SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Corneal Inlay

Device Trade Name: Raindrop® Near Vision Inlay

Device Procode: LQE

Applicant's Name and Address: ReVision Optics, Inc.
25651 Atlantic Ocean Drive, Suite A-1
Lake Forest, CA 92630

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P150034

Date of FDA Notice of Approval: June 29, 2016

II. INDICATIONS FOR USE

The Raindrop® Near Vision Inlay is indicated for intrastromal implantation to improve near vision in the non-dominant eye of phakic, presbyopic patients, 41 to 65 years of age, who have manifest refractive spherical equivalent of +1.00 diopters (D) to -0.50 D with less than or equal to 0.75 D of refractive cylinder, who do not require correction for clear distance vision, but who do require near correction of +1.50 D to +2.50 D of reading add.

III. CONTRAINDICATIONS

The Raindrop® Near Vision Inlay is contraindicated in patients who:

- have a corneal thickness that does not allow for a minimum of 300 microns of stromal bed thickness below the flap;
- have an abnormal corneal topographic map of the eye to be implanted;
- have an active eye infection or active inflammation;
- an active autoimmune or connective tissue disease;
- severe dry eye syndrome;
- have keratoconus or is a keratoconus suspect;
- have a recent herpes eye infection or problems resulting from a previous infection;
- have uncontrolled diabetes; or
- have uncontrolled glaucoma.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Raindrop® Near Vision Inlay labeling.

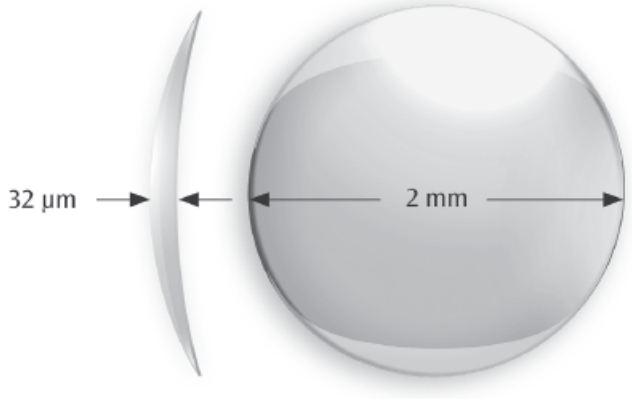
V. DEVICE DESCRIPTION

The Raindrop® Near Vision Inlay **(Figure 1)** is a biocompatible hydrogel corneal inlay designed to be implanted permanently under a femtosecond-laser-created corneal flap onto the stromal bed of the cornea and centered over a light-constricted pupil.

The Raindrop® Near Vision Inlay reshapes the central region of the cornea to provide a zone of increased power for focusing on near objects, resulting in improvement in near vision.

The proprietary, hydrogel material, which is clear and permeable to water, glucose, and oxygen, has a light transmittance in the visible spectrum of 99.7% and a water content of approximately 77%. The refractive index of the hydrogel material is 1.373, effectively the same as that of the human cornea (i.e., 1.376). The Raindrop® Near Vision Inlay is meniscus-shaped with an anterior curvature of 8.53 mm, a posterior curvature of 10.0 mm, a diameter of 2.0 mm, a central thickness of 32 µm, and edge thickness of 12 µm (Figure 1). The Raindrop® Near Vision Inlay is implanted intrastromally under a femtosecond laser flap and centered over the light constricted pupil in the treated eye (non-dominant), where it remains in position without the use of sutures. The Raindrop® Near Vision Inlay provides no significant optical power since its index of refraction is essentially the same as that of the cornea. The presence of the Raindrop® Near Vision Inlay steepens the anterior corneal curvature, increasing the optical power of the eye to provide improved uncorrected near vision in presbyopic patients who do not require distance vision correction. If necessary, the device can be removed after lifting the corneal flap.

Figure 1

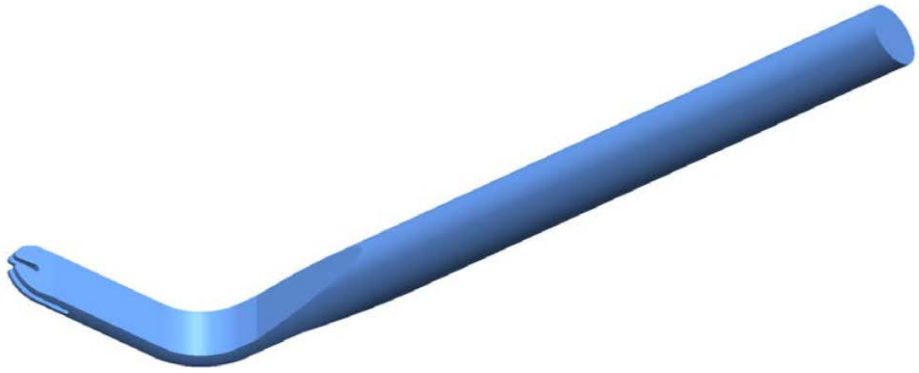


The Raindrop® Near Vision Inlay is pre-loaded into the Inlay Inserter and packaged in a glass vial, which is placed in an inner cup and sealed with a Tyvek lid. The device then undergoes terminal moist heat sterilization. The inner cup is then placed in a larger outer cup, which is placed in a shelf box for shipping and storage. The shelf box packaging of the Raindrop® Near Vision Inlay includes a 5-mL syringe and 22-gauge blunt tip cannula in sterile barrier peel

pouches. The Raindrop® Near Vision Inlay may be distributed either in a single-pack configuration or a 4-pack configuration.

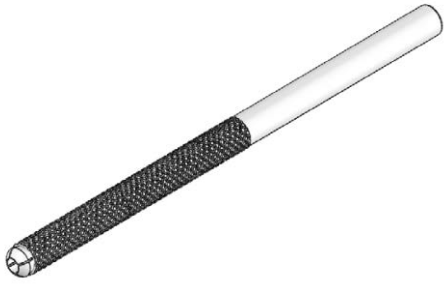
The Inlay Inserter is similar in shape to a hockey stick and made of unalloyed, commercially pure titanium. The hydrated inlay is loaded into the inlay nest at the distal end of the Inserter and a polytetrafluoroethylene (PTFE) cap is placed over the posterior end. The PTFE cap encloses the tip of the Inserter to keep the inlay in place throughout terminal sterilization, transportation, and shelf life. The figure below (**Figure 2**) depicts the Inlay Inserter without the cap.

Figure 2



The Inlay Inserter Chuck Handle (or Inserter Handle) is used in conjunction with the Inlay Inserter to extend the length of the device for ease of use while delivering the Raindrop® Near Vision Inlay. The Inserter Handle is distributed non-sterile and has three components: the handle, the sleeve, and the chuck. Prior to use, it is the responsibility of the user to thoroughly clean and sterilize each component of the instrument, and then assemble it according to the instructions for use. The image below (**Figure 3**) depicts the assembled Inlay Inserter Chuck Handle.

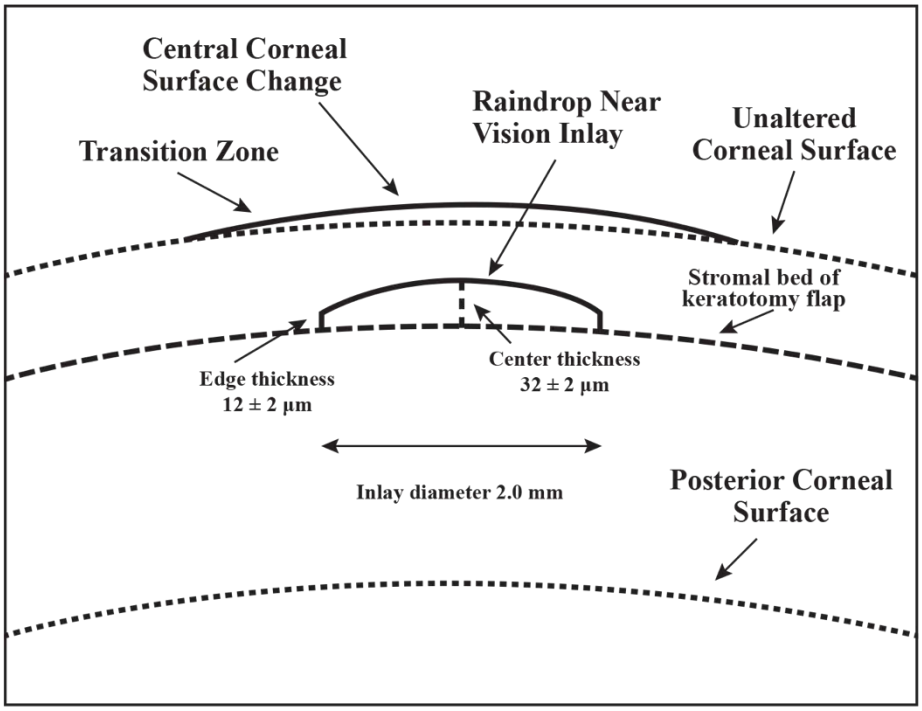
Figure 3



Principle of Operation

When the Raindrop® Near Vision Inlay is placed onto the stromal bed, the inlay volume biomechanically raises the stroma anterior to the device (**Figure 4**). The slight rise in the corneal surface increases the central anterior corneal curvature, thereby increasing the central power of the cornea.

Figure 4



VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of presbyopia. They include the following:

Glasses: Bifocal, trifocal, "reader", and/or progressives glasses have prescription for one, two, or more distances (a range from near to far) in the same lens.

Contact Lenses (monovision, bifocal, trifocal, and multifocal): In monovision, one eye is corrected for distance vision (or no contact lens is used if the uncorrected distance vision is good) and the other eye is corrected for near visionIn addition, there are monofocal, bifocal, trifocal, or multifocal contact lenses that have powers to correct for one, two, or more distances (a range from near to far) in the same contact lens.

Laser Correction (monovision LASIK [Laser-Assisted in Situ Keratomileusis]): Monovision LASIK uses an excimer laser to correct one eye for near vision and the other eye for distance vision.

Conductive Keratoplasty: Conductive keratoplasty is a treatment to reshape the corneal curvature to improve near vision in one eye.

Corneal Inlays: Another commercially marketed inlay is available. orneal inlays are designed to correct presbyopia by implanting a small device in the cornea of one eye.
Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the most appropriate method for that individual.

VII. MARKETING HISTORY

The Raindrop® Near Vision Inlay is commercially available in the European Union and has been distributed in the following countries: Hungary, United Kingdom, Germany, Belgium, Spain, and Portugal. The Raindrop® Near Vision Inlay has not been withdrawn from any country for any reason related to safety and 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.

Implantation of the Raindrop Near Vision Inlay may make the patient's best-corrected distance vision and/or uncorrected distance vision worse than it was before surgery.

In some cases after implantation of the Raindrop Near Vision Inlay, patients may still require glasses or contact lenses for certain activities, such as reading small print.

Vision and Ocular Symptoms. Raindrop Near Vision Inlay implantation may cause or worsen problems with glare, halos, foreign body sensation, and pain. Some of these symptoms may be improved with additional treatment including artificial tears and punctal plugs. However, these symptoms may not resolve, even with treatment.

Contrast Sensitivity. Raindrop Near Vision Inlay implantation may cause decreased contrast sensitivity most noticeable in the inlay implanted eye and under certain lighting conditions, like when driving at night or in very bright light. There could be a further reduction in contrast if the inlay implanted eye were to develop corneal haze and/or either eye were to develop a cataract, glaucoma, macular degeneration, or were to be implanted with a multifocal intraocular lens.

Eye Infections. There is a risk of infection and/or inflammation to the anterior segment of the eye as a result of Raindrop Near Vision Inlay implantation.

Dry Eyes. There is a risk of developing a new dry eye condition or exacerbation of an existing dry eye condition after the implantation procedure. A patient experiencing dry eye symptoms may require treatment with artificial tears, punctal plugs, and/or other therapy depending on the severity of the dry eye condition.

Corneal Complications. Risk of complications to the cornea include, but are not limited to:

- corneal haze
    - in low light conditions greater losses of contrast sensitivity may be experienced
    - best-corrected distance visual acuity may decrease
    - additional steroid therapy may be needed to treat this condition, which may result in an increase in intraocular pressure and faster cataract development than with normal aging (see **Intraocular Pressure**)
- corneal ectasia
    - in a severe case, a corneal transplant might be necessary
- scarring
- epithelial ingrowth requiring a second surgery to remove them
- inlay extrusion, inlay shifts in position, or misaligned flap
- epithelial defects or recurrent corneal erosion
- inflammation, such as diffuse lamellar keratitis (DLK)
- corneal melting or corneal swelling resulting in corneal decompensation that can cause loss of vision and may require transplant of healthy tissue from a donor

Cataract Formation. There is a risk of developing a cataract in the implanted eye as a result of normal aging, which could impact vision in the eye sooner, and to a greater degree, with the inlay present.

Refractive Error Change. When the Raindrop Near Vision Inlay creates a smooth gradient of power, it is inducing a zone of increased negative spherical aberration in the center of the eye which could have the potential for a decrease in uncorrected distance vision. In some cases, removal of the inlay will improve the patient's vision but may take many months. In other cases, removal of the inlay will not improve his or her vision and the decreased vision could become permanent.

Intraocular Pressure. There is a potential risk for intraocular pressure to increase as a result of using ophthalmic medication drops needed to suppress inflammation from inlay implantation following the surgery.

Secondary Surgical Intervention. After Raindrop Near Vision Inlay implantation, a second surgical intervention may be needed to either remove the inlay permanently or to exchange the inlay, primarily due to misalignment over the light-constricted pupil. Other types of surgery may also be needed to treat complications, such as lifting the corneal flap under which the inlay is implanted. Each of these additional surgeries has its own risks, and may or may not completely resolve the problem.

Posterior Segment Complications. There is a potential risk for a retinal detachment or posterior segment vascular event due to the implantation of the Raindrop Near Vision Inlay.

Vision Loss. There is a potential risk for losing best-corrected distance visual acuity after the surgery. In some cases, removal of the inlay will improve the best-corrected distance vision but may take many months. In other cases, removal of the inlay will not improve the vision and the decreased vision could become permanent.

Managing Eye Problems. Cataract surgery may be possible with the inlay in place. However, you may choose to remove the inlay before such surgery. The presence of the inlay may affect eye pressure measurements, making it difficult to detect changes in eye pressure compared to before surgery. Even though the inlay is transparent, viewing, imaging, and treating other eye conditions or structures may be difficult due to the presence of the inlay.

