SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name:	Excimer Laser System
Device Trade Name:	WaveLight EX500 Laser System
Device Procode:	LZS
Applicant's Name and Address:	Alcon Laboratories, Inc. ("Alcon") 6201 South Freeway Fort Worth, Texas 76134-2099
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P020050/S043
Date of FDA Notice of Approval:	March 5, 2025

The original PMA for the parent laser system, the WaveLight EX500 laser system, PMA P020050, was approved on October 7, 2003, and was indicated for the reduction or elimination of myopia of up to - 12.00 diopters (D) of sphere and up to - 6.00 D of astigmatism at the spectacle plane. The device then gained approval for expansion of the indication for the Laser Assisted In-Situ Keratomileusis (Wavefront Optimized LASIK) treatments for the reduction or elimination of hyperopic refractive errors up to + 6.00 D of sphere with and without astigmatic refractive errors up to + 5.00 D at the spectacle plane, with a maximum manifest refraction spherical equivalent (MRSE) of + 6.00 D in P030008 (October 10, 2003). The indications for use was expanded again in P030008/S004 (April 19, 2006) to include the reduction or elimination of naturally occurring mixed astigmatism of up to 6.00 D at the spectacle plane. Use of the parent system in conjunction with Wavefront-Guided Laser Assisted In-Situ Keratomileusis (Wavefront-Guided LASIK) treatment was approved in P020050/S004 (July 26, 2006). Use of the parent system in conjunction with Topography-Guided Laser Assisted In-Situ Keratomileusis (Topography -Guided LASIK) treatment was approved in P020050/S012 (August 27, 2013). Lastly, use of the parent system in conjunction with Photorefractive Keratectomy (PRK) treatment was approved in P020050/S023 (November 21, 2016).

II. INDICATIONS FOR USE

The WaveLight EX500 laser system, in conjunction **with INNOVEYES Sightmap**, is indicated for use in **INNOVEYES Laser Assisted In-Situ Keratomileusis ("wavelight plus"[1] LASIK)** treatments:

- for the reduction or elimination of myopia or myopia with astigmatism, in eyes with spherical equivalent (SE) more than -1.00 and up to -9.00 diopters (D), with up to -8.00 D of spherical component (in minus cylinder format) and up to -3.00 D of astigmatic component at the spectacle plane, based on the INNOVEYES Sightmap Measured Refraction,
- in patients with magnitude of the spherical equivalent (SE) difference between the Manifest Refraction (MRSE) and the Sightmap measured refraction SE being less than 0.75D,
- in patients who are 18 years of age or older, and
- for patients with documentation of a stable manifest refraction defined as ≤ 0.5 D preoperative spherical equivalent shift over one year prior to surgery.

III. CONTRAINDICATIONS

INNOVEYES LASIK treatments using the WaveLight EX500 lasers are contraindicated if any of the following conditions exist. Potential contraindications are not limited to those included in this list:

- patients with severe dry eyes,
- patients with a thin cornea and a calculated residual stromal bed thickness that is less than 250 microns,
- pregnant or nursing women,
- patients with a weakened immune system including diagnosed collagen vascular, autoimmune or immunodeficiency disease or connective tissue disease, which can cause corneal melting,
- patients with degenerations of structure of the cornea including diagnosed keratoconus or any clinical pictures suggestive of keratoconus,
- patients with a recurrent corneal erosion,
- patients with uncontrolled diabetes,
- patients with uncontrolled glaucoma. It is unknown whether LASIK is safe and effective for such patients,
- patients with active eye infections or active inflammations (e.g. keratitis, iritis, or uveitis) and
- patients with recent herpes eye infections or problems resulting from past herpes eye infections.

1 "wavelight plus" is alternative equivalent trade name for "INNOVEYES™" treatments.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the WaveLight EX500 and INNOVEYES Sightmap labeling.

V. DEVICE DESCRIPTION

Table 1 – WaveLight EX500 Laser System Specifications

Laser Device	Excimer laser / ArF Laser class 4 (IEC 60825-1)
Wavelength	193 nm
Maximum Permissible Exposure	30 J/m^2
Ablation Diameter	0.95 mm Gaussian beam profile
Pulse Duration	6 ± 2 ns
Pulse Frequency	500 Hz
Max. Output Energy	5 mJ
Average Power	< 2.5 W
Eyetracker Frequency	1050 Hz type synchronized with laser pulse frequency 500 Hz Active IR-eyetracker system
Aiming Beam	Diode 635 nm, cw (red, continuous wave) Average power: < 0.3 mW
Working Distance	9.84 inch (25 cm)

The system consists of 3 devices (WaveLight EX500 Laser System, WaveNet Planning Software (WPS), and INNOVEYES Sightmap diagnostic device) that work together to produce INNOVEYES Treatment.

The **WaveLight EX500 excimer laser system** (WaveLight EX500) is an FDA-approved stationary scanning-spot excimer laser system indicated for use in refractive surgery for the treatment of myopia, myopic astigmatism, hyperopia, hyperopic astigmatism, and mixed astigmatism, including customized refractive surgery based on data delivered by WaveLight diagnostic devices. The system consists of a compact excimer laser with high pulse frequency, a galvanometer scanner for positioning the laser spot and a fast eyetracker for determining eye position and laser-beam direction. The Gaussian shaped beam profile of the individual pulses and an ablation diameter of approximately 0.95 mm (0.68 mm FWHM - Full Width at Half Maximum) assure the desired contour and minimize surface irregularities during ablation.

All currently approved WaveLight treatment methods use profiles with certain theoretical assumptions (e.g., theoretical eye model), not real values from the multi-lens structure of the eye. For the INNOVEYES procedure, the model data is replaced by measured diagnostic data of the individual patient, taken using the Sightmap diagnostic device:

- Wavefront analysis (currently used for calculation of the approved Wavefront-guided treatment)
- Tomographic data (topographic data of the front surface of the cornea is currently used for calculation of the approved topography-guided treatment)
- Eye length (for current treatments, a mean value from literature is used)

By combining these data, an individual ablation profile (shot profile) is generated from the calculated individual eye model based on an iterative "Ray Tracing" calculation. **INNOVEYES Ray Tracing-Guided Vision Correction (INNOVEYES)** is the tradename of the software and treatment which uses the ray tracing algorithm and is intended for treatment of myopia, with and without astigmatism. INNOVEYES creates a virtual model of the patient's eye using ocular measurement data captured by the INNOVEYES Sightmap Diagnostic Device (Sightmap).

The **WaveNet Planning Software (WPS)** allows the physician to plan treatments on a portable notebook computer outside the surgical area exactly the same way as if directly on the WaveLight devices. The software is made available to the surgeon on a standard DVD-ROM and can be used with a notebook computer meeting the hardware requirements.

The **Sightmap** is a noncontact ophthalmic diagnostic device designed to capture measurements of the anterior segment of the eye, wavefront to analyze the optical aberrations of the entire eye, and axial length for use in INNOVEYES. Data from the Sightmap are stored electronically and can be exported within the WaveLight network for use with INNOVEYES in combination with the Alcon laser systems (i.e., EX500) to perform INNOVEYES treatments.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several alternative methods for the correction of myopic refractive error with or without astigmatism, nonsurgical and surgical, which include: wearing spectacles (glasses), wearing contact lenses, other types of LASIK (conventional, topography-guided, or wavefront-guided), photorefractive keratectomy (PRK), refractive lenticule extraction surgery, refractive lens exchange, phakic intraocular lenses (phakic IOL), and radial keratotomy (RK). Each alternative has its own advantages and disadvantages. A prospective patient should fully discuss all alternatives with the healthcare provider to select the method that best meets the patient's needs, expectations, and lifestyle.

VII. MARKETING HISTORY

The WaveLight EX500 is the 3rd generation of the WaveLight stationary scanning-spot Excimer laser systems. The 1st and 2nd generations are the ALLEGRETTO WAVE and the ALLEGRETTO WAVE EYE-Q, respectively. The WaveLight EX500 laser system has been commercially distributed in more than fifty (50) countries.

The INNOVEYES Sightmap device has been commercialized in Australia, China, Greece, and India.

Neither the WaveLight EX500 nor INNOVEYES Sightmap has been withdrawn from any country or market for reasons of safety or effectiveness.

In the US, the WaveLight EX500 was approved for the first time under P020050/S006 & P030008/S006 on November 23, 2011.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects (e.g., complications) associated with LASIK surgery include, but are not limited to, the following:

Intraoperative:
- Miscreated flap (perforated, incomplete, lost, too thin, misplaced, misaligned, buttonhole, etc.) or tissue damage from difficulty lifting flap
- Ocular penetration
- Subconjunctival hemorrhage or other bleeding
- Treatment interruption

Postoperative:
- Flap complications such as wrinkles (striae/microstriae), debris or foreign body under flap, epithelial ingrowth under flap, flap melting, any of which may require a flap lift or other additional surgery
- Corneal complications such as epithelial defects, haze, scarring, persistent edema (swelling), decompensation, ulcer, perforation, or anterior basement membrane dystrophy
- Corneal ectasia (thinning)
- Infection and/or Inflammation such as conjunctivitis, microbial keratitis, endophthalmitis, corneal infiltrates/ulcer, diffuse lamellar keratitis (DLK), superficial punctate keratopathy (SPK), uveitis, iritis, lamellar keratitis, sterile inflammation, central toxic keratopathy (CTK), corneal decompensation, etc.
- Grittiness (foreign body sensation) and/or ocular pain or soreness
- Dry eye syndrome with related symptoms
- Decreased vision or fluctuating visual acuity (for both uncorrected visual acuity and/or best corrected visual acuity while wearing glasses or contact lenses)
- Inadequate treatment result (over- or under-correction, induced or residual cylinder, and/or decentered ablation)
- Visual symptoms (new symptoms and/or worsening of pre-existing symptoms) such as glare, halos, starbursts, hazy or blurred vision, distortion, double or ghost images, fluctuation of vision, focusing difficulty, difficulty with depth perception, light sensitivity (e.g. transient light-sensitivity syndrome (TLSS), etc.
- Headache or eyestrain due to imbalance between the eyes

- Difficulty with night driving or other low light tasks
- Decreased contrast sensitivity
- Discomfort or pain, potentially including chronic eye pain that is resistant to therapy (neuropathic corneal pain)
- Retinal or posterior vitreous detachment and/or vascular accidents
- Ptosis (droopy eyelid)
- Increase in intraocular pressure (IOP)
- Cataract
- Medication intolerance (allergic reaction, etc.)
- Potential risk of psychological harm
- Corneal aberrations, leading to visual changes such as glare, halo, or star-burst patterns around lights
- Need for secondary surgical intervention

Difficulties with future ophthalmic assessments:

- After refractive surgery, there may be difficulties with future ophthalmic assessments, such as:
    - Selecting an appropriate intraocular lens (IOL) for implantation during cataract surgery, and/or
    - Measuring intraocular pressure (IOP)

  It is recommended that physicians consider whether it may be useful to provide the patient their pre-operative values prior to undergoing LASIK surgery.
- Patients around 40 years of age or older may need eyeglasses for close work such as reading, due to presbyopia.

