverse events, including secondary surgical interventions (SSIs) related to the optical properties of the IOL, in first eyes through study exit (No specific success criteria were pre-specified.)
- The rate of secondary surgical interventions due to the optical properties of the lens for first eyes through study exit (No specific success criteria were pre-specified.)
- The incidence of adverse events in first eyes compared to ISO Safety and Performance Endpoint (SPE) rates as defined in ISO 11979-7 through study exit (Success criteria for each type of event was a rate not statistically greater than the control rate.)

Secondary Safety Endpoints

- The rates of visual disturbances reported as "severe" by subjects, as well as the rates of visual disturbances reported as "very" bothersome by subjects, using the QoV questionnaire measure through Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation)
- Mean photopic contrast sensitivity with glare and mesopic contrast sensitivity with and without glare at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) and Post-Operative Visit 5 (Day 330 to 420 after second eye IOL implantation)
- Incidence of the types of AEs specified in the co-primary safety endpoints, but for fellow and "all" eyes
- Incidence of all other types of adverse events in primary eyes, fellow eyes, and "all" eyes

Other safety endpoints included:

- Binocular defocus curve sub study
- OCT sub study (evaluate image quality)
- Manifest refraction
- Slit Lamp Examination
- Device Deficiencies
- Intraocular Pressure
- Dilated Fundus Examination
- Fundus Visualization

With regards to effectiveness:

Primary Effectiveness Endpoints

- Photopic monocular best-corrected distance visual acuity (BCDVA) in first eyes at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) (The success criteria was statistical non-inferiority of BCDVA compared to the control. The non-inferiority margin was set at 0.10 logMAR.)
- Photopic monocular distance-corrected near visual acuity (DCNVA) in first eyes at 40 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) (The success criteria was statistical superiority of DCNVA compared to the control. The superiority margin was set at 0.0 logMAR.)
- Photopic monocular distance-corrected intermediate visual acuity (DCIVA) in first eyes at 66 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) (The success criteria was statistical superiority of DCIVA compared to the control. The superiority margin was set at 0.0 logMAR.)

Secondary Effectiveness Endpoints

- Photopic binocular distance-corrected near visual acuity (DCNVA) at 40 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation)
- Photopic binocular uncorrected near visual acuity (UCNVA) at 40 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation)
- Photopic binocular distance-corrected intermediate visual acuity (DCIVA) at 66 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation)
- Photopic binocular uncorrected intermediate visual acuity (UCIVA) at 66 cm at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation)
- First eye BCDVA, DCNVA, and DCIVA evaluated at Visit 5 (Day 330 to 420 after second eye IOL implantation)

Other effectiveness endpoints included:

- Astigmatic Blur Sub study: photopic logMAR monocular visual acuities at distance, intermediate and near with and without induced astigmatism to evaluate impact of residual astigmatism

With regard to study success, all primary safety and effectiveness endpoints with success criteria were required to demonstrate statistical study success. Individual subject success was not defined.

**Intent-to-Treat (ITT) Set**

The ITT Set included all randomized subjects.

**Modified Intent-to-Treat (mITT) Set**

The mITT Set included all randomized subjects with at least one eye in which the IOL touches the eye with a study lens. Randomized subjects excluded from this set were identified prior to database lock and unmasking.

**Modified Safety Set**
The Modified Safety set included all subjects with at least one eye in which the IOL touched the eye with a study lens.

## B. ACCOUNTABILITY OF THE PMA COHORT

At the time of the database lock, of 501 patients enrolled in the PMA, 91.8% (460) patients are available for analysis at the completion of the study, the approximately 12-month post-operative visit. The ITT Set, mITT Set, and the Modified Safety Set all included all 501 randomized subjects and 998 of the 1002 randomized eyes (**Table 10**). The disposition of all 501 randomized subjects is summarized in **Table 11**.

## Table 10: Subject Accountability by Visit up to Visit 5 (11-14 months)

| Modified Intent-to-Treat Set<br><br>Treatment: All Subjects | | | | | | |
|---|---|---|---|---|---|---|
| | **Total Number** | **Visit 0A/B (Pre-Op) n (%)** | **Operative Visit 00A n (%)** | **Visit 1A n (%)** | **Visit 2A n (%)** | **Visit 3A n (%)** |
| All Subjects | 501 | - | - | - | - | - |
| Subjects with an Eye Touched with Study IOL | 501 | - | - | - | - | - |
| Implanted Subjects | 501 | - | - | - | - | - |
| Available for Analysis (1) | - | 501 (100.0) | 501 (100.0) | 501 (100.0) | 493 (98.4) | 480 (95.8) |
| Discontinued (2) | - | 0 | 0 | 0 | 0 | 1 (0.2) |
| Missing at Scheduled Visit but Seen Later (3) | - | 0 | 0 | 0 | 8 (1.6) | 19 (3.8) |
| Not Seen but Accounted for (4) | - | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-up | - | 0 | 0 | 0 | 0 | 1 (0.2) |
| % Accountability | - | 100.0 | 100.0 | 100.0 | 98.4 | 96.0 |

| | **Operative Visit 00B n (%)** | **Visit 1B n (%)** | **Visit 2B n (%)** | **Visit 3B n (%)** | **Visit 4 n (%)** | **Visit 5 n (%)** |
|---|---|---|---|---|---|---|
| Available for Analysis (1) | 499 (99.6) | 495 (98.8) | 486 (97.0 | 481 (96.0) | 470 (93.8 | 460 (91.8) |
| Discontinued (2) | 1 (0.2) | 1 (0.2) | 2 (0.4) | 3 (0.6) | 10 (2.0) | 20 (4.0) |
| Missing at Scheduled Visit but Seen Later (3) | 0 | 3 (0.6) | 10 (2.0) | 14 (2.8) | 17 (3.4 | 16 (3.2) |
| Not Seen but Accounted for (4) | 0 | 0 | 0 | 0 | 0 | 0 |
| Lost to Follow-up | 1 (0.2) | 2 (0.4) | 3 (0.6) | 3 (0.6) | 4 (0.8) | 5 (1.0) |
| % Accountability | 99.8 | 99.0 | 97.4 | 96.6 | 95.7 | 95.6 |

Abbreviations: IOL = Intraocular Lens; Op = Operative.
Note: Percentages are based on the total number of subjects in the analysis population. % Accountability = 100*(Available for Analysis)/(All Modified Intent-to-Treat Subjects – Discontinued).
[1] Represents the total number of subjects for whom data are available at the visit
[2] Represents the total number of subjects that have discontinued treatment prior to the visit for any reason (e.g., death or device replacement), but does not include subjects that are lost to follow-up.
[3] Represents the total number of subjects that were seen outside the time window associated with the visit.
[4] Represents the total number of subjects that were missing at the scheduled visit but were accounted for by being contacted (e.g., by phone).

**Table 11: Subject Disposition (All Subjects)**

| Subject Disposition | enVista Trifocal IOL (N=332) | enVista Monofocal IOL (N=169) | All Participants (N=501) |
|---|---|---|---|
| Screen Failures (n) | - | - | 166 |
| Randomized (n) | 332 | 169 | 501 |
| Discontinued Prior to Attempted Implantation (n) | 0 | 0 | 0 |
| Attempted Implantation (n) | 332 (100%) | 169 (100%) | 501 (100%) |
| Successful First Implantation (n) | 332 (100%) | 169 (100%) | 501 (100%) |
| Completed Study (n) | 319 (96.1%) | 157 (92.9% | 476 (95.0% |
| Discontinued after First Implantation (n) | 13 (3.9%) | 12 (7.1% | 25 (5.0%) |

## C. STUDY POPULATION DEMOGRAPHICS AND BASELINE PARAMETERS

The demographics of the study population are typical for a randomized, prospective, multicenter clinical study of intraocular lenses performed in the US. All 501 subjects randomized were implanted (enVista trifocal IOL group, n=332; enVista monofocal IOL group, n=169). Of 1002 eyes randomized, 996 were implanted (enVista trifocal IOL group, n=659; enVista monofocal IOL group, n=337); 2 subjects each had 1 eye (OS- Left eye and OD- Right eye, respectively) that was touched by an IOL that was not implanted.

The Modified Safety Set population was primarily White (92.0%), not Hispanic/Latino (88.0%), and female (63.9%; **Table 12**). The mean ± SD age of the population was 68.0 ± 7.76 years. Similar demographics were observed across treatment groups.

## Table 12: Demographics (Modified Safety Set)

| Variable | enVista Trifocal IOL (N=332) | enVista Monofocal IOL (N=169) | All Participants (N=501) |
|---|---|---|---|
| Age, years | | | |
| n | 332 | 169 | 501 |
| Mean (SD) | 67.6 (7.89) | 68.8 (7.46) | 68.0 (7.76) |
| Median | 68.0 | 70.0 | 69.0 |
| Minimum, maximum | 32, 85 | 41, 85 | 32, 85 |
| Age categories, n (%) | | | |
| 18−64 years | 95 (28.6) | 35 (20.7) | 130 (25.9) |
| 65−84 years | 235 (70.8) | 133 (78.7) | 368 (73.5) |
| ≥85 years | 2 (0.6) | 1 (0.6) | 3 (0.6) |
| Gender, n (%) | | | |
| Male | 120 (36.1) | 61 (36.1) | 181 (36.1) |
| Female | 212 (63.9) | 108 (63.9) | 320 (63.9) |
| Race, n (%) | | | |
| American Indian/Alaska Native | 0 | 0 | 0 |
| Asian | 11 (3.3) | 4 (2.4) | 15 (3.0) |
| Chinese | 1 (0.3) | 1 (0.6) | 2 (0.4) |
| Non-Chinese | 10 (3.0) | 3 (1.8) | 13 (2.6) |
| Black/African American | 14 (4.2) | 9 (5.3) | 23 (4.6) |
| Native Hawaiian/Pacific Islander | 1 (0.3) | 0 | 1 (0.2) |
| White | 305 (91.9) | 156 (92.3) | 461 (92.0) |
| Multiple [a] | 1 (0.3) | 0 | 1 (0.2) |
| Other | 0 | 0 | 0 |
| Ethnicity, n (%) | | | |
| Hispanic/Latino | 40 (12.0) | 20 (11.8) | 60 (12.0) |
| Not Hispanic/Latino | 292 (88.0) | 149 (88.2) | 441 (88.0) |
| First eye, n (%) | | | |
| OD | 218 (65.7) | 95 (56.2) | 313 (62.5) |
| OS | 114 (34.3) | 74 (43.8) | 188 (37.5) |
| Study phase under which participant enrolled, n (%) | | | |
| Phase I/Pilot | 29 (8.7) | 13 (7.7) | 42 (8.4) |
| Phase II | 49 (14.8) | 24 (14.2) | 73 (14.6) |
| Phase III | 254 (76.5) | 132 (78.1) | 386 (77.0) |

eCRF = electronic Case Report Form; IOL = intraocular lens; OD = right eye; OS = left eye; SD = standard deviation.
[a] Participants who selected more than 1 race on the eCRF are grouped into the "Multiple" category.

## D. SAFETY AND EFFECTIVENESS RESULTS

### 1. Safety Results

The analysis of safety was based on the safety cohort of 501 implanted subjects: 332 enVista Envy subjects (327 bilaterally implanted) and 169 monofocal subjects (168 bilaterally implanted) available for the 12-month evaluation. Implanted subjects were followed for approximately 12 months (i.e., for 330-420 days after fellow eye implantation at Operative Visit 00B, which occurred 7-30 days after initial eye implantation at Operative Visit 00A [range 337-450 days]). The key safety outcomes for this study are presented below in **Tables 13 to 20**. Ocular (Serious and Non-Serious) Adverse Events are reported in **Tables 13 and 14**. ISO Grid Adverse Events are reported in **Tables 15 and 16**. Ocular Adverse Events based on a Modified Version of the American Academy of Ophthalmology (AAO) Consensus (Masket, 2017) are reported in **Tables 17 and 18**. Ocular Treatment-Emergent Serious Adverse Events by Treatment are reported in **Tables 19 and 20**.

**Co-primary Safety Endpoints**

- The incidence of all serious adverse events, including secondary surgical interventions (SSIs) related to the optical properties of the IOL, in first eyes through study exit
- The rate of secondary surgical interventions due to the optical properties of the lens for first eyes through study exit
- The incidence of adverse events in first eyes compared to ISO Safety and Performance Endpoint (SPE) rates as defined in ISO 11979-7 through study exit

No SSIs related to the optical properties of the IOLs were reported in the clinical study. All SPE rates for the enVista Envy IOL were below the SPE threshold as set forth by ISO 11979-7:2018 (**Tables 15 and 16**).

**Secondary Safety Endpoints**

- The rates of visual disturbances reported as "severe" by subjects, as well as the rates of visual disturbances reported as "very" bothersome by subjects, using the QoV questionnaire measure through Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) (**Table 21**)
- Mean photopic contrast sensitivity with glare and mesopic contrast sensitivity with and without glare at Post-Operative Visit 4 (Day 120 to 180 after second eye IOL implantation) and Post-Operative Visit 5 (Day 330 to 420 after second eye IOL implantation) (**Figures 2- 4; Tables 22-24**)
- Incidence of the types of AEs specified in the co-primary safety endpoints, but for fellow and "all" eyes (**Table 14**)
- Incidence of all other types of adverse events in primary eyes, fellow eyes, and "all" eyes (**Tables 16, 18, and 20**)

The differences in mean binocular contrast sensitivity between the Trifocal and Monofocal IOLs were clinically insignificant, i.e.; <0.15 log unit for 4 of the 12 test conditions (Mesopic with and without glare at 1.5 cpd, Mesopic without glare at 3 and 12 cpd); clinically significant differences favored the Monofocal IOL for the remaining test conditions. The mean binocular contrast sensitivity was worse in the trifocal cohort than monofocal cohort for all tested conditions, except for the lowest spatial frequency tested (i.e., thickest stripes) for the mesopic with glare, and mesopic without glare conditions.