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

IX. SUMMARY OF PRECLINICAL STUDIES

A. Laboratory Studies

1. Biocompatibility

Biocompatibility testing was performed for the corneal inlay and for the inserter and was conducted in conformance with FDA's blue book memorandum #G95-1, "Use of International Standard ISO 10993, Biological Evaluation of Medical Devices, Part 1: Evaluation and Testing," and with the relevant parts of ISO 10993. All biocompatibility testing was performed in compliance with Good Laboratory Practices.

Due to the small size of the corneal inlay, the biocompatibility testing was performed on facsimile samples. These test articles consist of the same materials used to manufacture the Raindrop® Near Vision Inlay that have undergone the same manufacturing and sterilization procedure as the finished device. According to G-95 memorandum, the corneal inlay is categorized as a permanent (over 30 days) implant device. **Table 1** provides the summary of the biocompatibility tests and the results of each test. The results showed that the facsimile samples satisfied the acceptance criteria for all tests.

Table 1: Biocompatibility – Raindrop® Near Vision Inlay (facsimile samples)

Test	Test Method	Test System	Results
Cytotoxicity	MEM Elution ISO 10993-5	L929 mammalian fibroblast cells	Non-cytotoxic
Sensitization	Maximization (SCI and Cottonseed Oil Extracts) ISO 10993-10	Guinea Pig	Non-sensitizer

Acute Systemic Toxicity	USP Systemic Injection (SCI* and Cottonseed Oil Extracts) ISO 10993-11	Mouse	Non-toxic
Subchronic Toxicity (4 weeks)	Subcutaneous Implantation (Test article disks) ISO 10993-6	Rat	Non-toxic
Mutagenicity - Reverse Mutation (Ames)	Ames ISO10993-3	*Salmonella typhimurium* (5 strains) and one strain of E.coli (with and without S-9 metabolic activation)	Non-mutagenic
Mutagenicity - Chromosomal Aberration	McCoy's 5a Culture Medium Extract ISO10993-3	Chinese Hamster Ovary Cells (with and without S-9 metabolic activation)	Negative for inducing chromosomal aberration
Mutagenicity - Mouse Micronucleus	SCI ISO10993-3	Mouse	Non-genotoxic
Implantation (12 weeks)	Intramuscular Implantation ISO 10993-6	Rabbit	Non-irritant
*SCI = 0.9% USP Sodium Chloride Solution			

Additionally, a 12-month eye implant study in swine was conducted to assess the long-term biocompatibility of the corneal inlay in the mammalian cornea. The results of the ocular implantation demonstrate that the test facsimile is biocompatible with the swine's cornea for the duration of the study.

The testing for the delivery device was performed on the finished, sterile Raindrop® Near Vision Inlay Inserter. The Raindrop® Near Vision Inlay Inserter is categorized as a surface device with limited (less than 24 hours) contact. **Table 2** provides the summary

of the biocompatibility testing conducted and the results of each test. These results showed that the Raindrop® Near Vision Inlay Inserter satisfied the acceptance criteria for all tests.

Table 2: Biocompatibility – Raindrop® Near Vision Inserter

Test	Test Method	Test System	Results
Cytotoxicity	MEM Elution ISO 10993-5:1999	L-929 mouse fibroblast cells	Non-cytotoxic
Sensitization – Murine Local Lymph Node Assay	Mouse LLNA (SCI* and DMSO**) ISO 10993-10:2002	Mouse	Non-sensitizer
Intracutaneous Reactivity	Intracutaneous Reactivity (SCI and Sesame Oil Extracts) ISO 10993-10:2002	New Zealand White Rabbit	Non-irritant
Ocular Irritation	Ocular Irritation (SCI* and Sesame Oil Extracts) ISO 10993-10:2002	New Zealand White Rabbit	Macroscopic findings unremarkable Histology findings - Mild irritant compared to control
Acute Systemic Toxicity	Systemic Injection (SCI* and Sesame Oil Extracts) ISO 10993-11:2006	Mouse	Non-toxic
* SCI = 0.9% USP Sodium Chloride Solution ** DMSO = Dimethylsulfoxide			

2. Physicochemical Tests

Preclinical studies were performed on Raindrop® Near Vision Inlay and Raindrop® Near Vision Inlay Inserter. Physicochemical tests were performed to demonstrate long

term safety and stability of the properties of the material used to manufacture the Raindrop® Inlay. See **Table 3** for summary of results.

Table 3: Physicochemical Testing – Raindrop® Inlay Material

Test	Purpose	Test Article Tested	Results
Infrared Scanning	Test for acceptance and identity of raw material.	Raindrop® Near Vision Inlay material and individual base polymer material	Pass
Exhaustive Extraction	Determine the identity/ amount of extractable substances from the materials used in the fabrication of the Raindrop® Near Vision Inlay.	Facsimile samples*	Pass
Testing for Leachables	Identify and quantify any extractable additives and other leachables from materials used in the fabrication of the Raindrop® Near Vision Inlay under physiologic conditions.	Facsimile samples*	Pass
Hydrolytic Stability	Demonstrate the hydrolytic stability of the materials used in the fabrication of the Raindrop® Near Vision Inlay for a time period equivalent to 5 years of real time hydrolytic exposure.	Facsimile samples*	Pass

Photostability	Evaluate stability of device when exposed to UV radiation for the equivalent of 20 years under anticipated conditions of normal exposure.	Raindrop® Near Vision Inlay	Pass

* Due to the small size of the device some of the testing was performed on facsimile samples. Facsimile samples were comprised of the same polymer material as the Raindrop® Near Vision Inlay. In addition, facsimile samples were exposed to the same manufacturing processes as the Raindrop® Near Vision Inlay.

3.Physical Tests

Testing was conducted to verify that the synthesis of the 7822 hydrogel material produces inlays that satisfy physical characterization and optical specifications. Where applicable, the testing was conducted in conformance with relevant provisions of ISO 11979-2:2000 – Ophthalmic Implants – Intraocular Lenses. Part 2: Optical properties and test methods. Testing was performed on three lots of material from polymerized rods which were selected from the beginning, middle and end of the filling process. The following tests (see **Table 4.1**) were conducted from material cut from these rods to evaluate the physical and optical properties of the material.

Table 4.1: Physical Testing – Raindrop® Inlay Material

Test	Purpose	Acceptance Criteria	Results
UV/Vis analysis	To determine light transmittance (100µm thickness)	>93% between 300 nm and 1100 nm	Transmittance ranged from 99.0% to 99.5%, with a mean of 99.2%, passed
Water content	To determine water content across lots (700µm thickness)	Water content should be between 70% and 80%	Water content ranged from 76% to 78%, with a mean of 77%, passed
Refractive index (RI) analysis	To determine consistency of refractive index across lots (700µm thickness)	Refractive index should be 1.376+/- 0.004	RI ranged from 1.372 to 1.375, with a mean of 1.373, passed

Additional physical testing was also performed on the final inlay which evaluated for resolutions efficiency (see **Table 4.2**).

Table 4.2: Physical Testing – Raindrop® Near Vision Inlay Test Article

Test	Purpose	Acceptance Criteria	Results
Resolution efficiency	To evaluate image quality of the lens in order to meet optical specifications – ISO 11979-2	Resolution efficiency ≥60%	Resolution efficiency ranged from 80% to 90%, passed

B. Additional Studies

1. Sterilization, Shelf Life, and Transport Stability

The Raindrop® Inlay is provided pre-loaded into the distal end of the Inserter. The Inserter and Inlay are placed into a saline filled glass vial. A stopper is placed on the vial and a polytetrafluoroethylene (PTFE) cap is secured over the stopper to closure. The glass vial is placed into a polypropylene inner cup, which is heat sealed with a Tyvek® lid. Following sterilization, the sterilized inner cup is placed in an outer cup, topped with a lid, and the entire assembly is then placed into a shelf box with appropriate labeling. The shelf box packaging of the Raindrop® Near Vision Inlay includes a 5-mL Syringe and 22-gauge blunt tip Cannula. The shelf box is provided in either a single pack configuration or a 4-pack shipping configuration.

The Raindrop® Inlay in the inner cup configuration is terminally sterilized by subjecting the finished device to moist heat sterilization. The moist heat sterilization cycle was validated in accordance with ISO 17665-1, "Sterilization of health care products –Moist heat – Part 1: Requirements for the development, validation and routine control of sterilization process for medical devices" and EN 556-1: "Sterilization of Medical Devices – Requirements for Medical Devices to be designated Sterile." The sterilization parameters were validated to achieve a Sterility Assurance Level (SAL) of 10^{-6}.

Shelf life studies have been conducted to verify that the packaging for the Raindrop® Near Vision Inlay maintains a sterile barrier and adequately protects the device through the expiration date on the package label, which is 3 years from the date of sterilization. Shelf life testing has also been conducted to verify that device physical and optical properties satisfy the requirements of the engineering drawings and product specification document through the 3 year labeled expiration date.

The testing was conducted in accordance with the relevant provisions of ISO 11979-6:2007 - Ophthalmic implants – Intraocular lenses - Part 6: Shelf-life and transport stability. Test samples consisted of packaged, finished Raindrop® Inlays that were stored at temperatures ranging from 18º C – 30º C for 3 years from the date of manufacture. The Raindrop® Near Vision Inlay, Inserter, and packaging satisfy sterile

barrier and device performance requirements through the 3 year expiration date on the device label.

Transport stability testing has been conducted on the packaged Raindrop® Near Vision Inlay to verify that the packaging provides adequate protection to the device during transportation, handling, and storage. Test samples consisted of packaged, finished Raindrop® Near Vision Inlays that were packaged in the current shipping configurations. The shipping packaging configurations have been subjected to transport challenges to verify that the device and sterile-barrier packaging is adequately protected from damage during anticipated "worst-case" conditions of transport and handling. The testing was conducted in accordance with the relevant provisions of ISO 11979-6:2007 - Ophthalmic implants – Intraocular lenses - Part 6: Shelf-life and transport stability. All test samples satisfied all acceptance criteria (see **Table 5**).

Table 5: Sterility, Shelf Life, and Transport Stability Testing

Test	Purpose	Acceptance Criteria	Results
Moist Heat Sterilization Validation	Evaluate sterility	No positive biological indicators	Pass
Bacterial endotoxin	Evaluate sterility	< 0.2 EU/device	Pass
Package Evaluation - Inner Cup Dye Penetration Testing	Evaluate whole package integrity	No evidence of dye across seal by a defined channel	Pass
Package Evaluation - Inner Cup Burst Test	Evaluate whole package integrity	Mean burst pressure ≥ 46.1 in H_2O	Pass
Package Evaluation - Vial and Rubber Stopper Bubble Emission Test	Evaluate whole package integrity	No bubbles visible around seal of vial and stopper	Pass
Transport Stability	Evaluate package integrity	Manufacturing specifications met after being subjected	Pass

	and stability of device	to anticipated "worse case" conditions of transportation and handling	

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical trial in the US under IDE G090149 to establish reasonable assurance of safety and effectiveness of implantation of the Raindrop® Near Vision Inlay in the corneal stroma to improve near vision in phakic, presbyopic subjects. Data from this clinical trial were the basis for the PMA approval decision. A summary of the clinical trial outcomes is presented below.

A. Study Design

The first subject was implanted with the Raindrop® Near Vision Inlay on April 6, 2010 and the last subject was implanted on August 20, 2013. The database for this PMA reflected data collected through June 2015 and included 373 subjects. There are 11 investigational sites.

This study is an ongoing, prospective, single-armed, non-masked, non-randomized, multicenter, interventional, clinical trial. A total of 373 consecutive subjects were implanted in their non-dominant eye with the Raindrop® Near Vision Inlay. All subjects are to be followed through 36-months postoperatively at 11 clinical sites. Enrollment of the study was phased in the United States. Thirty eyes were enrolled in the initial phase. During phases two and three, 75 and 268 eyes were enrolled, respectively. Enrollment was closed after 373 subjects were enrolled.

Postoperative evaluations are scheduled at 1 day, 1 week, 1, 3, 6, 9, 12, 18, 24, and 36 months. Additionally, postoperative visits were added at 2, 4, 8, and 30 months during the trial. The primary time point for effectiveness and safety analysis is at 24 month postoperatively. The applicant submitted the PMA after all subjects had reached the 24-month postoperative visit.

The sample size for this study was first calculated based on the criteria below for the primary effectiveness objective, and then adjusted by the need for an adequate sample size to evaluate the safety of the procedure. The primary effectiveness endpoint is the percentage of eyes with improvement in uncorrected near visual acuity (UCNVA) of 20/40 or better at 24 months postoperatively with a target of 75%. The criteria for sample size calculation were:

- The detectable difference (Δ) in the success rate is 10%.
- Significance level is 0.025 (using a lower one-sided exact boundary).
- Statistical power is at least 90%.

- Simulation with exact confidence interval calculation is used in calculating the sample size.

The sample size needed to meet the above requirements was 234 eyes, and with an anticipated 10% dropout rate, a total of 260 eyes had to be enrolled. In order to have a 95% confidence for at least one incidence of a safety event with a rate of 1% being observed, 300 eyes were required. Therefore, a sample size of 400 eyes was proposed in order to ensure a sufficient number of eyes available for follow-up at 36 months.

1. Clinical Inclusion and Exclusion Criteria

   Enrollment in the clinical trial was limited to subjects who met the following inclusion criteria:

   1. Subjects must provide informed consent, have signed the written informed consent form, and been given a copy.
   2. Subjects must be presbyopic adults, needing from +1.50 D to +2.50 D of reading add.
   3. Subjects must have uncorrected near visual acuity worse than 20/40 and better than 20/200 in the non-dominant eye.
   4. Subjects must have an uncorrected distance visual acuity of 20/25 or better in both eyes.
   5. Subjects must have distance visual acuity correctable to at least 20/20 in both eyes.
   6. Subjects must have a near visual acuity correctable to at least 20/20 in both eyes.
   7. Subjects must have a manifest refraction spherical equivalent (MRSE) between -0.50 and +1.00 D with no more than 0.75 D of refractive cylinder in the non-dominant eye.
   8. Subjects must report stable vision, i.e. no change in distance vision and/or MSRE within 0.50 D over prior 12 months.
   9. Subjects must have a tear break-up time (TBUT) of ≥8 seconds
   10. Subjects who are contact lens wearers must discontinue hard or rigid gas permeable lenses for at least 3 weeks and discontinue soft lenses for at least 1 week prior to baseline examination.
   11. Subjects who are contact lens wearers must have two (2) central keratometry readings with regular mires and two (2) manifest refractions taken at least one week apart, with no contact lens wear between. Keratometric values must not differ by more than ±0.50 D in any meridian in the eye to be implanted. Manifest refraction spherical equivalent (MRSE) values must not differ more than ±0.50 D in the non-dominant eye.
   12. Subjects must have a minimum central corneal thickness of ≥ 500 microns in the non-dominant eye.