For the specific list of adverse events observed during the clinical study, refer to **Tables 10** and **11** in section X, Summary of Clinical Studies, below.

IX. SUMMARY OF NON-CLINICAL STUDIES

A. Laboratory Studies

1. Accuracy and repeatability of wavefront analysis were evaluated by comparing sphere and cylinder measurements on test eyes from the Sightmap to an on-market device. Cylinder performance evaluation was conducted on a set of known trial lenses. Accuracy based on spherical equivalent and cylinder results was verified to be accurate to within ±0.25 D from nominal values. Additionally, Sightmap exhibited lower measurement variability and larger measurement range compared to the on-market device.

2. Accuracy and repeatability of tomographic data were evaluated by comparing anterior cornea surface curvature measurements from the Sightmap to an on-market device. This evaluation was conducted on 12 artificial eyes with known curvature. The difference in the average measurements between the two devices remained within ±0.25 D, meeting the predefined equivalence criterion of ±0.27

D (±50 µm) for a 6.5 mm optical zone. Additionally, the reproducibility of Sightmap Measurements was confirmed to be withing ±0.06 D (±13 µm).

3. Accuracy and repeatability of eye length measurements were demonstrated by measuring the length of multiple calibration bodies using the Sightmap and an on-market device. Sightmap measurements were in general closer to the nominal values of the calibration bodies. The average measurement differences between the two devices remained within the predefined equivalence criterion of ±70 µm for all calibration bodies tested. Additionally, Sightmap exhibited lower measurement variability.

B. Animal Studies

Not Applicable.

C. Additional Studies

1. Optical radiation safety of the INNOVEYES Sightmap was evaluated as per IEC 60825-1 (Safety of Laser Products, Part 1-Equipment Classification) and ANSI Z80.36 (American National Standard for Ophthalmics - Light Hazard Protection for Ophthalmic Instruments). The super luminescence diode (SLD) used for axial length measurement was classified according to IEC 60825-1 as a Class 1 laser and the other illuminators of the INNOVEYES Sightmap were found to meet the requirements of ANSI Z80.36.

2. Electrical Safety and Electromagnetic Compatibility of the INNOVEYES Sightmap was evaluated as per IEC 60601-1 (General Requirements for Basic Safety and Essential Performance) and IEC 60601-1-2 (Medical Electrical Equipment – Part 1-2: General Requirements for Safety – Collateral Standard: Electromagnetic Compatibility – Requirements and Tests). The purpose of the testing was to ensure continuous device function in a noisy electromagnetic field environment. The results demonstrated the INNOVEYES Sightmap remains functional within specifications in the presence of a range of electromagnetic frequency signals and when subjected to electrostatic discharge.

3. Software/Firmware and Cybersecurity/Interoperability of the INNOVEYES Sightmap was evaluated as per FDA software guidance “Content of Premarket Submissions for Device Software Functions” and FDA cybersecurity guidance “Cybersecurity in Medical Devices: Quality System Considerations and Content of Premarket Submissions”. The subject device also complies with the IEC 62304 standard. The results of the full software and cybersecurity validation testing demonstrate that INNOVEYES Sightmap meets the system specifications

for performance and accuracy.

4. Biocompatibility was evaluated as per the ISO 10993 series and FDA's guidance "Use of International Standard ISO 10993-1, 'Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process'". The Biocompatibility Risk Evaluation addressed all biological endpoints needed for this surface device with intact skin contact and less than 24-hour contact duration.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant (Alcon) performed a clinical study to establish a reasonable assurance of safety and effectiveness of INNOVEYES LASIK for the correction of myopia with and without astigmatism using the WaveLight EX500 excimer laser system with INNOVEYES software in conjunction with the Sightmap device. The study protocol allowed enrollment of subjects with up to -11.00 diopters (D) of sphere and up to -4.50 D of astigmatism at the spectacle plane measured by the Sightmap (wavefront objective refraction at 4 mm analysis zone) in the US under G190259. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The study was a prospective, single-arm, multi-center, unmasked, interventional study conducted at 9 investigational sites in the US. The study initiated on March 09, 2020, and completed on November 09, 2022. A total of 168 patients (336 eyes) with myopia with or without astigmatism had bilateral INNOVEYES LASIK treatment. The postoperative state of each treated eye was compared to the preoperative state (control) of the same eye. Patients were followed for 12 months after treatment.

Patients who agreed to participate in the clinical study provided informed consent and underwent the required screening procedures to determine study eligibility, including preoperative refractive errors within the specified range (myopia up to -11.00 D with or without astigmatism up to -4.50 D, with spherical equivalent no more than -12.00 D as shown from Sightmap Measured Refraction). INNOVEYES LASIK was planned using the preoperative data from the Sightmap. All eyes were targeted for emmetropia; nomograms were not used.

The safety analysis set (SAF) included all eyes that underwent surgery or attempted surgery (defined as eyes that had received topical eye drop medication prior to initiation of flap treatment). The full analysis set (FAS) included all eyes that successfully underwent refractive surgery. The consistent cohort (CC) included all eyes in the FAS that had manifest refraction data at all post-operative visits from one month up to and including the visit where refractive stability was established.

Descriptive statistics and frequency distributions were used to summarize clinical outcomes. For analysis of refractive outcomes, the sphere component of the manifest refraction (as tested at a distance of 4.0 m) was adjusted for optical infinity by adding -0.25 D to the sphere magnitude. Similarly, mean refraction spherical equivalent (MRSE) was calculated using the adjusted manifest sphere value. Analyses of Snellen lines were based on the conversion from logMAR line ± 2 letters (e.g., 20/20 Snellen = -0.04 to 0.04 logMAR).

1. <u>**Inclusion and Exclusion Criteria**</u>

Enrollment in the INNOVEYES study was limited to patients who met the following inclusion criteria:

- At least of 18 years of age
- Myopia up to -11.00 D, with or without astigmatism up to -4.50 D, with spherical equivalent no more than -12.00 D, as shown from INNOVEYES Sightmap Measured Refraction
- Best corrected photopic distance visual acuity of 20/20 or better (≤ 0.04 logMAR)
- Uncorrected photopic distance visual acuity of 20/40 or worse (≥ 0.34 logMAR)
- Less than 0.75 D MRSE difference between cycloplegic and subjective manifest refractions
- Less than 0.75 D (SE) difference between Sightmap Measured Refraction and manifest refraction
- Stable refraction (within ± 0.50 D) as determined by MRSE for a minimum of 12 months prior to surgery
- Stable refraction for contact lens wearers within ± 0.5 D MRSE on two consecutive exam dates 7 days apart after lenses are not worn for at least 3 weeks (rigid or toric contact lenses) or 1 week (soft contact lenses)

Patients were <u>not</u> permitted to enroll in the INNOVEYES study if they met any of the following exclusion criteria:

- Women who were pregnant or breastfeeding
- Acute or chronic disease or illness that would increase the operative risk
- Systemic medications that may confound the outcome of the study or increase the risk to the subject, including, but not limited to steroids, antimetabolites, isotretinoin, or amiodarone hydrochloride
- Ocular condition that may predispose the subject to future complications (e.g., history or evidence of active or inactive corneal disease, evidence of retinal vascular disease, keratoconus or keratoconus suspect, glaucoma)
- Previous intraocular or corneal surgery
- Predicted residual stromal bed thickness < 250 µm
- Intended to have monovision treatment

2. Follow-up Schedule

Table 2 Clinical Study Follow-Up Schedule

Exam	Visit Window
Preoperative Evaluation	1 to 30 days prior to Surgery
Visit 0	Operative Visit
Visit 1 1 Day	Day 1 postoperative
Visit 2 1 Week	Day 5 to 9 postoperative
Visit 3 1 Month	Day 21 to 35 postoperative
Visit 4 3 Months	Day 70 to 98 postoperative
Visit 5 6 Months	Day 147 to 182 postoperative
Visit 6 9 Months	Day 245 to 301 postoperative
Visit 7 12 Months	Day 330 to 420 postoperative

All patients were scheduled to be evaluated at the visits listed above (Table 2).

Parameters assessed pre-operatively and post-operatively during the study included: manifest subjective refraction (MR), cycloplegic refraction (CR), mesopic pupil size, uncorrected distance and uncorrected near visual acuity (UCDVA, UCNVA), best corrected distance visual acuity (BCDVA), contrast sensitivity (mesopic with and without glare), intraocular pressure (IOP), INNOVEYES Sightmap measurements (aberrometry, biometry, keratometry, corneal pachymetry, corneal topography, wavefront refraction), slit-lamp evaluation of the anterior segment, dilated fundus exam, Patient Reported Outcomes with LASIK (PROWL) questionnaire (including visual symptoms and satisfaction, driving difficulty, and dry eye symptoms). Adverse events (AEs) and complications were recorded at all visits.

Treatment plans were based on preoperative Sightmap measurements.

3. Clinical Endpoints

Safety endpoints evaluated at the time of refractive stability were as follows:

- Percentage of eyes with best-corrected distance visual acuity (BCDVA) worse than 20/40 in eyes with BCDVA of 20/20 or better pre-op baseline (Target ≤ 1%).
- Percentage of eyes that lose 2 or more lines BCDVA from baseline (Target ≤5%).
- Percentage of eyes that have an increase of manifest refractive astigmatism of greater than 2.00 D of absolute cylinder as compared to the preoperative refraction (Target ≤ 5%)
- Percentage of eyes with a serious, non-flap related, ocular adverse event at the postoperative visits (Target ≤ 1%)
- Additional supportive analyses of safety included, but not limited to, Ocular Adverse Events, Patient Reported Outcomes, change in best-corrected

distance Contrast Sensitivity (mesopic, with and without glare), and mean Aberrations.

Effectiveness endpoints evaluated at refractive stability were as follows:

- Percentage of eyes with uncorrected distance visual acuity (UCDVA) of 20/40 or better (in eyes with preoperative BCDVA of 20/20 or better) at refractive stability (Target ≥ 85%)
- Percentage of eyes with MRSE within 0.50 D of intended, at refractive stability (Target ≥ 50%)
- Percentage of eyes with MRSE within 1.00 D of intended, at refractive stability (Target ≥ 75%)
- Percentage of eyes that achieve refractive stability (Target ≥ 95%)
- Additional supportive effectiveness analyses included but not limited to, predictability of MR sphere, predictability of MR cylinder, percentage of eyes over-corrected or under-corrected by > 1.00 D MRSE, percentage of eyes having UCDVA of 20/20 or better, percentage of eyes having UCDVA equal to or better than preoperative BCDVA, and vector analyses (for eyes treated for astigmatism).

