SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: Intraocular Lens

Device Trade Name: Clareon™ Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) (Model Number: SY60WF)

Clareon™ Toric Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) (Model Numbers: CNW0T3, CNW0T4, CNW0T5, CNW0T6, CNW0T7, CNW0T8 and CNW0T9)

Clareon™ Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) with the AutonoMe™ Pre-loaded Delivery System (Model Number: CNA0T0)

Clareon™ Toric Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) with the AutonoMe™ Pre-loaded Delivery System (Model Numbers: CNA0T3, CNA0T4, CNA0T5, CNA0T6, CNA0T7, CNA0T8 and CNA0T9)

Device Procode: Intraocular Lens (HQL) and Lens, Intraocular, Toric Optics (MJP)

Applicant's Name and Address: Alcon Research, Ltd.
6201 South Freeway
Fort Worth, Texas 76134-2099

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P190018

Date of FDA Notice of Approval: January 7, 2020

II. INDICATIONS FOR USE

Clareon Aspheric Hydrophobic Acrylic Intraocular Lens (IOL)
The Clareon™ Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed.

Clareon Toric Aspheric Hydrophobic Acrylic Intraocular Lens (IOL)
The Clareon™ Toric Aspheric Hydrophobic Acrylic Intraocular Lenses (IOLs) are indicated for primary implantation in the capsular bag in the posterior chamber of the eye for visual correction of aphakia and pre-existing corneal astigmatism to reduce residual refractive cylinder and improve uncorrected distance vision in adult patients in whom a cataractous lens has been removed.

Clareon Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) with the AutonoMe Pre-loaded Delivery System
The Clareon™ Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) is indicated for primary implantation in the capsular bag in the posterior chamber of the eye for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed.

Clareon Toric Aspheric Hydrophobic Acrylic Intraocular Lens (IOL) with the AutonoMe Pre-loaded Delivery System
The Clareon™ Toric Aspheric Hydrophobic Acrylic Intraocular Lenses (IOLs) are indicated for primary implantation in the capsular bag in the posterior chamber of the eye for visual correction of aphakia and pre-existing corneal astigmatism to reduce residual refractive cylinder and improve uncorrected distance vision in adult patients in whom a cataractous lens has been removed.

III. CONTRAINDICATIONS

There are no known contraindications.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the respective Clareon™ IOL product labeling.

V. DEVICE DESCRIPTION

The Clareon™ and Clareon™ Toric Aspheric Hydrophobic Acrylic IOLs are ultraviolet and blue light filtering foldable single-piece posterior chamber intraocular lenses, intended as an optical implant for the replacement of the human crystalline lens in the visual correction of aphakia in adult patients following cataract surgery. Each IOL model is a single-piece design with a central optic and two open-loop haptics (**Figure 1**). Each lens has an optical portion and mechanical support elements (haptics) composed of a high refractive index soft hydrophobic acrylic material capable of being folded prior to insertion, which contains a covalently bonded blue light filtering chromophore. Alcon's proprietary chromophore filters blue light in a manner that approximates the human crystalline lens in the 400 to 475 nm wavelength range (Boettner and Wolter, 1962). The optic portion is biconvex and includes an aspheric surface. After surgical insertion into the eye, the lens gently unfolds to a full-size lens body. The haptics provide proper positioning of the lens optic within the capsular bag. The physical properties of these lenses are described in **Figure 2** and **Tables 1-2**.

The anterior aspheric surface of the Clareon™ and Clareon™ Toric IOLs is designed with negative spherical aberration to compensate for the positive spherical aberration of an average cornea. The Clareon™ Toric IOL has a toric component on the posterior surface with axis marks to denote the flat meridian (plus cylinder axis). Alignment of the toric axis marks with the post-operative steep corneal meridian allows the lens to correct preexisting corneal astigmatism. The astigmatic correction at the corneal plane for each model is shown in **Table 3.**

Figure 1: Physical Characteristics of the Lenses and AutonoMe Injector (all dimensions in millimeters)

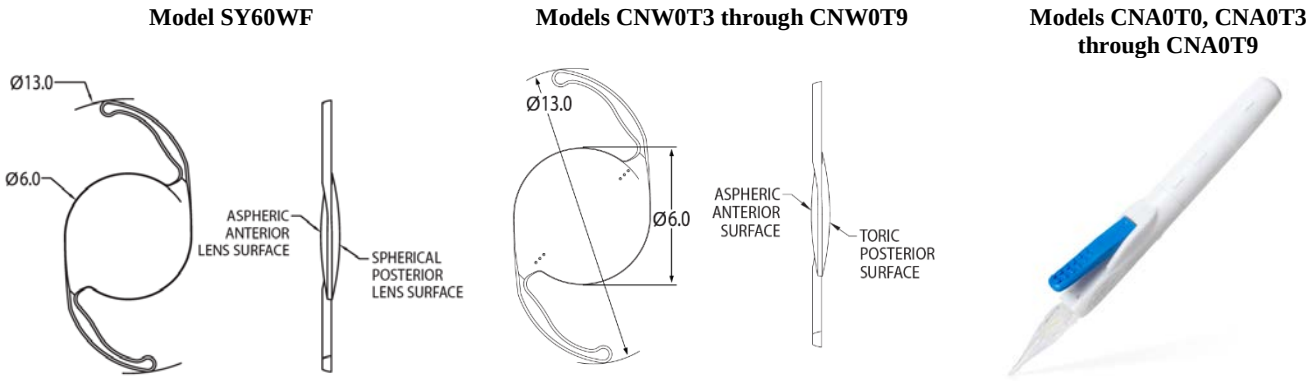

Figure 2: Spectral Transmittance

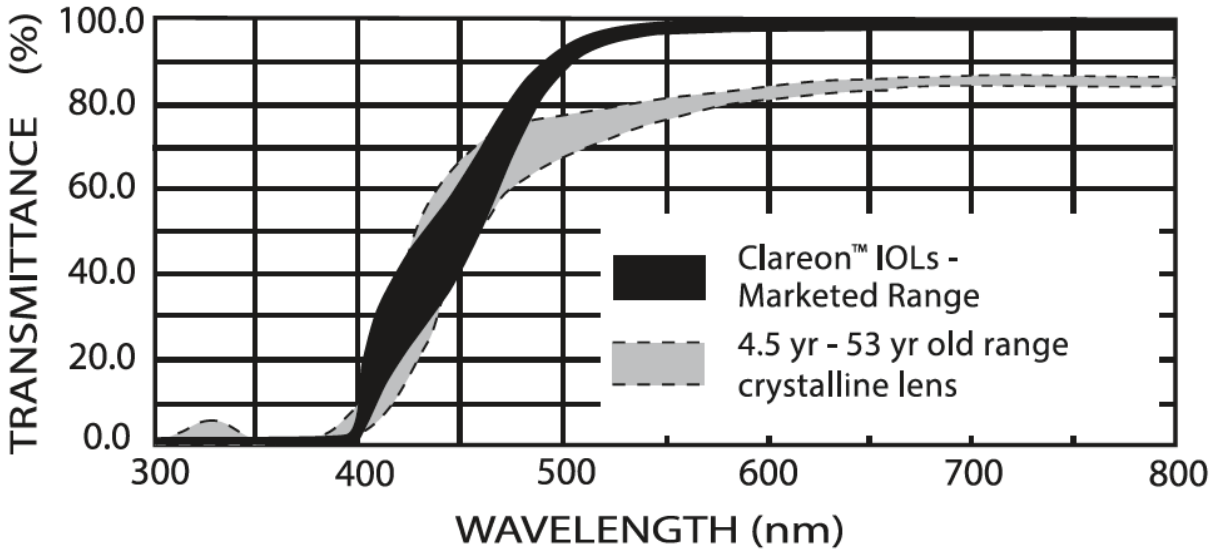

Table 1: Physical Characteristics of the Clareon™ IOL

Physical Characteristics	Description
Model	SY60WF
Optic Type	Anterior Asymmetric Biconvex
Optics Material	Ultraviolet and Blue Light Filtering Hydrophobic Acrylate/Methacrylate Copolymer

Spectral Transmission	10% transmittance at 403 nm (UV) for +20.0 diopter IOL
Index of Refraction	1.55 at 35°C
Optic Powers	+6.0 to +30.0 diopters (in 0.5 diopter increments)
Haptic Configuration	STABLEFORCE™ Modified-L Haptics
Haptic Material	Ultraviolet and Blue Light Filtering Hydrophobic Acrylate/Methacrylate Copolymer
Optic Diameter/$Ø_B$ (mm)	6.0
Overall Length/$Ø_T$ (mm)	13.0
Haptic Angle	0°