Subjects in the Trifocal group stated a greater frequency of halos (36.9% [116/314] quite often or very often) compared to the control (7.1% [11/154]) with 6.1% (19/309) of the Trifocal subjects describing the halos as severe and 7.1% (22/309) calling them very bothersome. Moderate to severe difficulty with focusing and depth perception was reported by 8.8% (27/309) and 5.5% (15/310) of subjects with the Trifocal group compared to 13.2% (20/151) and 7.9% (10/151) of subjects in the Monofocal group respectively.

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

The ocular adverse events (serious and non-serious) for both the study and control lens, first eye, are presented in **Table 13.** A similar proportion of subjects and eyes across treatment groups had at least 1 ocular TEAE (trifocal IOL, 49.4% (164/332) of subjects and 37.7% (249/661) of all eyes; monofocal IOL, 40.8% (69/169) of subjects and 28.8% 97/337) of all eyes ). The most common ocular TEAEs in both treatment groups were punctate keratitis, intraocular pressure increased, and vitreous detachment. All other adverse events in the first eyes were reported at a rate of < 2.4% in both groups. Results for the second eyes were similar to first eyes, **Table 14**.

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

| | enVista Trifocal IOL (N=332) | | | enVista Monofocal IOL (N = 169) | | |
|---|---|---|---|---|---|---|
| **Preferred Term** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Punctate keratitis | 48 (14.5) | 10.86, 18.71 | 53 | 13 7.7 | (4.16, 12.79) | 14 |
| Intraocular pressure increased | 26 7.8 | (5.18, 11.26) | 27 | 15 (8.9) | (5.05, 14.22) | 15 |
| Vitreous detachment | 22 (6.6) | (4.20, 9.86) | 22 | 10 (5.9) | (2.87, 10.61) | 10 |
| Dry eye | 7 2.1 | (0.85, 4.30) | 7 | 3 (1.8) | (0.37, 5.10) | 4 |
| Blepharitis | 5 (1.5) | (0.49, 3.48) | 5 | 4 (2.4) | (0.65, 5.95) | 4 |
| Meibomian gland dysfunction | 5 (1.5) | (0.49, 3.48) | 5 | 3 (1.8) | (0.37, 5.10) | 3 |
| Visual acuity reduced | 5 (1.5) | (0.49, 3.48) | 5 | 2 (1.2) | (0.14, 4.21) | 2 |
| Cystoid macular oedema | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Vitreous floaters | 2 (0.6) | 0.07, 2.16 | 2 | 1 (0.6) | (0.01, 3.25) | 1 |
| Diplopia | 3 (0.9) | (0.19, 2.62) | 3 | 0 | (0.00, 2.16) | 0 |
| Iritis | 3 (0.9) | (0.19, 2.62) | 3 | 1 (0.6) | (0.01, 3.25) | 1 |
| Blepharochalasis | 2 (0.6) | 0.07, 2.16 | 2 | 1 (0.6) | (0.01, 3.25) | 1 |

| | enVista Trifocal IOL (N=332) | | | enVista Monofocal IOL (N = 169) | | |
|---|---|---|---|---|---|---|
| **Preferred Term** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Macular fibrosis | 3 (0.9) | (0.19, 2.62) | 3 | 0 | (0.00, 2.16) | 0 |
| Chalazion | 3 (0.9) | (0.19, 2.62) | 3 | 0 | (0.00, 2.16) | 0 |
| Glare | 1 (0.3) | 0.01, 1.67 | 1 | 1 (0.6) | (0.01, 3.25) | 1 |
| Halo vision | 2 (0.6) | 0.07, 2.16 | 2 | 0 | (0.00, 2.16) | 0 |
| Conjunctivitis allergic | 1 (0.3) | 0.01, 1.67 | 1 | 1 (0.6) | (0.01, 3.25) | 1 |
| Eye irritation | 2 (0.6) | 0.07, 2.16 | 2 | 0 | (0.00, 2.16) | 0 |
| Eyelid irritation | 2 (0.6) | 0.07, 2.16 | 2 | 0 | (0.00, 2.16) | 0 |
| Conjunctival hyperaemia | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Conjunctivochalasis | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Diabetic retinopathy | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Iridocyclitis | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Retinal tear | 2 (0.6) | 0.07, 2.16 | 2 | 0 | (0.00, 2.16) | 0 |
| Corneal epithelium defect | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Eye pruritus | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Macular hole | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Retinal vein occlusion | 1 (0.3) | 0.01, 1.67 | 2 | 0 | (0.00, 2.16) | 0 |
| Trichiasis | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Ulcerative keratitis | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Vitreous haemorrhage | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Seidel test positive | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Cataract operation complication | 1 (0.3) | 0.01, 1.67 | 1 | 2 (1.2) | (0.14, 4.21) | 2 |
| Corneal abrasion | 2 (0.6) | 0.07, 2.16 | 2 | 0 | (0.00, 2.16) | 0 |
| Foreign body in eye | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Ocular procedural complication | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Conjunctivitis | 1 (0.3) | 0.01, 1.67 | 1 | 1 (0.6) | (0.01, 3.25) | 1 |
| Hordeolum | 1 (0.3) | 0.01, 1.67 | 1 | 2 (1.2) | (0.14, 4.21) | 2 |
| Ophthalmic herpes simplex | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Ophthalmic herpes zoster | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 2 |
| Visual field defect | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Dermatitis contact | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |
| Madarosis | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Seasonal allergy | 1 (0.3) | 0.01, 1.67 | 1 | 0 | (0.00, 2.16) | 0 |

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

| | enVista Trifocal IOL (N=329) | | | enVista Monofocal IOL (N = 168) | | |
|---|---|---|---|---|---|---|
| **Preferred Term** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Punctate keratitis | 46 (14.0) | (10.42, 18.21) | 50 | 11 (6.5) | (3.31, 11.41) | 12 |
| Intraocular pressure increased | 26 7.9 | 5.23, 11.37 | 26 | 8 (4.8) | (2.08, 9.17) | 8 |

| | enVista Trifocal IOL (N=329) | | | enVista Monofocal IOL (N = 168) | | |
|---|---|---|---|---|---|---|
| **Preferred Term** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Vitreous detachment | 21 (6.4) | (3.99, 9.59) | 21 | 7 4.2 | (1.69, 8.40) | 7 |
| Dry eye | 6 (1.8) | 0.67, 3.93 | 6 | 4 (2.4) | (0.65, 5.98) | 5 |
| Blepharitis | 5 (1.5) | (0.50, 3.51) | 5 | 4 (2.4) | (0.65, 5.98) | 4 |
| Meibomian gland dysfunction | 5 (1.5) | (0.50, 3.51) | 5 | 4 (2.4) | (0.65, 5.98) | 4 |
| Visual acuity reduced | 4 (1.2) | (0.33, 3.08) | 4 | 2 (1.2) | (0.14, 4.23) | 2 |
| Cystoid macular oedema | 3 (0.9) | (0.19, 2.64) | 3 | 3 (1.8) | (0.37, 5.13) | 4 |
| Vitreous floaters | 0 | (0.00, 1.11) | 0 | 4 (2.4) | (0.65, 5.98) | 5 |
| Diplopia | 3 (0.9) | (0.19, 2.64) | 3 | 0 | (0.00, 2.17) | 0 |
| Iritis | 2 (0.6) | 0.07, 2.18 | 2 | 0 | (0.00, 2.17) | 0 |
| Blepharochalasis | 2 (0.6) | 0.07, 2.18) | 2 | 0 | (0.00, 2.17) | 0 |
| Macular fibrosis | 1 (0.3) | (0.01, 1.68) | 1 | 1 (0.6) | (0.02, 3.27) | 1 |
| Chalazion | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Glare | 1 (0.3) | (0.01, 1.68) | 1 | 1 (0.6) | (0.02, 3.27) | 1 |
| Halo vision | 2 (0.6) | 0.07, 2.18 | 2 | 0 | (0.00, 2.17) | 0 |
| Conjunctivitis allergic | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Eye irritation | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Eyelid irritation | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Ocular hypertension | 2 (0.6) | 0.07, 2.18 | 2 | 1 (0.6) | (0.02, 3.27) | 1 |
| Conjunctival hyperaemia | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Conjunctivochalasis | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Diabetic retinopathy | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Iridocyclitis | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Anterior chamber cell | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Conjunctival cyst | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Conjunctival haemorrhage | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Eye discharge | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Eye inflammation | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Eye pain | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Photopsia | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Vitreous prolapse | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |
| Seidel test positive | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Cataract operation complication | 1 (0.3) | (0.01, 1.68) | 1 | 1 (0.6) | (0.02, 3.27) | 2 |
| Corneal abrasion | 2 (0.6) | 0.07, 2.18 | 2 | 0 | (0.00, 2.17) | 0 |
| Iris injury | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Conjunctivitis | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Endophthalmitis | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Visual field defect | 2 (0.6) | 0.07, 2.18 | 2 | 0 | (0.00, 2.17) | 0 |
| Dermatitis contact | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Corneal dystrophy | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Device dislocation | 0 | (0.00, 1.11) | 0 | 1 (0.6) | (0.02, 3.27) | 1 |

The incidences of cumulative adverse events for the enVista Envy IOL and the control Monofocal IOL as compared to the ISO 11979-7:2018 historical grid (SPE) rates are

provided in **Table 15** and **Table 16**. If the same event occurred multiple times in an eye, only the first occurrence is counted in the table below. All SPE rates for the enVista Envy IOL were not statistically significantly above the SPE thresholds as set forth by ISO 11979-7:2018. The results of adverse events analyses based on the consensus definitions as set forth by American Academy of Ophthalmology's Task Force (Masket et al. Ophthalmology 2017) are shown in **Table 17** and **Table 18**.

**Table 15: ISO Grid Adverse Events (First Eyes; Modified Safety Set)**

| Adverse Event | Observed Event Rate for enVista Trifocal IOL n (%) | 2-sided 95% CI | 1-sided 95% Lower CL | SPE Rate (%) [b] |
|---|---|---|---|---|
| Cumulative [a] | N=332 | | | |
| Cystoid macular oedema[c] | 0 | (0.00, 1.10) | 0.00 | 3.0 |
| Hypopyon | 0 | (0.00, 1.10) | 0.00 | 0.3 |
| Endophthalmitis | 0 | (0.00, 1.10) | 0.00 | 0.1 |
| Lens dislocated from posterior chamber[d] | 0 | (0.00, 1.10) | 0.00 | 0.1 |
| Pupillary block | 0 | (0.00, 1.10) | 0.00 | 0.1 |
| Retinal detachment[e] | 0 | (0.00, 1.10) | 0.00 | 0.3 |
| SSI | 3 (0.9) | (0.19, 2.62) | 0.25 | 0.8 |
| Persistent [a] | N=314 | | | |
| Corneal stroma oedema[f] | 0 | (0.0, 1.17 | 0.00 | 0.3 |
| Cystoid macular oedema | 0 | (0.0, 1.17 | 0.00 | 0.5 |
| Iritis[g] | 0 | (0.0, 1.17 | 0.00 | 0.3 |
| Raised IOP requiring treatment[h] | 0 | (0.0, 1.17 | 0.00 | 0.4 |

AE = adverse event; IOL = intraocular lens; IOP = intraocular pressure; ISO = International Organization of Standardization; SPE = Safety and Performance Endpoint, SSI = secondary surgical intervention.

[a] For cumulative AEs, observed AE rate is calculated as 100 multiplied by the number of eyes with the specific treatment-emergent event divided by the number of eyes (m). For persistent AE rates, the number of eyes (m) present at Visit 5 (11-14 months) is the denominator.

[b] The ISO standard SPE rate in ISO 11979-7:2018.

[c] Per protocol, the definition of Cystoid Macular Oedema (CME) on this study was cystoid macular edema diagnosed by clinical exam and adjunct testing (e.g. Optical Coherence Tomography [OCT], Fluorescein Angiography [FA] or other method), resulting in BCDVA of ≤ 20/40 at Visit 3 or later. No participants were diagnosed with CME based on OCT alone.

[d] IOL decentration or tilt likely to affect visual outcome and resulting in secondary intervention

[e] Partial or complete Retinal Detachment associated with retinal tear. There were no retinal detachments without retinal tears.

[f] Corneal or corneal wound edema resulting in BCDVA of ≤20/40 at Visit 3A or later in the first implanted eye or at Visit 3B or later in the second implanted eye, or any persistent corneal or corneal wound edema present at Visit 5 (11-14 months).

[g] Iritis/cells/flare characterized by grade 1+ cells or greater using Standardization of Uveitis Nomenclature (SUN) criteria 37 if persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the participant is maintained on therapy for more than 3 months to control inflammation.

[h] Elevation of IOP by ≥ 10 mmHg above baseline (pre-operative) to a minimum of 25 mmHg (Masket S, et al. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. Ophthalmology 2017;124 1):142-144) after IOL implantation, or elevated IOP requiring treatment if present at Visit 5.

The three secondary surgical interventions that occurred with the first eye for the enVista Envy IOL were suturing of a Seidel positive wound, a Pars Plana Vitrectomy with internal limiting membrane peeling due to a macular hole and an Argon laser retinopexy for an operculated retinal hole. These SSIs were determined not to be related to the optical properties of the IOL.