NOTE: Refractive stability is generally accepted to have been achieved at the latter of two postoperative refractions performed at least 3 months apart, if all of the following criteria are met:

- At least 95% of the treated eyes have a change ≤ 1.00 D of MRSE between the two refractions;
- The mean rate of change in MRSE, as determined by a paired analysis, is <0.5 D per year (0.04 D/month) over the same time period;
- The mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero or a rate of change attributable to normal aging;
- The 95% confidence interval for the mean rate of change includes zero or a rate of change attributable to normal aging; and
- Stability is confirmed at least 3 months after the initial stability time point, by a statistically adequate subgroup.

Regarding success/failure criteria, the effectiveness endpoints were considered met if the percentage of eyes met or exceeded the target rate at the time of refractive stability. Additionally, the safety endpoints were considered to have been met if the percentage of eyes was less than or equal to the target rate at the time of refractive stability for all the primary safety endpoints.

B. Accountability of PMA Cohort

At the completion of the study, 163 of the 168 treated patients (326/336 treated eyes, 97%) were available for analysis having reached the 12-month postoperative visit.

(**Table 3**). The SAF consisted of 336 eyes. The FAS consisted of 334 eyes. The CC included 326 eyes.

Table 3

Accountability by Postoperative Visit by Eye (Safety Analysis Set)

Eye Status (n/N (%))	1 Day	1 Week	1 Month	3 Months	6 Months	9 Months	12 Months
Enrolled and Treated (N) 336							
Available for Analysis	336/336 (100.0)	332/336 (98.8)	336/336 (100.0)	330/336 (98.2)	334/336 (99.4)	324/336 (96.4)	326/336 (97.0)
Active	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)
Missed Visit:							
Discontinued	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	4/336 (1.2)	4/336 (1.2)
Retreatment	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)
Adverse Event	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)
Withdrawal by Subject	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	4/336 (1.2)	4/336 (1.2)
Other causes	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)
Lost to Follow-up	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	4/336 (1.2)	6/336 (1.8)
Missed visit, but seen at a later visit	0/336 (0.0)	4/336 (1.2)	0/336 (0.0)	6/336 (1.8)	2/336 (0.6)	4/336 (1.2)	0/336 (0.0)
Not Seen, But Status Obtained	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)	0/336 (0.0)
% Accountability	100.0	98.8	100.0	98.2	99.4	97.6	98.2

C. Study Population Demographics and Baseline Parameters

The mean age of the study population was 33.3 years (standard deviation (SD) 6.98; range 21 to 56) at the time of screening, **Table 4**. The patient population consisted of 37.1% male and 62.9% female patients and was predominantly white (76.6%), of non-Hispanic or Latino ethnicity (85.6%).

Table 4

Demographic Statistics (Full Analysis Set)

Parameter	INNOVEYES
Age (Years)	
N	167
Mean (SD)	33.3 (6.98)
Median	32.0
(Min, Max)	(21, 56)
Age Group, n/N (%)	
≤21	3/167 (1.8)
>21	164/167 (98.2)
Sex, n/N (%)	
Female	105/167 (62.9)
Male	62/167 (37.1)
Unknown	0/167 (0.0)
Undifferentiated	0/167 (0.0)
Ethnicity, n/N (%)	
Hispanic or Latino	23/167 (13.8)
Not Hispanic or Latino	143/167 (85.6)
Not Reported	1/167 (0.6)
Unknown	0/167 (0.0)
Race, n/N (%)	
White	128/167 (76.6)
Black or African American	10/167 (6.0)
American Indian or Alaska Native	1/167 (0.6)
Asian	16/167 (9.6)

Parameter	INNOVEYES
Native Hawaiian or Other Pacific Islander	1/167 (0.6)
Multi-Racial	2/167 (1.2)
Other	9/167 (5.4)

N = Number of patients
n = Number of patients with non-missing response
SD = Standard deviation

Tables 5 and 6 present the preoperative refractive error bin distributions for the study population, based on preoperative Sightmap Measured Refraction. The approved refractive treatment ranges for the approved Indications for Use are represented by un-shaded areas of **Tables 5** and **6** (those with outcomes available for more than 20 eyes per dioptric bin), and the shaded areas of these tables are locked out by the INNOVEYES software.

Table 5
Preoperative Refractive Error Stratified by INNOVEYES Sightmap Measured Refraction Sphere and Cylinder (Full Analysis Set)

	INNOVEYES Sightmap Measured Cylinder						
INNOVEYES Sightmap Measured Sphere	**0 to ≤ -0.50 D n/N (%)**	**> -0.50 to ≤ -1.00 D n/N (%)**	**>-1.00 to ≤ -2.00 D n/N (%)**	**>-2.00 to ≤ -3.00 D n/N (%)**	**>-3.00 to ≤ -4.00 D n/N (%)**	**>-4.00 to ≤ -4.50 D n/N (%)**	**Total n/N (%)**
0 to ≤ -1.0 D	2/334 (0.6)	2/334 (0.6)	8/334 (2.4)	12/334 (3.6)	5/334 (1.5)	0/334 (0.0)	29/334 (8.7)
> -1.0 to ≤ -2.0 D	12/334 (3.6)	16/334 (4.8)	11/334 (3.3)	4/334 (1.2)	3/334 (0.9)	1/334 (0.3)	47/334 (14.1)
> -2.0 to ≤ -3.0 D	20/334 (6.0)	6/334 (1.8)	9/334 (2.7)	7/334 (2.1)	2/334 (0.6)	0/334 (0.0)	44/334 (13.2)
> -3.0 to ≤ -4.0 D	11/334 (3.3)	8/334 (2.4)	11/334 (3.3)	3/334 (0.9)	2/334 (0.6)	0/334 (0.0)	35/334 (10.5)
> -4.0 to ≤ -5.0 D	16/334 (4.8)	9/334 (2.7)	3/334 (0.9)	4/334 (1.2)	4/334 (1.2)	0/334 (0.0)	36/334 (10.8)
> -5.0 to ≤ -6.0 D	16/334 (4.8)	14/334 (4.2)	5/334 (1.5)	5/334 (1.5)	1/334 (0.3)	0/334 (0.0)	41/334 (12.3)
> -6.0 to ≤ -7.0 D	12/334 (3.6)	25/334 (7.5)	7/334 (2.1)	3/334 (0.9)	1/334 (0.3)	0/334 (0.0)	48/334 (14.4)
> -7.0 to ≤ -8.0 D	15/334 (4.5)	7/334 (2.1)	10/334 (3.0)	2/334 (0.6)	0/334 (0.0)	0/334 (0.0)	34/334 (10.2)
> -8.0 to ≤ -9.0 D	7/334 (2.1)	6/334 (1.8)	1/334 (0.3)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	14/334 (4.2)
> -9.0 to ≤ -10.0 D	3/334 (0.9)	3/334 (0.9)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	6/334 (1.8)
> -10.0 to ≤ -11.0 D	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)
Total	114/334 (34.1)	96/334 (28.7)	65/334 (19.5)	40/334 (12.0)	18/334 (5.4)	1/334 (0.3)	334/334 (100.0)

% Percentage is calculated by dividing the total number of eyes in the bin (n)/ by the total number of eyes N (334) x 100
Treatment of diopter ranges indicated by shaded rows and columns is locked out by INNOVEYES software.

Table 6
Preoperative Refractive Error Stratified by INNOVEYES Sightmap Measured Refraction Spherical Equivalent and Cylinder (Full Analysis Set)

	INNOVEYES Sightmap Measured Cylinder						
INNOVEYES Sightmap Measured Refraction Spherical Equivalent	**0 to ≤ -0.50 D n/N (%)**	**> -0.50 to ≤ -1.00 D n/N (%)**	**>-1.00 to ≤ -2.00 D n/N (%)**	**>-2.00 to ≤ -3.00 D n/N (%)**	**>-3.00 to ≤ -4.00 D n/N (%)**	**>-4.00 to ≤ -4.50 D n/N (%)**	**Total n/N (%)**
0 to ≤ -1.0 D	0/334 (0.0)	0/334 (0.0)	1/334 (0.3)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	1/334 (0.3)
> -1.0 to ≤ -2.0 D	13/334 (3.9)	14/334 (4.2)	11/334 (3.3)	9/334 (2.7)	2/334 (0.6)	0/334 (0.0)	49/334 (14.7)
> -2.0 to ≤ -3.0 D	15/334 (4.5)	8/334 (2.4)	11/334 (3.3)	6/334 (1.8)	4/334 (1.2)	0/334 (0.0)	44/334 (13.2)
> -3.0 to ≤ -4.0 D	13/334 (3.9)	6/334 (1.8)	7/334 (2.1)	7/334 (2.1)	2/334 (0.6)	1/334 (0.3)	36/334 (10.8)
> -4.0 to ≤ -5.0 D	17/334 (5.1)	6/334 (1.8)	10/334 (3.0)	4/334 (1.2)	2/334 (0.6)	0/334 (0.0)	39/334 (11.7)
> -5.0 to ≤ -6.0 D	18/334 (5.4)	15/334 (4.5)	2/334 (0.6)	3/334 (0.9)	4/334 (1.2)	0/334 (0.0)	42/334 (12.6)
> -6.0 to ≤ -7.0 D	12/334 (3.6)	22/334 (6.6)	9/334 (2.7)	6/334 (1.8)	3/334 (0.9)	0/334 (0.0)	52/334 (15.6)
> -7.0 to ≤ -8.0 D	13/334 (3.9)	16/334 (4.8)	5/334 (1.5)	1/334 (0.3)	1/334 (0.3)	0/334 (0.0)	36/334 (10.8)
> -8.0 to ≤ -9.0 D	9/334 (2.7)	4/334 (1.2)	9/334 (2.7)	3/334 (0.9)	0/334 (0.0)	0/334 (0.0)	25/334 (7.5)
> -9.0 to ≤ -10.0 D	4/334 (1.2)	4/334 (1.2)	0/334 (0.0)	1/334 (0.3)	0/334 (0.0)	0/334 (0.0)	9/334 (2.7)
> -10.0 to ≤ -11.0 D	0/334 (0.0)	1/334 (0.3)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	0/334 (0.0)	1/334 (0.3)
Total	114/334 (34.1)	96/334 (28.7)	65/334 (19.5)	40/334 (12.0)	18/334 (5.4)	1/334 (0.3)	334/334 (100.0)

% Percentage is calculated by dividing the total number of eyes in the bin (n)/ by the total number of eyes N (334) x 100
Treatment of diopter ranges indicated by shaded rows and columns is locked out by INNOVEYES software.

D. Safety and Effectiveness Results

1. Refractive Stability

Refractive stability was evaluated for the Consistent Cohort analysis set (*criteria that at least 95% eyes change MRSE ≤1.00 D over the visit interval, with change MRSE <0.04D/month (extrapolates to <0.5D/year) and decreases monotonically over time, and confidence interval includes zero* . Refractive stability was initially achieved at 3 months and confirmed at 6 months (**Table 7**). Therefore, key safety and effectiveness study endpoints were evaluated at 3 months, according to the study protocol which specified that safety and effectiveness endpoints were to be based on outcomes at the point of stability.