Table 2: Physical Characteristics of the Clareon™ Toric IOL

Physical Characteristics	Description						
IOL Model	CNW0T3	CNW0T4	CNW0T5	CNW0T6	CNW0T7	CNW0T8	CNW0T9
Optic Type	Biconvex Toric Aspheric Optic						
Optic Material	Ultraviolet and Blue Light Filtering Hydrophobic Acrylate/Methacrylate Copolymer						
Spectral Transmission	10% transmittance at 403 nm (UV) for +20.0 diopter IOL						
Index Of Refraction	1.55 at 35°C						
Optic Powers	+6.0 to +30.0 diopters (in 0.5 diopter increments)						
IOL Cylinder Powers (D)	1.50	2.25	3.00	3.75	4.50	5.25	6.00
Haptic Configuration	STABLEFORCE™ Modified-L Haptics						
Haptic Material	Ultraviolet and Blue Light Filtering Hydrophobic Acrylate/Methacrylate Copolymer						
Optic Diameter $Ø_B$ (mm)	6.0						
Overall Length $Ø_T$ (mm)	13.0						
Haptic Angle	0º						

Table 3: Astigmatic Correction at the Corneal Plane for Clareon™ Toric IOLs

IOL Model	Cylinder Power	
	IOL Power (Diopters)	Corneal Plane (Diopters)[a]
CNW0T3	1.50	0.98
CNW0T4	2.25	1.47
CNW0T5	3.00	1.96
CNW0T6	3.75	2.45
CNW0T7	4.50	2.94
CNW0T8	5.25	3.43
CNW0T9	6.00	3.92
[a]Based on an average pseudophakic human eye using an SRK/T optical A-constant of 119.1		

An Alcon web-based calculator is used in conjunction with the Clareon™ Toric IOL to determine the appropriate intraocular alignment and cylinder power for the patient.

The AutonoMe™ Pre-loaded Delivery System (Figure 1 above) is a single-use lens injector delivery system that contains an Alcon Single-Piece IOL to facilitate a repeatable, controlled delivery of the IOL into the capsular bag. This device is provided as a fully assembled, single-use device with the IOL positioned within the lens bay and has a speed-control-lever user interface. IOL advancement is driven by an internal compressed gas cylinder, which provides speed modulation by varying speed-control-lever depression. The AutonoMe™ Pre-loaded Delivery System nozzle features an external depth guard that functions as an insertion stop to limit the amount of the nozzle tip inserted into the incision. Once inserted into the incision, the lens is implanted by the

surgeon. After insertion, the delivery device is removed and discarded. **Table 4** shows the combinations of nozzle size and IOL diopter range.

Table 4: Combinations of Nozzle Size and IOL Diopter Range

Lens Model	Diopter Range	Nozzle Size
CNA0T0	6.0 - 25.0 D	AutonoMe™ Nozzle
	25.5 – 30.0 D	AutonoMe™ C-size Nozzle

Lens Model	Diopter Range	Nozzle Size
CNA0T3	6.0 - 25.0 D	AutonoMe™ Nozzle
	25.5 – 30.0 D	AutonoMe™ C-size Nozzle
CNA0T4-CNA0T6	6.0 - 21.0 D	AutonoMe™ Nozzle
	21.5 – 30.0 D	AutonoMe™ C-size Nozzle
CNA0T7-CNA0T9	6.0 - 18.0 D	AutonoMe™ Nozzle
	18.5 – 30.0 D	AutonoMe™ C-size Nozzle

The qualified ophthalmic viscoelastic devices (OVDs) that can be used with the Clareon™ IOL in the AutonoMe™ Delivery System are listed in **Table 5.**

Table 5: Qualified OVDs for Use with the Clareon™ IOL in the AutonoMe™ Delivery System

Lens Model	Qualified OVD
CNA0T0	VISCOAT™ OVD
	DISCOVISC™ OVD
	PROVISC™ OVD

Models	Qualified OVD
CNA0T3-CNA0T9	VISCOAT™ OVD DISCOVISC™ OVD PROVISC™ OVD

Refer to the Physician Labeling for additional details.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

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

VII. MARKETING HISTORY

The Clareon™ and Clareon™ Toric Aspheric Hydrophobic Acrylic Intraocular Lens with and without the AutonoMe™ Pre-loaded Delivery System is currently commercially available in the European Union, Japan, Australia and many countries within Asia, South America and the Middle East. The devices have 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.

Potential adverse events and complications accompanying cataract or implant surgery may include, but are not limited to the following: lens epithelial cell on-growth, corneal endothelial damage, infection (endophthalmitis), toxic anterior segment syndrome (TASS), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, cyclitic membrane, iris prolapse, hypopyon, anterior uveitis, hyphema, pigment dispersion, posterior capsule opacification, transient or persistent glaucoma, and secondary surgical intervention. Secondary surgical interventions include, but are not limited to: lens repositioning, lens replacement, vitreous aspiration or iridectomy for pupillary block, wound leak repair, and retinal detachment repair.

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

IX. SUMMARY OF NONCLINICAL STUDIES

Biocompatibility Testing

The Clareon™ IOL material, polymer formula AL-8726 with 0.04% AL-8739, is a flexible acrylate/ methacrylate copolymer with UV and blue light absorbing chromophores intended for use as an ocular implant.

A comprehensive battery of toxicity studies were performed on the test material (test sample representative of the finished sterile device) and demonstrated that the Clareon™ IOL is non-cytotoxic, non-mutagenic, non-clastogenic, non-irritating, non-sensitizing and resulted in no untoward intraocular irritation/tissue pathology following a six-month ocular implantation study in rabbits (refer to **Table 6**). The toxicology studies were conducted in accordance with the requirements of International Standard Organization (ISO) 11979-5, *Ophthalmic implants – Intraocular lenses – Part 5: Biocompatibility* standard and relevant parts of ISO 10993-1: Biological evaluation of medical devices - Part 1: Evaluation and testing within a risk management process. The studies were conducted in accordance with Good Laboratory Practices (GLP).

Table 6: Biocompatibility Testing

Biological Endpoint	Test method	Test Result
Cytotoxicity	MEM Elution Assay	Negative for cytotoxicity

Biological Endpoint	Test method	Test Result
Cytotoxicity	Indirect Contact (Agar Diffusion Assay)	Negative for cytotoxicity
Cytotoxicity	Indirect Contact (Agar Diffusion Assay with Nd-YAG Laser Saline Extract)	Negative for cytotoxicity
Cytotoxicity	Cell Growth Inhibition Assay (9-point)	Positive for cell growth inhibition – determined to be low risk
Cytotoxicity	Colony Formation Assay (MEM Elution)	Negative for colony growth inhibition
Cytotoxicity	Colony Formation Assay (Direct Contact)	Negative for colony growth inhibition
Cytotoxicity	Colony Formation Assay (Nd-YAG Laser Saline Extract)	Negative for colony growth inhibition
Sensitization	Guinea Pig Maximization Assay	Negative for contact sensitization
Genotoxicity	Bacterial Reverse Mutation Assay	Negative for mutagenic potential
Genotoxicity	Mouse Lymphoma Assay	Negative for mutagenic potential
Implantation	Intramuscular Implantation (One and Four-Weeks) in Rabbits	No significant biological local response
Implantation	Intraocular Implantation (Four and Six-Months) in Rabbits	No significant biological local response

According to Annex A of EN ISO 10993-1, the AutonoMe Pre-loaded Delivery System is categorized as a device with limited (≤ 24 hours for injector device) contact duration with tissue/bone. The Clareon™ IOLs packaged within the AutonoMe Pre-loaded Delivery

System are permanent contact devices. The AutonoMe Pre-loaded Delivery System is intended for single-use.

Chemical Characterization

As demonstrated in **Table 7**, chemical characterization was conducted on Clareon™ IOL material (AL-8739) to meet the requirements of EN ISO 11979-5, *Ophthalmic implants – Intraocular lenses – Part 5: Biocompatibility*.