## Table 16: ISO Grid Adverse Events (Second Eyes; Modified Safety Set)

| Adverse Event | Observed Event Rate for enVista Trifocal IOL n (%) | 2-sided 95% CI | 1-sided 95% LCL | SPE Rate (%) [b] |
|---|---|---|---|---|
| Cumulative [a] | N=329 | | | |
| Cystoid macular oedema [c] | 3 (0.9) | (0.19, 2.64) | 0.25 | 3.0 |
| Hypopyon | 0 | (0.00, 1.11) | 0.00 | 0.3 |
| Endophthalmitis | 1 (0.3) | (0.01, 1.68) | 0.02 | 0.1 |
| Lens dislocated from posterior chamber [d] | 0 | (0.00, 1.11) | 0.00 | 0.1 |
| Pupillary block | 0 | (0.00, 1.11) | 0.00 | 0.1 |
| Retinal detachment [e] | 0 | (0.00, 1.11) | 0.00 | 0.3 |
| SSI | 2 (0.6) | (0.07, 2.18) | 0.11 | 0.8 |
| Persistent [a] | N=314 | | | |
| Corneal stroma oedema [f] | 0 | (0.0, 1.17 | 0.00 | 0.3 |
| Cystoid macular oedema | 0 | (0.0, 1.17 | 0.00 | 0.5 |
| Iritis [g] | 0 | (0.0, 1.17 | 0.00 | 0.3 |
| Raised IOP requiring treatment [h] | 0 | (0.0, 1.17 | 0.00 | 0.4 |

AE = adverse event; CI = confidence interval; IOL = intraocular lens; IOP = intraocular pressure; ISO = International Organization of Standardization; LCL = lower confidence limit; SPE = Safety and Performance Endpoint, SSI = secondary surgical intervention.
[a] For cumulative AEs, observed AE rate is calculated as 100 multiplied by the number of eyes with the specific treatment-emergent event divided by the number of eyes (m). For persistent AE rates, the number of eyes (m) present at Visit 5 (11-14 Months) is the denominator.
[b] The ISO standard SPE rate in ISO 11979-7:2018 and ISO 11979-7:2018.
[c] Per protocol, the definition of CME on this study was cystoid macular edema diagnosed by clinical exam and adjunct testing (e.g. OCT, FA or other method), resulting in BCDVA of ≤ 20/40 at Visit 3 or later. No participants were diagnosed with CME based on OCT alone.
[d] IOL decentration or tilt likely to affect visual outcome and resulting in secondary intervention
[e] Partial or complete Retinal Detachment associated with retinal tear. There were no retinal detachments without retinal tears.
[f] Corneal or corneal wound edema resulting in BCDVA of ≤20/40 at Visit 3A or later in the first implanted eye or at Visit 3B or later in the second implanted eye, or any persistent corneal or corneal wound edema present at Visit 5 (11-14 months).
[g] Iritis/cells/flare characterized by grade 1+ cells or greater using Standardization of Uveitis Nomenclature (SUN) criteria 37 if persistent for greater than 3 months after surgery, or relapses in less than 3 months after discontinuation of therapy, or the participant is maintained on therapy for more than 3 months to control inflammation.
[h] Elevation of IOP by ≥ 10 mmHg above baseline (pre-operative) to a minimum of 25 mmHg (Masket S, et al. Special Report: The American Academy of Ophthalmology Task Force Consensus Statement on Adverse Events with Intraocular Lenses. Ophthalmology 2017;124 1):142-144) after IOL implantation, or elevated IOP requiring treatment if present at Visit 5.

The two secondary surgical interventions that occurred with the second eyes for the enVista Envy IOL were a Pars Plana Vitrectomy for endophthalmitis and removal of a retained lens fragment. Among second eyes, the trifocal IOL group had 3/329 subjects (95% Confidence interval between 0.2-2.6) with cystoid macular edema, which was not statistically significantly greater than the SPE rate of 3.0%, and 1/329 subject (0.3%, 95% CI: 0.0- 1.7) with endophthalmitis, which was not significantly greater than the SPE rate of 0.1%. In addition, 2/329 participants (0.6%, 95% CI: 0.07-2.18%) had secondary surgical interventions, which was not significantly greater than the SPE rate of 0.8% (**Table 16**).

None of the other ISO grid cumulative AEs or any persistent AEs were reported in the trifocal IOL group.

**Table 17: Ocular Adverse Events based on a Modified Version of AAO Consensus (Masket *et al.*, 2017), First Eye (Modified Safety Set)**

| | enVista Trifocal IOL (N=332) | | | enVista Monofocal IOL (N=169) | | |
|---|---|---|---|---|---|---|
| **Adverse Event** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Chronic anterior uveitis | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Clinically significant cystoid macular edema | 0 | (0.00, 1.10) | 0 | 1 (0.6) | (0.01, 3.25) | 1 |
| Visually significant corneal edema | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Endophthalmitis | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Mechanical pupillary block | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Increased IOP | 26 (7.8) | (5.18, 11.26) | 27 | 15 (8.9) | (5.05, 14.22) | 15 |
| Rhegmatogenous Retinal Detachment | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Toxic anterior segment syndrome | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Secondary IOL intervention - Exchange | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Secondary IOL intervention - Removal | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |
| Secondary IOL intervention - Reposition | 0 | (0.00, 1.10) | 0 | 0 | (0.00, 2.16) | 0 |

**Table 18: Ocular Adverse Events based on a Modified Version of AAO Consensus (Masket *et al.*, 2017), Second Eye (Modified Safety Set)**

| | enVista Trifocal IOL (N=329) | | | enVista Monofocal IOL (N=168) | | |
|---|---|---|---|---|---|---|
| **Adverse Event** | **n (%)** | **2-sided 95% CI** | **E** | **n (%)** | **2-sided 95% CI** | **E** |
| Chronic anterior uveitis | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Clinically significant cystoid macular edema | 3 (0.9) | (0.19, 2.64) | 3 | 3 (1.8) | (0.37, 5.13) | 4 |
| Visually significant corneal edema | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Endophthalmitis | 1 (0.3) | (0.01, 1.68) | 1 | 0 | (0.00, 2.17) | 0 |
| Mechanical pupillary block | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Increased IOP | 26 (7.9) | (5.23, 11.37) | 26 | 8 (4.8) | (2.08, 9.17) | 8 |
| Rhegmatogenous Retinal Detachment | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Toxic anterior segment syndrome | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Secondary IOL intervention - Exchange | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Secondary IOL intervention - Removal | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |
| Secondary IOL intervention - Reposition | 0 | (0.00, 1.11) | 0 | 0 | (0.00, 2.17) | 0 |

### Deaths, Other Serious Adverse Events, and Other Significant Adverse Events

Four deaths, all of which were unrelated to the control or test IOLs, occurred during this study.

### Serious Adverse Events

Five of 332 subjects (1.5%) in the trifocal IOL group and 2/169 subjects (1.2%) in the monofocal IOL group experienced ocular TE-SAEs. The ocular TE-SAEs, occurring in 1 subject each, were macular hole, retinal tear, retinal vein occlusion, endophthalmitis, and Seidel test positive in the trifocal IOL group and ophthalmic herpes zoster and cataract operation complication in the monofocal IOL group. See **Table 19** and **Table 20** below.

## Table 19: Ocular Treatment-Emergent Serious Adverse Events by Treatment (First Eyes; Modified Safety Set)

| Adverse Event Term | enVista Trifocal IOL (N=332) n (%) | enVista Monofocal IOL (N=169) n (%) |
|---|---|---|
| All ocular TE-SAEs | 4 (1.2) | 1 (0.6) |
| Macular hole | 1 (0.3) | 0 |
| Retinal tear | 1 (0.3) | 0 |
| Retinal vein occlusion | 1 (0.3) | 0 |
| Ophthalmic herpes zoster | 0 | 1 (0.6) |
| Seidel test positive | 1 (0.3) | 0 |

IOL = intraocular lens
Note: When reporting incidence, an eye is counted only once if the eye experiences more than 1 event within the system organ class or individual preferred term. System organ classes and preferred terms are based on MedDRA Version 21

## Table 20: Ocular Treatment-Emergent Serious Adverse Events Treatment (Second Eyes and All Eyes; Modified Safety Set)

| | Second Eyes | | All Eyes | |
|---|---|---|---|---|
| Adverse Event Term | enVista Trifocal IOL (N=329) n (%) | enVista Monofocal IOL (N=168) n (%) | enVista Trifocal IOL (N=661) n (%) | enVista Monofocal IOL (N=337) n (%) |
| All ocular TE-SAEs | 1 (0.3) | 1 (0.6) | 5 (0.8) | 2 (0.6) |
| Macular hole | 0 | 0 | 1 (0.2) | 0 |
| Retinal tear | 0 | 0 | 1 (0.2) | 0 |
| Retinal vein occlusion | 0 | 0 | 1 (0.2) | 0 |
| Endophthalmitis | 1 (0.3) | 0 | 1 (0.2) | 0 |
| Ophthalmic herpes zoster | 0 | 0 | 0 | 1 (0.3) |
| Cataract operation complication | 0 | 1 (0.6) | 0 | 1 (0.3) |
| Seidel test positive | 0 | 0 | 1 (0.2) | 0 |

IOL = intraocular lens; MedDRA, Medical Dictionary for Regulatory Activities; TE-SAE = treatment-emergent serious adverse event.
Note: When reporting incidence, an eye is counted only once if the eye experiences more than 1 event of the same type. Adverse event term is coded from the verbatim using the Medical Dictionary for Regulatory Activities (MedDRA V 21).

**Visual Disturbances**

A Patient Reported Outcome Measure instrument was developed and validated for use in this clinical study to assess visual disturbances. While the clinical study was not designed to determine which lens had higher rates of each visual disturbance, study findings can help identify trends in potential differences between this lens and the monofocal control. Subjects were first asked if they experienced a particular visual disturbance. If the subject responded affirmatively, he or she was asked to rate the severity, frequency, and bothersomeness. A single subject may report multiple symptoms.

As demonstrated in **Table 21**, 4-6 months after surgery, results show a trend of more subjects who received this lens (enVista Trifocal IOL) reporting having halos compared to subjects who received the monofocal lens although 80% (247/309) of the Trifocal group reported the halos as being not at all to a little bothersome. About 10% (31/311) more subjects experienced glare and starbursts at least occasionally in the Trifocal group compared to the monofocal group.

Subjects in the Trifocal group stated a greater frequency of halos (36.9% [116/314] quite often or very often  compared to the Monofocal IOL (7.1% [11/154]). Moderate to severe difficulty with focusing and depth perception was reported by 8.8%  27/309) and 5.5% (15/310) of subjects with the Trifocal group compared to 13.2%  20/151) and 7.9%  10/151) of subjects in the Monofocal group respectively.

## Table 21: Quality of Vision Questionnaire Responses at Visit 4 (4-6 months) Modified Safety Set

| | | Frequency n (%) | | | | Severity n (%) | | | | Bothersome n (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Visual Disturbance** | **Device** | **Never** | **Occasionally** | **Quite often** | **Very often** | **Not at all** | **Mild** | **Moderate** | **Severe** | **Not at all** | **A little** | **Quite** | **Very** |
| **Glare** | | N=154 | | | | N=151 | | | | N=151 | | | |
| | Monofocal | 73 47.4 | 67 (43.5) | 9 (5.8) | 5 (3.2) | 76 (50.3) | 49 (32.5) | 23 (15.2) | 3 (2.0) | 85 (56.3) | 48 (31.8) | 16 (10.6) | 2 (1.3) |
| | | N=314 | | | | N=310 | | | | N=310 | | | |
| | This device | 118 37.6 | 152 (48.4) | 28 (8.9) | 16 (5.1) | 124 (40.0) | 129 (41.6) | 47 (15.2) | 10 (3.2) | 148 47.7 | 125 (40.3) | 23 7.4 | 14 (4.5) |
| | | N=154 | | | | N=151 | | | | N=151 | | | |
| **Halos** | Monofocal | 91 (59.1) | 52 (33.8) | 8 (5.2) | 3 (1.9) | 95 (62.9) | 41 (27.2) | 13 (8.6) | 2 (1.3) | 104 (68.9) | 36 (23.8) | 9 (6.0) | 2 (1.3) |
| | | N=314 | | | | N=309 | | | | N=309 | | | |
| | This device | 84 (26.8) | 114 (36.3) | 62 (19.7) | 54 (17.2) | 90 (29.1) | 114 (36.9) | 86 (27.8) | 19 (6.1) | 126 (40.8) | 120 (38.8) | 41 (13.3) | 22 (7.1) |
| | | N=154 | | | | N=151 | | | | N=151 | | | |
| **Starbursts** | Monofocal | 101 (65.6) | 41 (26.6) | 6 (3.9) | 6 (3.9) | 109 (72.2) | 29 (19.2) | 7 (4.6) | 6 (4.0) | 118 (78.1) | 23 (15.2) | 4 (2.6) | 6 (4.0) |
| | | N=314 | | | | N=311 | | | | N=311 | | | |
| | This device | 168 (53.5) | 106 (33.8) | 28 (8.9) | 12 (3.8) | 175 (56.3) | 91 (29.3) | 37 (11.9) | 8 (2.6) | 204 (65.6) | 78 (25.1) | 19 (6.1) | 10 (3.2) |
| | | N=154 | | | | N=152 | | | | N=152 | | | |
| **Hazy Vision** | Monofocal | 102 (66.2) | 44 (28.6) | 6 (3.9) | 2 (1.3) | 101 (66.4) | 36 (23.7) | 14 (9.2) | 1 (0.7) | 104 (68.4) | 37 (24.3) | 11 (7.2) | 0 (0.0) |
| | | N=314 | | | | N=311 | | | | N=311 | | | |
| | This device | 211 (67.2) | 81 (25.8) | 17 (5.4) | 5 (1.6) | 214 (68.8) | 73 (23.5) | 22 (7.1) | 2 (0.6) | 222 (71.4) | 64 (20.6) | 21 (6.8) | 4 (1.3) |
| | | N=153 | | | | N=153 | | | | N=154 | | | |
| **Blurred Vision** | Monofocal | 82 (53.6) | 55 (35.9) | 13 (8.5) | 3 (2.0) | 86 (56.2) | 48 (31.4) | 17 (11.1) | 2 (1.3) | 93 (60.4) | 46 (29.9) | 13 (8.4) | 2 (1.3) |
| | | N=314 | | | | N=311 | | | | N=311 | | | |
| | This device | 195 (62.1) | 103 (32.8) | 12 (3.8) | 4 (1.3) | 200 (64.3) | 92 (29.6) | 15 (4.8) | 4 (1.3) | 214 (68.8) | 76 (24.4) | 15 (4.8) | 6 (1.9) |
| | | N=154 | | | | N=151 | | | | N=151 | | | |
| **Distortion** | Monofocal | 130 (84.4) | 23 (14.9) | 1 (0.6) | 0 (0.0) | 128 (84.8) | 20 (13.2) | 3 (2.0) | 0 (0.0) | 129 (85.4) | 19 (12.6) | 2 (1.3) | 1 (0.7) |
| | | N=313 | | | | N=310 | | | | N=310 | | | |
| | This device | 280 (89.5) | 29 (9.3) | 4 (1.3) | 0 (0.0) | 281 (90.6) | 25 (8.1) | 4 (1.3) | 0 (0.0) | 283 (91.3) | 22 (7.1) | 5 (1.6) | 0 (0.0) |
| | | N=154 | | | | N=152 | | | | N=152 | | | |
| **Double or Multiple Images** | Monofocal | 127 (82.5) | 20 (13.0) | 6 (3.9) | 1 (0.6) | 127 (83.6) | 15 (9.9) | 9 (5.9) | 1 (0.7) | 128 (84.2) | 19 (12.5) | 4 (2.6) | 1 (0.7) |
| | | N=314 | | | | N=309 | | | | N=309 | | | |