Table 7
Criteria for Refractive Stability (Consistent Cohort Analysis Set)

		1 Month to 3 Months (N = 326)	3 Months to 6 Months (N = 326)	6 Months to 9 Months (N = 316)	9 Months to 12 Months (N = 314)
Change in MRSE by ≤ 1.0 D [a]	n/N (%)	324/326 (99.4)	321/326 (98.5)	315/316 (99.7)	312/314 (99.4)
Change in MRSE by ≤ 0.5 D	n/N (%)	304/326 (93.3)	306/326 (93.9)	300/316 (94.9)	305/314 (97.1)
Change in MRSE in Diopters	Mean	-0.011	0.010	-0.018	0.000
	SD	0.3063	0.3232	0.2946	0.2674
Change in MRSE per Month [b]	Mean	-0.005	0.003	-0.006	0.000
	SD	0.1532	0.1077	0.0982	0.0891
Change in Cylinder by ≤ 1.0 D	n/N (%)	326/326 (100.0)	326/326 (100.0)	316/316 (100.0)	314/314 (100.0)
Change in Cylinder by ≤ 0.5 D	n/N (%)	316/326 (96.9)	321/326 (98.5)	308/316 (97.5)	309/314 (98.4)
Change in Cylinder in Diopters	Mean	0.026	0.004	-0.017	0.021
	SD	0.2698	0.2492	0.2367	0.2105
Change in Cylinder per Month	Mean	0.013	0.001	-0.006	0.007
	SD	0.1349	0.0831	0.0789	0.0702

N = Number of eyes with data at all visits
n = Number of eyes in specified category
SD = Standard deviation,
[a]Refractive stability criterion: at least 95% of eyes with change ≤1.00 D of MRSE between the 2 refractions
[b]Refractive stability criterion: mean change of ≤0.04 D per month (≤0.5 D per year) as determined by paired analysis

2. Safety Results

In the safety analysis set, there were 330 eyes available at the 3-month visit. The key safety outcomes for this study are presented in **Table 8**. No eyes (0/330, 0%) had a co-primary safety endpoint observation at 3 months.

Table 8
Co-Primary Safety Endpoints at Refractive Stability (Safety Analysis Set)

Outcome	INNOVEYES n/N (%)	Target Rate (%)
BCDVA loss of 2 lines (10 letters) or more from pre-op	0/330 (0.0)	≤ 5%
BCDVA worse than 20/40 (with BCDVA 20/20 or better pre-op)	0/329 (0.0)	≤ 1%
Increase of manifest refractive astigmatism >2.00 D of absolute cylinder compared to pre-op	0/330 (0.0)	≤ 5%
Non-Flap related, ocular serious adverse events*	0/330 (0.0)	≤ 1%

N = Number of eyes in Safety Analysis Set
n = Number of eyes in specified category
Refractive stability achieved at 3 months
*Cumulative number of events reported at refractive stability or earlier
Line difference categories determined using logMAR values; a 0.1 difference in logMAR equals a 1 line difference.
Snellen lines were based on the conversion from logMAR line +/- 2 letters (e.g., 20/20 Snellen = -0.04 to 0.04 logMAR).

Safety endpoint outcomes throughout the 12-month study are provided in **Table 9**:

Table 9
Co-Primary Safety Endpoints at Any Postoperative Visit (Safety Analysis Set)

Outcome	InnovEyes n/N (%)
BCDVA loss of 2 lines (10 letters) or more from pre-op	4/336 (1.2)
BCDVA worse than 20/40 (with BCDVA 20/20 or better pre-op)	0/335 (0.0)
Increase of manifest refractive astigmatism >2.00 D of absolute cylinder compared to pre-op	0/336 (0.0)
Non-Flap related, ocular serious adverse events	4/336 (1.2)

<u>Adverse Events</u>:
A summary of ocular adverse events (AEs) that occurred during the study are presented in **Table 10**. Ocular AEs were reported in 37 of 336 eyes (11.0%). The most common ocular AEs included corneal flap complication (3.3%) and blepharitis (1.2%); these were nonserious and mild. All other ocular AEs occurred at an incidence ≤ 0.9%. The reported incidence of Dry Eye was 0.9%. Non-ocular AEs were infrequent; the most common was coronavirus infection which resolved in all cases. No patients discontinued the study due to a treatment-emergent AE. There were no ocular or non-ocular adverse device effects reported in the study.

Table 10
Incidence of Ocular Adverse Events by Preferred Term (Safety Analysis Set)

	INNOVEYES n/N (%)	E
Any Event	37/336 (11.0)	58
Corneal flap complication	11/336 (3.3)	12
Blepharitis	4/336 (1.2)	4
Conjunctivitis	3/336 (0.9)	3
Conjunctivitis allergic	3/336 (0.9)	3
Corneal operation	3/336 (0.9)	3
Diffuse lamellar keratitis	3/336 (0.9)	3
Dry eye	3/336 (0.9)	3
Punctate keratitis	3/336 (0.9)	4
Visual acuity reduced	3/336 (0.9)	3
Corneal opacity	2/336 (0.6)	2
Eye allergy	2/336 (0.6)	2
Punctal plug insertion	2/336 (0.6)	2
Retinal laser coagulation	2/336 (0.6)	2
Retinal tear	2/336 (0.6)	2
Vision blurred	2/336 (0.6)	2
Abscess drainage	1/336 (0.3)	1
Abscess of eyelid	1/336 (0.3)	1
Chalazion	1/336 (0.3)	1
Chorioretinal atrophy	1/336 (0.3)	1
Corneal abrasion	1/336 (0.3)	1
Corneal disorder	1/336 (0.3)	1
Hordeolum	1/336 (0.3)	1
Vitreous disorder	1/336 (0.3)	1

N = Total number of eyes; n = Number of eyes with the events; E = Number of events.

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE.
Events are counted each time in the event (E) column.
Adverse events coded using MedDRA version 22.0

Ocular serious adverse events (SAEs) were reported in 4 eyes (1.2%) of 3 patients (**Table 11**) across all study visits. One subject had a retinal tear in each eye on Day 167; 1 subject had visual acuity reduced in left eye on Day 250 and corneal opacity on Day 213; and 1 subject had visual acuity reduced in left eye on Day 336. All events were reported as not related to the device and all recovered. No non-ocular SAEs were reported.

Table 11
Incidence of Ocular Serious Adverse Events by Preferred Term (Safety Analysis Set)

	INNOVEYES n/N (%)	E
Any Event	4/336 (1.2)	5
Retinal tear	2/336 (0.6)	2
Visual acuity reduced	2/336 (0.6)	2
Corneal opacity	1/336 (0.3)	1

N = Total number of eyes; n = Number of eyes with the events; E = Number of events.
If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n) for the corresponding AE.

Preservation of BCDVA:

The change in lines of BCDVA compared to baseline is presented in **Table 12**. At 3 months, 97.9% (319/326) of eyes had no change or had improvement in BCDVA compared to preoperative. No eyes were reported with loss of >2 lines of BCDVA at any postoperative visit, and 4 eyes were reported with loss of 2 lines across all study visits. At the 12-month final visit, 1 eye (0.3%) was reported with loss of 2 lined of BCDVA compared to baseline.

Table 12
BCDVA Line Differences from Preoperative (Full Analysis Set)

Difference from Preoperative	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
> 2 lines better	0/330 (0.0)	0/334 (0.0)	0/326 (0.0)	0/330 (0.0)	0/320 (0.0)	0/322 (0.0)
2 lines better	1/330 (0.3)	4/334 (1.2)	5/326 (1.5)	3/330 (0.9)	7/320 (2.2)	6/322 (1.9)
1 line better	35/330 (10.6)	62/334 (18.6)	61/326 (18.7)	72/330 (21.8)	72/320 (22.5)	80/322 (24.8)
0 lines	253/330 (76.7)	247/334 (74.0)	253/326 (77.6)	244/330 (73.9)	232/320 (72.5)	229/322 (71.1)
1 line worse	40/330 (12.1)	20/334 (6.0)	7/326 (2.1)	11/330 (3.3)	8/320 (2.5)	6/322 (1.9)
2 lines worse	1/330 (0.3)	1/334 (0.3)	0/326 (0.0)	0/330 (0.0)	1/320 (0.3)	1/322 (0.3)
> 2 lines worse	0/330 (0.0)	0/334 (0.0)	0/326 (0.0)	0/330 (0.0)	0/320 (0.0)	0/322 (0.0)

N = Number of eyes with data at visit
n = Number of eyes in category
Line difference categories determined using logMAR values; a 0.1 difference in logMAR equals a 1 line difference.

<u>Patient Reported Outcomes:</u>

The Patient Reported Outcomes with LASIK (PROWL) questionnaire was administered preoperatively and at all postoperative visits at refractive stability and later. Visual symptoms were reported at a lower prevalence both at 3 months and 12 months compared to preoperative (**Table 13**).

Table 13
Categorical Statistics for PROWL Questionnaire: Reported Visual Symptoms at Refractive Stability Visit and Later (Safety Analysis Set)