Table 7: Chemical testing

Test	Test Substance	Test Description	Test Results
Material Stability Aging and Leachability	Clareon™ IOLs with Blue Light Filtering (BLF)	Hydrolytic stability per ISO 11979-5, Annex C:extractable content and optical quality	IOLs chemically, mechanically and optically stable under physiological conditions through at least 5 years of simulated exposure
Material Extraction	Clareon™ BLF material and Clareon™ IOLs with BLF	Exhaustive Extraction and Test for Leachables per ISO 11979-5, Annex A and B	No safety concern due to extractable content and no change in spectral transmittance after extraction in acetone or aqueous mediums
Insoluble Inorganics	Clareon™ IOLs with BLF	Evaluation of insoluble inorganics per ISO 11979-5, Section 5.7	IOLs contained no insoluble inorganic within a 10 ppm detection limit
Fourier Transform / Infrared Spectroscopy	Clareon™ IOLs with BLF	Infrared Absorption Spectra of lens material	Confirm expected material composition
Nd-YAG Laser Exposure	Clareon™ IOLs with BLF Exposed to YAG laser	Light and Scanning Electron Microscopy, Extractables and ISO Agarose Overlay Assay V79 Colony Extract Method	PASS: Material stability and negative for cytotoxicity

Components of the AutonoMe™ Pre-loaded Delivery System that have direct or indirect patient contact were evaluated for extractable content per ISO 10993 *Biological evaluation of medical devices – Part 18: Chemical characterization of materials*. The chemistry results demonstrated an equivalent extractable and leachable profile between Clareon™ IOLs provided in the wagon wheel lens case and those provided in the AutonoMe™ Pre-loaded Delivery System. There were no higher than expected levels for residual monomers, additives, degradation products, process contaminants and/or packaging components that introduced any new biological risks that would affect the patient risk profile for the Clareon™ IOL material.

Optical/Mechanical Testing

Pre-clinical optical / mechanical tests were performed with the Clareon™ and Clareon™ Toric IOLs and were measured in accordance with EN ISO 11979-2 Ophthalmic Implants – Intraocular Lenses – Part 2: Optical Properties and Test Methods and EN ISO 11979-3 Ophthalmic Implants – Intraocular Lenses – Part 3: Mechanical Properties and Test Methods. Test results are presented in **Tables 8 and 9**. Optical validation testing was performed to characterize the haze of the Clareon™ IOLs with results presented in **Table 10**.

Table 8: Optical Testing of Clareon™ IOLs

Optical Testing	**Standard**	**Test Results**
Effective Focal Length (EFL)	EN ISO 11979-2, Sections 4.2. ANSI Z80.7, Section 5.2.1.	Passed
Modulation Transfer Function(MTF) in ISO Model Eye	EN ISO 11979-2, Section 4.3. ANSI Z80.7, Section 5.2.2.	Passed
Modulation Transfer (MTF) in the 0.2 µm Spherical Aberration (SA) Modified ISO Model Eye	EN ISO 11979-2, Section 4.3. ANSI Z80.7, Section 5.2.2.	Passed
Spectral Transmittance	EN ISO 11979-2, Section 4.4. ANSI Z80.7, Section 5.2.3.	Acceptable

Table 9: Optical Testing of Clareon™ Toric IOLs

Optical Testing	**Standard**	**Test Results**
Spherical Equivalent Power & Cylinder Power	EN ISO 11979-2, Sections 4.2. ANSI Z80.7, Section 5.2.1.	Passed
Modulation Transfer Function (MTF) in the ISO Model Eye	EN ISO 11979-2, Section 4.3. ANSI Z80.7, Section 5.2.2.	Passed
Spectral Transmittance	EN ISO 11979-2, Section 4.4. ANSI Z80.7, Section 5.2.3.	Acceptable

Table 10: Haze Testing of Clareon™ IOLs

Testing	Test Method	Test Results
Cosmetic Haze Inspection - Assessment of cosmetic haze on the IOL.	Lenses from multiple lots were visually inspected and both anterior and posterior optic surfaces were graded for surface haze according to clear, light, medium, and heavy based on a photographic scale.	Lenses exhibited clear surface appearance (no haze).

Sterilization

The sterilization cycle for the Clareon™ and Clareon™ Toric IOLs has been validated in accordance with the following standards, and has passed the tests listed in **Tables 11-12** below:

- EN ISO 11135 Sterilization of health-care products – Ethylene oxide – Requirements for the development, validation and routine control of a sterilization process for medical devices
- EN 556-1 Sterilization of medical devices – Requirements for medical devices to be designated 'STERILE' – Part 1: Requirements for terminally sterilized medical devices.

Table 11: Clareon™ and Clareon™ Toric IOLs in the Wagon Wheel Lens Case Sterilization Acceptance Specifications

Description	Specifications
Sterility Assurance Level (SAL)	The Clareon™ sterilization qualification verified a Sterility Assurance Level in excess of the required SAL of $\leq 1.0 \times 10^{-6}$, which meets EN ISO 11135 and EN 556-1.
Residual Ethylene Oxide (EO)-Lens	Residual analysis conducted within the qualification verified that the residual ethylene oxide was below both the ISO 10993-7 limits ($\leq$ 0.5 µg/IOL/day and $\leq$ 1.25 µg/IOL) and Alcon internal limits ($\leq$ 0.5 µg/IOL).
Residual Ethylene Chlorohydrin (ECH)-Lens	Residual analysis conducted within the qualification verified that the residual ethylene chlorohydrin was below both the ISO 10993-7 limits ($\leq$ 2 µg/IOL/day and $\leq$ 5 µg/IOL) and Alcon internal limits ($\leq$ 0.5 µg/IOL).

Table 12: Clareon™ and Clareon™ Toric IOLs (with AutonoMe) Sterilization Acceptance Specifications

Description	Specifications
Sterility Assurance Level (SAL)	The AutonoMe™ Sterilization qualification verified a Sterility Assurance Level in excess of the required SAL of $\leq 1.0 \times 10^{-6}$, which meets EN ISO 11135 and EN 556-1.
Residual Ethylene Oxide (EO)-Lens	Residual analysis conducted within the qualification verified that the residual ethylene oxide was below both the ISO 10993-7 limits ($\leq$ 0.5 µg/IOL/day and $\leq$ 1.25 µg/IOL) and Alcon internal limits ($\leq$ 0.5 µg/IOL).
Residual Ethylene Chlorohydrin (ECH)-Lens	Residual analysis conducted within the qualification verified that the residual ethylene chlorohydrin was below both the ISO 10993-7 limits ($\leq$ 2 µg/IOL/day and $\leq$ 5 µg/IOL) and Alcon internal limits ($\leq$ 0.5 µg/IOL).
Residual Ethylene Oxide (EO) -Device	Residual analysis of the AutonoMe™ nozzle and plunger (tissue contact) verified the residual ethylene oxide was below ISO 10993-7 limits and Alcon internal limits (both $\leq$ 1.25 µg/device)
Residual Ethylene Chlorohydrin (ECH)-Device	Residual analysis of the AutonoMe™ nozzle and plunger (tissue contact) verified the residual ethylene chlorohydrin was below ISO 10993-7 limits and Alcon internal limits (both $\leq$ 5 µg/device)

Microbiology

The finished Clareon™ products are tested for bacterial endotoxin post-ethylene oxide sterilization. A validated bacterial endotoxin test (BET) is conducted and requires that both the Clareon™ IOL and the AutonoMe™ Pre-loaded Delivery System shall be tested within each sterilization batch and must meet the specification of not more than 0.2 EU/device. The bacterial endotoxin testing is based on the FDA Guidance for Industry and FDA Staff: Endotoxin Testing Recommendations for Single-Use Intraocular Ophthalmic Devices (issued August 17, 2015).

Shelf-Life

Clareon™ and Clareon™ Toric IOL in the Wagon Wheel Lens Case

The shelf life and transport stability of the Clareon™ and Clareon™ Toric IOLs in the Wagon Wheel lens case has been established as 3.4 years, which will be reflected in the product labeling. The Clareon IOL in the wagon wheel packaging, exposed to two ethylene oxide sterilization cycles, has demonstrated at least a 3.4-year equivalent real time shelf life at ambient storage room conditions ($\leq$ 30°C or 86°F). The IOL and its packaging also meet the transport stability requirements of EN ISO 11979-6.

Clareon™ IOL and Clareon™ Toric IOL in the AutonoMe™ Pre-loaded Delivery System

The shelf life and transport stability of the Clareon™ IOLs in the AutonoMe™ Pre-loaded Delivery System has been established as 2 years when stored at 30° C. The Clareon™ IOL in the AutonoMe™ Pre-loaded Delivery System, exposed to two ethylene oxide sterilization cycles, has demonstrated at least a 2-year equivalent real time shelf life at ambient storage room conditions (≤ 30°C or 86°F).