| | | Frequency n (%) | | | | Severity n (%) | | | | Bothersome n (%) | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| **Visual Disturbance** | **Device** | **Never** | **Occasionally** | **Quite often** | **Very often** | **Not at all** | **Mild** | **Moderate** | **Severe** | **Not at all** | **A little** | **Quite** | **Very** |
| | This device | 276 (87.9) | 32 (10.2) | 5 (1.6) | 1 (0.3) | 275 (89.0) | 24 (7.8) | 9 (2.9) | 1 (0.3) | 275 (89.0) | 25 (8.1) | 7 (2.3) | 2 (0.6) |
| | | N=154 | | | | N=153 | | | | N=153 | | | |
| **Fluctuation in Vision** | Monofocal | 78 (50.6) | 72 (46.8) | 4 (2.6) | 0 (0.0) | 84 (54.9) | 62 (40.5) | 7 (4.6) | 0 (0.0) | 95 (62.1) | 52 (34.0) | 5 (3.3) | 1 (0.7) |
| | | N=314 | | | | N=311 | | | | N=311 | | | |
| | This device | 179 (57.0) | 119 (37.9) | 14 (4.5) | 2 (0.6) | 187 (60.1) | 102 (32.8) | 18 (5.8) | 4 (1.3) | 207 (66.6) | 88 (28.3) | 11 (3.5) | 5 (1.6) |
| | | N=154 | | | | N=151 | | | | N=151 | | | |
| **Focusing Difficulties** | Monofocal | 70 (45.5) | 67 (43.5) | 16 (10.4) | 1 (0.6) | 72 (47.7) | 59 (39.1) | 20 (13.2) | 0 (0.0) | 75 (49.7) | 62 (41.1) | 13 (8.6) | 1 (0.7) |
| | | N=314 | | | | N=309 | | | | N=309 | | | |
| | This device | 134 (42.7) | 159 (50.6) | 17 (5.4) | 4 (1.3) | 146 (47.2) | 136 (44.0) | 24 (7.8) | 3 (1.0) | 172 (55.7) | 116 (37.5) | 17 (5.5) | 4 (1.3) |
| | | N=154 | | | | N=151 | | | | N=151 | | | |
| **Judging Distance or Depth Perception** | Monofocal | 108 (70.1) | 35 (22.7) | 9 (5.8) | 2 (1.3) | 107 (70.9) | 32 (21.2) | 8 (5.3) | 4 (2.6) | 110 (72.8) | 31 (20.5) | 6 (4.0) | 4 (2.6) |
| | | N=314 | | | | N=310 | | | | N=310 | | | |
| | This device | 224 (71.3) | 79 (25.2) | 10 (3.2) | 1 (0.3) | 228 (73.5) | 65 (21.0) | 16 (5.2) | 1 (0.3) | 231 (74.5) | 64 (20.6) | 14 (4.5) | 1 (0.3) |

Abbreviations: IOL = Intraocular Lens; Op = Operative. This Device= enVista MX60EF Trifocal IOL, Monofocal=enVista MX60E monofocal IOL

### Sub-Study: Binocular Contrast Sensitivity

Binocular best corrected distance contrast sensitivity was performed using a sine wave grating produced on a high-resolution monitor. Testing was performed using the M&S Clinical Trial Suite (CTS; M&S Technologies, Niles, IL) at 6 months under three conditions: photopic with glare, mesopic without glare, and mesopic with glare (**Tables 22-24**). Chart luminances were 85 cd/m$^2$ for photopic conditions and 2.5-3.2 cd/m$^2$ for mesopic conditions. This analysis uses the modified safety set. The mean and 95% confidence intervals results are shown in **Figures 2, 3, and 4**.

The differences in mean binocular contrast sensitivity between the Trifocal and Monofocal IOLs were clinically insignificant, i.e., <0.15 log unit for 4 of the 12 test conditions Mesopic with and without glare at 1.5 cpd, Mesopic without glare at 3 and 12 cpd); clinically significant differences favored the Monofocal IOL for the remaining test conditions. The mean binocular contrast sensitivity was worse in the trifocal cohort than monofocal cohort for all tested conditions, except for the lowest spatial frequency tested (i.e., thickest stripes) for the mesopic with glare, and mesopic without glare conditions.

Monocular contrast sensitivity is a more accurate assessment of individual IOL performance compared to binocular contrast sensitivity, and results for monocular contrast sensitivity would be expected to be reduced compared to binocular contrast sensitivity results.

**Figure 2: Binocular Contrast Sensitivity – Photopic Lighting With Glare by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

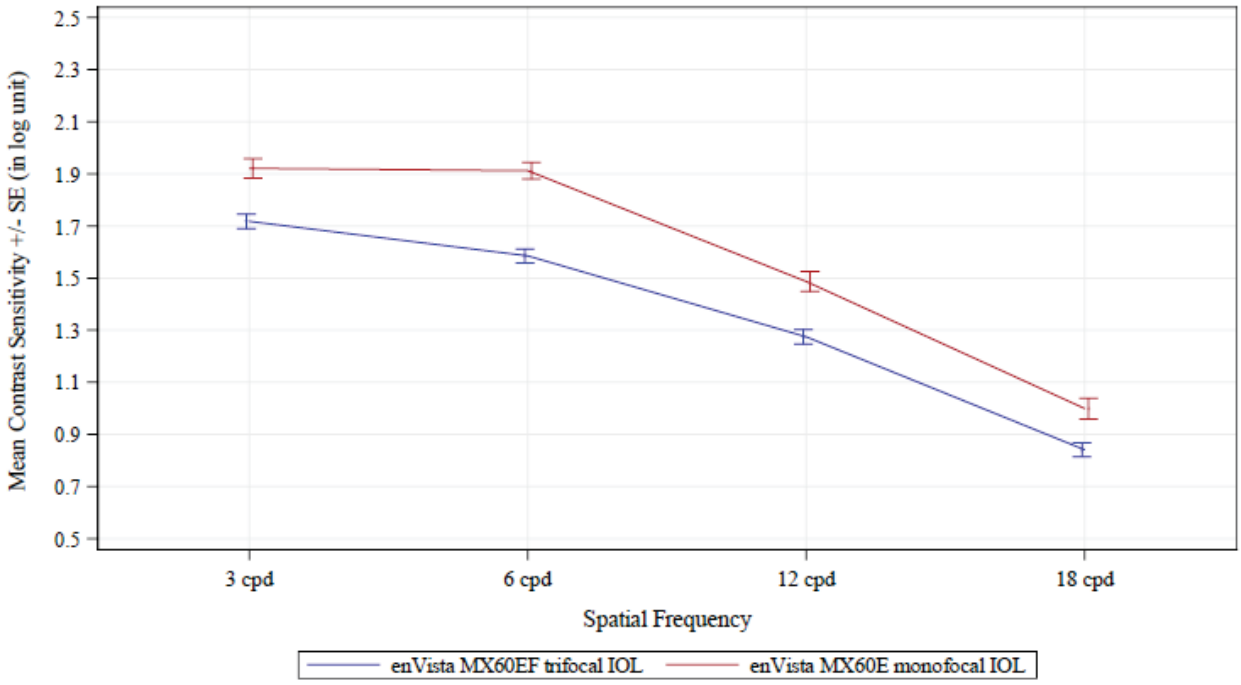


**Figure 3: Binocular Contrast Sensitivity – Mesopic Lighting With Glare by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

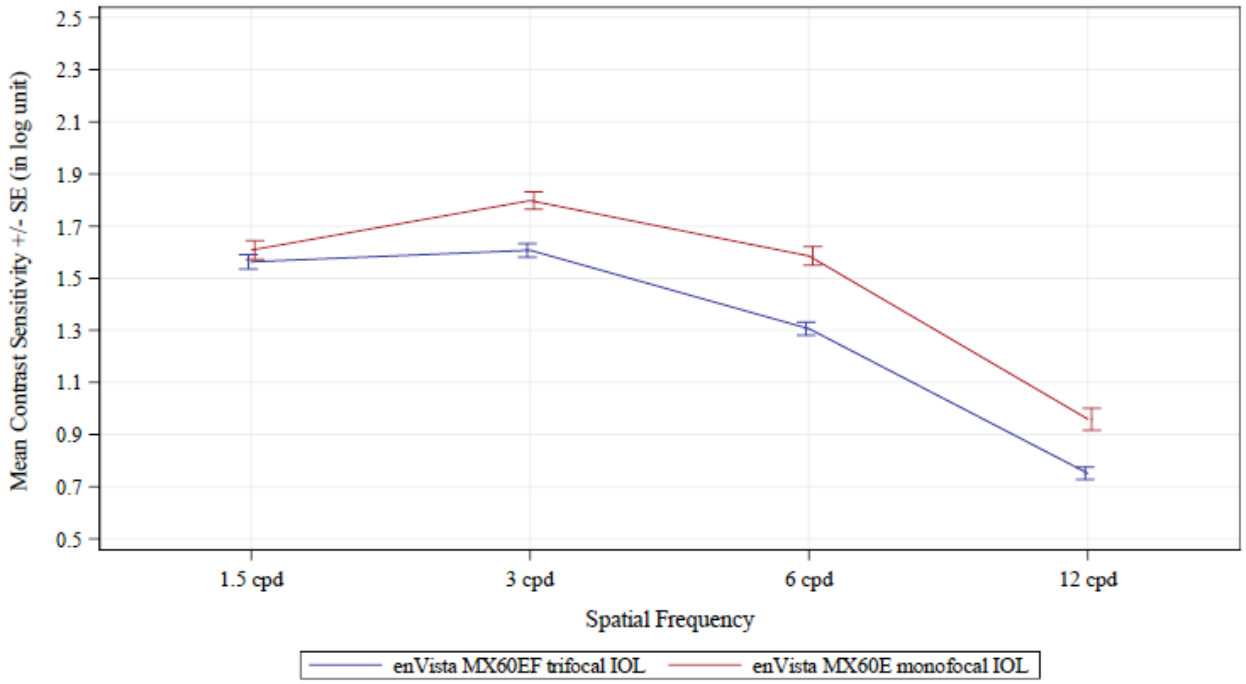



**Figure 4: Binocular Contrast Sensitivity – Mesopic Lighting Without Glare by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

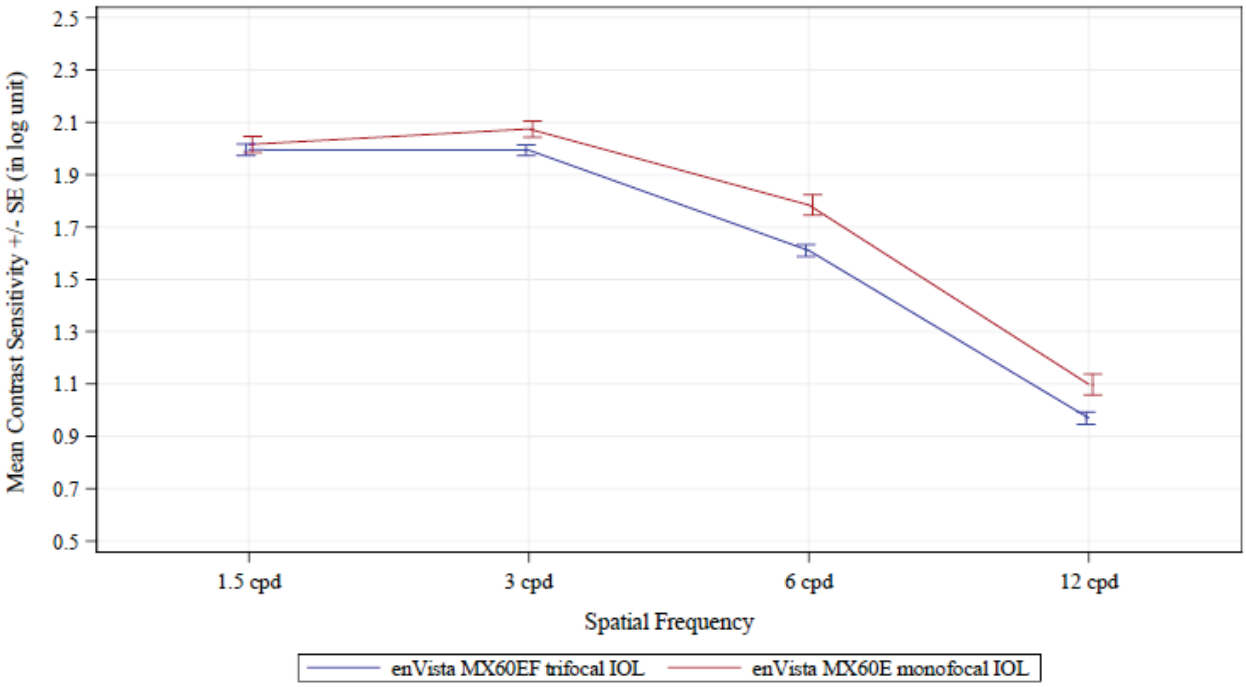


**Table 22: Photopic Binocular Contrast Sensitivity With Glare in Log Value by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

| | enVista Trifocal IOL (N=327) | enVista Monofocal IOL (N=168) |
|---|---|---|
| Photopic CS with glare at 3 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.718 (0.3642) | 1.921 (0.3114) |
| Median | 1.750 | 1.925 |
| Minimum, maximum | 0.00, 2.40 | 0.60, 2.40 |
| 95% CI for mean | 1.662, 1.773 | 1.847, 1.995 |
| Mean difference (trifocal – monofocal) | -0.203 | |
| 95% CI for mean difference | -0.301, -0.105 | |
| Photopic CS with glare at 6 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.585 (0.3468) | 1.912 (0.2712) |
| Median | 1.625 | 1.925 |
| Minimum, maximum | 0.00, 2.24 | 1.27, 2.40 |
| 95% CI for mean | 1.532, 1.638 | 1.847, 1.977 |
| Mean difference (trifocal – monofocal) | -0.327 | |
| 95% CI for mean difference | -0.418, -0.235 | |
| Photopic CS with glare at 12 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.274 (0.3635) | 1.487 (0.3238) |
| Median | 1.300 | 1.548 |
| Minimum, maximum | 0.00, 2.00 | 0.57, 2.20 |
| 95% CI for mean | 1.219, 1.330 | 1.409, 1.564 |
| Mean difference (trifocal – monofocal) | -0.212 | |
| 95% CI for mean difference | -0.311, -0.114 | |
| Photopic CS with glare at 18 cpd, log units | | |
| n | 166 | 69 |
| Mean (SD) | 0.841 (0.3384) | 0.999 (0.3294) |
| Median | 0.875 | 1.000 |
| Minimum, maximum | 0.00, 1.80 | 0.28, 1.85 |
| 95% CI for mean | 0.789, 0.893 | 0.920, 1.078 |
| Mean difference (trifocal – monofocal) | -0.158 | |
| 95% CI for mean difference | -0.253, -0.064 | |