Outcomes[a]	Symptom	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Symptom Prevalence[b,c]	Any type of symptom	130/167 (77.8)	88/165 (53.3)	66/167 (39.5)	64/162 (39.5)	57/163 (35.0)
	Double Images	76/167 (45.5)	10/165 (6.1)	12/167 (7.2)	10/162 (6.2)	4/163 (2.5)
	Glare	76/167 (45.5)	47/165 (28.5)	37/167 (22.2)	29/162 (17.9)	22/163 (13.5)
	Halos	92/167 (55.1)	68/165 (41.2)	53/167 (31.7)	49/162 (30.2)	39/163 (23.9)
	Starbursts	110/167 (65.9)	63/165 (38.2)	51/167 (30.5)	44/162 (27.2)	49/163 (30.1)
Symptom Development[b,d]	No symptoms of any type to at least 1 symptom		12/37 (32.4)	6/37 (16.2)	4/35 (11.4)	3/35 (8.6)
	Double Images		5/91 (5.5)	5/91 (5.5)	3/87 (3.4)	1/88 (1.1)
	Glare		14/89 (15.7)	10/90 (11.1)	10/85 (11.8)	3/86 (3.5)
	Halos		24/75 (32.0)	15/75 (20.0)	14/71 (19.7)	7/72 (9.7)
	Starbursts		11/57 (19.3)	7/57 (12.3)	7/55 (12.7)	8/55 (14.5)
Symptom Resolution[b,e]	Any type of symptom to none at all		51/127 (40.2)	70/129 (54.3)	67/126 (53.2)	73/127 (57.5)
	Double Images		68/73 (93.2)	68/75 (90.7)	68/74 (91.9)	71/74 (95.9)
	Glare		42/75 (56.0)	49/76 (64.5)	57/76 (75.0)	57/76 (75.0)
	Halos		45/89 (50.6)	54/91 (59.3)	56/90 (62.2)	58/90 (64.4)
	Starbursts		55/107 (51.4)	65/109 (59.6)	69/106 (65.1)	66/107 (61.7)
Difficulty Performing Activities Due to Symptoms[f,g]	Any type of symptom	4/167 (2.4)	4/165 (2.4)	2/167 (1.2)	1/162 (0.6)	1/163 (0.6)
	Double Images	0/167 (0.0)	1/165 (0.6)	0/167 (0.0)	0/162 (0.0)	0/163 (0.0)
	Glare	1/167 (0.6)	1/165 (0.6)	0/167 (0.0)	0/162 (0.0)	0/163 (0.0)
	Halos	0/167 (0.0)	2/165 (1.2)	1/167 (0.6)	0/162 (0.0)	1/163 (0.6)
	Starbursts	3/167 (1.8)	1/165 (0.6)	1/167 (0.6)	1/162 (0.6)	0/163 (0.0)
No Difficulty Performing Activities Due to Symptoms[f]	No difficulty due to any symptom	97/167 (58.1)	117/165 (70.9)	132/167 (79.0)	125/162 (77.2)	135/163 (82.8)
	Double Images	154/167 (92.2)	163/165 (98.8)	161/167 (96.4)	156/162 (96.3)	162/163 (99.4)
	Glare	128/167 (76.6)	140/165 (84.8)	152/167 (91.0)	146/162 (90.1)	151/163 (92.6)
	Halos	122/167 (73.1)	138/165 (83.6)	147/167 (88.0)	135/162 (83.3)	141/163 (86.5)
	Starbursts	110/167 (65.9)	134/165 (81.2)	143/167 (85.6)	135/162 (83.3)	140/163 (85.9)
Very or Extremely Bothersome Symptoms[f]	Any type of symptom	22/167 (13.2)	4/165 (2.4)	4/167 (2.4)	2/162 (1.2)	1/163 (0.6)
	Double Images	2/167 (1.2)	1/165 (0.6)	1/167 (0.6)	0/162 (0.0)	0/163 (0.0)
	Glare	10/167 (6.0)	1/165 (0.6)	2/167 (1.2)	0/162 (0.0)	0/163 (0.0)
	Halos	7/167 (4.2)	3/165 (1.8)	2/167 (1.2)	2/162 (1.2)	0/163 (0.0)
	Starbursts	15/167 (9.0)	1/165 (0.6)	4/167 (2.4)	1/162 (0.6)	1/163 (0.6)

N = Number of patients in specified category
Preoperative = Screening visit
a The percentages may add up to more than 100% because the categories are not mutually exclusive and patients may have more than 1 symptom
b The symptom was considered present if it was experienced either with or without optical correction
c The number of patients with a symptom divided by the number of patients with both eyes treated who completed the questionnaire at the scheduled visits
d Analysis includes only patients with no symptom of the relevant type preoperatively who completed the questionnaire at the postoperative visit
e Analysis includes only patients with a symptom of the relevant type preoperatively who completed the questionnaire at the postoperative visit

f Responses are based on wearing an optical correction preoperatively and wearing no optical correction postoperatively
g Rates based on either of the following responses: 'A lot of difficulty' or 'So much difficulty that I can no longer do some of my usual activities

Dry eye symptoms were assessed using the **Ocular Surface Disease Index (OSDI)** scores. The percentage of patients with moderate or severe OSDI scores at 3 months (4.8%) and 12 months (5.5%) was lower than the percentage of patients at preoperative (24.5%). Development of dry eye symptoms was reported in 11.5% of patients at 3 months and 11.7% of patients at 12 months. Furthermore, most patients who reported dry eye symptoms (mild, moderate, or severe) pre-operatively experienced a resolution in dry eye symptoms both at 3 months (70.6%) and 12 months (72.1%) (**Table 14**). However, improvement in symptoms of dry eye is likely related to treatment of dry eye symptoms during the post-operative time period, rather than due to the device/procedure.

Table 14
Categorical Statistics for PROWL Questionnaire: Ocular Surface Disease Index (OSDI) Scores at Refractive Stability Visit and Later (Safety Analysis Set)

Measure	Response	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Distribution of OSDI Scores[a]	Normal	98/167 (58.7)	134/165 (81.2)	132/167 (79.0)	128/162 (79.0)	133/163 (81.6)
	Mild	28/167 (16.8)	23/165 (13.9)	24/167 (14.4)	24/162 (14.8)	21/163 (12.9)
	Moderate	22/167 (13.2)	6/165 (3.6)	8/167 (4.8)	9/162 (5.6)	7/163 (4.3)
	Severe	19/167 (11.4)	2/165 (1.2)	3/167 (1.8)	1/162 (0.6)	2/163 (1.2)
Development of Dry Eye Symptoms[b]	Total		11/96 (11.5)	13/97 (13.4)	12/94 (12.8)	11/94 (11.7)
	Mild		8/96 (8.3)	9/97 (9.3)	8/94 (8.5)	7/94 (7.4)
	Moderate		1/96 (1.0)	2/97 (2.1)	3/94 (3.2)	3/94 (3.2)
	Severe		2/96 (2.1)	2/97 (2.1)	1/94 (1.1)	1/94 (1.1)
Resolution of Dry Eye Symptoms[c]			48/68 (70.6)	47/69 (68.1)	45/67 (67.2)	49/68 (72.1)

n = Number of patients in specified category
Preoperative = Screening visit
OSDI based on composite score from 0 to 100; scores were categorized as normal (0-12), mild (13-22), moderate (23-32), and severe (33-100) dry eye disease
[a] N = Number of patients with both eyes treated who completed the questionnaire at the scheduled visits
[b] N = Number of patients with a normal OSDI score at preoperative visit who submitted a questionnaire at the postoperative visits (normal OSDI score at preoperative visit to worse-than-normal score at postoperative visit)
[c] N = Number of patients with a worse-than-normal OSDI score at preoperative visit who submitted a questionnaire at the postoperative visits (worse-than-normal OSDI score at preoperative visit to normal score at postoperative visit

Preoperatively, 2/167 (1.2%) of subjects reported not using glasses or contact lenses for vision in a typical day. Following INNOVEYES LASIK, 149/163 (91.4%) of subjects reported not using glasses or contacts at 12 months. Of the 163 subjects, 9.2% (12 who wore glasses, 3 who wore contact lenses) reported needing correction when reading (**Table 15**).

Table 15
Categorical Statistics for PROWL Questionnaire: Spectacle/Contact Lens Use at Refractive Stability Visit and Later (Safety Analysis Set)

Question	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
In a typical day:					
I do not use glasses or contact lenses	2/167 (1.2)	150/165 (90.9)	152/167 (91.0)	147/162 (90.7)	149/163 (91.4)
I use glasses to correct my vision for distance	139/167 (83.2)	3/165 (1.8)	2/167 (1.2)	3/162 (1.9)	2/163 (1.2)
I use glasses to correct my vision for reading	59/167 (35.3)	13/165 (7.9)	13/167 (7.8)	12/162 (7.4)	12/163 (7.4)
I use soft contact lenses to correct my vision for distance	105/167 (62.9)	2/165 (1.2)	2/167 (1.2)	1/162 (0.6)	1/163 (0.6)
I use soft contact lenses to correct my vision for reading	31/167 (18.6)	2/165 (1.2)	2/167 (1.2)	3/162 (1.9)	3/163 (1.8)
I use hard (rigid gas permeable) contact lenses to correct my vision for distance	3/167 (1.8)	0/165 (0.0)	0/167 (0.0)	0/162 (0.0)	0/163 (0.0)
I use hard (rigid gas permeable) contact lenses to correct my vision for reading	2/167 (1.2)	0/165 (0.0)	0/167 (0.0)	1/162 (0.6)	0/163 (0.0)

N = Number of subjects with both eyes treated with data at visit
n = Number of subjects in specified category
Subjects can have more than 1 response
Preoperative = Screening visit
PROWL = Patient Reported Outcomes with LASIK

At 12 months, 158/161 (98.1%) of subjects who drove reported no difficulty driving during the daytime in familiar places; 3/161 (1.9%) reported a little difficulty. Throughout the postoperative period, no subjects reported giving up driving due to vision.” (**Table 16**).

Table 16
Categorical Statistics for PROWL Questionnaire: NEI-VFQ-25 Driving Scale at Refractive Stability Visit and Later (Safety Analysis Set)

Question	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Have you ever driven a car?					
Yes	166/167 (99.4)	165/165 (100.0)	166/167 (99.4)	161/162 (99.4)	162/163 (99.4)
No	1/167 (0.6)	0/165 (0.0)	1/167 (0.6)	1/162 (0.6)	1/163 (0.6)
Do you currently drive?					
Yes	164/166 (98.8)	162/165 (98.2)	165/166 (99.4)	160/161 (99.4)	161/162 (99.4)
No	2/166 (1.2)	3/165 (1.8)	1/166 (0.6)	1/161 (0.6)	1/162 (0.6)
If you gave up driving, was that mainly because of your vision, mainly for some other reason, or because of both your vision and other reasons?					
Mainly vision	0/2 (0.0)	0/3 (0.0)	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)

Question	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Mainly other reasons	1/2 (50.0)	3/3 (100.0)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)
Both vision and other reasons	1/2 (50.0)	0/3 (0.0)	0/1 (0.0)	0/1 (0.0)	0/1 (0.0)
Because of your vision, how much difficulty do you have driving during the daytime in familiar places? Would you say you have:					
No difficulty at all	146/164 (89.0)	156/162 (96.3)	159/165 (96.4)	158/160 (98.8)	158/161 (98.1)
A little difficulty	15/164 (9.1)	4/162 (2.5)	6/165 (3.6)	2/160 (1.3)	3/161 (1.9)
Moderate difficulty	3/164 (1.8)	0/162 (0.0)	0/165 (0.0)	0/160 (0.0)	0/161 (0.0)
A lot of difficulty	0/164 (0.0)	1/162 (0.6)	0/165 (0.0)	0/160 (0.0)	0/161 (0.0)
Never drive during the daytime because of vision	0/164 (0.0)	1/162 (0.6)	0/165 (0.0)	0/160 (0.0)	0/161 (0.0)
Never drive during the daytime for other reasons	0/164 (0.0)	0/162 (0.0)	0/165 (0.0)	0/160 (0.0)	0/161 (0.0)

N = Number of subjects with both eyes treated with data at visit
n = Number of subjects in specified category
Preoperative = Screening visit
PROWL = Patient Reported Outcomes with LASIK
NEI-VFQ = National Eye Institute Visual Function Questionnaire

At both 3 months and 12 months post-operative, most patients were either very satisfied (30.3% at 3 months; 18.4% at 12 months) or completely satisfied (65.5% at 3 months; 79.1% at 12 months) with their vision (**Table 17**).