As all Clareon™ Toric IOL models in the AutonoMe™ Pre-loaded Delivery System share material, design, processing and packaging commonalities, as well as substantial similarities to the Clareon™ monofocal IOL, Clareon™ Toric IOLs in the AutonoMe™ Pre-loaded Delivery System are considered to be qualified for up to 2 years of shelf life when stored at 30° C. The IOL, delivery system and its packaging also meet the transport stability requirements of EN ISO 11979-6.

Conclusion: The overall results of the preclinical tests were acceptable from biocompatibility, physiochemical, optical, mechanical and microbiological perspectives. Shelf-life and transport stability have been established.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Clareon™ and Clareon™ Toric IOLs for the proposed indications in the US under IDE #G170112. 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 conducted under IDE G170112 was a prospective, multicenter, single-arm, unmasked, safety and performance study in adult (≥ 22 years of age) subjects requiring cataract surgery at 16 investigational sites. Upon meeting study eligibility criteria, 350 subjects were unilaterally implanted in the study eye with a Clareon™ IOL.

Subjects attended a total of 7 study visits, including a preoperative screening visit (Visit 0), an operative visit (Visit 00), and postoperative visits on Day 1-2 (Visit 1/Day 1), Day 7-14 (Visit 2/Week 1), Day 30-45 (Visit 3/Month 1), Day 120-180 (Visit 4/Month 6) and Day 330-420 (Visit 5/Month 12). Unscheduled visits were conducted if needed for medical attention.

The primary endpoint data were collected at the final visit (Visit 5/Month 12). The study was considered successful if the data indicated a favorable outcome in relation to the control safety and performance end point (SPE) rates as reported in EN ISO 11979-7:2014.

A sub-study to assess the rotational stability of the Clareon™ IOL was also conducted, using a slit-lamp photographic method. This was planned to include at least 125 subjects to achieve at least 100 evaluable subjects at 6 study sites. Toric axis markings were incorporated on the Clareon™ monofocal IOL for evaluation of rotational stability.

Patients were treated between July 2017 and February 2019. The database for this PMA reflected data collected through February 2019 and included 350 patients at 16 investigational sites.

The statistical analyses were frequentist. The study design, end points, sample size, and other variables were based on recommendations as set forth by ISO 11979-7:2014 "Ophthalmic Implants - Intraocular Lenses - Part 7: Clinical Investigations of Intraocular Lenses for the Correction of Aphakia."

1. **Clinical Inclusion and Exclusion Criteria**

Enrollment in the Clareon™ IOL study was limited to patients who met the following key inclusion criteria:

- Subjects 22 years or older in need of cataract surgery in at least 1 eye
- Calculated lens power within the available range of the Clareon™ IOL
- Clear intraocular media other than cataract
- Subjects for whom postoperative emmetropia planned (±0.5 D SE)

Patients were not permitted to enroll in the Clareon™ IOL study if they met any of the following key exclusion criteria:

- Any disease or pathology, other than cataract, that was expected to reduce the potential postoperative BCDVA to a level worse than 0.30 logMAR (including, but not limited to the following: amblyopia, clinically severe corneal dystrophy (eg, epithelial, stromal, or endothelial dystrophy), diabetic retinopathy, extremely shallow anterior chamber not due to swollen cataract, microphthalmos, previous retinal detachment, previous corneal transplant, recurrent severe anterior or posterior segment inflammation of unknown etiology, iris neovascularization, uncontrolled glaucoma, aniridia, optic nerve atrophy, clinically significant macular degeneration, or diagnosis of pseudoexfoliation)
- Previous corneal surgery
- Rubella or traumatic cataract
- Ocular trauma or previous refractive surgery
- Current or recent use of an alpha-1-selective adrenoceptor blocking agent or an antagonist of alpha1A adrenoceptor (eg, Flomax (tamsulosin HCL), Hytrin, or Cardura) that, in the opinion of the Investigator, would potentially require mechanical or surgical manipulation to enlarge the pupil

- Any other ocular or systemic condition that, in the opinion of the Investigator, should exclude the subject from the study

Subjects requiring additional procedures due to intraoperative complications, mechanical or surgical intervention to manipulate the pupil, excessive iris mobility, significant vitreous loss, significant anterior chamber hyphema, zonular capsular rupture or other unrecognized ocular conditions that could compromise the IOL position, as well as any inability to place the IOL in the capsular bag due to surgical complications were discontinued from the study during the surgery as well. These subjects were not considered screen failures, but did not receive implantation with the study lens.

2. **Follow-up Schedule**

All patients were scheduled to return for follow-up examinations on postoperative Day 1-2 (Visit 1/Day 1), Day 7-14 (Visit 2/Week 1), Day 30-45 (Visit 3/Month 1), Day 120-180 (Visit 4/Month 6) and Day 330-420 (Visit 5/Month 12). Unscheduled visits were conducted if needed for medical attention.

The visit schedule and clinical evaluations are presented in **Table 13, below.** Adverse events and complications were recorded at all visits. The key timepoints are shown below in the tables summarizing safety and effectiveness.

Table 13: **Schedule of Visits**

Activity	Visit 0	Visit 00	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5[9]
	Day -30 to 0 Preoperative	Day 0 Operative Visit	1-2 Days Postoperative	7-14 Days Postoperative	30-45 Days Postoperative	120-180 Days Postoperative	330-420 Days Postoperative\ Early Exit
Informed Consent	X						
Demographics	X						
Medical History	X						
Concomitant Medications	X	X	X	X	X	X	X
Urine Pregnancy Test[1]	X						
Inclusion/Exclusion	X	X					
Keratometry	X						
Axial Length	X						
Operative Eye		X					
Surgery/Treatment		X					

Activity	Visit 0 Day -30 to 0 Preoperative	Visit 00 Day 0 Operative Visit	Visit 1 1-2 Days Postoperative	Visit 2 7-14 Days Postoperative	Visit 3 30-45 Days Postoperative	Visit 4 120-180 Days Postoperative	Visit 5[9] 330-420 Days Postoperative\ Early Exit
Surgical Report • Lens power • Lens power calculation formula • A-constant • Incision size • Implant success • Target refractive error • Intended axis of placement • FLACS Procedures[2]		X					
Problems During Surgery		X					
Other Surgical Procedures		X					
Monocular UCDVA	X		X	X	X	X	X
Manifest Refraction (4 m)	X			X	X	X	X
Monocular BCDVA	X			X	X	X	X
IOP	X		X	X	X	X	X
Slit-Lamp Exam	X		X	X	X	X[7]	X[7]
PCO Assessment[3]			X	X	X	X	X
IOL Position Change[4]			X	X	X	X	X
Slit-lamp photography, if applicable[5,7]			X	X	X	X	X
IOL Axis of Orientation Slit-Lamp Imaging[6, 7]		X	X	X	X	X	X[10]
Dilated Fundus Exam[8]	X					X	X
Adverse Events (Including SSIs)	X	X	X	X	X	X	X
Device Deficiencies		X	X	X	X	X	X

[1] Required for women of child-bearing potential

[2] FLACS is only permitted for the following procedures: capsulorhexis, lens fragmentation, and/or primary and sideport incisions

[3] If a posterior capsulotomy has been performed, document in EDC.

[4] Includes Tilt and Decentration

[5] See MOP for Slit-lamp Photography requirements

[6] Sites participating in rotational stability sub-study

[7] Subject must be dilated for assessment

[8] Data is reported in EDC at the surgical visit, but may be collected from medical records if assessed within 30 days prior to screening visit

[9] If possible, perform Visit 5 procedures for an early exiting subject

[10] Only required if subject is exiting the study early; at, or prior to, Visit 4

3. **Clinical Endpoints**

The Clareon™ IOL clinical study design, objectives, endpoints and other variables were based on the recommendations as set forth by EN ISO 11979-7:2014. **Table 14** shows a summary of the effectiveness objectives, endpoints and statistical methods. **Table 15** describes the safety objectives, endpoints and statistical methods.

Table 14: Summary of Effectiveness - Objectives, Endpoints and Statistical Methods

Objective	Endpoint	Summary Statistics Used for Analysis
Primary To demonstrate favorable **Visual Acuity (VA)** outcomes for the Clareon IOL **compared to historical SPE rates**, as reported in EN ISO 11979-7:2014.	Co-Primary • Percentage of all-implanted subjects (AAS) achieving monocular best corrected distance visual acuity (BCDVA) of 0.3 logMAR or better at Month 12 • Percentage of best-case subjects (BAS) achieving monocular BCDVA of 0.3 logMAR or better at Month 12	Co-Primary The number and percent of eyes with BCDVA of 0.3 logMAR or better at Month 12 postoperative (Visit 5) along with the one-sided exact 95% Upper Confidence Limit (UCL). Study success was concluded if the one-sided exact 95% UCL for monocular BCDVA of 0.3 logMAR or better was greater than or equal to the SPE rates of 92.5% for the AAS and 96.7% for the BAS.