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

**Table 23: Mesopic Binocular Contrast Sensitivity With Glare in Log Value by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

| | enVista Trifocal IOL (N=327) | enVista Monofocal IOL (N=168) |
|---|---|---|
| Mesopic CS with glare at 1.5 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.563 (0.3597) | 1.608 (0.2981) |
| Median | 1.648 | 1.670 |
| Minimum, maximum | 0.25, 2.34 | 0.63, 2.40 |
| 95% CI for mean | 1.508, 1.618 | 1.537, 1.679 |
| Mean difference (trifocal – monofocal) | -0.045 | |
| 95% CI for mean difference | -0.141, 0.051 | |
| Mesopic CS with glare at 3 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.607 (0.3373) | 1.798 (0.2796) |
| Median | 1.650 | 1.820 |
| Minimum, maximum | 0.45, 2.34 | 0.80, 2.30 |
| 95% CI for mean | 1.556, 1.659 | 1.731, 1.864 |
| Mean difference (trifocal – monofocal) | -0.190 | |
| 95% CI for mean difference | -0.280, -0.100 | |
| Mesopic CS with glare at 6 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.306 (0.3309) | 1.585 (0.3019) |
| Median | 1.323 | 1.610 |
| Minimum, maximum | 0.50, 2.24 | 0.75, 2.24 |
| 95% CI for mean | 1.256, 1.356 | 1.513, 1.657 |
| Mean difference (trifocal – monofocal) | -0.279 | |
| 95% CI for mean difference | -0.370, -0.189 | |
| Mesopic CS with glare at 12 cpd, log units | | |
| n | 167 | 69 |
| Mean (SD) | 0.751 (0.3139) | 0.959 (0.3528) |
| Median | 0.750 | 1.020 |
| Minimum, maximum | 0.10, 1.77 | 0.25, 1.70 |
| 95% CI for mean | 0.703, 0.799 | 0.874, 1.044 |
| Mean difference (trifocal – monofocal) | -0.208 | |
| 95% CI for mean difference | -0.300, -0.116 | |

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

**Table 24: Mesopic Binocular Contrast Sensitivity Without Glare in Log Value by Spatial Frequency at Visit 4 (4-6 months) (Modified Safety Set)**

| | enVista Trifocal IOL (N=327) | enVista Monofocal IOL (N=168) |
|---|---|---|
| Mesopic CS without glare at 1.5 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.995 (0.2899) | 2.015 (0.2634) |
| Median | 2.050 | 2.075 |
| Minimum, maximum | 0.80, 2.40 | 1.15, 2.40 |
| 95% CI for mean | 1.951, 2.039 | 1.953, 2.078 |
| Mean difference (trifocal – monofocal) | -0.020 | |
| 95% CI for mean difference | -0.100, 0.059 | |
| Mesopic CS without glare at 3 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.993 (0.2722) | 2.075 (0.2576) |
| Median | 2.075 | 2.125 |
| Minimum, maximum | 0.95, 2.40 | 1.49, 2.40 |
| 95% CI for mean | 1.952, 2.035 | 2.013, 2.136 |
| Mean difference (trifocal – monofocal) | -0.081 | |
| 95% CI for mean difference | -0.156, -0.006 | |
| Mesopic CS without glare at 6 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 1.610 (0.2877) | 1.784 (0.3248) |
| Median | 1.620 | 1.770 |
| Minimum, maximum | 0.77, 2.30 | 1.05, 2.34 |
| 95% CI for mean | 1.566, 1.654 | 1.706, 1.861 |
| Mean difference (trifocal – monofocal) | -0.174 | |
| 95% CI for mean difference | -0.258, -0.090 | |
| Mesopic CS without glare at 12 cpd, log units | | |
| n | 168 | 70 |
| Mean (SD) | 0.969 (0.2998) | 1.098 (0.3358) |
| Median | 0.950 | 1.110 |
| Minimum, maximum | 0.15, 1.85 | 0.30, 1.75 |
| 95% CI for mean | 0.924, 1.015 | 1.018, 1.178 |
| Mean difference (trifocal – monofocal) | -0.129 | |
| 95% CI for mean difference | -0.216, -0.042 | |

CI = confidence interval; cpd = cycles per degree; CS = contrast sensitivity; IOL = intraocular lens; SD = standard deviation.

### Fundus Visualization

On the dilated fundus exam performed at Visit 3A/B (30-60 days), 1/629 eyes in the Trifocal IOL group and zero eyes in the Monofocal IOL group revealed an inadequate clarity of the fundus upon visualization. Similarly at Visit 4 (120-180 days), zero eyes in the Trifocal IOL group and 1/312 eyes in the monofocal IOL group revealed an inadequate clarity of fundus on visualization.

### Device Failures

Two subjects required a surgical exchange of the IOL during the initial phacoemulsification and IOL procedure due to bent haptics and both incidences were recorded as a device deficiency as there was no other adverse event.

## 2. Effectiveness Results

The analyses of effectiveness were based on the 470 evaluable subjects at the 6-month time point. Key effectiveness outcomes are presented in **Tables 34-37**.

### Co-primary Effectiveness Endpoints

All of the co-primary effectiveness endpoints on this study were met, with the trifocal IOL showing statistical noninferiority to the monofocal IOL in photopic monocular BCDVA, satisfactory BCDVA performance compared to the International Organization for Standardization (ISO) grid performance standards, and statistical superiority to the monofocal IOL in photopic monocular DCNVA and DCIVA (both $P < 0.0001$) (**Table 25**).

Visual Acuity was assessed using a computerized test system (CTS, M&S Technologies, Niles, IOL). The first co-primary effectiveness endpoint (non-inferiority of mean monocular BCDVA) was met. The second co-primary effectiveness endpoint (superiority of DCNVA) was met with both a statistically significant and clinically meaningful difference between the enVista Envy and monofocal control arm of about 4 logMAR lines. The third co-primary effectiveness endpoint (superiority of mean monocular DCIVA) was also met with a statistically significant and clinically meaningful difference of 2 logMAR lines between arms.

**Table 25: Photopic Monocular (First Eyes) BCDVA (4 m) at Visit 4 (4-6 months) (mITT Set)**

| BCDVA, logMAR | enVista Trifocal IOL (N=332) | enVista Monofocal IOL (N=169) |
|---|---|---|
| n | 312 | 156 |
| Mean (SD/SE) | 0.022 (0.0950/0.0054) | -0.017 (0.0897/0.0072) |
| Median | 0.000 | 0.000 |
| Minimum, maximum | -0.18, 0.58 | -0.30, 0.40 |
| LS mean (SE) [a] | 0.032 (0.0058) | -0.008 (0.0076) |
| LS mean difference (SE) [a] | 0.040 (0.0085) | |
| 2-sided 90% CI [a] | 0.026, 0.054 | |

ANCOVA = analysis of covariance; BCDVA = best-corrected distance visual acuity; CI = confidence interval; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; SD = standard deviation; SE = standard error.
[a] Statistics are based on an ANCOVA model with BCDVA as the dependent variable and treatment and site as fixed factors.

In the mITT Set at Visit 4 (4-6 months), photopic monocular BCDVA of 20/40 or better was achieved by 98.7% of first eyes in the trifocal IOL group versus 92.5%, which is the ISO standard SPE rate for the mITT Set; the observed proportion was not statistically significantly worse than the SPE rate (P > 0.9999; **Table 26**).

**Table 26: Proportion of First Eyes That Achieved 0.30 logMAR (20/40) or Better in Photopic Monocular BCDVA (4 m) at Visit 4 (4-6 months) (mITT Set and Best Case Set)**

| Population | enVista Trifocal IOL (N=332) |
|---|---|
| mITT Set | m=312 |
| n (%) | 308 (98.7) |
| 90% CI | 97.1, 99.6 |
| 1-sided p-value[a] | >0.9999 |
| Best Case Set | m=310 |
| n (%) | 306 (98.7) |
| 90% CI | 97.1, 99.6 |
| 1-sided p-value[b] | 0.9920 |

BCDVA = best-corrected distance visual acuity; CI = confidence interval; IOL = intraocular lens; ISO = International Organization for Standardization; logMAR = logarithm of the minimum angle of resolution; mITT = Modified Intent-to-Treat; SPE = Safety and Performance Endpoint.
[a] p-value based on a 1-sided exact binomial test comparing the proportion of eyes achieving BCDVA 0.3 logMAR or better to the ISO standard SPE rate of 92.5% for the mITT Set.
[b] p-value based on a 1-sided exact binomial test comparing the proportion of eyes achieving BCDVA 0.3 logMAR or better to the ISO standard SPE rate of 96.7% for the Best Case Set.

For each endpoint, if the p-value from the MI analysis of treatment effect was ≤ 0.05 and the treatment effect was ≤ -0.10 logMAR units for DCIVA or DCNVA, then it was concluded that the test IOL is statistically and clinically successful in the corresponding outcome.

Mean ± SD photopic monocular DCNVA at Visit 4 (4-6 months) in first eyes (excluding Phase I subjects) was 0.152 ± 0.1342 logMAR in the trifocal IOL group and 0.545 ± 0.1703 logMAR in the monofocal IOL group (**Table 27**). The LS mean ± SE difference between treatment groups was -0.392 ± 0.0142 logMAR, for a statistically significant difference

demonstrating superiority of the trifocal IOL over the control IOL (P < 0.0001). Moreover, the treatment effect of -0.392 logMAR exceeded the protocol-defined performance standard for clinical significance of -0.10 logMAR. Similar results were observed for the PP Set.

Mean ± SD photopic monocular DCIVA at Visit 4 (4-6 months) in first eyes (excluding Phase I subjects) was 0.122 ± 0.1199 logMAR in the trifocal IOL group and 0.349 ± 0.1592 logMAR in the monofocal IOL group (**Table 28**). The LS mean ± SE difference between treatment groups was -0.225 ± 0.0133 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL (P < 0.0001). Moreover, the treatment effect of -0.225 logMAR exceeded the protocol-defined performance standard for clinical significance of -0.10 logMAR. Similar results were observed for the PP Set.

**Table 27: Photopic Monocular (First Eyes) DCNVA (40 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set; MI)**

| DCNVA, logMAR | enVista Trifocal IOL (N=303) | enVista Monofocal IOL (N=156) |
|---|---|---|
| n | 297 | 152 |
| Mean (SD) | 0.152 (0.1342) | 0.545 (0.1703) |
| Median | 0.120 | 0.560 |
| Minimum, maximum | -0.17, 0.72 | -0.05, 1.03 |
| LS mean (SE) [a] | 0.148 (0.0095) | 0.539 (0.0126) |
| LS mean difference (SE) [a] | -0.392 (0.0142) | |
| 2-sided 95% CI [a] | -0.419, -0.364 | |
| p-value [a] | <0.0001 | |

ANCOVA = analysis of covariance; CI = confidence interval; DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; MI = multiple imputation; SD = standard deviation; SE = standard error.
Note: Missing data are imputed using the Markov chain Monte Carlo MI method. An ANCOVA model with DCNVA as the dependent variable and treatment and site as fixed factors is performed to obtain effect size and SE for each of complete imputed datasets.
[a] Overall statistics are from the MI method. The p-value is for a 2-sided treatment difference test.

**Table 28: Photopic Monocular (First Eyes) DCIVA (66 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set; MI)**

| DCIVA, logMAR | enVista Trifocal IOL (N=303) | enVista Monofocal IOL (N=156) |
|---|---|---|
| n | 297 | 152 |
| Mean (SD) | 0.122 (0.1199) | 0.349 (0.1592) |
| Median | 0.100 | 0.350 |
| Minimum, maximum | -0.26, 0.68 | -0.08, 0.90 |
| LS mean (SE) [a] | 0.124 (0.0089) | 0.349 (0.0119) |
| LS mean difference (SE) [a] | -0.225 (0.0133) | |
| 2-sided 95% CI [a] | -0.251, -0.199 | |
| p-value [a] | <0.0001 | |

ANCOVA = analysis of covariance; CI = confidence interval; DCIVA = distance-corrected intermediate visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; LS = least-squares; MI = multiple imputation; SD = standard deviation; SE = standard error.
Note: Missing data are imputed using the Markov chain Monte Carlo MI method. An ANCOVA model with DCIVA as the dependent variable and treatment and site as fixed factors is performed to obtain effect size and SE for each of complete imputed datasets.
[a] Overall statistics are from the MI method. The p-value is for a 2-sided treatment difference test.

**Secondary Effectiveness Variables**

Mean ± SD/SE photopic binocular DCNVA at Visit 4; 4-6 months (excluding Phase I subjects) was 0.080 ± 0.0977/0.0058 logMAR in the trifocal IOL group and 0.453 ± 0.1526/0.0128 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.374 ± 0.0114 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

Mean ± SD photopic binocular UNVA at Visit 4; 4-6 months (excluding Phase I subjects) was 0.096 ± 0.1056 logMAR in the trifocal IOL group and 0.418 ± 0.1454 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.321 ± 0.0119 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL $P < 0.0001$).