Table 17
Categorical Statistics for PROWL Questionnaire: Satisfaction with Current Vision at Refractive Stability Visit and Later (Safety Analysis Set)

Question	Preoperative n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
In general, how satisfied or dissatisfied are you with your present vision?					
Completely satisfied	26/167 (15.6)	108/165 (65.5)	125/167 (74.9)	112/162 (69.1)	129/163 (79.1)
Very satisfied	65/167 (38.9)	50/165 (30.3)	37/167 (22.2)	46/162 (28.4)	30/163 (18.4)
Somewhat satisfied	47/167 (28.1)	6/165 (3.6)	4/167 (2.4)	3/162 (1.9)	4/163 (2.5)
Somewhat dissatisfied	11/167 (6.6)	0/165 (0.0)	1/167 (0.6)	0/162 (0.0)	0/163 (0.0)
Very dissatisfied	12/167 (7.2)	1/165 (0.6)	0/167 (0.0)	1/162 (0.6)	0/163 (0.0)
Completely dissatisfied	6/167 (3.6)	0/165 (0.0)	0/167 (0.0)	0/162 (0.0)	0/163 (0.0)

N = Number of patients with both eyes treated with data at visit
n = Number of patients in specified category

Contrast Sensitivity:

Contrast sensitivity was evaluated preoperatively and postoperatively under mesopic (3 cd/m^2) conditions with and without glare at 4 spatial frequencies (1.5, 3, 6, and 12 cycles per degree, cpd). Eight eyes which were unable to see the reference pattern at a particular spatial frequency were excluded from the analysis. **Table 18** shows that contrast sensitivity improved from baseline, across most spatial frequencies, at refractive stability (3 months).

Table 18
Descriptive Statistics for Change from Baseline for Best Corrected Distance Mesopic Contrast Sensitivity (log unit) at Refractive Stability Visit (Safety Analysis Set)

Visit	Spatial Frequency	n	Mean +/- SD	Median	Percentiles 25%, 75%	Min, Max
Without Glare	1.5 CPD	330	0.018 +/- 0.2982	0.000	-0.100, 0.200	-1.20, 1.30
	3 CPD	330	0.050 +/- 0.2611	0.000	-0.100, 0.200	-1.10, 1.00
	6 CPD	330	0.118 +/- 0.3726	0.100	-0.100, 0.340	-1.10, 1.10
	12 CPD	330	0.074 +/- 0.4172	0.075	-0.200, 0.300	-1.20, 1.60
With Glare	1.5 CPD	330	0.096 +/- 0.4594	0.060	-0.200, 0.340	-2.00, 1.80
	3 CPD	330	0.115 +/- 0.4129	0.100	-0.100, 0.360	-1.40, 1.30
	6 CPD	328	0.168 +/- 0.4514	0.145	-0.135, 0.440	-1.40, 1.70
	12 CPD	326	0.174 +/- 0.4758	0.200	-0.150, 0.500	-1.30, 1.60

SD = Standard deviation, CPD = Cycles per degree
n = Number of eyes with contrast sensitivity test

A clinically significant change in contrast sensitivity was defined as a difference of ≥ 0.30 log unit decrease (loss)/increase (gain) at 2 or more spatial frequencies from preoperative. As shown in **Table 19**, most eyes had either no change in clinically significant contrast sensitivity or an increase in clinically significant contrast sensitivity at all months compared to preoperative under mesopic conditions with or without glare.

Table 19
Incidence of Clinically Significant Changes in Best Corrected Distance Contrast Sensitivity at Refractive Stability Visit and Later (Safety Analysis Set)

Condition	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Mesopic With Glare				
Decrease	52/330 (15.8)	52/334 (15.6)	40/324 (12.3)	46/326 (14.1)
No Change	147/330 (44.5)	142/334 (42.5)	137/324 (42.3)	134/326 (41.1)
Increase	132/330 (40.0)	142/334 (42.5)	152/324 (46.9)	147/326 (45.1)
Mesopic Without Glare				
Decrease	33/330 (10.0)	34/334 (10.2)	31/324 (9.6)	26/326 (8.0)
No Change	216/330 (65.5)	209/334 (62.6)	213/324 (65.7)	208/326 (63.8)
Increase	83/330 (25.2)	93/334 (27.8)	81/324 (25.0)	93/326 (28.5)

N = Number of eyes with data at visit
n = Number of eyes in specified category
Decrease/Increase categories are not mutually exclusive.
Data for eyes that were unable to see the reference patterns were excluded.

Aberrations:

Aberrations were calculated from the Zernike coefficients collected from the INNOVEYES Sightmap. Zernike coefficients were rescaled to represent pupil diameters of either 4 mm and 5.5 mm (**Table 20**). Overall, there was small increase in average root-mean-squared (RMS; absolute value) higher-order aberrations (HOA) at 3 months following surgery, evident with the 5.5 mm standardized wavefront diameter, due to a slight increase in coma. Trefoil was unchanged and there was a decrease in mean RMS spherical aberration.

Table 20
Descriptive Statistics for Aberrometry Results
(Safety Analysis Set)

	4 mm OZ		5.5 mm OZ	
	Preoperative (n=336)	3 Months (n=328)	Preoperative (n=336)	3 Months (n=326)
Parameter	Mean +/- SD	Mean +/- SD	Mean +/- SD	Mean +/- SD
Astigmatism (µm)	0.398 +/- 0.3450	0.164 +/- 0.1209	0.760 +/- 0.6526	0.260 +/- 0.1926
Sphere (µm)	2.641 +/- 1.2135	-0.090 +/- 0.2720	5.202 +/- 2.3237	-0.096 +/- 0.4986
Trefoil (µm)	0.052 +/- 0.0289	0.054 +/- 0.0357	0.109 +/- 0.0586	0.107 +/- 0.0694
Coma (µm)	0.056 +/- 0.0300	0.085 +/- 0.0515	0.125 +/- 0.0646	0.208 +/- 0.1256
Spherical Aberration (µm)	0.034 +/- 0.0293	-0.005 +/- 0.0385	0.109 +/- 0.0854	0.052 +/- 0.1112
Total Higher Order Aberrations (RMSh) (µm)	0.116 +/- 0.0322	0.134 +/- 0.0553	0.254 +/- 0.0713	0.314 +/- 0.1266

OZ = optical zone
n = Number of eyes with data at visit
SD = Standard deviation
RMSh = root mean square, higher order aberrations

2. **Effectiveness Results:**

The analysis of effectiveness was based on the 326 evaluable eyes at the 3-month time point. Key effectiveness outcomes are presented in **Table 21**. At refractive stability (3 months) all primary effectiveness targets were exceeded.

Table 21
Primary Effectiveness Endpoints at Refractive Stability (Full Analysis Set)

Co-Primary Endpoints	INNOVEYES n/N	(%)	Target Rate (%)
UCDVA of 20/40 or better (with pre-op BCDVA of 20/20 or better)	325/325	(100.0)	≥85%
MRSE within ±0.50 D	300/326	(92.0)	≥50%
MRSE within ±1.00 D	321/326	(98.5)	≥75%

N = Number of eyes with data
n = Number of eyes in specified category
Refractive stability achieved at 3 months
Snellen lines were based on the conversion from logMAR line +/- 2 letters (e.g., 20/20 Snellen = -0.04 to 0.04 logMAR).

Primary effectiveness endpoints at 3 months, stratified by preoperative spherical equivalent by INNOVEYES Sightmap Measured Refraction, are presented in **Table 22**. All preoperative groups achieved the effectiveness study targets for UCDVA 20/40 or better (target 85%) and MRSE within 0.50 D (target 50%) and MRSE within 1.00 D (target 75%).

Table 22

Primary Effectiveness Endpoints at Refractive Stability by Preoperative INNOVEYES Sightmap Measured Refraction Spherical Equivalent (Full Analysis Set)

Preoperative INNOVEYES Sightmap Measured Refraction Spherical Equivalent	UCDVA 20/40 or better n/N (%)	MRSE within ±0.50 D n/N (%)	MRSE within ±1.00 D n/N (%)
All Eyes (N)	325/325 (100.0)	300/326 (92.0)	321/326 (98.5)
0 to ≤ -1 D (n=1)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)
> -1 to ≤ -2 D (n=49)	49/49 (100.0)	49/49 (100.0)	49/49 (100.0)
> -2 to ≤ -3 D (n=42)	42/42 (100.0)	42/42 (100.0)	42/42 (100.0)
> -3 to ≤ -4 D (n=34)	33/33 (100.0)	31/34 (91.2)	33/34 (97.1)
> -4 to ≤ -5 D (n=35)	35/35 (100.0)	34/35 (97.1)	35/35 (100.0)
> -5 to ≤ -6 D (n=42)	42/42 (100.0)	39/42 (92.9)	42/42 (100.0)
> -6 to ≤ -7 D (n=52)	52/52 (100.0)	43/52 (82.7)	51/52 (98.1)
> -7 to ≤ -8 D (n=36)	36/36 (100.0)	32/36 (88.9)	35/36 (97.2)
> -8 to ≤ -9 D (n=25)	25/25 (100.0)	19/25 (76.0)	23/25 (92.0)
> -9 to ≤ -10 D (n=9)	9/9 (100.0)	9/9 (100.0)	9/9 (100.0)
> -10 to ≤ -11 D (n=1)	1/1 (100.0)	1/1 (100.0)	1/1 (100.0)
> -11 to ≤ -12 D (n=0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)

UCDVA of 20/40 or better in eyes with preoperative BCDVA of 20/20 or better
n and N = Number of eyes with data
Numerators = Number of eyes in specified outcome category
Refractive stability achieved at 3 months
Snellen lines were based on the conversion from logMAR line +/- 2 letters (e.g., 20/20 Snellen = -0.04 to 0.04 logMAR).
Treatment of diopter ranges indicated by shaded rows and columns is locked out by INNOVEYES software.

Manifest Refraction:

Predictability of refraction is shown in **Table 23**. At 3 months post-op, the majority of eyes, 92% (300/326), were within 0.5 D of target from the point of refractive stability. Most eyes, 91.1 % (297/326), were within 0.50 D of target sphere refraction at the point of refractive stability. At Month 3, 96.1% (174/181) of eyes treated for astigmatism (> -0.50 D) were within ± 1.00 D of cylinder target (zero), and 88.4% (160/181) were within ± 0.50 D of cylinder target.