Secondary To demonstrate IOL **rotational stability** at Month 6	Secondary • IOL rotation, defined as the difference between axis of IOL orientation on day of surgery and at Month 6 (Visit 4) in the rotational analysis set (RAS)	Secondary For IOL rotation, the number and percent of eyes from day of surgery to Month 6 compared to the following performance targets • less than 10 degrees in 90 % of eyes in the RAS • less than 20 degrees in 95 % of eyes in the RAS • less than 30 degrees in 99 % of eyes in the RAS • Descriptive statistics including, sample size, number in category, and percent in category, for categorical variables, and sample size, mean, median, SD, min, max, and two-sided 95% CIs for continuous parameters.

Table 15: Summary of Safety - Objectives, Endpoints and Statistical Methods

Objective	Endpoint	Summary Statistics Used for Analysis
To demonstrate favorable **Adverse Event (AE)** outcomes for the Clareon IOL **compared to historical SPE rates** as reported in EN ISO 11979-7:2014.	Rate of AEs, including secondary surgical interventions (SSI)	Descriptive statistics including n and %, and 2-sided 95% CI, and SPE rate. The one-sided exact 95% LCL for incidence rates observed for study eyes compared to the cumulative and persistent AE SPE rates that includes SSIs.

B. Accountability of PMA Cohort

At the time of database lock, of 376 patients enrolled in the PMA study, 342 patients (97.7%) are available for analysis at the completion of the study, the 12-month post-operative visit. As summarized in **Table 16**, 376 subjects provided informed consent and were enrolled in the clinical study. A total of 26 subjects were considered screen failures for not meeting the study eligibility criteria. Eight subjects were discontinued after implantation with the study IOL as described in **Table 16**.

Table 16: Subject Disposition (All Enrolled subjects)

	n (%)
Total enrolled	376
Discontinued prior to Attempted Implantation	26

	n (%)
Screen Failure	26
Attempted Implantation	350 (100.0)
Successful Implantation	350 (100.0)
Completed Study	342 (97.7)
Discontinued after Attempted Implantation	8 (2.3)
Death	2 (0.6)
Lost to Follow Up	4 (1.1)
Withdrawal by Subject	2 (0.6)

Total enrolled = Total number of subjects consented.
Discontinuation prior to attempted implantation will comprise screen failure and other reasons for discontinuation.
Completed the study indicated by Subject Status on CRF Subject Derivations.
N = Number of subjects with attempted implantation
n = Number of subjects in specified category
Percentages are calculated as (n/N) * 100

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an IOL study performed in the US, as reported in **Tables 17-18** below.

Table 17: Demographic Statistics (All Implanted Analysis set)

Parameter	(N = 350)
Age (Years), n (%)	
<65	69 (19.7)
≥65	281 (80.3)
Mean (SD)	69.7 (6.44)
Median	70.0
(Min, Max)	(45, 86)
Sex, n (%)	
Female	213 (60.9)
Male	137 (39.1)
Unknown	0 (0.0)
Undifferentiated	0 (0.0)
Race, n (%)	
White	273 (78.0)
Black or African American	36 (10.3)
American Indian or Alaska Native	0 (0.0)
Asian	29 (8.3)
Native Hawaiian or Other Pacific Islander	1 (0.3)
Multi-Racial	0 (0.0)
Other	11 (3.1)
Ethnicity, n (%)	
Hispanic or Latino	11 (3.1)
Not Hispanic or Latino	336 (96.0)
Not Reported	2 (0.6)
Unknown	1 (0.3)

N = Number of subjects in the analysis set
n = Number of subjects in specified category
Percentages are calculated as (n/N) * 100
SD = Standard Deviation

Table 18: Baseline Characteristics (All-Implanted Analysis Set)

	(N = 350)
Best Corrected Distance VA (logMAR)	
n	350
Mean (SD)	0.191 (0.2060)
Median	0.16
(Min, Max)	(-0.18, 1.70)
Axial Length (mm)	
n	350
Mean (SD)	23.867 (0.9620)
Median	23.75
(Min, Max)	(21.28, 27.05)
Axial Length Category	
Total	350
Short (<21 mm)	0 (0.0)
Medium (21-26 mm)	343 (98.0)
Long (>26 mm)	7 (2.0)
Corneal astigmatism = abs (K1-K2)	
n	350
Mean (SD)	0.647 (0.4181)
Median	0.57
(Min, Max)	(0.00, 3.15)

N = Number of eyes in the analysis set
Total = Number of eyes with data
n = Number of eyes in specified category
Percentages are calculated as (n/Total) * 100
SD = Standard Deviation
Baseline = Preoperative

D. Safety and Effectiveness Results

1. Safety Results

The safety analysis set included all eyes with attempted IOL implantation (successful or aborted after contact with eye). The safety analysis was based on the safety analysis cohort of 350 patients available for 12 month evaluation.

The primary safety goal for the Clareon™ IOL clinical study was met, as the exact one-sided 95% lower confidence limit (LCL) of cumulative and persistent AEs were within limits compared to the historical SPE rates reported in EN ISO 11979-7:2014. Based on the results of this study, the Clareon™ IOL was concluded to be safe for implantation in the capsular bag in the posterior chamber for the visual correction of aphakia, and no unanticipated risks associated with Clareon™ IOL were identified. The rate of secondary surgical interventions (SSIs) did not exceed the SPE rate as the 1-sided 95% lower CL for an AE is less

than the SPE%. There were no device-related SSIs reported during the study. No subjects underwent a Secondary IOL Intervention as described by Masket, et al (2017).

Adverse effects that occurred in the PMA clinical study:
The incidences of cumulative adverse events for the Clareon™ IOL as compared to the ISO 11979-7:2014 SPE rates are provided in **Table 19** below, less than the threshold in ISO 11979-7:2014. There were no device-related SSIs reported.

Table 19: Cumulative and Persistent Adverse Events in the Safety Analysis Set, Clareon™ IOL

	(N = 350)			
	n (%)	2-sided 95% CI	1-sided 95% Lower CL	SPE %
Cumulative Serious Adverse Events				
Cystoid macular oedema	3 (0.9)	(0.18, 2.48)	0.23	3.0
Hypopyon	0 (0.0)	(0.00, 1.05)	0.00	0.3
Endophthalmitis	0 (0.0)	(0.00, 1.05)	0.00	0.1
Lens dislocated from posterior chamber	0 (0.0)	(0.00, 1.05)	0.00	0.1
Pupillary block	0 (0.0)	(0.00, 1.05)	0.00	0.1
Retinal detachment	0 (0.0)	(0.00, 1.05)	0.00	0.3
Secondary surgical intervention*	6 (1.7)	(0.63, 3.69)	0.75	0.8
Other				
Herpes virus infection	1 (0.3)	(0.01, 1.58)	0.01	NA
Macular fibrosis	1 (0.3)	(0.01, 1.58)	0.01	NA
Macular hole	1 (0.3)	(0.01, 1.58)	0.01	NA
Punctate keratitis	1 (0.3)	(0.01, 1.58)	0.01	NA
Retinal tear	2 (0.6)	(0.07, 2.05)	0.10	NA
Persistent Serious Adverse Events				
Corneal stroma oedema	0 (0.0)	(0.00, 1.05)	0.00	0.3
Cystoid macular oedema	1 (0.3)	(0.01, 1.58)	0.01	0.5
Iritis	0 (0.0)	(0.00, 1.05)	0.00	0.3
Raised IOP requiring treatment	0 (0.0)	(0.00, 1.05)	0.00	0.4

CI = Confidence Interval
CL = Confidence Limit
SPE = Safety and Performance Endpoint
Persistent = Present or ongoing at the final scheduled visit
IOP = Intraocular Pressure
SPE rates are from BS EN ISO 11979-7:2014, Ophthalmic Implants - Intraocular Lenses - Part 7: Clinical Investigations, Table B.2 - Posterior Chamber IOL Adverse Event Safety and Performance Endpoint Rates
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.
"Other" includes the MedDRA Preferred Term for ocular SAEs that do not belong to any predefined SPE categories.
Percentages are calculated as (n/N) * 100.
The SPE rate is considered not exceeded if the 1-sided 95% lower CL for an AE is less than the SPE%.
*None of these secondary surgical interventions were related to the IOL.