13. Subjects must have an average corneal power of ≥ 41.00 D and ≤ 47.00 D in the non-dominant eye.
14. Subjects must have mesopic pupil <7.0 mm and photopic pupil >3.0 mm in the non-dominant eye.
15. Subjects aged ≤ 45 years must have an endothelial cell count ≥ 2200 cells/mm^2 in the eye to be implanted. Subjects aged ≥ 46 years must have an endothelial cell count of ≥ 2000 cells/mm^2 in the non-dominant eye.
16. Subjects must be willing and able to return for scheduled follow-up examinations for 36 months after surgery.
17. Subjects must have documented monovision tolerance.

Potential subjects were not permitted to enroll in the clinical trial if they met any of the following exclusion criteria:

1. Subjects with a difference of > 0.75 D between the manifest refraction spherical equivalent and the cycloplegic refraction spherical equivalent.
2. Subjects with anterior segment pathology, including clinically significant cataracts, in the non-dominant eye.
3. Subjects with residual, recurrent, active ocular or uncontrolled eyelid disease, or any corneal abnormality (including endothelial dystrophy, guttata, recurrent corneal erosion, etc.) in the non-dominant eye.
4. Subjects with ophthalmoscopic signs of keratoconus (or keratoconus suspect) in the non-dominant eye.
5. Subjects with clinically significant dry eyes, as determined by Tear Breakup time (TBUT) of < 8 seconds or the presence of greater than mild symptoms of dryness or discomfort or SPK greater than grade 1.
6. Subjects with distorted or unclear corneal mires on topography maps of the non-dominant eye.
7. Subjects who require canthotomy to generate a corneal flap in the non- dominant eye.
8. Subjects with macular degeneration, retinal detachment, or any other fundus pathology that would prevent an acceptable visual outcome in the non-dominant eye.
9. Subjects who have undergone previous intraocular or corneal surgery including cataract and LASIK surgery in the non-dominant eye.
10. Subjects with a history of herpes zoster or herpes simplex keratitis.
11. Subjects who have a history of steroid-responsive rise in intraocular pressure (IOP), preoperative IOP >21 mm Hg, glaucoma, or are a glaucoma suspect.
12. Subjects using systemic medications with significant ocular side effects.

13. Subjects who are pregnant, lactating, or planning to become pregnant during the course of the study.

14. Subjects with known sensitivity to planned study concomitant medications.

15. Subjects who are participating in any other ophthalmic drug or device clinical trial during the time of this clinical investigation.

2. Follow-up Schedule

Subjects are scheduled to return for follow-up examinations according to the following schedule:

Table 6: Follow-up Schedule

Visit	Visit Window
Preoperative Evaluation	Day -90 to Day -1
Operative Evaluation	Day 0
Day 1	1 to 2 days postoperative
1 Week	5 to 9 day postoperative
1 Month	3 to 6 weeks postoperative
2 Months*	7 to 9 weeks postoperative
3 Months	10 to 14 weeks postoperative
4 Months*	15 to 19 weeks postoperative
6 Months	20 to 26 weeks postoperative
8 Months*	27 to 34 weeks postoperative
9 Months	35 to 43 weeks postoperative
12 Months	11 to 14 months postoperative
18 Months	17 to 20 months postoperative
24 Months	22 to 26 months postoperative
30 Months	28 to 32 months postoperative
36 Months	34 to 39 months postoperative

* Visits added in Supplement 12 of G090149 study after enrollment and initial follow-up for a subset of subjects were completed.

The schedule of examinations post-explant is as follows:

- 1 Day
- 1 Week
- 1 Month
- 3 Months
- 6 Months
- Annually after 6-Months if BCDVA is not within 2 lines of baseline.

The evaluations to be performed at each visit are as follows:

1. Ocular dominance: Preoperative
2. Monovision tolerance: Preoperative
3. Near vision with Contact Lens (ETDRS, photopic) 40 cm: Preoperative
4. Pupil size measurement: Preoperative, 6 months

5. Pinhole Acuity (day 1 only)
    - Distance (6 m /20 ft.)
6. Manifest refraction (no auto-refraction): Preoperative, week 1; months 1, 2, 3, 4, 6, 8, 9, 12, 18, 24, 30 (take measurement in both eyes at this time point), 36 (take measurement in both eyes at this time point) and all unscheduled visits.
7. Monocular and Binocular uncorrected visual acuity (ETDRS, photopic): Preoperative, week 1, months 1, 3, 6, 9, 12, 18, 24, 30 (take measurements in both eyes at this time point), 36 (take measurements in both eyes at this time point) and all unscheduled visits.
    - Distance (6 m /20 ft.)
    - Intermediate (80 cm /32 in.)
    - Near (40 cm / 16 in.)
8. Monocular best corrected visual acuity (ETDRS, photopic): Preoperative, week 1; months 1, 2, 3, 4, 6, 8, 9, 12, 18, 24, 30 (take measurements in both eyes at this time point), 36 (take measurements in both eyes at this time point) and all unscheduled visits.
    - Distance (6 m / 20 ft.)
    - Near (40 cm / 16 in.)
9. Monocular distance-corrected near visual acuity (ETDRS, photopic): Preoperative, months 1, 3, 6, 9, 12, 18, 24, 30, 36 and during unscheduled visits when indicated.
10. Monocular and binocular mesopic (with and without glare) and photopic (without glare) contrast sensitivity testing: Preoperative, months 3, 6, 12, 18, 24, 30, 36 and during unscheduled visits when indicated.
11. Slit lamp examination: Preoperative, day 1, week 1; months 1, 2, 3, 4, 6, 8, 9, 12, 18, 24, 30 (take measurement in both eyes at this time point), 36 (take measurement in both eyes at this time point) and all unscheduled visits.
12. Keratometry: Preoperative; months 3, 6, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator.
13. Corneal topography: Preoperative; months 3, 6, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator.
14. Wavefront aberrometry: Preoperative; months 1, 3, 6, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator.
15. Specular microscopy of the corneal endothelium on both eyes: Preoperative, months 3, 6, 9, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator
16. Pachymetry: Preoperative, day 0, and at months 3, 6, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator.

17. Applanation intraocular pressure (Goldmann and Tono-pen): Preoperative, week 1, months 1, 2, 3, 4, 6, 8, 9, 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator
18. Cycloplegic refraction, performed at least 30 minutes after, but no more than 60-75 minutes following two drops of, 1% cyclopentolate hydrochloride separated by five minutes: Preoperative, months 12, 18, 24, 30, 36 and during unscheduled visits when deemed necessary by the investigator
19. Dilated fundus examination: Preoperative, months 12, 18, 24, 30, 36 months and during unscheduled visits when deemed necessary by the investigator.
20. National Eye Institute subject questionnaire: Preoperative, months 3, 6, 12, 18, 24, 30, 36.
21. Visual symptom assessment questionnaire: Preoperative, months 1, 3, 6, 9, 12, 18, 24, 30, 36.

In addition, defocus testing was performed preoperatively and at the 12-month postoperative visits on a subgroup of 30 subjects to assess the effect of the device on vision through the full depth of focus (-5.0 D to +5.0 D).

Adverse events and complications were recorded at all visits.

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

3. Clinical Endpoints

The primary safety endpoint stated in the protocol is as follows:

- Preservation of best corrected visual acuity (primary safety endpoint): less than 5% of eyes should have a loss of two (2) or more lines of best corrected distance visual acuity (BCDVA) and best corrected near visual acuity (BCNVA) at six (6) months and all subsequent visits. Less than 1% of eyes with preoperative BCDVA and BCNVA of 20/20 should have BCDVA and BCNVA worse than 20/40 at six (6) months and all subsequent visits.

However, there is no hypothesis testing in the protocol based upon this stated primary safety endpoint.

The other key safety endpoints specified in the protocol are as follows:

- Refractive Stability: the change in manifest refractive spherical equivalent (MRSE) between two (2) time points performed at least three (3) months apart, should be no more than 0.50 D in 50% of eyes and no more than 1.00 D in 95% of eyes. The mean rate of change in MRSE, as determined by a paired analysis is $\leq$ 0.5 D per year (0.04 D /month) over the same time period. The mean

difference in MRSE should have 95% CI that include zero, or a rate of change attributed to normal aging. The mean rate of change of MRSE decreases monotonically over time, with a projected asymptote of zero, or a rate of change attributed to normal aging. Stability is confirmed at least three (3) months after the stability time point.

- Induced astigmatism: less than 5% of eyes should have postoperative manifest refractive astigmatism at 6 months and all subsequent visits that increases from preoperative baseline by greater than 2.00 D.

- Adverse events and complications: adverse events should occur in no more than 5% of eyes. Any single adverse event should occur in no more than 1% of eyes.

Again, there is no hypothesis testing specified in the protocol for these endpoints.

Additional assessments for safety include intraocular pressure, contrast sensitivity, endothelial cell density, and visual and ocular symptoms.

The primary effectiveness endpoint is defined as follows:

- Improvement in UCNVA (40 cm/16 in) at 24 months postoperatively.
  75% of eyes should achieve UCNVA of 20/40 or better.

For the primary analysis of this effectiveness endpoint, all subjects whose inlays were explanted at or before 24 months were imputed as effectiveness failures, and the 24-month outcomes after inlay exchange were used for subjects who received an inlay exchange at or before 24 months.

According to the protocol, the trial is to be considered a success if both the primary safety (preservation of best corrected visual acuity) and effectiveness (improvement in uncorrected near vision) endpoints meet their targets.

B. Accountability of PMA Cohort

Accountability is shown in **Tables 7.1** through the 6-month post-implantation visit, in **Table 7.2** for the 8- to 36-month post-implantation visits, and in **Table 7.3** for the post-removal visits. At the time of database lock, of 373 subjects enrolled in the PMA study, 92% (344/373) were available for analysis at the 24-month postoperative visit, the primary time point analysis of the safety and effectiveness endpoints, when counting those subjects that had removals as discontinued.

Table 7.1: Accountability (Day 1 – Month 6)

Available for Analysis	Day 1 N=373	Week 1 N=373	Month 1 N=373	Month 2 N=317	Month 3 N=373	Month 4 N=343	Month 6 N=373
	373 (100%)	373 (100%)	371 (99%)	310 (98%)	366 (98%)	332 (97%)	365 (98%)
Post-exchange Data Included in Available for	18	18	18	16	16	16	16
Discontinued	0 (0%)	0 (0%)	2 (1%)	3 (1%)	4 (1%)	5 (1%)	5 (1%)
Explant	0 (0%)	0 (0%)	2 (1%)	2 (1%)	3 (1%)	4 (1%)	4 (1%)
Deceased	0 (0%)	0 (0%)	0 (0%)	1 (0%)	1 (0%)	1 (0%)	1 (0%)
Active[1]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lost to Follow-up[2]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (0%)	1 (0%)	1 (0%)
Missed Visit[3]	0 (0%)	0 (0%)	0 (0%)	4 (1%)	2 (1%)	5 (1%)	2 (1%)
% Accountability[4]	100%	100%	100%	99%	99%	98%	99%

* Interim visits replaced missed visits for 2 subjects at each of 9 and 12 months, and 1 subject at each of 24 and 30 months. All visit-specific testing to be included in the analyses was performed at the interim visits.
[1] Active eyes: eyes not yet seen or not yet eligible for the interval.
[2] Lost to follow-up: eyes that would not be examined at the scheduled visit and are not considered active or discontinued.
[3] Missed visit: eyes not examined at the scheduled visit, but may be seen at a subsequent visit.
[4] % Accountability = [available for analysis / (enrolled-discontinued-active)] x 100

Table 7.2: Accountability (8 - 36 months)

Available for Analysis	Month 8 N=343	Month 9 N=373	Month 12 N=373	Month 18 N=373	Month 24 N=373	Month 30 N=373	Month 36 N=373
	334 (97%)	364 (98%)	361 (97%)	351 (94%)	344 (92%)	175 (47%)	129 (35%)
Post-exchange Data Included in Available for Analysis	16	16	16	16	14	5	3
Discontinued	5 (1%)	6 (2%)	8 (2%)	15 (4%)	21 (6%)	27 (7%)	28 (8%)
Explant	4 (1%)	5 (1%)	7 (2%)	14 (4%)	20 (5%)	26 (7%)	27 (7%)
Deceased	1 (0%)	1 (0%)	1 (0%)	1 (0%)	1 (0%)	1 (0%)	1 (0%)
Active[1]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	161 (43%)	209 (56%)
Lost to Follow-up[2]	1 (0%)	2 (1%)	3 (1%)	4 (1%)	5 (1%)	7 (2%)	7 (2%)
Missed Visit[3]	3 (1%)	1 (0%)	1 (0%)	3 (1%)	3 (1%)	3 (1%)	0 (0%)
% Accountability[4]	99%	99%	99%	98%	98%	95%	95%

* Interim visits replaced missed visits for 2 subjects at each of 9 and 12 months, and 1 subject at each of 24 and 30 months. All visit-specific testing to be included in the analyses was performed at the interim visits.
[1] Active eyes: eyes not yet seen or not yet eligible for the interval.
[2] Lost to follow-up: eyes that would not be examined at the scheduled visit and are not considered active or discontinued.
[3] Missed visit: eyes not examined at the scheduled visit, but may be seen at a subsequent visit.
[4] % Accountability=[available for analysis / (enrolled-discontinued-active)] x 100

Table 7.3: Accountability (Post removal visits)

	Day 1 Post Removal N=27	Week 1 Post Removal N=27	Month 1 Post Removal N=27	Month 3 Post Removal N=27	Month 6 Post Removal N=27
Available for Analysis	26 (96%)	24 (89%)	23 (85%)	19 (70%)	18 (67%)
Discontinued	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
Withdrew Consent	0 (0%)	0 (0%)	0 (0%)	0 (0%)	1 (4%)
Active[1]	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Lost to Follow-up[2]	0 (0%)	1 (4%)	2 (7%)	4 (15%)	7 (26%)
Missed Visit[3]	1 (4%)	2 (7%)	2 (7%)	4 (15%)	1 (4%)
% Accountability[4]	96%	89%	85%	70%	69%

[1] Active eyes: eyes not yet seen or not yet eligible for the interval.
[2] Lost to follow-up: eyes that would not be examined at the scheduled visit and are not considered active or discontinued.
[3] Missed visit: eyes not examined at the scheduled visit, but may be seen at a subsequent visit.
[4] % Accountability=[available for analysis / (enrolled-discontinued-active)] x 100

C. Study Population Demographics and Baseline Parameters

As indicated in **Table 8**, the mean age of the study subjects was 51.3 years, ranging from 41 to 65 years. Of the 373 subjects enrolled in the study, 204 (55%) were females and 169 (45%) were males. Seventy-eight percent of subjects were Caucasian, and the other largest ethnic group was Hispanic (14%). The mean mesopic pupil size was 5.41 mm, and the mean photopic pupil size was 4.04 mm. The majority or 64% (240/373) of non-dominant/operated eyes was the left eye.