Mean ± SD/SE photopic binocular DCIVA at Visit 4; 4-6 months (excluding Phase I subjects) was 0.041 ± 0.0976/0.0058 logMAR in the trifocal IOL group and 0.268 ± 0.1485/0.0125 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.225 ± 0.0111 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL ($P < 0.0001$).

Mean ± SD photopic binocular UIVA at Visit 4; 4-6 months (excluding Phase I subjects) was 0.064 ± 0.0988 logMAR in the trifocal IOL group and 0.217 ± 0.1442 logMAR in the monofocal IOL group. The LS mean ± SE difference between treatment groups was -0.151 ± 0.0115 logMAR, for a statistically significant difference demonstrating superiority of the trifocal IOL over the control IOL $P < 0.0001$).

At Visit 5 (11-14 months), mean ± SD photopic monocular BCDVA in first eyes was 0.027 ± 0.0920 logMAR in the trifocal IOL group and -0.020 ± 0.0826 logMAR in the monofocal IOL group (**Table 29**). At Visit 5 (11-14 months), mean ± SD photopic monocular DCNVA in first eyes (excluding Phase I subjects) was 0.143 ± 0.1284 logMAR in the trifocal IOL group and 0.533 ± 0.1843 logMAR in the monofocal IOL group. At Visit 5 (11-14 months), mean ± SD photopic monocular DCIVA in first eyes (excluding Phase I subjects) was 0.120 ± 0.1147 logMAR in the trifocal IOL group and 0.343 ± 0.1594 logMAR in the monofocal IOL group.

All of the secondary effectiveness endpoints that were tested for superiority were met, with the trifocal IOL showing statistical superiority to the monofocal IOL in photopic binocular DCNVA, UNVA, DCIVA, and UIVA (all $P < 0.0001$).

**Table 29: Photopic Monocular (First Eyes) BCDVA (4 m), DCNVA (40 cm), and DCIVA (66 cm) at Visit 5 (11-14 months) (mITT Set)**

| | enVista Trifocal IOL (N=332) | enVista Monofocal IOL (N=169) |
|---|---|---|
| BCDVA (4 m), logMAR | | |
| n | 308 | 152 |
| Mean (SD) | 0.027 (0.0920) | -0.020 (0.0826) |
| Median | 0.000 | -0.010 |
| Minimum, maximum | -0.16, 0.46 | -0.26, 0.30 |
| DCNVA (40 cm), excluding Phase I participants, logMAR | | |
| n | 280 | 139 |
| Mean (SD) | 0.143 (0.1284) | 0.533 (0.1843) |
| Median | 0.120 | 0.540 |
| Minimum, maximum | -0.12, 0.52 | 0.04, 1.00 |
| DCIVA (66 cm), excluding Phase I participants, logMAR | | |
| n | 280 | 139 |
| Mean (SD) | 0.120 (0.1147) | 0.343 (0.1594) |
| Median | 0.100 | 0.360 |
| Minimum, maximum | -0.10, 0.60 | -0.10, 1.00 |

BCDVA = best-corrected distance visual acuity; DCIVA = distance-corrected intermediate visual acuity; DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

**Supportive Effectiveness Variables**

Supportive effectiveness analyses included categorical summaries of photopic monocular and binocular corrected (BCDVA, DCNVA, and DCIVA) and uncorrected (UDVA, UNVA, and UIVA) VAs.

**BCDVA**

Photopic binocular BCDVA of 20/20-2 or better at Visit 4 (4-6 months) was achieved by 85.3% of subjects in the trifocal IOL group and 89.7% of subjects in the monofocal IOL group; BCDVA of 20/40 or better was achieved by 100.0% of subjects in both treatment groups (**Table 30**).

In the mITT Set, photopic monocular BCDVA of 20/40-2 or better at Visit 4 (4-6 months) was achieved by 98.7% of first eyes in the trifocal IOL group versus 99.4% of first eyes in the monofocal IOL group, by 99.0% of second eyes in the trifocal IOL group versus 100.0% of second eyes in the monofocal IOL group, and by 98.9% of all eyes in the trifocal IOL group versus 99.7% of all eyes in the monofocal IOL group; none of these percentages were statistically significantly worse than the ISO grid performance standard.

**Table 30: Categorical Analysis of Photopic Binocular BCDVA (4 m) at Visit 4 (4-6 months) (mITT Set)**

| BCDVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 312 | 156 |
| 20/20-2 or better | 266 (85.3) | 140 (89.7) |
| 20/25-2 or better | 304 (97.4) | 154 (98.7) |
| 20/32-2 or better | 311 (99.7) | 156 (100.0) |
| 20/40-2 or better | 312 (100.0) | 156 (100.0) |
| logMAR VA | | |
| 0.00 or better | 220 (70.5) | 133 (85.3) |
| 0.10 or better | 299 (95.8) | 154 (98.7) |
| 0.20 or better | 309 (99.0) | 156 (100.0) |
| 0.30 or better | 312 (100.0) | 156 (100.0) |

BCDVA = best-corrected distance visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

**UDVA**

Photopic binocular UDVA of 20/20-2 or better was achieved at Visit 4 (4-6 months) by 57.5% of subjects in the trifocal IOL group and 73.1% of subjects in the monofocal IOL group; UDVA of 20/40-2 or better was achieved by 99.7% of subjects in the trifocal IOL group and 100.0% of subjects in the monofocal IOL group (**Table 31**).

**Table 31: Categorical Analysis of Photopic Binocular UDVA (4 m) at Visit 4 (4-6 months) (mITT Set)**

| UDVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 313 | 156 |
| 20/20-2 or better | 180 (57.5) | 114 (73.1) |
| 20/25-2 or better | 276 (88.2) | 144 (92.3) |
| 20/32-2 or better | 306 (97.8) | 154 (98.7) |
| 20/40-2 or better | 312 (99.7) | 156 (100.0) |
| logMAR VA | | |
| 0.00 or better | 125 (39.9) | 93 (59.6) |
| 0.10 or better | 253 (80.8) | 139 (89.1) |
| 0.20 or better | 302 (96.5) | 153 (98.1) |
| 0.30 or better | 311 (99.4) | 156 (100.0) |
| 0.40 or better | 312 (99.7) | 156 (100.0) |

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UDVA = uncorrected distance visual acuity; VA = visual acuity.

**DCNVA**

Photopic binocular DCNVA of 20/20-2 or better (excluding Phase I subjects) was achieved at Visit 4 (4-6 months) by 44.0% of subjects in the trifocal IOL group and no subjects in the monofocal IOL group; DCNVA of 20/40-2 or better (excluding Phase I subjects) was achieved by 98.9% of subjects in the trifocal IOL group and 24.6% of subjects in the monofocal IOL group (**Table 32**).

**Table 32: Categorical Analysis of Photopic Binocular DCNVA (40 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set)**

| DCNVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 284 | 142 |
| 20/20-2 or better | 125 (44.0) | 0 |
| 20/25-2 or better | 225 (79.2) | 1 (0.7 |
| 20/32-2 or better | 271 (95.4) | 12 (8.5) |
| 20/40-2 or better | 281 (98.9) | 35 (24.6) |
| logMAR VA | | |
| 0.00 or better | 79 (27.8) | 0 |
| 0.10 or better | 181 (63.7) | 0 |
| 0.20 or better | 260 (91.5) | 8 (5.6) |
| 0.30 or better | 279 (98.2) | 27 (19.0) |
| 0.40 or better | 283 (99.6) | 64 (45.1) |
| 0.50 or better | 284 (100.0) | 98 (69.0) |

DCNVA = distance-corrected near visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

**UNVA**

Photopic binocular UNVA of 20/20-2 or better (excluding Phase I subjects) was achieved at Visit 4 (4-6 months) by 38.4% of subjects in the trifocal IOL group and no subjects in the monofocal IOL group; UNVA of 20/40-2 or better (excluding Phase I subjects) was achieved by 99.3% of subjects in the trifocal IOL group and 31.5% of subjects in the monofocal IOL group (**Table 33**).

**Table 33: Categorical Analysis of Photopic Binocular UNVA (40 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set)**

| UNVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 284 | 143 |
| 20/20-2 or better | 109 (38.4) | 0 |
| 20/25-2 or better | 208 (73.2) | 4 (2.8) |
| 20/32-2 or better | 262 (92.3) | 22 (15.4) |
| 20/40-2 or better | 282 (99.3) | 45 (31.5) |
| logMAR VA | | |
| 0.00 or better | 64 (22.5) | 0 |
| 0.10 or better | 174 (61.3) | 1 (0.7 |
| 0.20 or better | 248 (87.3) | 10 (7.0) |
| 0.30 or better | 278 (97.9) | 38 (26.6) |
| 0.40 or better | 283 (99.6) | 78 (54.5) |

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UNVA = uncorrected near visual acuity; VA = visual acuity.

**DCIVA**

Photopic binocular DCIVA of 20/20-2 or better measured at a distance of 66 cm (excluding Phase I subjects) was achieved at Visit 4 (4-6 months) by 61.5% of subjects in the trifocal IOL group and 2.8% of subjects in the monofocal IOL group; DCIVA of 20/40-2 or better measured at a distance of 66 cm (excluding Phase I subjects) was achieved by 98.6% of subjects in the trifocal IOL group and 73.9% of subjects in the monofocal IOL group (**Table 34**).

**Table 34: Categorical Analysis of Photopic Binocular DCIVA (66 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set)**

| DCIVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 283 | 142 |
| 20/20-2 or better | 174 (61.5) | 4 (2.8) |
| 20/25-2 or better | 257 (90.8) | 34 (23.9) |
| 20/32-2 or better | 276 (97.5) | 69 (48.6) |
| 20/40-2 or better | 279 (98.6) | 105 (73.9) |
| logMAR VA | | |
| 0.00 or better | 119 (42.0) | 1 (0.7 |
| 0.10 or better | 235 (83.0) | 21 (14.8) |
| 0.20 or better | 274 (96.8) | 57 (40.1) |
| 0.30 or better | 278 (98.2) | 95 (66.9) |
| 0.40 or better | 279 (98.6) | 120 (84.5) |

DCIVA = distance-corrected intermediate visual acuity; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; VA = visual acuity.

**UIVA**

Photopic binocular UIVA of 20/20-2 or better measured at a distance of 66 cm (excluding Phase I subjects) was achieved at Visit 4 (4-6 months) by 51.8% of subjects in the trifocal IOL group and 14.7% of subjects in the monofocal IOL group; UIVA of 20/40-2 or better measured at a distance of 66 cm (excluding Phase I subjects) was achieved by 98.6% of subjects in the trifocal IOL group and 84.6% of subjects in the monofocal IOL group (**Table 35**).

**Table 35: Categorical Analysis of Photopic Binocular UIVA (66 cm) at Visit 4 (4-6 months) – Excluding Phase I Participants (mITT Set)**

| UIVA | enVista Trifocal IOL n (%) | enVista Monofocal IOL n (%) |
|---|---|---|
| N | 284 | 143 |
| 20/20-2 or better | 147 (51.8) | 21 (14.7) |
| 20/25-2 or better | 237 (83.5) | 50 (35.0) |
| 20/32-2 or better | 273 (96.1) | 89 (62.2) |
| 20/40-2 or better | 280 (98.6) | 121 (84.6) |
| logMAR VA | | |
| 0.00 or better | 93 (32.7) | 12 (8.4) |
| 0.10 or better | 210 (73.9) | 38 (26.6) |
| 0.20 or better | 268 (94.4) | 75 (52.4) |
| 0.30 or better | 280 (98.6) | 116 (81.1) |
| 0.40 or better | 282 (99.3) | 132 (92.3) |

IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; UIVA = uncorrected intermediate visual acuity; VA = visual acuity.

**Sub-Study: Binocular Defocus Curves**

Binocular defocus curves were evaluated at Visit 4 (4-6 months) for a subset of subjects, 53 in the trifocal IOL group and 41 in the monofocal IOL group.

**Figure 5** shows that both treatment groups had similar corrected distance vision, as shown by the similar peaks near 20/20 at 0.0 D. However, in the intermediate and near vision range (-1.5 to -2.5 D), the trifocal IOL group demonstrated a plateau at approximately 20/25, whereas the monofocal IOL group decreased from approximately 20/40 to nearly 20/80. The trifocal IOL advantage was maintained throughout the extended near vision range (-2.5 to -3.5 D).

Subjects were also subdivided by photopic pupil size. Those with the smallest pupil sizes <3.0 mm; trifocal IOL group, n=12; monofocal IOL group, n=9) and those with medium pupil sizes 3.0 − 4.0 mm; trifocal IOL group, n 21; monofocal IOL group, n=23 showed a similar advantage for the trifocal IOL group in the intermediate and near vision ranges (**Figure 6** and **Figure 7**, respectively). Those subjects with the largest pupil sizes >4.0 mm; trifocal IOL group, n=18; monofocal IOL group, n=9) showed the largest advantage for the trifocal IOL group in the intermediate and near vision ranges (**Figure 8**).

As measured by the binocular defocus curves from the data collected with a subset of subjects (n=94), both IOL groups had similar distance vision, while the trifocal IOL group showed better VA compared with the monofocal IOL group in the intermediate vision range and maintained this throughout the near vision range. Photopic pupil size impacted depth of focus, with large pupil sizes demonstrating the largest VA benefit of the trifocal IOL.