Tables 20-21 below further characterize AEs as reported for the clinical study:

Table 20: All Ocular AEs (Serious and Non-Serious AEs combined) (Safety Analysis Set)

Preferred Term	(N = 350) n (%)	2-sided 95% CI	E
Posterior capsule opacification	19 (5.4)	(3.30, 8.35)	19
Intraocular pressure increased	17 (4.9)	(2.85, 7.66)	18
Punctate keratitis	8 (2.3)	(0.99, 4.45)	9
Vitreous detachment	8 (2.3)	(0.99, 4.45)	8
Dry eye	7 (2.0)	(0.81, 4.08)	7
Conjunctival haemorrhage	5 (1.4)	(0.47, 3.30)	5
Corneal oedema	4 (1.1)	(0.31, 2.90)	5
Cystoid macular oedema	4 (1.1)	(0.31, 2.90)	5
Blepharoplasty	4 (1.1)	(0.31, 2.90)	4
Iritis	4 (1.1)	(0.31, 2.90)	4
Visual impairment	4 (1.1)	(0.31, 2.90)	4
Vitreous floaters	4 (1.1)	(0.31, 2.90)	4
Eyelid ptosis	3 (0.9)	(0.18, 2.48)	4
Diabetic retinopathy	3 (0.9)	(0.18, 2.48)	3
Visual acuity reduced	3 (0.9)	(0.18, 2.48)	3
Iridocyclitis	2 (0.6)	(0.07, 2.05)	3
Blepharitis	2 (0.6)	(0.07, 2.05)	2
Blepharochalasis	2 (0.6)	(0.07, 2.05)	2
Diplopia	2 (0.6)	(0.07, 2.05)	2
Foreign body sensation in eyes	2 (0.6)	(0.07, 2.05)	2
Inflammation of wound	2 (0.6)	(0.07, 2.05)	2
Lacrimation increased	2 (0.6)	(0.07, 2.05)	2
Macular fibrosis	2 (0.6)	(0.07, 2.05)	2
Macular hole	2 (0.6)	(0.07, 2.05)	2
Photopsia	2 (0.6)	(0.07, 2.05)	2
Retinal drusen	2 (0.6)	(0.07, 2.05)	2
Retinal laser coagulation	2 (0.6)	(0.07, 2.05)	2

Preferred Term	(N = 350) n (%)	2-sided 95% CI	E
Retinal tear	2 (0.6)	(0.07, 2.05)	2
Vitrectomy	2 (0.6)	(0.07, 2.05)	2
Corneal operation	1 (0.3)	(0.01, 1.58)	2
Allergy to surgical sutures	1 (0.3)	(0.01, 1.58)	1
Chalazion	1 (0.3)	(0.01, 1.58)	1
Congenital optic nerve anomaly	1 (0.3)	(0.01, 1.58)	1
Conjunctival hyperaemia	1 (0.3)	(0.01, 1.58)	1
Conjunctivitis	1 (0.3)	(0.01, 1.58)	1
Corneal abrasion	1 (0.3)	(0.01, 1.58)	1
Corneal dystrophy	1 (0.3)	(0.01, 1.58)	1
Corneal epithelium defect	1 (0.3)	(0.01, 1.58)	1
Corneal neovascularisation	1 (0.3)	(0.01, 1.58)	1
Corneal striae	1 (0.3)	(0.01, 1.58)	1
Dacryostenosis acquired	1 (0.3)	(0.01, 1.58)	1
Dermatitis allergic	1 (0.3)	(0.01, 1.58)	1
Device dislocation	1 (0.3)	(0.01, 1.58)	1
Diabetic retinal oedema	1 (0.3)	(0.01, 1.58)	1
Eye naevus	1 (0.3)	(0.01, 1.58)	1
Eye swelling	1 (0.3)	(0.01, 1.58)	1
Herpes virus infection	1 (0.3)	(0.01, 1.58)	1
Herpes zoster	1 (0.3)	(0.01, 1.58)	1
Iris neovascularisation	1 (0.3)	(0.01, 1.58)	1
Keratitis	1 (0.3)	(0.01, 1.58)	1
Lacrimation decreased	1 (0.3)	(0.01, 1.58)	1
Meibomian gland dysfunction	1 (0.3)	(0.01, 1.58)	1
Ophthalmologic treatment	1 (0.3)	(0.01, 1.58)	1
Optic ischaemic neuropathy	1 (0.3)	(0.01, 1.58)	1
Photophobia	1 (0.3)	(0.01, 1.58)	1
Retinal degeneration	1 (0.3)	(0.01, 1.58)	1

Preferred Term	(N = 350) n (%)	2-sided 95% CI	E
Retinal exudates	1 (0.3)	(0.01, 1.58)	1
Retinal haemorrhage	1 (0.3)	(0.01, 1.58)	1
Retinopathy hypertensive	1 (0.3)	(0.01, 1.58)	1
Retinoschisis	1 (0.3)	(0.01, 1.58)	1
Vision blurred	1 (0.3)	(0.01, 1.58)	1
Visual acuity reduced transiently	1 (0.3)	(0.01, 1.58)	1
Vitreous haemorrhage	1 (0.3)	(0.01, 1.58)	1
Xanthelasma	1 (0.3)	(0.01, 1.58)	1

If an eye has multiple occurrences of an AE, the eye is presented only once in the respective eye count column (n).
Events are counted each time in the event (E) column.
N = Number of eyes in the analysis set; n = Number of eyes with event; E = Number of events; CI = Confidence Interval.
Percentages are calculated as (n/N) * 100.
Adverse events are coded using MedDRA version 20.0.

Table 21: Supportive Analysis of AEs (AAO Task Force consensus, Masket 2017) (Safety Analysis Set)

Adverse Event	(N = 350) n (%)	2-sided 95% CI	E
Chronic anterior uveitis	2 (0.6)	(0.07, 2.05)	2
Clinically significant cystoid macular oedema	2 (0.6)	(0.07, 2.05)	2
Corneal oedema	2 (0.6)	(0.07, 2.05)	3
Endophthalmitis	0 (0.0)	(0.00, 1.05)	0
Mechanical pupillary block	0 (0.0)	(0.00, 1.05)	0
Increased IOP	15 (4.3)	(2.42, 6.97)	16
Rhegmatogenous RD	0 (0.0)	(0.00, 1.05)	0
Toxic anterior segment syndrome	0 (0.0)	(0.00, 1.05)	0
Secondary IOL intervention - Exchange	0 (0.0)	(0.00, 1.05)	0
Secondary IOL intervention - Removal	0 (0.0)	(0.00, 1.05)	0

Secondary IOL intervention - Reposition	0 (0.0)	(0.00, 1.05)	0

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 are based on a modified version of AAO Consensus (Masket, 2017).
N = Number of eyes in the analysis set; n = Number of eyes with event; E = Number of events; CI = Confidence Interval.
Percentages are calculated as (n/N) * 100. IOP = Intraocular Pressure

2. **Effectiveness Results**

The analysis of effectiveness was based on the 350 evaluable patients at the 12-month time point. Key effectiveness outcomes are presented in **Tables 22 to 40**.

The All-Implanted Analysis Set (AAS) was the primary set for the analyses of effectiveness endpoints and included all eyes with successful IOL implantation. Additional analyses, including for one co-primary endpoint, were conducted using the Best-Case Analysis Set. The Best-Case Analysis Set (BAS) included all eyes successfully implanted with the IOL that had at least 1 postoperative visit, no preoperative ocular pathology, no macular degeneration at any time, and no previous surgery for the correction of refractive errors. The Rotational Analysis Set (RAS) included all eyes with successful IOL implantation from the subset of sites that examined subjects for rotational stability.

Monocular Visual Acuity (VA) was measured in this study using the Fast ETDRS Method (Camparini 2001). This adaptive psychophysical method of VA determination allows for a reduction of the number of letter presentations when the subject is far from threshold and retains the same letter-by-letter accuracy of the standard ETDRS method near threshold level (Camparini 2001, Tong 2002).

The co-primary effectiveness endpoints were met as the one-sided exact 95% upper confidence limit for the percentage of subjects with monocular Best Corrected Distance VA of 0.3 logMAR or better at Month 12 was greater than the SPE rates for both the AAS and BAS. Key effectiveness results are provided in **Table 22**.