Table 8: Population Demographics

	N=373
Race	
Caucasian	290 (78%)
African American	10 (3%)
Asian	6 (2%)
Hispanic	52 (14%)
Other*	15 (4%)
Gender	
Male	169 (45%)
Female	204 (55%)
Age at Consent (Years)	
N	373
Mean (SD)	51.3 (4.3)
Median	51.0
Min, Max	41, 65
Non-Dominant/Op Eye	
OD	133 (36%)
OS	240 (64%)
Photopic Pupil Size (mm)	
n	373
Mean (SD)	4.04 (0.70)
Median	3.90
Min, Max	3.0, 6.9
Mesopic Pupil Size (mm)	
n	373
Mean (SD)	5.41 (0.78)
Median	5.40
Min, Max	3.6, 6.9

	N=373

* Other races: 50% Asian, 50% Caucasian; Armenian; Asian + Caucasian + Hawaiian; Chinese-Hawaiian-Caucasian; Filipino-Spanish; Hawaiian 50%, Caucasian 50%; Hawaiian-Chinese; Hawaiian-Filipino; Hawaiian-Filipino-Italian; Korean-Caucasian; Middle Eastern (N=2); Native American; Pacific Islander; and Polynesian

The distribution of central corneal thickness (CCT) values across the cohort is presented in **Figure 5**.

Figure 5: Distribution of Corneal Thickness

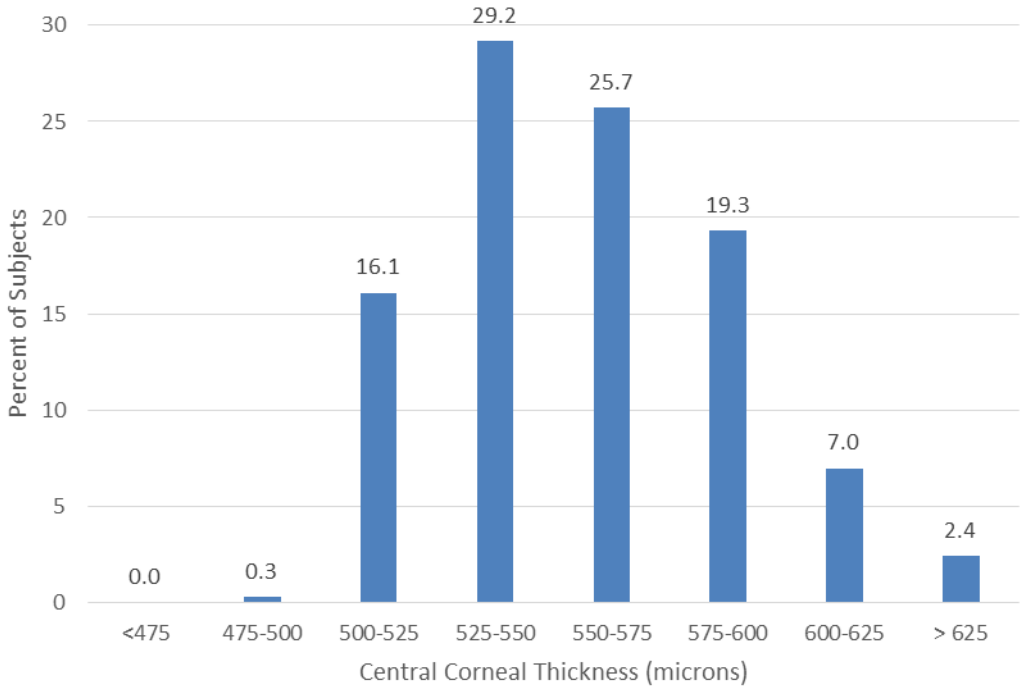


Table 9 provides a summary of the preoperative refractive parameters for all subjects. Mean MRSE was +0.24 D, ranging from -0.50 D to +1.00 D. Mean add power was +1.82 D, ranging from +1.50 D to +2.50 D. Mean cylinder was -0.23 D, with a range from -0.75 D to 0.00 D.

Table 9: Mean Preoperative Refractive Parameters

	Sphere (D)	Cylinder (D)	MRSE (D)	Add (D)
n	373	373	373	373
Mean (SD)	0.359 (0.353)	-0.234 (0.241)	0.242 (0.344)	1.816 (0.245)
Median	0.250	-0.250	0.250	1.750
Min, Max	-0.50, 1.25	-0.75, 0.00	-0.50, 1.00	1.50, 2.50

Not Reported	0	0	0	0

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the 373 subjects that underwent surgery. The key safety outcomes for this study are presented below in Tables **10.1** to **10.2**.

Adverse effects that occurred in the PMA clinical study:

Adverse effects are reported in Tables **10.1** to **10.2**.

Table 10.1: Incidence Of Ocular Adverse Events For Study Cohort

	Through 12 Months N = 373		Through 24 Months N = 373		Through 36 Months N = 373	
	# of Events	# (%) of Subjects	# of Events	# (%) of Subjects	# of Events	# (%) of Subjects
Corneal Epithelial Defect Involving the Keratectomy	2	2 (0.5%)	2	2 (0.5%)	2	2 (0.5%)
Melting of the Flap	0	0 (0.0%)	1	1 (0.3%)	1	1 (0.3%)
Ocular Infection	5	4 (1.1%)	6	5 (1.3%)	8	7 (1.9%)
Epithelial Ingrowth	11	10 (2.7%)	11	10 (2.7%)	11	10 (2.7%)
Lost, Misaligned, or Misplaced Flap	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)
Loss in BCDVA of > 2 Lines (>= 11 Letters) at 3 Months or Later	10	8 (2.1%)	13	10 (2.7%)	14	11 (2.9%)
Late Onset of Haze Beyond 6 Months with Loss of 2 Lines (10 Letters) or More BCVA	4	4 (1.1%)	4	4 (1.1%)	4	4 (1.1%)
Hospitalization	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)
Cataract (with Loss in BCDVA >= 2 Lines at Any Time	0	0 (0.0%)	1	1 (0.3%)	1	1 (0.3%)
Increase in IOP of > 10 mmHg Above Baseline	8	5 (1.3%)	9	6 (1.6%)	9	6 (1.6%)
Diffuse Lamellar Keratitis (DLK)	6	6 (1.6%)	6	6 (1.6%)	6	6 (1.6%)
Secondary Surgical Intervention	35	32 (8.6%)	45	41 (11.0%)	48	44 (11.8%)
Inlay Exchange	19	18 (4.8%)	19	18 (4.8%)	19	18 (4.8%)
Inlay Explant	14	14 (3.8%)	24	24 (6.4%)	27	27 (7.2%)
Flap Lift	2	2 (0.5%)	2	2 (0.5%)	2	2 (0.5%)
Posterior Vitreous Detachment	0	0 (0.0%)	0	0 (0.0%)	1	1 (0.3%)
Broken Orbital Bone	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)
Iritis	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)
Transient Visual Disturbance	1	1 (0.3%)	1	1 (0.3%)	1	1 (0.3%)

All data assigned to a visit, regardless of whether scheduled or not, were used in determining the presence of an adverse event at that visit.
n = number of subjects with the adverse event

Table 10.2: Incidence Of Complications For Study Cohort

	All Eyes N=373 n (%)
Peripheral corneal epithelial defect at 1 month or later	2 (0.5%)
Corneal edema between 1 week and 1 month after the procedure	13 (3.4%)
Central corneal haze	62 (16.6%)
Foreign body sensation at 1 month or later	33 (8.8%)

	All Eyes N=373 n (%)
Pain at 1 month or later	9 (2.4%)
Severe ghost or double images	1 (0.2%)
Severe glare or halos	3 (0.8%)
Severe dry eye beyond 6 months after procedure	1 (0.2%)
Other*	7 (1.8%)
All data assigned to a visit, regardless of whether it was scheduled or not, were used in deter mining complication presence at that visit. n = number of subjects with the complication	

*Other: mild epithelial defect at the flap hinge (n=2), epithelial sloughing causing an abrasion, allergic conjunctivitis, herpes zoster, meibomitis, and viral conjunctivitis.

Sixty-two (62) subjects were noted to have central corneal haze at some point during the three (3) year study. The haze resolved in 55 (89%) of these subjects. Forty (64%) of the subjects had a single incidence of haze with 22 (36%) experiencing recurrent haze.

The adverse event (AE) safety endpoint included two components: AEs should have occurred in less than 5% of eyes and any single AE should have occurred in less than 1% of eyes. The cumulative AE rate exceeded the target rate of 5%. Of the pre-specified 22 AE categories, 7 ocular AE categories exceeded the target rate of 1% as follows:

- Ocular infection: 7/373 (2%)
- Epithelial ingrowth: 10/373 (3%)
- Loss in BCDVA of > 2 lines (≥ 11 Letters) at 3 months or later: 11/373 (3%)
- Increase in IOP of > 10 mm Hg above baseline: 6/373 (2%)
- DLK: 6/373 (2%)
- Secondary Surgical Intervention: 44/373 (12%)
  - inlay exchange: 18/373 (5%)
  - inlay explant: 27/373 (7%)

The reasons for inlay removal are as follows:

- Subject Dissatisfaction With Visual Outcome After Three (3) Months Postoperative: 10/27 (37%)
- Decentration: 2/27 (7%)
- Epithelial Ingrowth: 2/27 (7%)
- Haze: 10/27 (37%)
- Patient's Request: 3/27 (11%)

Visual acuity results for the removal cohort (N=27) at the preoperative visit, the last available visit before inlay removal, one (1) month post removal, three (3) months post removal, six (6) months post removal, and at the last available visit post removal are summarized in **Table 11**.

Table 11: Monocular Best-Corrected Distance Visual Acuity For Removal Cohort

	Preop N=27	Last Available Before Removal N=27	1 Month Post Removal N=23	3 Month Post Removal N=19	6 Month Post Removal N=18	Last Available Post Removal N=27
20/20 or Better	27 (100%)	10 (37%)	15 (65%)	16 (84%)	14 (78%)	20 (80%)
20/25 or Better	27 (100%)	20 (74%)	21 (91%)	18 (95%)	18 (100%)	25 (100%)
20/32 or Better	27 (100%)	25 (93%)	23 (100%)	19 (100%)	18 (100%)	25 (100%)
20/40 or Better	27 (100%)	26 (96%)	23 (100%)	19 (100%)	18 (100%)	25 (100%)
Worse than 20/40	0 (0%)	1 (4%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0	0	2

One (1) subject with epithelial ingrowth was worse than 20/40 (i.e., 20/63) at the last available visit before removal and BCDVA resolved to 20/16 within one week of removal. At six (6) months post removal, BCDVA was 20/12.5 and the epithelial ingrowth had resolved for this subject. At the last available post removal visit, all subjects had 20/25 or better BCDVA.

Table 12 summarizes the change in lines of monocular UCDVA after inlay removal compared to baseline. At one (1) month post removal, five (5) subjects had a loss of ≥ 3 lines. At the subsequent post removal visits and the last available visit post removal, three (3) subjects had a loss of ≥ 2 lines. Twenty-three (23) subjects in the explant cohort had a loss or gain of < 2 lines at the last available visit post removal.

Table 12: Monocular UCDVA After Inlay Removal

	Last Available Before Removal N=27	1 Week Post Removal N=24	1 Month Post Removal N=23	3 Month Post Removal N=19	6 Month Post Removal N=18	Last Available Post Removal N=27
Gain of ≥ 3 lines (≥ 15 letters)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gain of ≥ 2 lines (≥ 10 letters)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gain of > 1 line (> 5 letters)	0 (0%)	0 (0%)	1 (4%)	1 (5%)	0 (0%)	1 (4%)
Within 1 line (± 5 letters)	7 (26%)	10 (43%)	14 (61%)	13 (68%)	13 (72%)	18 (69%)
Loss of > 1 line (> 5 letters)	20 (74%)	13 (57%)	8 (35%)	5 (26%)	5 (28%)	7 (27%)
Loss of ≥ 2 lines (≥ 10 letters)	16 (59%)	6 (26%)	5 (22%)	3 (16%)	3 (17%)	3 (12%)
Loss of ≥ 3 lines (≥ 15 letters)	11 (41%)	4 (17%)	5 (22%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	1	0	0	0	1

Only two adverse events occurred post-removal and these were observed in a single subject. This subject developed epithelial ingrowth at 1 week post removal. To treat the epithelial ingrowth, the investigator lifted the flap (secondary surgical intervention) at the 3 month post removal visit. Complications (i.e., central corneal haze) were reported in ten (10) subjects post removal. These complications resolved in 90% of the

subjects. Central corneal haze was unresolved in one (1) subject at the last post removal visit (6 months post removal).

Of the 373 subjects, 18 subjects had their inlays exchanged during the study. The post-exchange safety and effectiveness data is included in the analyses with the data from the rest of the cohort. The reasons for the exchanges were as follows:

- Inlay Misalignment: 12 subjects (67%)
- Epithelial Ingrowth: 1 subject (6%)
- Other: 5 subjects (28%).

Other includes epithelial nest, inlay not present at postoperative visit, interface debris, striae, and wrinkled inlay.