Table 23

Predictability of MRSE (Full Analysis Set)

Outcome	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Predictability of MRSE within ±0.50 D	287/330 (87.0)	291/334 (87.1)	300/326 (92.0)	300/330 (90.9)	291/320 (90.9)	304/322 (94.4)
Predictability of MRSE within ±1.00 D	320/330 (97.0)	327/334 (97.9)	321/326 (98.5)	324/330 (98.2)	317/320 (99.1)	321/322 (99.7)
Predictability of MRSE within ±2.00 D	330/330 (100.0)	334/334 (100.0)	326/326 (100.0)	330/330 (100.0)	320/320 (100.0)	322/322 (100.0)

Manifest Refraction Sphere (Full Analysis Set)						
Outcome	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Manifest refraction sphere within ±0.5 D	295/330 (89.4)	285/334 (85.3)	297/326 (91.1)	294/330 (89.1)	284/320 (88.8)	297/322 (92.2)
Manifest refraction sphere within ±1.0 D	325/330 (98.5)	324/334 (97.0)	320/326 (98.2)	320/330 (97.0)	312/320 (97.5)	318/322 (98.8)
Manifest Refraction Cylinder (Full Analysis Set with Preoperative Astigmatic Myopia)						
Outcome	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Manifest refraction cylinder ≤ -0.5 D	146/179 (81.6)	145/183 (79.2)	160/181 (88.4)	158/181 (87.3)	145/176 (82.4)	148/177 (83.6)
Manifest refraction cylinder ≤ -1.0 D	176/179 (98.3)	177/183 (96.7)	174/181 (96.1)	179/181 (98.9)	169/176 (96.0)	172/177 (97.2)

Astigmatic myopia is defined as eyes with preoperative manifest refraction cylinder > -0.5 D
N = Number of eyes with data at visit
n = Number of eyes in category

Over-correction and Under-Correction of MRSE:
Table 24 presents the proportion of treated eyes with MRSE over-corrected or under-corrected. At the 3-month refractive stability time point, 3 eyes (0.9%) were over-corrected by > 1.00 D (none by > 2.00 D) and 2 eyes (0.6%) were under-corrected by > 1.00 D (no eyes by > 2.00 D). At 12 months, 1 eye was reported with over-correction > 1.00 D and having UCDVA of 0.24 logMAR.

Table 24
Supportive Effectiveness Endpoint: Over-correction/Under-correction of MRSE (Full Analysis Set)

Outcome	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
Overcorrected by > 1.00 D	1/330 (0.3)	4/334 (1.2)	3/326 (0.9)	6/330 (1.8)	3/320 (0.9)	1/322 (0.3)
Overcorrected by > 2.00 D	0/330 (0.0)	0/334 (0.0)	0/326 (0.0)	0/330 (0.0)	0/320 (0.0)	0/322 (0.0)
Undercorrected by > 1.00 D	9/330 (2.7)	3/334 (0.9)	2/326 (0.6)	0/330 (0.0)	0/320 (0.0)	0/322 (0.0)
Undercorrected by > 2.00 D	0/330 (0.0)	0/334 (0.0)	0/326 (0.0)	0/330 (0.0)	0/320 (0.0)	0/322 (0.0)

N = Number of eyes with data at visit
n = Number of eyes in category
Refractive stability achieved at 3 months

Uncorrected Distance Visual Acuity:
Table 25 presents the distribution of UCDVA results over time for all myopic eyes. All eyes (100%) achieved UCDVA of 20/40 or better at 3 months post-op and later. The majority (≥ 64.1%) of eyes achieved 20/16 or better UCDVA across all postoperative study visits after the point of refractive stability.

Table 25
UCDVA (Full Analysis Set)

Outcome	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
UCDVA of 20/40 or better	329/330 (99.7)	334/334 (100)	326/326 (100)	330/330 (100)	320/320 (100)	322/322 (100)
UCDVA of 20/20 or better	260/330 (78.8)	288/334 (86.2)	301/326 (92.3)	302/330 (91.5)	288/320 (90.0)	304/322 (94.4)
UCDVA equal to or better than the pre-op BCDVA	129/330 (39.1)	174/334 (52.1)	177/326 (54.3)	180/330 (54.5)	174/320 (54.4)	209/322 (64.9)
UCDVA of 20/10 or better	4/330 (1.2)	5/334 (1.5)	4/326 (1.2)	8/330 (2.4)	7/320 (2.2)	8/322 (2.5)
UCDVA of 20/12.5 or better	41/330 (12.4)	69/334 (20.7)	67/326 (20.6)	63/330 (19.1)	74/320 (23.1)	85/322 (26.4)
UCDVA of 20/16 or better	162/330 (49.1)	204/334 (61.1)	218/326 (66.9)	212/330 (64.2)	205/320 (64.1)	226/322 (70.2)
UCDVA of 20/20 or better	260/330 (78.8)	288/334 (86.2)	301/326 (92.3)	302/330 (91.5)	288/320 (90.0)	304/322 (94.4)
UCDVA of 20/25 or better	307/330 (93.0)	320/334 (95.8)	320/326 (98.2)	324/330 (98.2)	314/320 (98.1)	318/322 (98.8)
UCDVA of 20/32 or better	324/330 (98.2)	330/334 (98.8)	325/326 (99.7)	330/330 (100)	319/320 (99.7)	322/322 (100)

N = Number of eyes with data at visit
n = Number of eyes in category
Snellen lines were based on the conversion from logMAR line +/- 2 letters (e.g., 20/20 Snellen = -0.04 to 0.04 logMAR).

Table 26 presents the line difference in postoperative UCDVA achieved compared to preoperative best corrected visual acuity (BCDVA) for all myopic eyes. At 3 months, 85.3% (278/326) of eyes achieved the same or better uncorrected visual acuity than their preoperative best corrected visual acuity.

Table 26
Line Differences for Postoperative UCDVA Compared to Preoperative BCDVA (Full Analysis Set)

Difference from Preoperative	1 Week n/N (%)	1 Month n/N (%)	3 Months n/N (%)	6 Months n/N (%)	9 Months n/N (%)	12 Months n/N (%)
> 2 lines better	0/330 (0.0)	0/334 (0.0)	0/326 (0.0)	0/330 (0.0)	1/320 (0.3)	0/322 (0.0)
2 lines better	0/330 (0.0)	3/334 (0.9)	1/326 (0.3)	1/330 (0.3)	1/320 (0.3)	5/322 (1.6)
1line better	25/330 (7.6)	31/334 (9.3)	41/326 (12.6)	42/330 (12.7)	52/320 (16.3)	40/322 (12.4)
0 lines	197/330 (59.7)	231/334 (69.2)	236/326 (72.4)	235/330 (71.2)	215/320 (67.2)	245/322 (76.1)
1 line worse	76/330 (23.0)	52/334 (15.6)	41/326 (12.6)	45/330 (13.6)	46/320 (14.4)	25/322 (7.8)
2 lines worse	25/330 (7.6)	12/334 (3.6)	4/326 (1.2)	5/330 (1.5)	3/320 (0.9)	6/322 (1.9)
> 2 lines worse	7/330 (2.1)	5/334 (1.5)	3/326 (0.9)	2/330 (0.6)	2/320 (0.6)	1/322 (0.3)

N = Number of eyes with data at visit
n = Number of eyes in category
Line difference categories determined using logMAR values; a 0.1 difference in logMAR equals a 1-line difference.

Cylinder Correction and Vector Analyses:
Table 27 presents the percent reduction of cylinder for eyes with preoperative myopic astigmatism (manifest refraction cylinder > -0.50 D) at refractive stability

stratified by preoperative cylinder. **Table 28** presents the proportions of eyes with residual manifest cylinder magnitude at 3 months and the absolute shift in axis from preoperative.

Table 27
Supportive Effectiveness Endpoint: Reduction of Absolute Cylinder at Refractive Stability (Full Analysis Set with Preoperative Astigmatic Myopia)

Preoperative Cylinder	**n**	**Percent Reduction of Absolute Cylinder Mean [range]**
All Eyes (N)	181	80.911 [-16.67,100.00]
> -0.50 to ≤ -1.00 D	76	76.645 [0.00,100.00]
> -1.00 to ≤ -2.00 D	57	83.496 [-16.67,100.00]
> -2.00 to ≤ -3.00 D	31	83.801 [44.44,100.00]
> -3.00 to ≤ -4.00 D	17	86.046 [46.15,100.00]
> -4.00 to ≤ -4.50 D	0	-

Astigmatic myopia is defined as eyes with preoperative manifest refraction cylinder > -0.5 D
n = Number of eyes with preoperative cylindrical component in category
Increases in cylinder are reported as negative numbers

Table 28
Residual Astigmatic Error at Refractive Stability (Full Analysis Set with Preoperative Astigmatic Myopia)

	Absolute Shift in Axis*					
Residual Cylinder Magnitude	≤5º n/N (%)	>5º to ≤10º n/N (%)	>10º to ≤15º n/N (%)	>15º to ≤30º n/N (%)	>30º n/N (%)	Total
All Eyes (N)						181
0.0 D*	87/181 (48.1)					
> 0.0 D to ≤ -0.5 D	4/181 (2.2)	3/181 (1.7)	3/181 (1.7)	5/181 (2.8)	58/181 (32.0)	
>-0.5 D to ≤ -1.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	14/181 (7.7)	
>-1.0 D to ≤ -2.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	7/181 (3.9)	
>-2.0 D to ≤ -3.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	
>-3.0 D to ≤ -4.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	
>-4.0 D to ≤ -5.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	
>-5.0 D to ≤ -6.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	
> -6.0 D	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	0/0 (0.0)	

Astigmatic myopia is defined as eyes with preoperative manifest refraction cylinder > -0.5 D
*Shifts are defined to be zero for eyes with zero residual cylinder magnitude
n = Number of eyes in category

Vector analysis summary statistics at 3 months are presented in **Table 29** for eyes with preoperative manifest refractive astigmatism of > -0.50 D. The mean absolute error vector (EV) magnitude was less than 0.50 D for all astigmatic eyes (0.240 D ± 0.3198 D), the mean correction ratio (CR) was close to 1.0 (1.138 ± 0.2925) and the mean error ratio (ER) was close to zero (0.186 ± 0.2647).

Table 29
Vector Analysis Summary at Refractive Stability
(Full Analysis Set with Preoperative Astigmatic Myopia)

Preoperative Cylinder	n	|IRC| (Mean ±SD)	|SIRC| (Mean ±SD)	|EV| (Mean ±SD)	CR (Mean ±SD)	ER (Mean ±SD)
All Eyes (N)	181	1.473 ± 0.8126	1.662 ± 0.9448	0.240 ± 0.3198	1.138 ± 0.2925	0.186 ± 0.2647
> -0.50 to ≤ -1.00 D	76	0.764 ± 0.1211	0.883 ± 0.3042	0.170 ± 0.2294	1.151 ± 0.3520	0.227 ± 0.3080
> -1.00 to ≤ -2.00 D	57	1.445 ± 0.2762	1.623 ± 0.4451	0.226 ± 0.3455	1.131 ± 0.2887	0.163 ± 0.2716
> -2.00 to ≤ -3.00 D	31	2.344 ± 0.3175	2.634 ± 0.4544	0.357 ± 0.3516	1.132 ± 0.1883	0.160 ± 0.1650
> -3.00 to ≤ -4.00 D	17	3.150 ± 0.2447	3.500 ± 0.4698	0.386 ± 0.4256	1.114 ± 0.1494	0.125 ± 0.1402
> -4.00 to ≤ -4.50 D	0	-	-	-	-	-

Astigmatic myopia is defined as eyes with preoperative manifest refraction cylinder > -0.5 D
IRC = Intended refractive correction; SIRC = Surgically induced refractive correction; EV = Error vector;
CR = Correction ratio; ER = Error ratio
N = Number of eyes with data
n = Number of eyes in specified category

3. **Subgroup Analyses:**
Evaluation of the co-primary effectiveness endpoints at refractive stability showed no clinically meaningful differences in outcomes based upon preoperative category of MRSE, MR cylinder, race, ethnicity, age, or sex, as well as based on InnovEyes Sightmap measured SE and cylinder. The percentage of eyes meeting the co-primary effectiveness endpoints exceeded prespecified targets when evaluated by preoperative subcategories. There were no eyes with any coprimary safety endpoint observations at refractive stability; therefore, evaluation of the safety endpoints by categories was not performed. The study was not specifically powered for these subgroups.