Table 22: Summary of Key Effectiveness Results

Objective	Endpoint/Criteria for Success	Outcome
Primary To demonstrate favorable VA outcomes for the Clareon IOL compared to historical SPE rates, as reported in EN ISO 11979-7:2014.	Co-Primary Percentage of all-implanted subjects achieving monocular BCDVA of 0.3 logMAR or better at 12 months postoperative (Visit 5) Percentage of best-case subjects achieving monocular BCDVA of 0.3 logMAR or better at 12 months postoperative (Visit 5)	Co-Primary • Monocular BCDVA 0.3 logMAR or better was achieved in 99.7% (341/342) of subjects in the all-implanted analysis set (AAS)[1] at month 12 with a one-sided 95% UCL of 99.99%. • Monocular BCDVA 0.3 logMAR or better was achieved in 99.7% (325/326) of subjects in the best-case analysis set (BAS)[2] at month 12 with a one-sided 95% UCL of 99.98%.
Secondary To demonstrate IOL rotational stability	Secondary IOL rotation, defined as the difference between axis of IOL orientation on day of surgery and at month 6 (Visit 4) The performance target in support of the secondary effectiveness objective is to show that IOL rotation at 6 months postoperative (Visit 4) is: • less than 10° in 90 % of eyes in the RAS[3] • less than 20° in 95 % of eyes in the RAS • less than 30° in 99 % of eyes in the RAS	Secondary • 98.4% (122/124) of subjects had absolute rotation < 10 degrees at month 6 • 99.2% (123/124) of subjects had absolute rotation < 20 degrees at month 6 • 99.2% (123/124) of subjects had absolute rotation < 30 degrees at Month 6 • Mean absolute rotation, was 2.2696

[1] The AAS was the primary set for the analyses of effectiveness endpoints and included all eyes with successful IOL implantation.
[2] The BAS included all eyes successfully implanted with the IOL that had at least 1 postoperative visit, no pre-operative ocular pathology, no macular degeneration at any time, and no previous surgery for the correction of refractive errors.
[3] The RAS included all eyes with successful IOL implantation from the subset of sites that examined subjects for rotational stability

a. Primary Effectiveness Outcomes - Monocular BCDVA:

Table 23: Categorical Statistics for Monocular BCDVA at 4 m (logMAR) (All-Implanted Analysis Set)

Visit	logMAR Category	(N =350) n	(%)

Visit	logMAR Category	(N =350) n	(%)
Preoperative	Total	350	
	0.0 logMAR or better	54	(15.4)
	0.1 logMAR or better	123	(35.1)
	0.2 logMAR or better	219	(62.6)
	0.3 logMAR or better	283	(80.9)
	Worse than 0.3 logMAR	67	(19.1)
1 Week	Total	349	
	0.0 logMAR or better	214	(61.3)
	0.1 logMAR or better	306	(87.7)
	0.2 logMAR or better	333	(95.4)
	0.3 logMAR or better	341	(97.7)
	Worse than 0.3 logMAR	8	(2.3)
1 Month	Total	348	
	0.0 logMAR or better	253	(72.7)
	0.1 logMAR or better	317	(91.1)
	0.2 logMAR or better	337	(96.8)
	0.3 logMAR or better	343	(98.6)
	Worse than 0.3 logMAR	5	(1.4)
6 Months	Total	344	
	0.0 logMAR or better	252	(73.3)
	0.1 logMAR or better	317	(92.2)
	0.2 logMAR or better	338	(98.3)
	0.3 logMAR or better	342	(99.4)
	Worse than 0.3 logMAR	2	(0.6)
1 Year	Total	342	
	0.0 logMAR or better	277	(81.0)
	0.1 logMAR or better	318	(93.0)
	0.2 logMAR or better	339	(99.1)
	0.3 logMAR or better	341	(99.7)
	Worse than 0.3 logMAR	1	(0.3)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

Table 24: Categorical Statistics for Monocular BCDVA at 4 m (logMAR) (Best-Case Analysis Set)

		(N =334)	
Visit	**logMAR Category**	**n**	**(%)**
Preoperative	Total	334	
	0.0 logMAR or better	53	(15.9)
	0.1 logMAR or better	120	(35.9)
	0.2 logMAR or better	212	(63.5)
	0.3 logMAR or better	270	(80.8)
	Worse than 0.3 logMAR	64	(19.2)
1 Week	Total	333	
	0.0 logMAR or better	210	(63.1)
	0.1 logMAR or better	297	(89.2)
	0.2 logMAR or better	321	(96.4)
	0.3 logMAR or better	327	(98.2)
	Worse than 0.3 logMAR	6	(1.8)
1 Month	Total	332	
	0.0 logMAR or better	247	(74.4)
	0.1 logMAR or better	307	(92.5)
	0.2 logMAR or better	325	(97.9)
	0.3 logMAR or better	328	(98.8)
	Worse than 0.3 logMAR	4	(1.2)
6 Months	Total	328	
	0.0 logMAR or better	247	(75.3)
	0.1 logMAR or better	307	(93.6)
	0.2 logMAR or better	323	(98.5)
	0.3 logMAR or better	326	(99.4)
	Worse than 0.3 logMAR	2	(0.6)
1 Year	Total	326	
	0.0 logMAR or better	271	(83.1)
	0.1 logMAR or better	307	(94.2)
	0.2 logMAR or better	323	(99.1)
	0.3 logMAR or better	325	(99.7)
	Worse than 0.3 logMAR	1	(0.3)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

Table 25: Best Corrected Visual Acuity in the Best Case Analysis Set at Month 12, Clareon™ IOL

Visual Acuity	n	%
0.0 logMAR or better	271	83.1
0.1 logMAR or better	307	94.2
0.2 logMAR or better	323	99.1
0.3 logMAR or better	325	99.7
Worse than 0.3 logMAR	1	0.3
ISO SPE Rate for % of 0.3 logMAR or better	96.7%	
N	326	
ISO SPE Rate = BS EN ISO 11979-7:2014, Ophthalmic Implants - Intraocular Lenses - Part 7: Clinical Investigations, Table B.4 - Posterior Chamber IOL Adverse Event Safety and Performance Endpoint Rates		

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 26: Best Corrected Visual Acuity in the All-Implanted Analysis Set at Month 12, Clareon™ IOL

Visual Acuity	n	%
0.0 logMAR or better	277	81.0
0.1 logMAR or better	318	93.0
0.2 logMAR or better	339	99.1
0.3 logMAR or better	341	99.7
Worse than 0.3 logMAR	1	0.3
ISO SPE Rate for % of 0.3 logMAR or better	92.5%	
N	342	
ISO SPE Rate = BS EN ISO 11979-7:2014, Ophthalmic Implants - Intraocular Lenses - Part 7: Clinical Investigations, Table B.3 - Posterior Chamber IOL Adverse Event Safety and Performance Endpoint Rates		

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 27: Best Corrected Visual Acuity in the Best Case Analysis Set at Month 12 (Snellen), Clareon™ IOL

Visual Acuity	n	%
20/20 or better	287	88.0
20/25 or better	316	96.9
20/32 or better	324	99.4
20/40 or better	325	99.7
Worse than 20/40	1	0.3
N	326	
Note: 20/20 = 0.04 logMAR 20/25 = 0.14 logMAR 20/32 = 0.24 logMAR 20/40 = 0.34 logMAR		

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 28: Best Corrected Visual Acuity in the All-Implanted Analysis Set at Month 12 (Snellen), Clareon™ IOL

Visual Acuity	n	%
20/20 or better	297	86.8
20/25 or better	331	96.8
20/32 or better	340	99.4
20/40 or better	341	99.7
Worse than 20/40	1	0.3
N	342	
Note: 20/20 = 0.04 logMAR 20/25 = 0.14 logMAR 20/32 = 0.24 logMAR 20/40 = 0.34 logMAR		

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 29: Uncorrected Visual Acuity in the Best Case Analysis Set at Month 12, Clareon™ IOL

Statistic	(N = 334)
n	326
Mean (SD)	0.042 (0.1348)
Median	-0.02
(Min, Max)	(-0.20, 0.70)
95% CI	(-0.027, -0.056)

Table 30: Uncorrected Visual Acuity in the All-Implanted Analysis Set at Month 12, Clareon™ IOL

Statistic	(N = 350)
n	342
Mean (SD)	0.043 (0.1339)
Median	0.02
(Min, Max)	(-0.20, 0.70)
95% CI	(0.029, 0.057)

Table 31: Summary of Supportive Effectiveness

Endpoint/Criteria for Success	Outcome
• Monocular UCDVA at 12 months postoperative (Visit 5) • Estimated IOL A-constant at Month 6	• Greater than 95% of subjects had monocular UCDVA of 0.3 logMAR or better at Month 12 • The LSMean for A-constant in the AAS and BAS sets were 119.199 and 119.196 with 0.05D standard error (of LSMean) in both data sets.

b. <u>Secondary Effectiveness Outcome – IOL Rotation:</u>

Toric axis markings were incorporated on Clareon™ monofocal investigational lenses for evaluation of rotational stability. The rotational stability of the Clareon™ IOL was evaluated using a photographic method utilizing retro-illumination and ocular anatomical landmarks under dilated condition. Assessments performed in a subset of the total study population, which included 141 subjects at 6 sites. Of the 141 subjects, 10 subjects had images at baseline which were not readable; therefore rotation could not be assessed at any other time points. The remaining 131 subjects were evaluated for rotation. IOL rotation, defined as the difference between IOL axis orientation on day of surgery and at the month 6 post-operative visit (Visit 4).