Preservation of Best Corrected Visual Acuity (Primary Safety Endpoint)

BCDVA is presented in **Table 13**. No subjects after the one (1) month visit had BCDVA worse than 20/40 at any scheduled postoperative visit. Change in BCDVA from preoperative to each postoperative visit is presented in **Table 14**. After the one (1) month postoperative visit, 0% to 2% of subjects experienced a BCDVA loss of ≥ 2 lines at each postoperative visit, which supports an observation that fewer than 5% of eyes should lose ≥ 2 lines of BCDVA at the six (6) month postoperative visit and all subsequent visits. Four (4) subjects experienced a loss of ≥ 2 lines of BCDVA at the 24 month visit.

Table 13: Monocular Best Corrected Distance Visual Acuity Across Study Visits

	Preop N=373	Month 6 N=365	Month 9 N=364	Month 12 N=361	Month 18 N=351	Month 24 N=344	Month 30 N=175	Month 36 N=129
20/20 or Better	373 (100%)	327 (90%)	309 (85%)	316 (88%)	310 (88%)	297 (86%)	151 (86%)	111 (86%)
20/25 or Better	373 (100%)	359 (98%)	359 (99%)	357 (99%)	346 (99%)	340 (99%)	171 (98%)	128 (99%)
20/32 or Better	373 (100%)	365 (100%)	362 (99%)	361 (100%)	351 (100%)	343 (100%)	175 (100%)	129 (100%)
20/40 or Better	373 (100%)	365 (100%)	364 (100%)	361 (100%)	351 (100%)	344 (100%)	175 (100%)	129 (100%)
Worse than 20/40	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
95% CI*	0.0%, 1.0%	0.0%, 1.0%	0.0%, 1.0%	0.0%, 1.0%	0.0%, 1.0%	0.0%, 1.1%	0.0%, 2.1%	0.0%, 2.8%
Not Reported	0	0	0	0	0	0	0	0

* Exact binomial 95% confidence interval for worse than 20/40

Table 14: Change From Preoperative Visit In Lines Of Monocular Best Corrected Distance Visual Acuity Across Study Visits

	Month 6 N=365	Month 9 N=364	Month 12 N=361	Month 18 N=351	Month 24 N=344	Month 30 N=175	Month 36 N=129
Gain of ≥ 2 lines (≥ 10 letters)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Gain of > 1 lines (> 5 letters)	3 (1%)	4 (1%)	0 (0%)	3 (1%)	2 (1%)	1 (1%)	2 (2%)
Within 1 line (± 5 letters)	332 (91%)	321 (88%)	324 (90%)	314 (89%)	309 (90%)	155 (89%)	110 (85%)
Loss of > 1 lines (> 5 letters)	30 (8%)	39 (11%)	37 (10%)	34 (10%)	33 (10%)	19 (11%)	17 (13%)
Loss of ≥ 2 lines (≥ 10 letters)	5 (1%)	7 (2%)	2 (1%)	4 (1%)	4 (1%)	4 (2%)	0 (0%)
95% CI*	0.4%, 3.2%	0.8%, 3.9%	0.1%, 2.0%	0.3%, 2.9%	0.3%, 3.0%	0.6%, 5.7%	0.0%, 2.8%

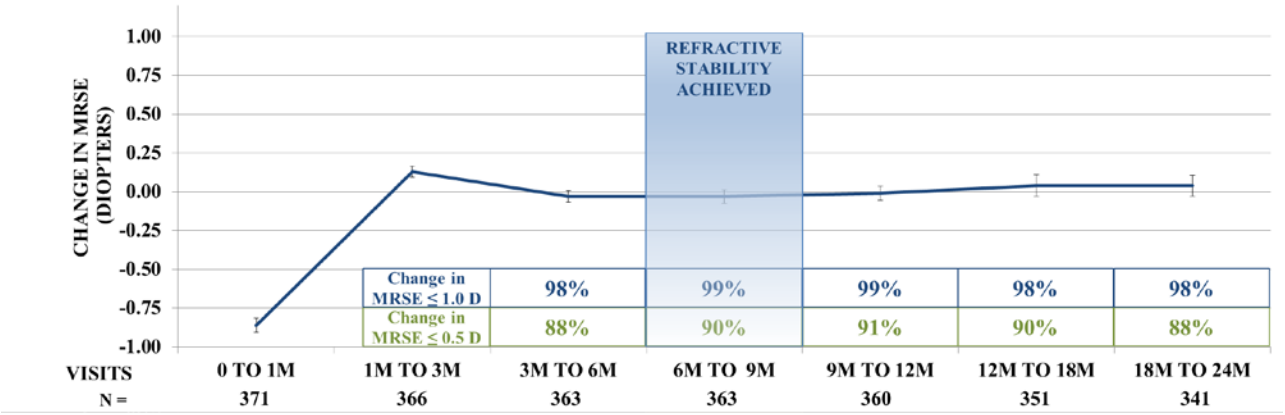
Not Reported	0	0	0	0	0	0	0
1 line = 5 letters * Exact binomial 95% confidence interval							

BCNVA is similar to the results of the BCDVA. One (1) subject reported BCNVA worse than 20/40 (i.e., 20/50) at any scheduled postoperative visit after 1 month (i.e., 9 months). This resolved at an interim visit 5 days later, where the subject had 20/20 BCNVA. A total of 0% to 3% of subjects experienced a BCNVA loss of ≥ 2 lines at each postoperative visit from one (1) month and later. One percent (3/344) of subjects experienced a loss of ≥ 2 lines of BCNVA at the 24 month postoperative visit.

Refractive Stability

Reported in **Figure 6**, stable refraction was demonstrated with at least 98% of subjects experiencing a change in MRSE within 1.0 D between all consecutive postoperative time points and at least 88% of subjects had a change in MRSE within 0.5 D between all consecutive postoperative time points. An annualized mean rate of change in MRSE, as determined by a paired analysis, was less than 0.5 D. Outcomes demonstrate that stability of MRSE following Raindrop® Near Vision Inlay implantation is achieved within six (6) months. The 95% CI for the mean rate of MRSE change includes zero at three (3) months and later.

Figure 6: Stability of Manifest Refraction Spherical Equivalent Over Time



Induced Astigmatism

There were no eyes with manifest refractive astigmatism that increased by greater than 2.00 D at one (1) month and later.

2. Effectiveness Results

   Ninety-two percent (92%, 336/364) of subjects at the 24-month postoperative visit achieved 20/40 or better UCNVA, and the lower bound of the 95% confidence interval (CI) was 89.1%. Therefore, the primary effectiveness endpoint was met.

3. Subgroup Analyses

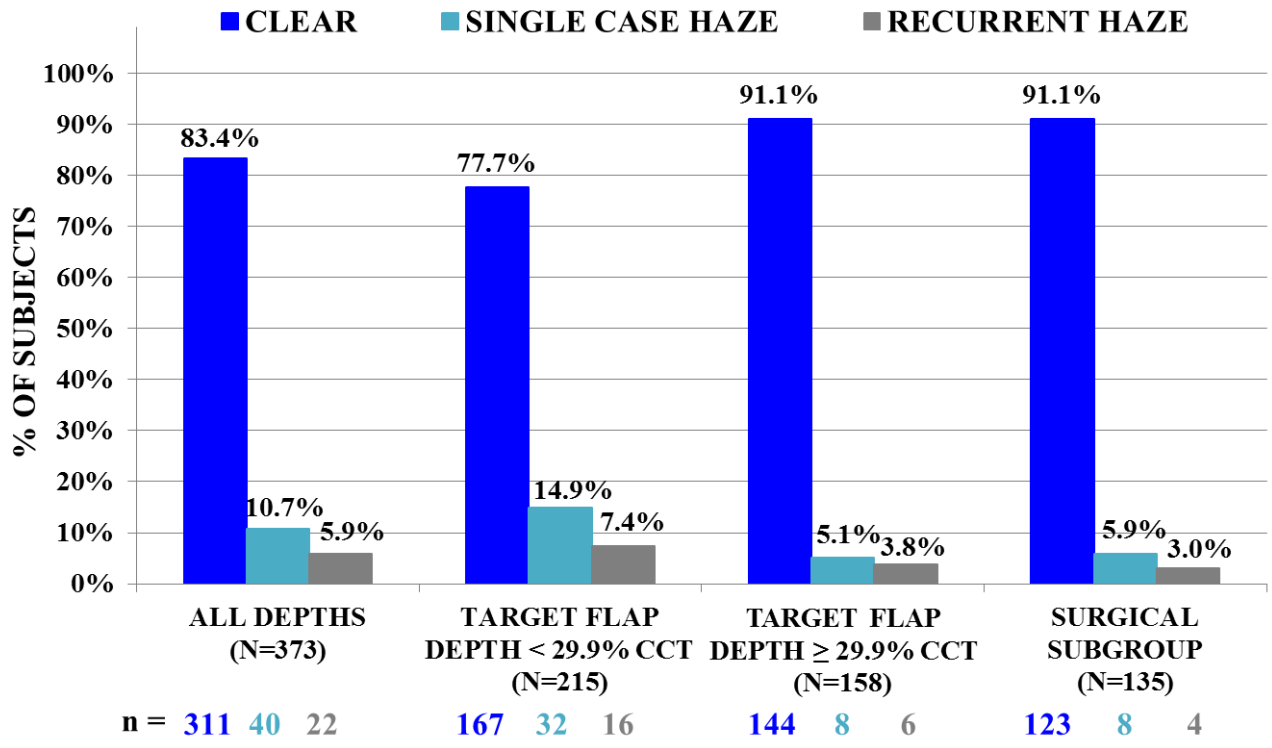
   The pivotal clinical trial was not powered for subgroup analyses.

   Comparison of results with the Raindrop® Near Vision Inlay among different manners in which surgery was performed and the way postoperative topical steroids were prescribed (tapered off within one month vs. tapered off within 3 months) during the clinical study suggest that certain outcomes may be somewhat better using particular surgical parameters

than others and tapering steroids more slowly, although the study was not designed for such comparisons. These comparisons are the basis for recommendations for the parameters in the instructions for use, i.e., targeting the flap depth to 30% of the central corneal thickness (CCT) with a minimum target depth of 150 µm and minimum residual stromal bed thickness of 300 µm, and a flap diameter of 8.0 mm or greater, and the recommendation for the steroid regimen.

There were 135 out of 373 subjects that had surgery performed in this manner using the single-bend inserter referred to as the Surgical Parameters Subgroup, or Surgical Subgroup. **Figure 7** illustrates the difference in incidence of corneal haze among the full cohort, the cohort that had a target flap depth of less than 29.9% of CCT, the cohort that had a target flap depth of greater than or equal to 29.9% of CCT, and the Surgical Subgroup. Out of the 135 Surgical Subgroup subjects, 12 (8.9%) developed central corneal haze postoperatively. Of these 12 subjects, 8 (75%) cases of haze were single incidence and 4 (25%) cases were recurrent haze.

Figure 7: Difference in Corneal Haze



There were 133/133 (100%) Surgical Subgroup subjects with UCNVA of 20/40 or better at 12 months and 128/128 (100%) with this level of vision at 24 months.

No subjects in the Surgical Parameters Subgroup had postoperative BCDVA worse than 20/40 at 1 month postoperatively and at all follow-up visits. After the one (1) month postoperative visit, 0% to 2% of subjects experienced a BCDVA loss of ≥ 2 lines at each postoperative visit, which supports an observation that fewer than 5% of eyes should lose ≥ 2 lines of BCDVA at the six (6) month postoperative visit and all subsequent visits. No subject experienced a loss of ≥ 2 lines of BCDVA at the 24 month visit.

In this subgroup, no subject had BCNVA worse than 20/40 at 1 month postoperatively and at all follow-up visits. After the one (1) month postoperative visit, no subject experienced a BCNVA loss of ≥ 2 lines, which supports an observation that fewer than 5% of eyes should lose ≥ 2 lines of BCNVA at the six (6) month postoperative visit and all subsequent visits.

Refractive stability was demonstrated from 12 months through 24 months. At 3 months and later, at least 97% of subjects experienced a change in MRSE within 1.0 D between consecutive postoperative time points and at least 84% of subjects had a change in MRSE within 0.5 D between all consecutive postoperative time points. An annualized mean rate of change in MRSE, as determined by a paired analysis, was less than 0.5 D from 3 months through 24 months. The 95% CI for the mean rate of MRSE change included zero between the 3-month and 6-month visits and later. Outcomes demonstrate that stability of MRSE following Raindrop® Near Vision Inlay implantation is achieved within six (6) months.

The cumulative rates of ocular adverse events that occurred through 36 months are (N=135):

- Ocular Infection: 1 subject (0.7%)
- Lost, Misaligned, or Misplaced Flap: 1 subject (0.7%)
- Increase in IOP of >10 mmHg Above Baseline: 2 subjects (1.5%)
- Diffuse Lamellar Keratitis: 1 subject (0.7%)
- Inlay Exchange: 5 subjects (3.7%)
- Inlay Removal: 5 subjects (3.7%)
- Iritis: 1 subject (0.7%)

The cumulative rates of complications that occurred through 36 months are (N=135):

- Peripheral Corneal Defect at 1 Month or Later: 1 subject (0.7%)
- Corneal Edema Between 1 Week and 1 Month After Procedure: 3 subjects (2.2%)
- Central Corneal Haze: 12 subjects (8.9%)
- Foreign Body Sensation at 1 Month or Later: 5 subjects (3.7%)
- Pain at 1 Month or Later: 1 subject (0.7%)
- Severe Dry Eye Beyond 6 Months After Procedure: 1 subject (0.7%)
- Herpes Zoster: 1 subject (0.7%)

The Surgical Parameters Subgroup had fewer subjects who eventually had inlays removed. There were 3.7% (5/135) removals in this subgroup. The reasons for removals (number of subjects = 5) were:

- Subject Dissatisfaction With Visual Outcome After 3 Months Postoperative: 2 subjects (40%, 2/5)
- Epithelial Ingrowth: 1 subject (20%, 1/5)
- Haze: 1 subject (20%,1/5)
- Subject's Request: 1 subject (20%, 1/5)

All subjects in this subgroup had BCDVA of 20/20 or better after inlay removal.