**Figure 5: Binocular Defocus Curves (logMAR) by Defocus Lens Power at Visit 4 (4-6 months) (mITT Set)**

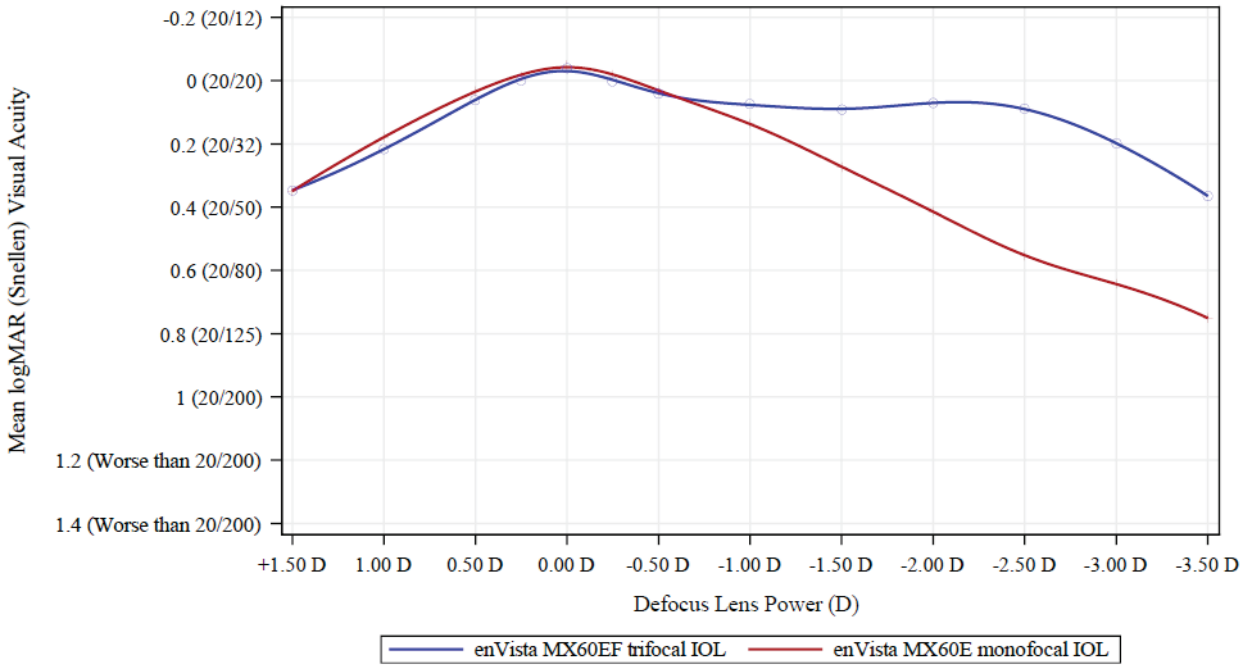


**Figure 6: Binocular Defocus Curves (logMAR) by Defocus Lens Power at Visit 4 (4-6 months) for Participants With Small (<3.0 mm) Pupil Size (mITT Set)**

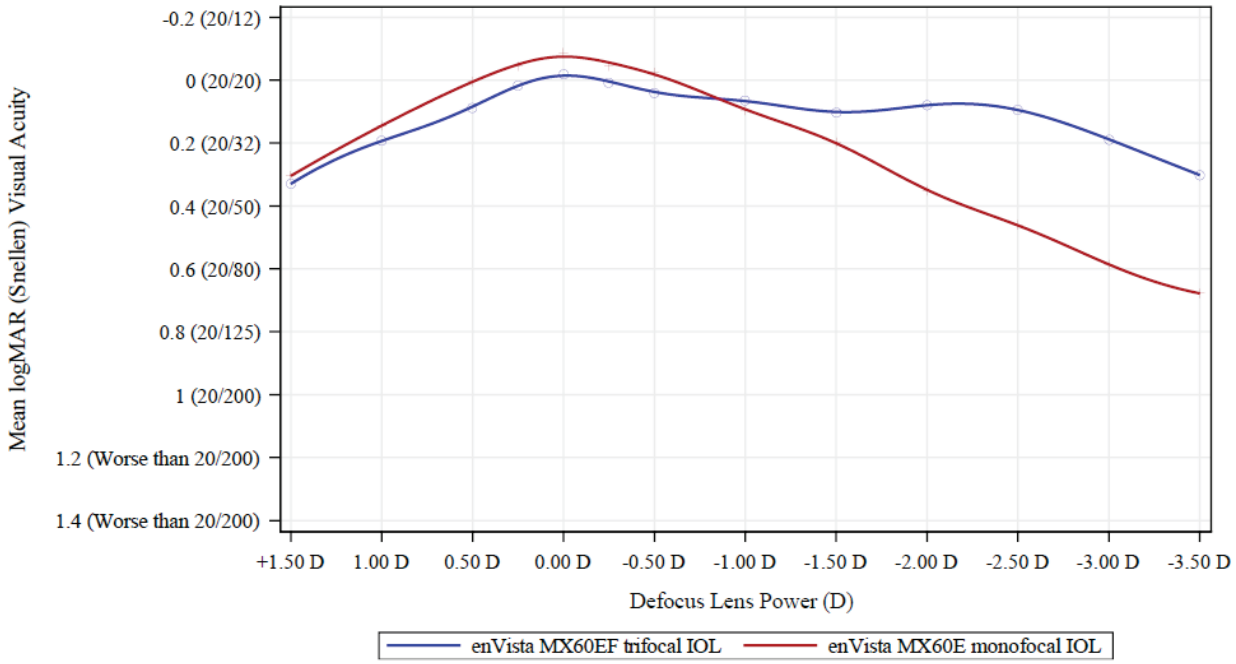



**Figure 7: Binocular Defocus Curves (logMAR) by Defocus Lens Power at Visit 4 (4-6 months) for Participants With Medium (3.0 – 4.0 mm) Pupil Size (mITT Set)**

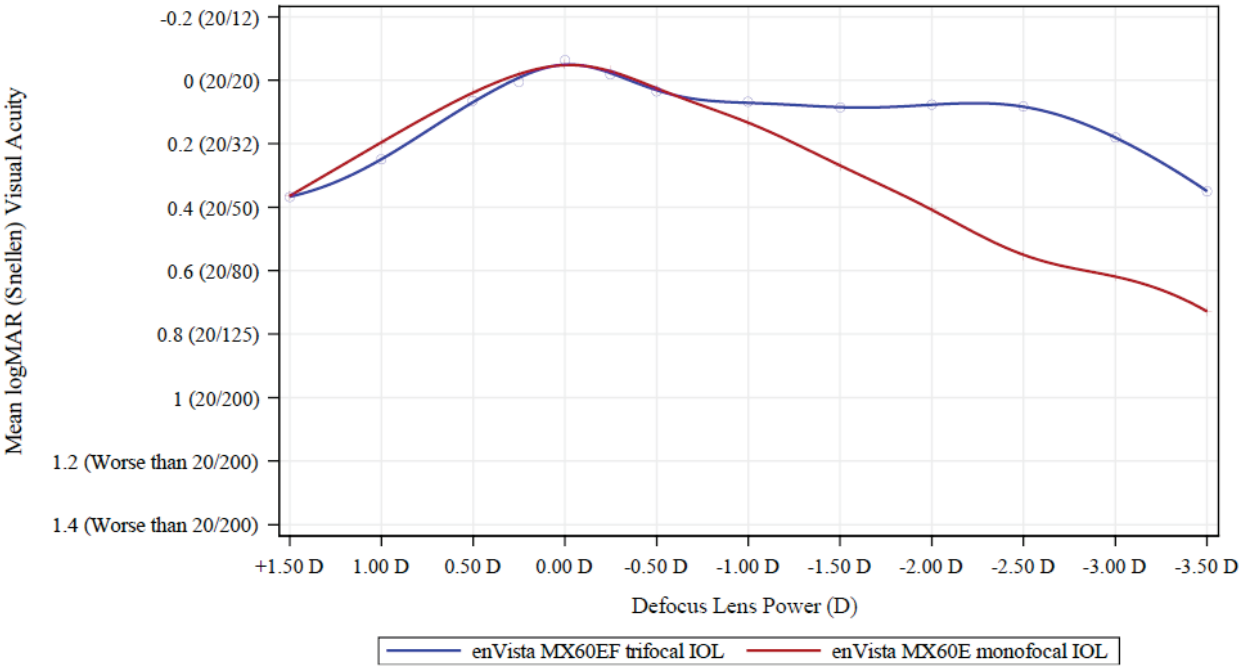
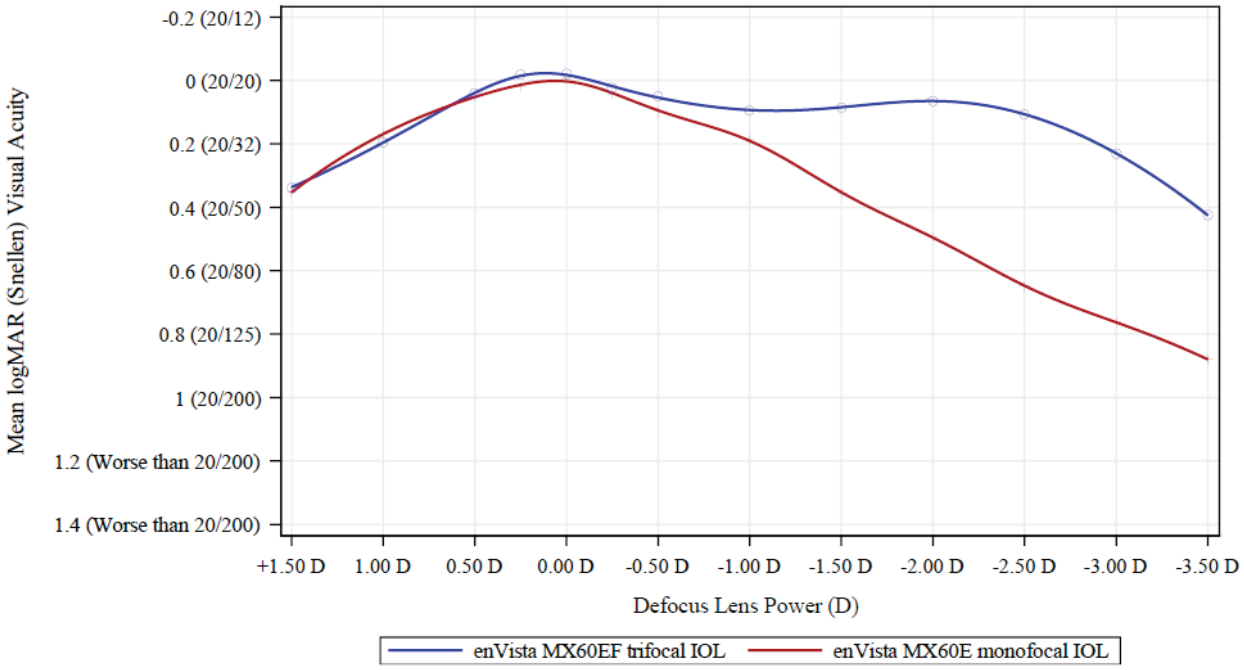


**Figure 8: Binocular Defocus Curves (logMAR) by Defocus Lens Power at Visit 4 (4-6 months) for Participants With Large (>4.0 mm) Pupil Size (mITT Set)**




**Sub-study: Trial Frame Astigmatism**

The Trial Frame astigmatism simulation was a sub-study conducted at Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5), at up to 10 sites. Approximately 30 Group 1 subjects and 15 Group 2 subjects were enrolled with a goal of a total of 50 subjects enrolled. Enrollment was sequential with consecutive subjects enrolled at each site in order of their completion of post-operative Visit 5 (11-14 months) and based on their eligibility. The sub-study noted a first subject on July 21, 2022, and a completion with last subject on February 21, 2023. The purpose of the Trial Frame Astigmatism Simulation sub-study was to assess the potential effect of residual astigmatism on visual performance. It was conducted in subjects implanted with the non-toric enVista Envy IOL and the study was performed to support approval of toric models with cylinder power greater than 3.75D in the IOL plane.

Eligibility was confirmed at completion of Visit 5 (11-14 months) and the subject once consented was brought back to undergo the trial frame evaluation at Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5). The Inclusion criteria included a completed Visit 5 (11-14 months) with a signed consent; a BCDVA of 20/25 or better at Visit 5 (11-14 months); no Adverse /Serious Adverse Events including corneal edema/ increased Intra Ocular Pressure and acceptance to complete the Visit 6 between 2 and 30 days after completion of Visit 5 (11-14 months). Subjects with oblique post-operative residual astigmatism (axis between 30 to 60 degrees or 120 to 150 degrees) were excluded.

To assess the potential effect of residual astigmatism on the visual performance of enVista Envy Trifocal IOL in relation to enVista monofocal IOL, various levels of astigmatic blur (1.00 D, 1.50 D, 2.00 D in with-the-rule and against-the-rule orientations) were added to each subject's distance corrected visual acuities. Visual acuity was tested at 4 m, 66 cm, and 40 cm for each eye of the participating subject using the Clinical Trial Suite system (M&S Technologies, Niles, IL). To ensure the spherical equivalent was kept at a constant, a correction (-0.50 sph added with +1.00 cylinder, -0.75 sph added with +1.50 cylinder, -1.00 sph added with +2.00 cylinder) was added to each plus cylinder power added to the trial frame to modify the spherical power.

The logMAR VA for each assessed combination of distance, cylinder power and axis were summarized by treatment group using the sample size, mean, standard deviation, minimum, first through third quartiles, and maximum. Also summarized was the within-eye difference in logMAR VA between without astigmatic correction (0.00 D cylinder power) and with astigmatic correction, for each combination of distance, non-zero cylinder power, and axis.

**Results**

A total of 33 subjects implanted with the enVista Envy Trifocal IOL (i.e., 66 eyes) and 17 implanted with enVista monofocal IOL (i.e., 34 eyes) consented to participate in the trial frame astigmatism sub-study. The mean age of the subjects was 65.4 ± 9.51 years in the enVista Envy Trifocal group and 71.3 ± 6.16 years in the enVista monofocal IOL group. Most of the study subjects were females in both groups 57.6%; 19/33 in the enVista Envy Trifocal group and 58.8%; 10/17 in the monofocal IOL group). In the enVista Envy Trifocal group, 97%; 32/33 of the subjects were White, and 3%; 1/33 were Asian, whereas in the enVista monofocal IOL group, all (100%; 17/17) of the study subjects were White with a larger subset of subjects falling under the non-Hispanic or non-Latino ethnicity in both groups. The mean photopic pupil size (for the first eye) was 4.0 ± 0.71 mm in the Envy Trifocal group and 3.9 ± 0.82 mm in the monofocal IOL group. The mesopic pupil size was 4.8 ± 0.74 mm in the enVista Envy Trifocal group and 4.5 ± 0.80 mm in the monofocal IOL group. The mean absolute refractive cylinder (in the first eye) was -0.60 ± 0.99 D in the Envy Trifocal group and 0.00 ± 0.74 D in the monofocal IOL group.