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

E. Financial Disclosure:
The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 9 principal investigators (PIs) and 33 sub-investigators (SubIs) of which none were full-time or part-time employees of the sponsor. Seven investigators (4 PIs and 3 SubIs) 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: 7
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

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

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

In accordance with the provisions of section 515(c)(2) of the act as amended by the Safe Medical Devices Act of 1990, this PMA was not referred to the Ophthalmic Devices Panel, an FDA advisory committee, for review and recommendation because the information in the PMA substantially duplicates information previously reviewed by this panel.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

Safety and effectiveness evaluation included clinical review interpretation of the observed descriptive reported outcomes for protocol-specified endpoints, considering outcomes that reflect the level of performance of recent refractive laser device approvals rather than the "minimal bar" target rates established in the 1996 FDA guidance document for refractive laser devices.

A. Safety Conclusions:

The risks of the device are based on nonclinical data, as well as data collected in a clinical study conducted to support PMA approval as described above. In the study, safety endpoint outcomes were superior to the target rates specified in the protocol for INNOVEYES LASIK with Sightmap for myopia with and without astigmatism. Refractive stability was achieved at 3 months. At the 3-month stability time point, the reported safety of treatments was superior to protocol endpoint targets, as reported for the proportion of eyes with:

- No eye (0%) with best-corrected distance visual acuity (BCDVA) worse than 20/40 (*for eyes with BCDVA of 20/20 or better pre-op baseline*) (Target ≤ 1%)
- No eye (0%) lost 2 or more lines BCDVA from baseline (Target ≤5%)
- No eye (0%) with increase of manifest refractive astigmatism of > 2.00 D of absolute cylinder as compared to baseline refraction (Target ≤ 5%)
- No eye (0%) had non-flap related SAE at the 3 month visit (Target ≤ 1%).
    - Additional analyses of adverse event safety outcomes included: Ocular Adverse Events (AEs), overall, were reported for 37 of 336 eyes (11.0%), the most common were corneal flap complication (3.3%) and blepharitis (1.2%), all reported as mild; all other ocular AEs were reported at low incidence ≤ 0.9% by type and types typical of LASIK devices.
    - Ocular Serious adverse events (SAEs) were reported for 4 eyes (1.2%) in 3 patients at all study visits after the time of refractive stability; none were deemed related to the procedure or device, and all resolved.
    - There were no adverse device effects reported.
- Additional supportive analyses of safety included:

- Patient Reported Outcomes from PROWL suggest that visual symptoms were similar to those typically following LASIK, and suggest a high rate of patient satisfaction.
- Improvements in mesopic contrast sensitivity with and without glare were reported at 3 months.
- Average post-operative HOA levels (RMS; absolute value) did not raise safety concerns.

B. <u>Effectiveness Conclusions:</u>

Effectiveness endpoint outcomes far exceeded target rates specified in the protocol for the clinical study of INNOVEYES LASIK with Sightmap for correction of myopia with and without astigmatism. Refractive stability was achieved at 3 months. At the 3-month stability time point, the effectiveness outcomes were reported as follows:

- 100% of eyes had uncorrected distance visual acuity (UCDVA) 20/40 or better (*for eyes with preoperative BCDVA of 20/20 or better)* (Target ≥ 85%)
- 92% of eyes with MRSE within 0.50 D of intended (Target ≥ 50%)
- 98.4% of eyes with MRSE within 1.00 D of intended (Target ≥ 75%)
- Additional supportive effectiveness analyses outcomes included:
    - 91.1% of eyes were within 0.50 D of the MR sphere target (i.e., predictability of MR sphere) at 3 months
    - 96.1% of eyes were within ± 1.00 D, and 88.4% were within ± 0.50 D of the MR cylinder target (zero), *in eyes treated for astigmatism > -0.50D (i.e., predictability of MR cylinder*)
    - 1 eye was over-corrected by > 1.00 D MRSE at month 12 and no eyes under-corrected by > 1.00 D
    - UCDVA of 20/20 or better: 92% of eyes at month 3, 94.4% at month 12
    - UCDVA equal to or better than baseline BCDVA: 85.3% of eyes at month 3
    - vector analyses (*for eyes treated for astigmatism*)

Endpoint outcomes far exceed study protocol success targets and are reasonable for recent LASIK device approvals. Lower success rates for higher levels of baseline MRSE are clinically anticipated; however, outcomes for eyes at the upper end of the indicated refractive range still far exceeds endpoint target rates.

C. <u>Benefit-Risk Conclusions</u>

The probable benefits of the device are based on data collected in the clinical study conducted to support PMA approval, as described above. Probable benefit for the INNOVEYES Sightmap is the evaluation of the anterior segment of the eye through the provision of diagnostic data and evaluation of the optical properties of the whole eye in one device that eases planning of customized LASIK. These diagnostic data may be used to screen out patients who are ineligible for surgery or for planning treatment in eligible patients with the intent of improving outcomes.

Additional factors were considered in determining probable risks and benefits for the INNOVEYES, including good quality of the clinical study design and conduct, robustness of analysis of study results, sufficient generalizability of results to the target population described in the indications for use, patient tolerance for risk, alternative available treatments for the refractive condition each with specific risks and benefits, and patient reported outcomes collected in the study. The probable risks of the device are also based on data from the clinical study that was conducted to support PMA approval as described above. Risks for the Sightmap include the possibility of inaccurate measurements from the device which could result in poor refractive outcomes or loss of BCDVA.

In conclusion, given the available information, the data support that for InnovEyes LASIK in conjunction with Sightmap, probable benefits outweigh probable risks.

1. Patient Perspectives:
   Patient perspectives were collected during the study using the Patient Reported Outcomes with LASIK (PROWL) questionnaire. Following INNOVEYES LASIK, a majority of patients reported lower prevalence of visual symptoms at all post-operative visits compared to preoperative (**Table 13**). The percentage of patients with dry eye symptoms was lower at post-operative visits than at preoperative. Although a small percentage of patients developed dry eye symptoms, most patients with preoperative dry eye symptoms experienced a resolution in dry eye symptoms post-operatively (**Table 14**). However, it is noted that improvement in symptoms of dry eye is likely related to treatment of dry eye symptoms during the post-operative time period rather than due to the device/procedure. Following INNOVEYES LASIK, most patients reported not using glasses or contacts (**Table 15**). Additionally, most patients who drove, reported no difficulty driving during the daytime in familiar places. Throughout the postoperative period, no patients reported giving up driving due to vision (**Table 16**). Results from the PROWL questionnaire also showed that most patients were either very satisfied or completely satisfied with their vision after INNOVEYES LASIK (**Table 17**).

In conclusion, given the available information above, the data support that for

"The WaveLight EX500 laser system, in conjunction **with INNOVEYES Sightmap**, is indicated for use in **INNOVEYES Laser Assisted In-Situ Keratomileusis ("wavelight plus"[2] LASIK)** treatments:

- for the reduction or elimination of myopia or myopia with astigmatism, in eyes with spherical equivalent (SE) more than -1.00 and up to -9.00 diopters (D), with up to -8.00 D of spherical component (in minus cylinder format) and up to -3.00 D of astigmatic component at the spectacle plane, based on the INNOVEYES Sightmap Measured Refraction,

2 "wavelight plus" is alternative equivalent trade name for "INNOVEYES™" treatments.

- in patients with magnitude of the spherical equivalent (SE) difference between the Manifest Refraction (MRSE) and the Sightmap measured refraction SE being less than 0.75D,
- in patients who are 18 years of age or older, and
- for patients with documentation of a stable manifest refraction defined as ≤ 0.5 D preoperative spherical equivalent shift over one year prior to surgery."

the probable benefits outweigh the probable risks.

D. Overall Conclusions:

The body of data in this application supports the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. Results from the clinical study demonstrate safety and effectiveness of INNOVEYES LASIK for the correction of myopia with and without astigmatism, as summarized in sections A and B, above. All safety endpoint targets were met at the 3-month stability time point; no eye (0%) had best-corrected distance visual acuity (BCDVA) worse than 20/40 (*for eyes with BCDVA of 20/20 or better pre-op baseline*), no eye (0%) lost 2 or more lines BCDVA from baseline, and no eye (0%) had increase of manifest refractive astigmatism of > 2.00 D of absolute cylinder as compared to baseline refraction), with low rates of adverse events, no unexpected safety findings observed, and AEs consistent with the types of events typically reported in refractive laser studies. In addition, all effectiveness endpoint outcomes far exceeded target rates at the 3-month stability time point; 100% of treated eyes had UCDVA 20/40 or better at 3 months postop, 92% had MRSE within ± 0.50 D of predicted, and 98.4% had MRSE within ± 1.00 D of predicted.

The refractive range included in the Indication for Use is supported by the clinical study cohort, for which there were outcomes available for ≥ 20 eyes per dioptric bin, for myopic sphere correction up to -8.00 D, for cylinder correction up to -3.00 D, and for spherical equivalent correction from more than -1.00 D up to -9.00 D. Since the study only reported 1 eye in the "0 to -1.00 D" bin for "Innoveyes Sightmap Measured Refraction Spherical Equivalent" as was performed in the clinical study and as intended for the marketed INNOVEYES device, the range 0 to -1.00 D is not included in the Indications for Use refractive range to be approved.

Probable benefit includes the potential for reduced dependence or elimination of need for spectacles (glasses) and/or contact lenses for correction of refractive error, due to reduction of manifest spherical equivalent (MRSE) and improvement of uncorrected visual acuity (UCVA). Duration of effect was not evaluated beyond 12 months in the clinical study, which is typical for refractive laser studies to support PMA approval; however, clinical experience provides evidence of long-term refractive outcome duration with some regression over time, of varying degree per individual patient characteristics. Risk mitigation includes patient labeling and professional user labeling, both with appropriate indications, contraindications, warnings, and precautions.

Overall, given the available information as summarized above, the data demonstrate reasonable assurance of safety and effectiveness for INNOVEYES LASIK for the correction of myopia with or without astigmatism for the proposed Indications for Use, and the probable benefits outweigh the probable risks.

XIII. CDRH DECISION

CDRH issued an approval order on March 5, 2025.

XIV. 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.