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CRF 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangements of, any clinical investigator conducting clinical studies covered by the regulation. The clinical study conducted under IDE G090149 and Protocol P09-0003 included 11 investigators and 30 sub-investigators of which none were full-time or part-time employees of the applicant during the time that they were investigators/sub-investigators. Ten of the investigators/subinvestigators had disclosable financial interests and/or arrangements as defined in 21 C.F.R. §§ 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: **none**
- Significant payment of other sorts: **9**
- Proprietary interest in the product tested held by the investigator: **none**
- Significant equity interest held by investigator in applicant of covered study: **4**

FDA determined that these financial interests/arrangements could have impacted the clinical study outcome. FDA determined the information provided did raise questions about the reliability of the data. The following additional actions were taken and deemed necessary to ensure the reliability of the data (21 CFR 54.5(c)). Therefore, the applicant was asked to perform analyses to determine whether the financial interests/arrangements of clinical investigators had any impact on the clinical study outcomes, which were reviewed by the FDA. The analyses showed that there was a statistically significant lower percentage of subjects who achieved the primary effectiveness endpoint at the sites with PIs with greater financial interests/arrangements, although the target was still met at these sites. Therefore, the FDA concluded that the financial interests/arrangements were unlikely to have influenced the clinical study outcomes in a positive way.

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The following additional results from the pivotal clinical trial were considered:

Contrast Sensitivity:

Contrast sensitivity with best correction was analyzed in the inlay eye and binocularly in mesopic with and without glare and in photopic without glare conditions. At 24 months, on average, subjects experienced a decrease in contrast sensitivity monocularly in each of the different lighting conditions compared to preoperative measurements, while binocularly subjects experienced less of a decrease in contrast sensitivity from preoperative measurements, and mainly under photopic conditions **(Figure 8, 9, and 10)**. For each lighting condition, there were subjects who had clinically significant losses of contrast sensitivity from preoperative measurements defined as a loss of more than 0.3 log units at two or more spatial frequencies or a change from seeing to not seeing the highest contrast test target available at any spatial frequency. The greatest proportions of subjects with clinically significant decreases in contrast sensitivity from preoperative measurement were in mesopic with glare conditions with 37% (127/344) of subjects having clinically significant monocular contrast sensitivity losses and 9% (31/344) having clinically significant binocular contrast sensitivity losses. Subjects that experienced central corneal haze postoperatively generally had greater losses of contrast sensitivity under mesopic with glare conditions than subjects who did not develop haze.

Figure 8: Contrast Sensitivity Mesopic Without Glare Monocular And Binocular Preop And At 24M At Different Spatial Frequencies

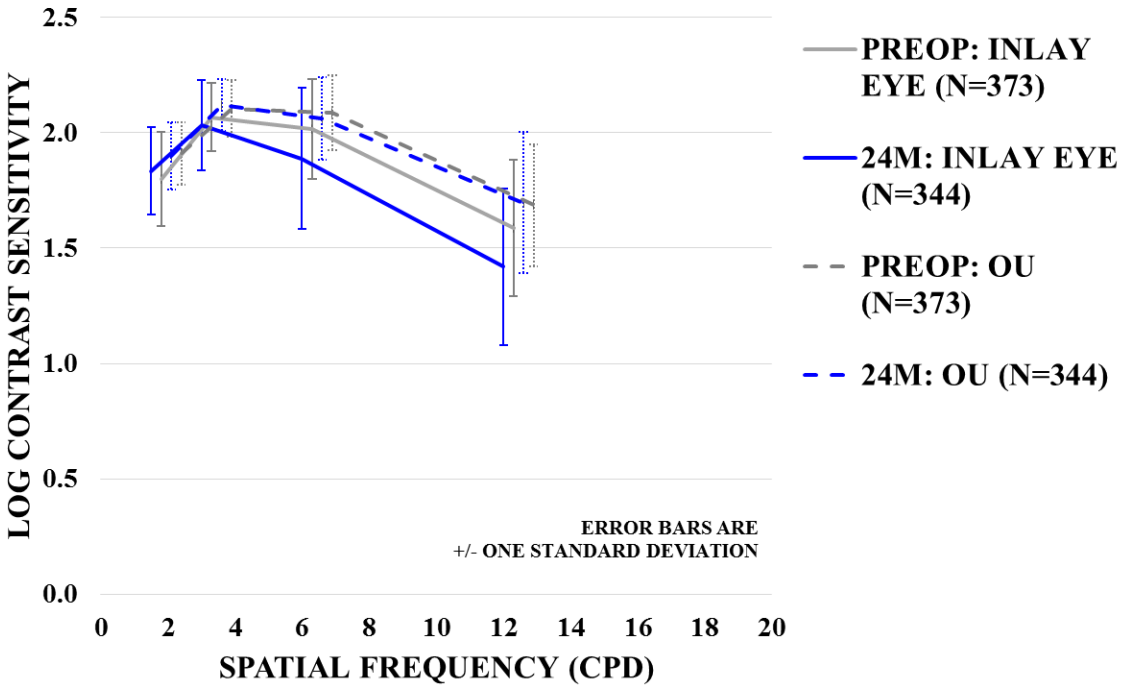


Figure 9: Contrast Sensitivity Mesopic With Glare Monocular And Binocular Preop And At 24M At Different Spatial Frequencies

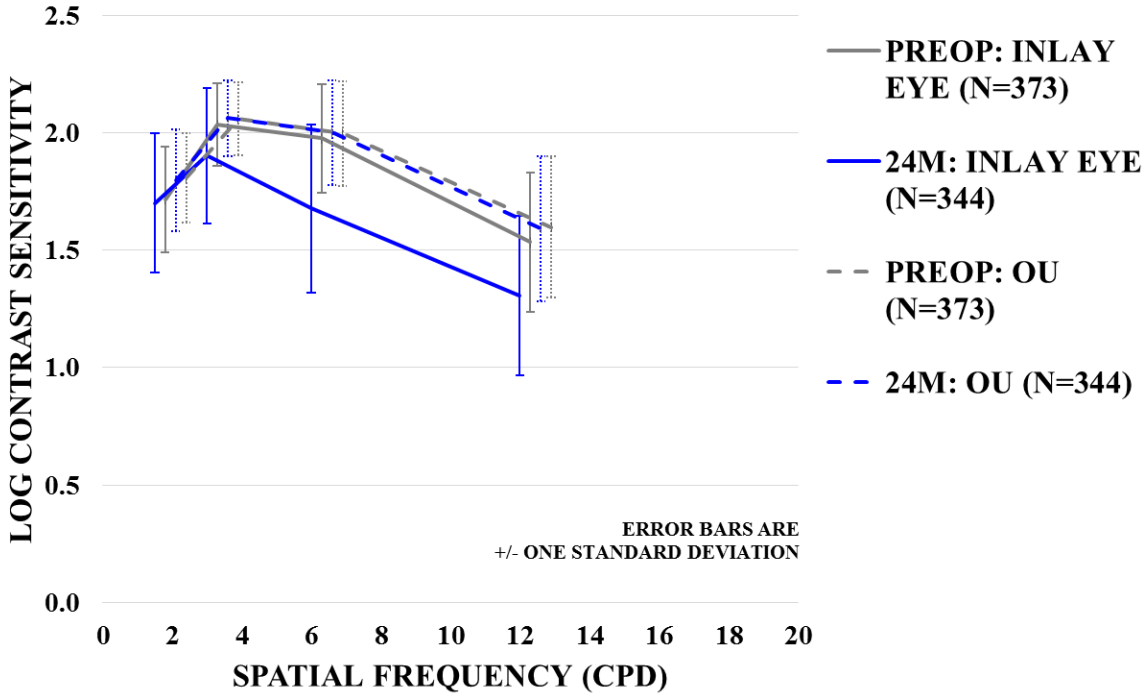
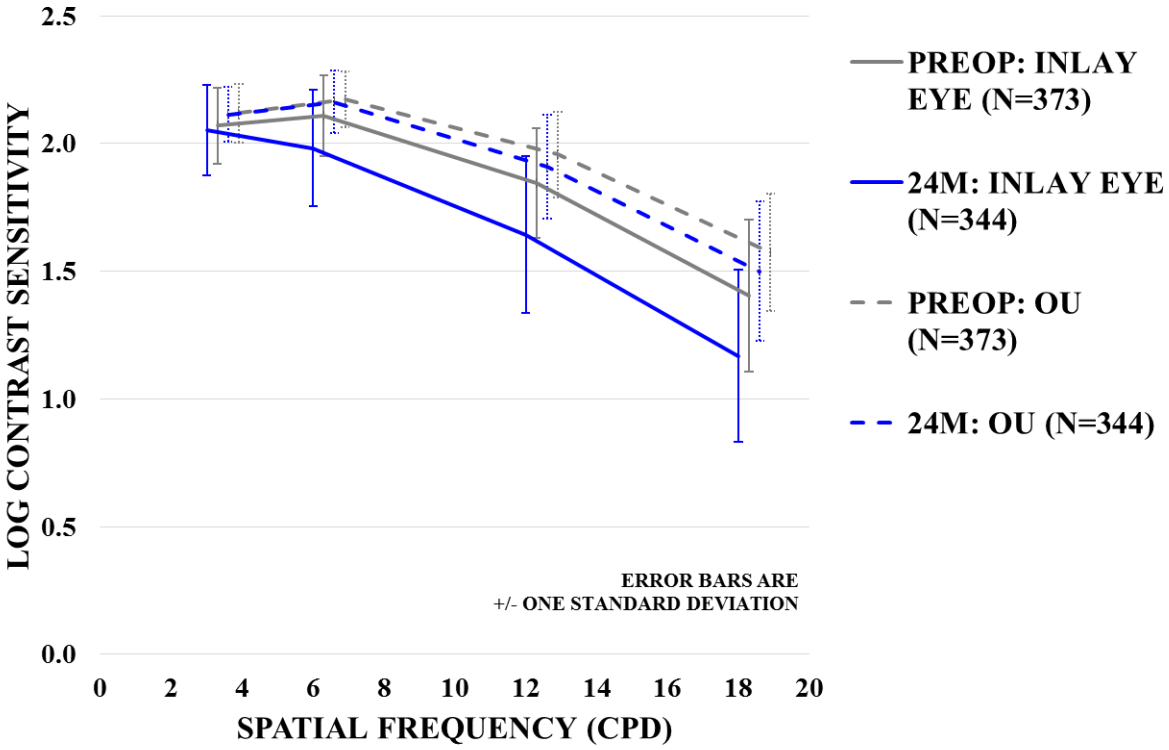


Figure 10: Contrast Sensitivity Photopic Without Glare Monocular And Binocular Preop And At 24M At Different Spatial Frequencies



Endothelial Cell Counts:
Age-related endothelial cell density (ECD) loss rate is estimated to be 0.6% annually. In the clinical trial, the ECD measurements were performed prior to surgery and subsequently at each scheduled follow up visit (3M, 6M, 9M, 12M, 18M, 24M, 30M, and 36M) on both eyes. The mean change from preoperative to any visit up to 24 months was no greater than -17.4 cells/mm^2 ECD loss. Percent change from preoperative mean ECD was also minimal, with no absolute mean change greater than 0.6% through 24 months postoperatively. At 24 months, no subjects lost more than 10% ECD from preoperative measurements and only 4% (14/344) lost between 5% and 10% ECD.

Pachymetry:
The mean change in CCT indicated a mean increase from baseline at all postoperative visits ranging from 20.4 µm at Month 3 to 30.3 µm at Month 30 in the operative eye after receiving the 32-µm thick inlay.

Intraocular Pressure (IOP):
IOP was measured by two instruments at each time point, and Goldmann and Tono-Pen tonometer measurements were compared at each visit. During the study, at each visit, the mean of the differences was < 0.5 mmHg and was not considered clinically relevant. Furthermore, the mean of the differences varied in sign indicating that the Goldmann and the Tono-Pen techniques measured relatively higher or lower at different visits, although on average, the Goldmann measurements tended to be slightly higher that the Tono-Pen measurements within subjects at most postoperative time points.

Using Goldmann, the preoperative mean IOP was 14.9 (SD 2.7) mmHg. The mean IOP postoperative ranged from 16.2 (SD 3.9) mmHg at one (1) month to 13.8 (SD 2.5) mmHg at 24 months. The mean change in IOP was greatest at month one (1) (1.3 mmHg, SD 3.5) and was approximately -1.0 mmHg at every time point from three (3) months through 24 months postoperative. Similar trends were seen with the Tono-Pen measurements, although the mean changes from the preoperative visit were slightly less with the Tono-Pen at every time point at 3 months and later.

Six (6) subjects experienced an IOP increase > 10 mmHg from the preoperative visit during the early postoperative period. All resolved.

Within-Subject Change in Uncorrected Near and Uncorrected Distance Visual Acuity:
After surgery, the average improvement in monocular UCNVA was 5 lines from baseline. At 24M, 97.6% (336/344) of subjects gained 2 or more lines of UCNVA in the inlay eye. The average change in monocular UCDVA after surgery was a decrease of 1.2 lines from baseline. At 24M, 43% (148/344) of subjects had a decrease of 1 or more lines of UCDVA in the inlay eye.