The tolerance to induced astigmatism, when assessed using trial frame astigmatism blur, showed that (**Table 36**):

- The baseline (no additional sphere, cylinder, or axis) mean BCDVA (± SD) among all eyes was 0.01 (±0.07) logMAR in the trifocal IOL group and 0.01 (± 0.11) logMAR in the monofocal IOL group.
- With simulated astigmatism, change from baseline mean BCDVA (± SD) ranged from 0.14 (± 0.14) logMAR (+1.00 D, cylinder 180°) to 0.46 (± 0.18) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from 0.08 (± 0.10) logMAR (+1.00 D, cylinder 180°) to 0.44 (±0.20) logMAR (+2.00 D, cylinder 90°) in the monofocal IOL group.

- The baseline (no additional sphere, cylinder, or axis) mean DCIVA (± SD) among all eyes was 0.12 (± 0.10) logMAR in the trifocal IOL group and 0.40(± 0.14) logMAR in the monofocal IOL group.
- With simulated astigmatism, change from baseline mean DCIVA (± SD) ranged from 0.04 (± 0.09) logMAR (+1.00 D, cylinder 180°) to 0.22 (± 0.14) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from -0.01 (± 0.12) logMAR (+1.00 D, cylinder 90°) to 0.03 (± 0.11) logMAR (+2.00 D, cylinder 180°) in the monofocal IOL group
- The baseline (no additional sphere, cylinder, or axis) mean DCNVA (± SD) was 0.15 (± 0.11) logMAR in the trifocal IOL group and 0.56 (± 0.14) logMAR in the monofocal IOL group
- With simulated astigmatism, change from baseline mean DCNVA (± SD) ranged from 0.08 (± 0.11) logMAR (+1.00 D, cylinder 180°) to 0.21 (± 0.15) logMAR (+2.00 D, cylinder 90°) in the trifocal IOL group and from -0.01 (± 0.09) logMAR (+1.00 D, cylinder 90°) to 0.04 ± 0.08 logMAR (+2.00 D, cylinder 180°) in the monofocal IOL group.

**Conclusion**

Visual acuity results for eyes with higher levels of induced astigmatism (1.50 D and 2.00 D) were generally reduced compared to visual acuity results for eyes without induced astigmatism. For DCNVA mean acuity was 2.2 lines of vision for all induced astigmatism levels compared to eyes with induced astigmatism with a mean difference of about 1.5 lines for 1.50 D and about 2.2 lines for 2.00 D.

The results of this clinical investigation indicate that the effects of 1.00 D of induced astigmatism on distance, intermediate and near visual acuities are about 1.4 to 2.0 lines, 0.4 to 0.7 lines, and 0.8 to 0.9 lines, respectively, compared to acuities without induced astigmatism. Non toric enVista Envy IOLs provide improved intermediate and near vision while preserving good distance vision compared to standard monofocal IOLs. The results from this simulation provide reasonable assurance that eyes implanted with high-cylinder toric enVista Envy trifocal IOLs may generally achieve reasonably similar results but indicate that eyes with significant toric lens misalignment from the intended position or errors in the estimated postoperative astigmatism are likely to achieve somewhat poorer results.

**Table 36: Photopic Monocular logMAR Distance Corrected Visual Acuities with the Trial Frame Astigmatism Simulation sub-study and within eye difference of logMAR Visual Acuities with and without astigmatic correction at Visit 6 (Day 2 to 30 after otherwise last visit/Postoperative Visit 5) (Modified Safety Set: All eyes).**

| DCVA, logMAR | Assignment | Baseline (No additional sphere, cylinder, or axis) | +2.00 D, cylinder 180° | +2.00 D, cylinder 90° | +1.50 D, cylinder 180° | +1.50 D, cylinder 90° | +1.00 D, cylinder 180° | +1.00 D, cylinder 90° |
|---|---|---|---|---|---|---|---|---|
| **Mean (SD) BCDVA** | enVista Trifocal IOL (N = 66) | 0.01 (0.07) | 0.39 (0.20) | 0.47 (0.17) | 0.27 (0.17) | 0.33 (0.15) | 0.15 (0.14) | 0.21 (0.15) |
| | enVista Monofocal IOL (N = 34) | 0.01 (0.11) | 0.27 (0.19) | 0.45 (0.22) | 0.17 (0.13) | 0.30 (0.20) | 0.09 (0.11) | 0.22 (0.20) |
| **Mean (SD) BCDVA: Change from baseline** | enVista Trifocal IOL (N = 66) | - | 0.38 (0.21) | 0.46 (0.18) | 0.26 (0.18) | 0.32 (0.14) | 0.14 (0.14) | 0.20 (0.14) |
| | enVista Monofocal IOL (N = 34) | - | 0.26 (0.19) | 0.44 (0.20) | 0.16 (0.15) | 0.29 (0.18) | 0.08 (0.10) | 0.21 (0.16) |
| **Mean (SD) DCIVA** | enVista Trifocal IOL (N = 66) | 0.12 (0.10) | 0.31 (0.13) | 0.34 (0.13) | 0.23 (0.12) | 0.26 (0.12) | 0.16 (0.11) | 0.19 (0.10) |
| | enVista Monofocal IOL (N = 34) | 0.40 (0.14) | 0.43 (0.14) | 0.39 (0.16) | 0.42 (0.16) | 0.40 (0.15) | 0.42 (0.14) | 0.39 (0.14) |
| **Mean (SD) DCIVA: Change from baseline** | enVista Trifocal IOL (N = 66) | - | 0.19(0.11) | 0.22(0.14) | 0.11(0.11) | 0.14(0.14) | 0.04(0.09) | 0.07(0.12 |
| | enVista Monofocal IOL (N = 34) | - | 0.03 (0.11) | -0.01(0.18) | 0.02(0.18) | 0.00(0.13) | 0.02(0.11) | -0.01(0.12) |

| DCVA, logMAR | Assignment | Baseline (No additional sphere, cylinder, or axis) | +2.00 D, cylinder 180° | +2.00 D, cylinder 90° | +1.50 D, cylinder 180° | +1.50 D, cylinder 90° | +1.00 D, cylinder 180° | +1.00 D, cylinder 90° |
|---|---|---|---|---|---|---|---|---|
| **Mean (SD) DCNVA** | enVista Trifocal IOL (N = 66) | 0.15(0.11) | 0.36(0.14) | 0.37(0.13 | 0.30(0.12) | 0.29(0.12) | 0.23(0.13) | 0.24(0.12) |
| | enVista Monofocal IOL (N = 34) | 0.56(0.14) | 0.61(0.14) | 0.56(0.15) | 0.60(0.13) | 0.57(0.15 | 0.60(0.13) | 0.55(0.15) |
| **Mean (SD) DCNVA: Change from baseline** | enVista Trifocal IOL (N = 66) | - | 0.21 (0.15) | 0.22 (0.15) | 0.15 (0.13) | 0.14 (0.13) | 0.08 (0.11) | 0.09(0.13) |
| | enVista Monofocal IOL (N = 34) | - | 0.05 (0.09) | 0.00 (0.09) | 0.04 (0.07) | 0.004 (0.08) | 0.04 (0.08) | -0.01 (0.09) |

DCVA = Distance corrected visual acuity, BCDVA = best-corrected distance visual acuity; DCIVA= Distance corrected intermediate visual acuity, DCNVA= Distance corrected near visual acuity, D = diopter; IOL = intraocular lens; logMAR = logarithm of the minimum angle of resolution; SD = standard deviation.

**Optical Coherence Tomography Imaging Sub-Study**

A total of 26 first eyes in Group 1 (test lens) and 13 first eyes in Group 2 (control lens) underwent imaging of the macula and/or optic nerve by anterior-segment OCT at 3 sites using the Zeiss Cirrus. Images were rated to have excellent quality in 37 eyes and good quality in 2 eyes. In all cases, the images were readable and provided sufficient information to diagnose the condition of the posterior segment (i.e., data on macular thickness and a clear image of Bruch's membrane in macular scans, retinal nerve fiber layer thickness, cup-to-disc ratio, and other parameters of optic disc morphology in optic nerve head scans).

**Manifest Refraction, Residual Refractive Error and Keratometric Cylinder**

**Table 37** presents residual refractive error and postoperative keratometric cylinder for first eyes. The mean sphere and spherical equivalent in both the Trifocal and Monofocal groups demonstrate refractive accuracy to target with values close to zero. Approximately 97% of all eyes in both treatment groups were within ± 1.00 D of intended spherical equivalent at the end of the study.

**Table 37: First Eye Residual Refractive Error and Keratometric Cylinder 4 to 6 Months after Surgery by Treatment Group (Modified Safety Set)**

| Parameter | Statistic | enVista Trifocal IOL (N=332) | enVista Monofocal IOL (N=169) |
|---|---|---|---|
| Sphere (D) | n | 312 | 156 |
| | Mean (SD) | 0.095 (0.4473) | 0.093 (0.4537) |
| | Median | 0.000 | 0.000 |
| | Min, Max | -1.25, 2.00 | -1.00, 1.25 |
| Cylinder (D) | n | 312 | 156 |
| | Mean (SD) | -0.460 (0.3913) | -0.465 (0.3518) |
| | Median | -0.500 | -0.500 |
| | Min, Max | -1.75, 0.00 | -1.50, 0.00 |
| Spherical Equivalent (D) | n | 312 | 156 |
| | Mean (SD) | -0.135 (0.3875) | -0.139 (0.4036) |
| | Median | -0.125 | -0.188 |
| | Min, Max | -1.25, 1.38 | -1.50, 1.00 |
| Keratometric Cylinder (D) | n | 310 | 156 |
| | Mean (SD) | 0.576 (0.4123) | 0.596 (0.3149) |
| | Median | 0.500 | 0.560 |
| | Min, Max | 0.00, 3.92 | 0.00, 1.58 |

**Intraocular Pressure**

Among all eyes, baseline mean ± SD IOP was 15.8 ± 2.85 mmHg in the trifocal IOL group and 15.4 ± 2.95 mmHg in the monofocal IOL group. At Visit 5 (11-14 months), mean ± SD IOP was 14.2 ± 2.66 mmHg (change from baseline, -1.6 ± 2.78 mmHg) in the trifocal IOL group and 13.8 ± 2.85 mmHg (change from baseline, -1.4 ± 2.96 mmHg) in the monofocal IOL group. Among all eyes, IOP showed a modest decline in both treatment groups from baseline to Visit 5 (11-14 months) (~1.5 mmHg).

### 3. Subgroup Analyses

No analyses were performed for any subgroups.

### 4. Pediatric Extrapolation

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

## XI. FINANCIAL DISCLOSURE

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 24 principal investigators of which none were full-time or part-time employees of the sponsor. The clinical study also included sub-investigators of which none were full-time or part-time employees of the sponsor. Among all investigators, three had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

- Compensation to the investigator for conducting the study where the value could be influenced by the outcome of the study: 0
- Significant payment of other sorts: 3
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

Bausch & Lomb has adequately disclosed the financial interest/arrangements with clinical investigators. The information provided does not raise any questions about the reliability of the data.

## XII. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

There is no supplemental clinical information.

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

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

## XIV. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

### A. Effectiveness Conclusions

All 3 co-primary effectiveness endpoints examined in this study were met, with the enVista Envy IOL showing statistical noninferiority to the monofocal IOL in photopic monocular BCDVA, satisfactory BCDVA performance compared to the ISO grid performance standards, and statistical superiority in photopic monocular DCNVA and DCIVA.

### B. Safety Conclusions

The risks of the device are based on nonclinical laboratory and animal studies, as well as data collected in clinical studies conducted to support PMA approval as described above. All 3 co-primary safety endpoints examined in this study were met. ISO grid cumulative or persistent AEs in first eyes of the enVista Envy IOL group did not exceed the SPE rates. No SSIs due to the optical properties of the study lens were reported in first eyes of the enVista Envy IOL group. No first eyes in the enVista Envy IOL group had an ocular TE-SAE that was related to the study device. No unexpected safety findings were observed.

### C. Benefit-Risk Determination

The probable benefits and risks of the enVista Envy IOL and enVista Envy toric IOL are based on data collected in a clinical study conducted to support PMA approval. This study has demonstrated statistically significant and clinically meaningful results with the enVista IOL showing statistical noninferiority to the monofocal IOL in photopic monocular BCDVA, satisfactory BCDVA performance compared to the ISO grid performance standards, and statistical superiority to the monofocal IOL in photopic monocular DCNVA and DCIVA.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. No unexpected safety findings were observed. Adverse event rates, including SSIs, were not clinically concerning for the enVista IOL.

Additional factors to be considered in determining probable risks and benefits for the enVista Envy IOL and enVista Envy toric IOL included:

1. Patient Perspective

   Patient perspectives considered during the review included:

   - Information on patients' experience of visual symptoms using the Quality of Vision (QoV) questionnaire, a patient reported outcome (PRO) measure

In conclusion, given the available information above, the data support that for the visual correction of aphakia (and corneal astigmatism for subjects receiving a toric IOL) in subjects for whom a cataract lens has been removed, while providing improved intermediate and near visual acuity and maintaining comparable distance visual acuity compared to a monofocal IOL, the probable benefits of the enVista Envy IOL and enVista Envy toric IOL outweigh the probable risks.

### D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Key effectiveness endpoints related to near, intermediate, and distance visual acuity were met, demonstrating the ability of the enVista Envy IOLs to provide clinically meaningful improvements in intermediate and near visual acuity, while maintaining comparable distance visual acuity compared to a monofocal IOL. Adverse events were compared favorably to grid rates established in an FDA-recognized international standard.

## XV. CDRH DECISION

CDRH issued an approval order on 10/10/24.

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

## XVI. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.