When the change in monocular UCNVA and monocular UCDVA are examined in combination, the proportion of subjects who did not gain 2 or more lines of UCNVA and who lost more than

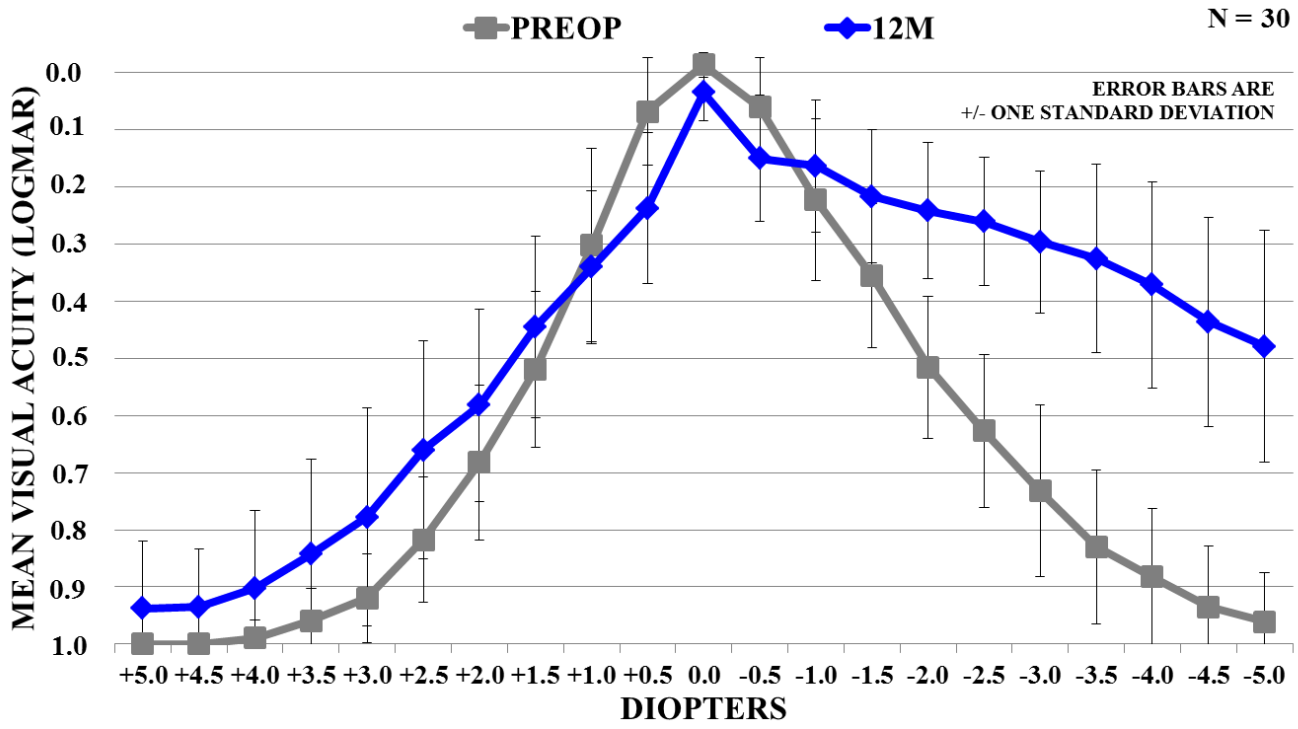
1 line of UCDVA was 1.4% (5/344) at 24 months, and 56.1% (193/344) of subjects gained 2 or more lines of UCNVA with a minimal loss of UCDVA (i.e., ≤ 1 line loss).

The ratio of the number of subjects with significant gain in UCNVA (i.e., ≥ 2 lines) with minimal loss of UCDVA (i.e., ≤ 1 line loss) over the subjects without significant gain in UCNVA with minimal loss of UCDVA was 39 (193/5).

Defocus Curve:

In a subset of subjects (n = 30), defocus curves in the implanted eye were tested preoperatively and at the 12-month follow-up visit. In **Figure 11**, the flatter postoperative defocus curve with negative defocus compared to the preoperative one supports the mechanism of action of the Raindrop® Near Vision Inlay – increasing the power of the cornea centrally to improve near vision.

Figure 11: Preoperative and Postoperative Monocular Defocus Curves



Ocular and Visual Symptoms:

Ocular and visual symptoms were self-reported and rated by the following five categories: Absent, Mild, Moderate, Marked, and Severe. Because the questionnaire used was not developed with patient input, the true symptoms rates and their severity may be different than the study rate. However, the estimates observed in the study are shown in **Tables 15 and 16** for all subjects by category preoperatively and postoperatively at 24 months.

Table 15: Ocular Symptoms Preop And At Month 24

	Pain		Foreign Body Sensation		Light Sensitivity	
	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344
Absent	371 (99%)	342 (99%)	366 (98%)	343 (100%)	349 (94%)	313 (91%)
Mild	2 (1%)	2 (1%)	7 (2%)	1 (<1%)	22 (6%)	29 (8%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	2 (1%)	2 (1%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0	0	0

	Tired Eyes		Dryness		Discomfort	
	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344
Absent	293 (79%)	302 (88%)	321 (86%)	201 (59%)	327 (88%)	315 (92%)
Mild	75 (20%)	37 (11%)	51 (14%)	119 (35%)	43 (12%)	28 (8%)
Moderate	5 (1%)	5 (1%)	1 (<1%)	23 (7%)	3 (1%)	1 (<1%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	1	0	0

Table 16: Visual Symptoms Preop and At Month 24

	Glare		Halos	
	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344
Absent	351 (94%)	235 (68%)	356 (95%)	234 (68%)
Mild	19 (5%)	101 (29%)	17 (5%)	99 (29%)
Moderate	3 (1%)	6 (2%)	0 (0%)	10 (3%)
Marked	0 (0%)	2 (1%)	0 (0%)	1 (<1%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0

	Blurred Vision		Double Vision		Fluctuation of Vision	
	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344	Preop N=373	Month 24 N=344
Absent	361 (97%)	253 (74%)	373 (100%)	310 (90%)	360 (97%)	253 (74%)
Mild	9 (2%)	80 (23%)	0 (0%)	28 (8%)	12 (3%)	85 (25%)
Moderate	3 (1%)	7 (2%)	0 (0%)	5 (1%)	1 (<1%)	5 (1%)
Marked	0 (0%)	3 (1%)	0 (0%)	1 (<1%)	0 (0%)	1 (<1%)
Severe	0 (0%)	1 (<1%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0	0	0

The estimates observed in the study for the Surgical Parameters Subgroup are shown in **Tables 17 and 18.**

Table 17: Ocular Symptoms Before Surgery And At The 24 Month Visit for Surgical Parameter Subgroup

	Pain		Foreign Body Sensation		Light Sensitivity	
	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128
Absent	135 (100%)	128 (100%)	135 (100%)	128 (100%)	131 (97%)	122 (95%)
Mild	0 (0%)	0 (0%)	0 (0%)	0 (0%)	4 (3%)	6 (5%)
Moderate	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0	0	0

	Tired Eyes		Dryness		Discomfort	
	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128
Absent	111 (82%)	115 (90%)	117 (87%)	78 (61%)	122 (90%)	122 (95%)
Mild	24 (18%)	12 (9%)	18 (13%)	44 (35%)	13 (10%)	5 (4%)
Moderate	0 (0%)	1 (1%)	0 (0%)	5 (4%)	0 (0%)	1 (1%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	1	0	0

Table 18: Visual Symptoms Before Surgery And At The 24 Month Visit for Surgical Parameter Subgroup

	Glare		Halos	
	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128
Absent	127 (94%)	90 (70%)	131 (97%)	89 (70%)
Mild	8 (6%)	38 (30%)	4 (3%)	38 (30%)
Moderate	0 (0%)	0 (0%)	0 (0%)	1 (1%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0

	Blurred Vision	Double Vision	Fluctuation of Vision

	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128	Preop N=135	Month 24 N=128
Absent	134 (99%)	95 (74%)	135 (100%)	120 (94%)	133 (99%)	91 (71%)
Mild	1 (1%)	30 (23%)	0 (0%)	6 (5%)	2 (1%)	36 (28%)
Moderate	0 (0%)	3 (2%)	0 (0%)	2 (2%)	0 (0%)	1 (1%)
Marked	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Severe	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)
Not Reported	0	0	0	0	0	0

Uncorrected Visual Acuity for the Full Cohort

The following figures represent supplemental information of parameters assessed during the trial and are provided in the physician labeling:

Figure 12: Monocular UCNVA At Preop And 24 Months Postop Visit

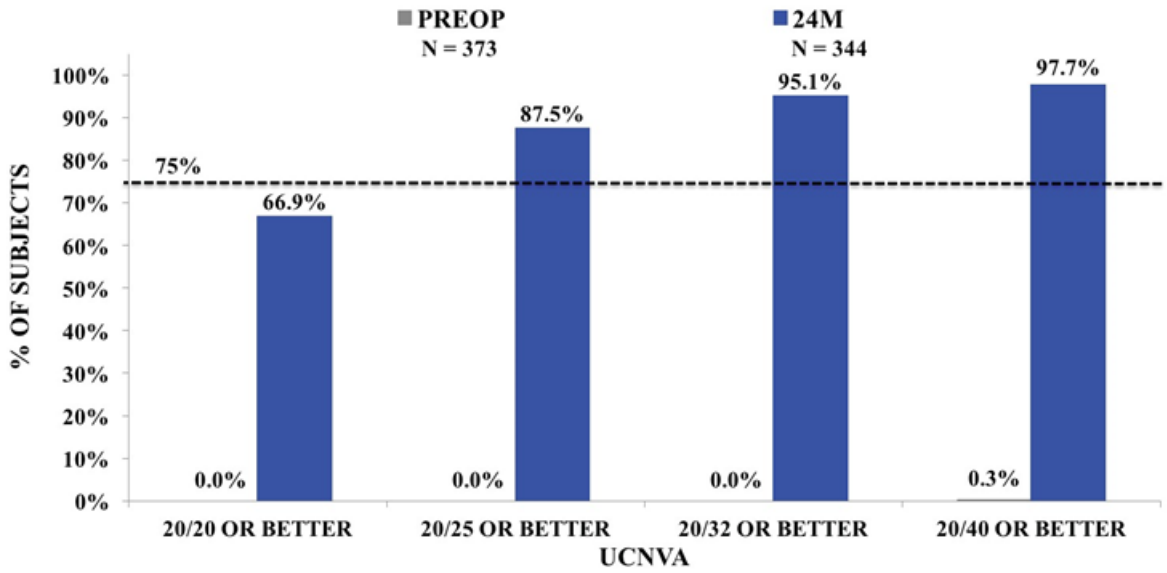


Figure 13: Monocular UCIVA At Preop And 24 Months Postop Visit

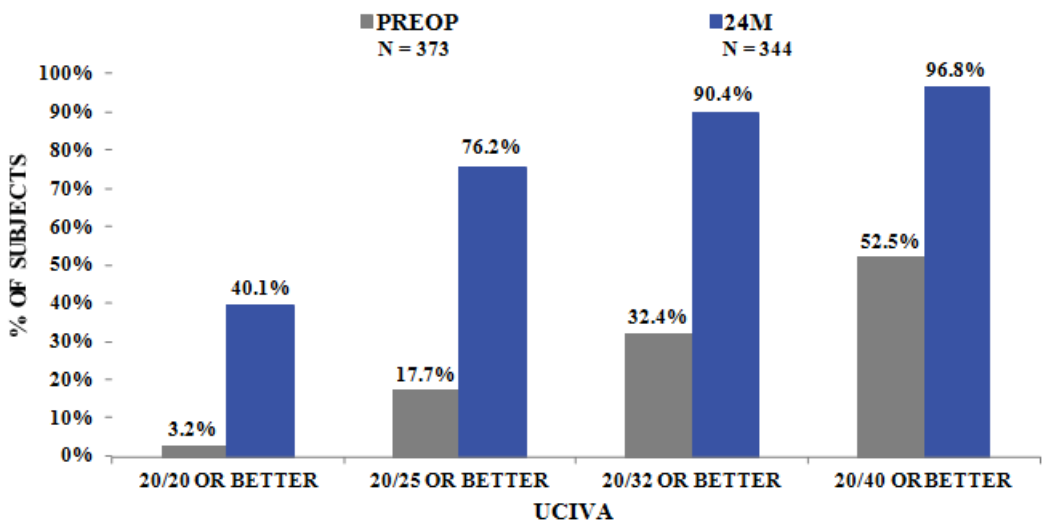


Figure 14: Mean Monocular Uncorrected Visual Acuity At Near, Intermediate, and Distance Across Study Visits

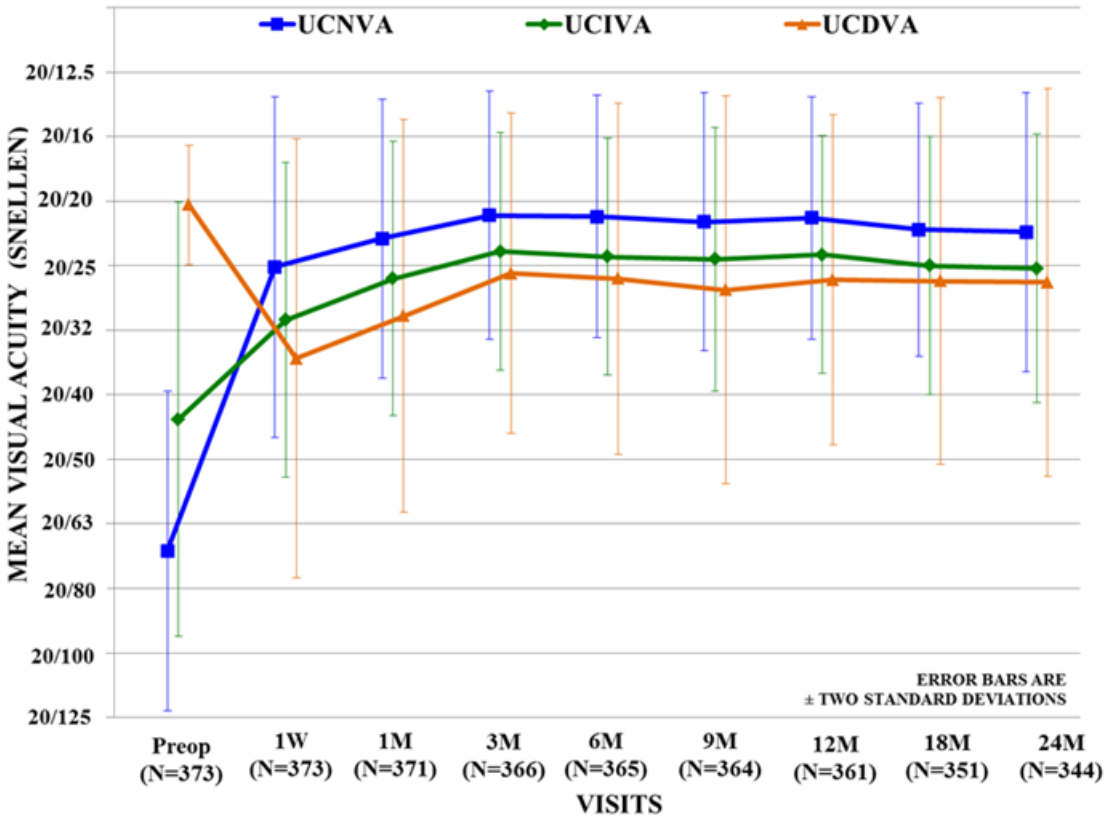


Figure 15: Mean Change in Lines from Preop Across Study Visits

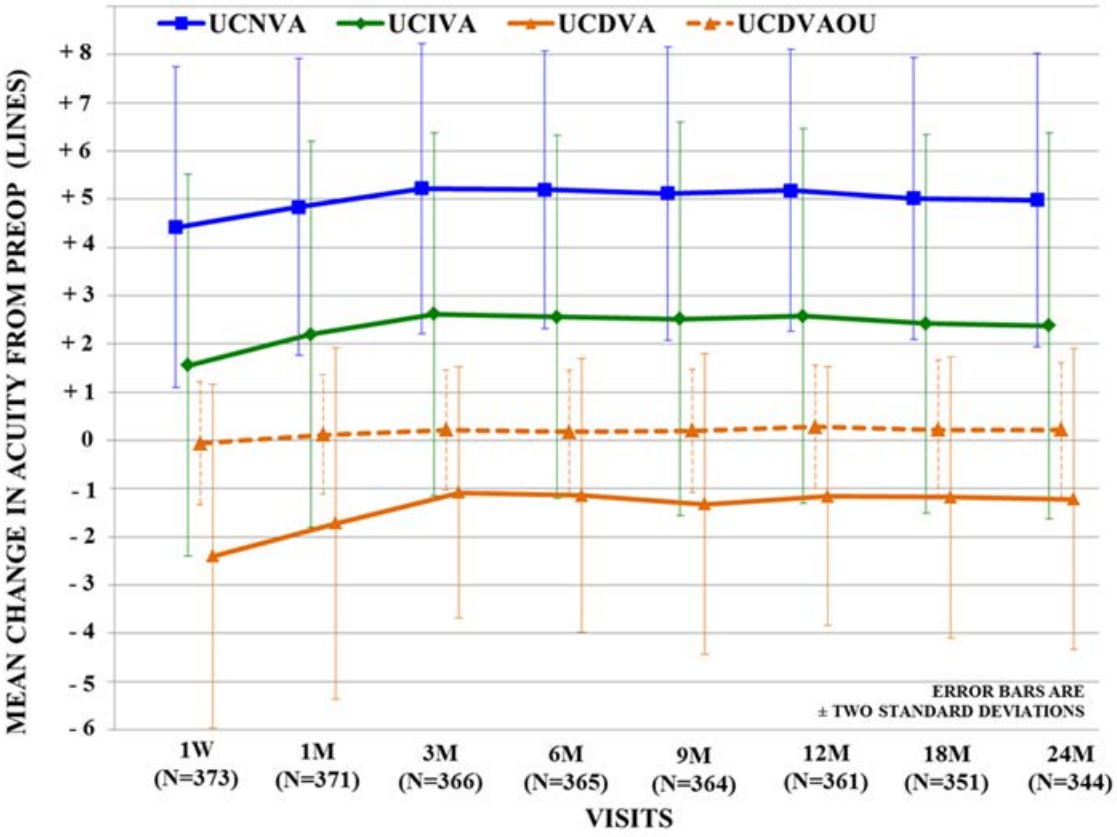
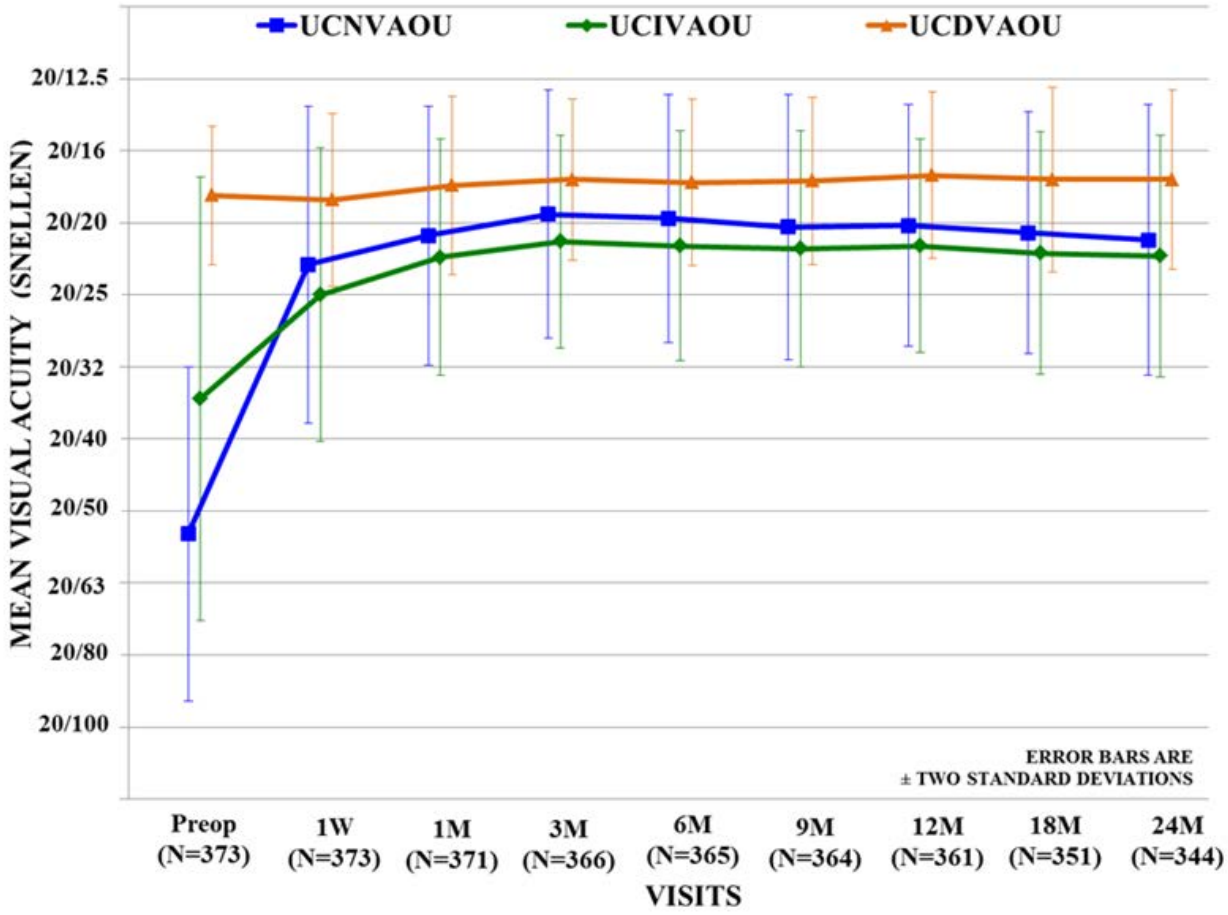


Figure 16: Mean Binocular Uncorrected Visual Acuity At Near, Intermediate, And Distance Across Study Visits



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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The target for the primary effectiveness endpoint of the clinical trial was met, and the success criterion was met.

B. Safety Conclusions

Although there was no hypothesis testing for the primary safety endpoint, the target for the primary safety endpoint of the clinical trial was met.

Since the primary effectiveness and safety endpoints were met, the clinical trial was considered a success per the pre-specified criteria in the protocol.

The risks of the device are based on the data collected in animal studies, the clinical trial conducted to support PMA approval as described above, as well as evidence from the literature. The risks of the Raindrop® Near Vision Inlay implantation include:

- Vision and Eye Symptoms, such as, glare, halos, blurred vision, double vision, fluctuation of vision, dryness, foreign body sensation, and pain.
- Decreased Contrast Sensitivity.
- Eye Infections.
- Dry Eye Syndrome.
- Corneal Complications, such as, haze, ectasia, scarring, epithelial ingrowth, inlay extrusion or malposition, flap dislocation, epithelial defect, inflammation, melting of the corneal tissue, edema.
- Increased Eye Pressure related to postoperative steroid therapy to prevent and treat complications of inlay implantation.
- Need for Inlay Removal or Other Additional Surgery, e.g., flap lift, inlay exchange.
- Vision Loss.
- Potential Retinal Complications.
- Potential Difficulty Diagnosing and Managing Eye Diseases, such as, retinal diseases, glaucoma, cataract.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in the clinical trial conducted to support PMA approval as described above.

The risks may be mitigated by the labeling, including recommendations regarding the following:

- Proper patient selection,
- Specific surgical parameters
- Postoperative medication regimens, including slow taper of postoperative steroids

Risks are also mitigated by the fact that the device is intended to be implanted in only one

eye.

Careful patient selection according to the labeling and a thorough informed consent process will be of the utmost importance.

1. Patient Perspectives

   A questionnaire was administered during the clinical trial to collect information on the rate and severity of patient symptoms. However, caution must be used in interpreting the data, given that patient input was not provided in developing the questionnaire; the true symptom rates and their severity may be different than the trial rates. A quality of life questionnaire was also administered, but the tool was not fit for purpose in this intended use population. Therefore, it did not play a role in the PMA decision and was not be included in the labeling.

In conclusion, given the available information, the probable benefits outweigh the probable risks of the Raindrop® Near Vision Inlay for intrastromal implantation to improve near vision in the non-dominant eye of phakic, presbyopic patients, 41 to 65 years of age, who have manifest refractive spherical equivalent of (MRSE) +1.00 diopters (D) to -0.50 D with less than or equal to 0.75 D of refractive cylinder, who do not require correction for clear distance vision, but who do require near correction of +1.50 D to +2.50 D of reading add.

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.

XIV. CDRH DECISION

CDRH issued an approval order on June 29, 2016. The final conditions of approval cited in the approval order are described below.

1. ODE Lead PMA Post-Approval Study – A Multicenter Postmarket Surveillance Study to Evaluate the Long Term Safety of the Revision Optics, Inc. Raindrop® Near Vision Inlay in Emmetropic Subjects: The Office of Device Evaluation (ODE) will have the lead for this clinical study. The Multicenter Postmarket Surveillance Study to Evaluate the Long Term Safety of the Revision Optics, Inc. Raindrop® Near Vision Inlay in Emmetropic Subjects (Protocol P15-0065-X4 received via e-mail on May 25, 2016) is a single-arm, prospective, multicenter, observational study to evaluate the long-term safety of the Raindrop® Near Vision Inlay in emmetropic patients who were previously enrolled in the single-arm, prospective, multicenter, interventional pivotal trial conducted under IDE G090149 to support the PMA.

   Subjects from G090149, whether currently enrolled or not, who have not passed the 60-month post-operative inlay implantation window or the 24-month post-removal window, whichever is longer after initial implantation, will be recruited. Subjects will be followed

until 60 months after initial inlay implantation, or 24 months after removal, whichever is longer.

The endpoints include the rate of persistent loss of 2 lines or more of best-corrected distance visual acuity at the last available visit from pre-operative baseline with a target of less than 5%, and the rate of secondary surgical interventions over 60 months postoperatively with a target of 10% or less.

2. OSB Lead PMA Post-Approval Study – *Raindrop® Near Vision Inlay New Enrollment Study*: The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The Raindrop® Near Vision Inlay New Enrollment Study is designed to evaluate the Raindrop® Near Vision Inlay in terms of long term safety, the effect of prescribed steroid medication regimens, and the impact of surgical parameters used during implantation on patient safety outcomes. This is a prospective, single-arm, multi-center registry study of newly enrolled patients.

   The study will enroll at least 528 eyes from 528 phakic, presbyopic patients (unilateral implantation in the non-dominant eye) between the ages of 41 and 65 years at up to 30 sites, to ensure that at least 422 patients (assuming an overall attrition rate of 20%) will be available for long-term follow-up at 60 months after implantation.

   The post-approval study will be conducted in two phases:

   Phase One:
   Phase one will occur prior to initiating enrollment for phase two of the post-approval study. In phase one, a questionnaire will be developed to elicit the reason(s) for device explantation including the experience of visual symptoms. The questionnaire will be assessed qualitatively through concept elicitation and cognitive debriefing interviews, ensuring concept saturation has been reached. The qualitative assessment will evaluate:

   (1) The clarity of the items within the instrument
   (2) How the respondents interpret the item(s)
   (3) Ease of completion of the patient-reported outcomes (PROs)
   (4) The comprehensiveness of the PROs
   (5) The appropriateness of the format, response scales, and recall period used in the PROs.

   Phase Two:
   Phase two will involve the conduct of the new-enrollment post-approval study, which will begin after results from phase one are accepted by the FDA. The questionnaire developed in phase one of the study will be assessed quantitatively and formally administered during phase two as a nested component of the post-approval study. The quantitative questionnaire assessment will evaluate the psychometric properties of the most up-to-date questionnaire including evaluations of (if appropriate):

   (a) Internal consistency reliability

(b) Test-retest reliability (in stable patients)
(c) Clinical validity
(d) Known groups validity
(e) Item Response Theory and/or Factor Analysis to understand the factor structure.

The co-primary endpoints for the post-approval study test the following hypotheses:

1. That fewer than 5% of eyes have a persistent (present at the subject's last visit) loss of two (2) lines or more of best corrected distance visual acuity (BCDVA) at 60 months after inlay implantation, or 24 months after removal, whichever is longer, with a one-sided alpha level of 0.025.
2. Fewer than 10% of eyes underwent device removal over the 60-months of follow-up with a one-sided alpha level of 0.025.

Both of the alternative hypotheses should be met in order to determine the safety of the inlay.

The secondary endpoints include:

1. The rate of secondary surgical interventions overall and by type (e.g. exchange); and
2. The rate of adverse events (especially those resulting in BCDVA loss of two or more lines) categorized as ocular, device and/or procedure related, unanticipated, or other.

Additional clinical observations include:

- Operative surgical parameters [spot/line separation, target flap depth (absolute value and as percentage of central corneal thickness), etc.]
- Refractive stability (manifest refractive spherical equivalent)
- Slit lamp observation (especially haze development, grading, and recurrence rate)
- Assessment of dry eye syndrome
- Intraocular pressure
- Additional steroid medication regimens prescribed (including number of patients, length of treatment, and reasons for treatment) and rate of sequelae due to chronic use
- Information about cataract development and management
- Uncorrected near visual acuity
- Ease of assessment of the retina.

The observed rate of persistent BCDVA loss of two or more lines and that of inlay removal during the 60-month follow-up period will be compared to their performance goals based on the exact binomial distribution with one-sided significance level of 0.025. All ocular adverse events (including secondary surgical interventions) will be summarized by the number and percent of patients reported with the corresponding events. The summary will also be stratified by device and/or procedure relationship. The number and percent of patients with haze and those with recurrent haze will also be provided. Descriptive statistics will be calculated for all other clinical parameters.

Assessments of patients will be performed at the following timepoints: preoperative visit (day -90 to -1), the day of operation (day 0), day 1, 1 week, and at 1, 3, 6, 9, and 12 months, and annually thereafter for 60 total months of follow-up. Explanted patients will be assessed at 1 day, 1 week, and at 1, 3, 6, 12, and 24 months after explant.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.