At month 6, the percentage of subjects with absolute IOL rotation of < 10 degrees and < 20 degrees was 98.4% (122/124) and 99.2% (123/124), respectively (**Tables 32 and 33**). The median absolute rotation at month 6 was 1.449 degrees (**Table 35**). The maximum rotation in either direction at month 6 was -40.003 degrees and 9.212 degrees (**Table 36**). The subject with -40.003 rotation had an AE reported at Day 1 for suspected ocular trauma, which resulted in haptic rotation and optic decentration. The investigator suggested that the decentration in the IOL might have caused huge rotation. The amount of rotation from Month 1 to Month 6 for this subject was 1.077 degrees.

Table 32: Categorical Statistics for Absolute IOL Rotation (10 Degrees Increment) at Month 6 from Day of Surgery, Rotation Analysis Set, Clareon™ IOL

	(N=141)	
Category	n	%
Total	124	-
Less than 10 degrees	122	98.4
Less than 20 degrees	123	99.2
Less than 30 degrees	123	99.2
Greater than 30 degrees	1	0.8

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

Table 33: Categorical Statistics for Absolute IOL Rotation (10 Degrees Increment) (Rotation Analysis Set)

		(N =141)	
Visit	**Category**	**n**	**(%)**
1 Day	Total	127	
	Less than 10 degrees	125	(98.4)
	Less than 20 degrees	126	(99.2)
	Less than 30 degrees	126	(99.2)
	Greater than 30 degrees	1	(0.8)
1 Week	Total	126	
	Less than 10 degrees	124	(98.4)
	Less than 20 degrees	125	(99.2)
	Less than 30 degrees	125	(99.2)
	Greater than 30 degrees	1	(0.8)
1 Month	Total	127	
	Less than 10 degrees	124	(97.6)
	Less than 20 degrees	126	(99.2)
	Less than 30 degrees	126	(99.2)
	Greater than 30 degrees	1	(0.8)
6 Months	Total	124	
	Less than 10 degrees	122	(98.4)
	Less than 20 degrees	123	(99.2)
	Less than 30 degrees	123	(99.2)
	Greater than 30 degrees	1	(0.8)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 34: Categorical Statistics for Absolute IOL Rotation (5 Degrees Increment) (Rotation Analysis Set)

		(N =141)	
Visit	**Category**	**n**	**(%)**
1 Day	Total	127	
	0 – 5 degrees	121	(95.3)
	>5 – 10 degrees	4	(3.1)
	>10 – 15 degrees	1	(0.8)
	>15 – 20 degrees	0	(0.0)
	>20 – 30 degrees	0	(0.0)
	>30 degrees	1	(0.8)
1 Week	Total	126	
	0 – 5 degrees	118	(93.7)
	>5 – 10 degrees	6	(4.8)
	>10 – 15 degrees	1	(0.8)
	>15 – 20 degrees	0	(0.0)
	>20 – 30 degrees	0	(0.0)
	>30 degrees	1	(0.8)
1 Month	Total	127	
	0 – 5 degrees	119	(93.7)
	>5 – 10 degrees	5	(3.9)
	>10 – 15 degrees	2	(1.6)
	>15 – 20 degrees	0	(0.0)
	>20 – 30 degrees	0	(0.0)
	>30 degrees	1	(0.8)
6 Months	Total	124	
	0 – 5 degrees	115	(92.7)
	>5 – 10 degrees	7	(5.6)
	>10 – 15 degrees	1	(0.8)
	>15 – 20 degrees	0	(0.0)
	>20 – 30 degrees	0	(0.0)
	>30 degrees	1	(0.8)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Percentages are calculated as (n/N) * 100

Table 35: Descriptive Statistics for Absolute IOL Rotation (Degrees), Rotation Analysis Set, Clareon™ IOL

Visit	Statistic	(N = 141)*
1 Day	n	127
	Mean (SD)	1.8483 (3.72254)
	Median	0.942
	(Min, Max)	(0.002, 38.232)
	95% CI	(1.1946, 2.5020)
1 Week	n	126
	Mean (SD)	1.9942 (3.86948)
	Median	1.213
	(Min, Max)	(0.020, 40.547)
	95% CI	(1.3119, 2.6764)
1 Month	n	127
	Mean (SD)	2.2335 (3.95863)
	Median	1.414
	(Min, Max)	(0.008, 41.110)
	95% CI	(1.5384, 2.9287)
6 Months	n	124
	Mean (SD)	2.2696 (3.87231)
	Median	1.449
	(Min, Max)	(0.014, 40.033)
	95% CI	(1.5812, 2.9579)

N = Number of eyes in the analysis set
n = Number of eyes at visit with data
SD = Standard Deviation, CI = Confidence Interval
* Of 141, 10 had images at baseline which were not readable and at each visit, individual subjects may have had images which were missing or not readable

Table 36: Descriptive Statistics for Signed IOL Rotation (Degrees) (Rotation Analysis Set)

Visit	Statistic	(N = 141)
1 Day	n	127
	Mean (SD)	-0.5120 (4.12751)
	Median	-0.197
	(Min, Max)	(-38.232, 7.315)
	95% CI	(-1.2368, 0.2128)
1 Week	n	126
	Mean (SD)	0.0657 (4.35627)
	Median	0.371
	(Min, Max)	(-40.547, 7.143)
	95% CI	(-0.7024, 0.8338)
1 Month	n	127
	Mean (SD)	0.4099 (4.53097)

Visit	Statistic	(N = 141)
	Median	0.770
	(Min, Max)	(-41.110, 10.296)
	95% CI	(-0.3858, 1.2056)
6 Months	n	124
	Mean (SD)	0.5632 (4.45734)
	Median	0.847
	(Min, Max)	(-40.033, 9.212)
	95% CI	(-0.2291, 1.3555)

N = Number of eyes in the analysis set
n = Number of eyes at visit with data
SD = Standard Deviation, CI = Confidence Interval

IOL axis rotation between 1 month and 6 months is described in **Tables 37-40**. The mean absolute rotation between 1 month and 6 months was 0.9782 degrees (**Table 37**). No subject had an absolute rotation of greater than 10 degrees from Month 1 to Month 6 in the study and 98.4% (127/129) of subjects had an absolute rotation between Month 1 and Month 6 of ≤ 5 degrees (**Tables 39** and **Table 40**) indicating stability over time.

Table 37: Descriptive Statistics for Absolute Change in IOL Axis (Degrees) Between 1 Month and 6 Months (Rotation Analysis Set)

Visit	Statistic	(N = 141)
6 Months	n	129
	Mean (SD)	0.9782 (1.07568)
	Median	0.677
	(Min, Max)	(0.003, 7.029)
	95% CI	(0.7908, 1.1656)

N = Number of eyes in the analysis set
n = Number of eyes at visit with data
SD = Standard Deviation, CI = Confidence Interval

Table 38: Descriptive Statistics for Signed Change in IOL Axis (Degrees) Between 1 Month and 6 Months (Rotation Analysis Set)

Visit	Statistic	(N = 141)
6 Months	n	129
	Mean (SD)	0.2030 (1.44222)

Visit	Statistic	(N = 141)
	Median	0.185
	(Min, Max)	(-7.029, 5.272)
	95% CI	(-0.0482, 0.4543)

N = Number of eyes in the analysis set
n = Number of eyes at visit with data
SD = Standard Deviation, CI = Confidence Interval

Table 39: Categorical Statistics for Absolute Change in IOL Axis Between 1 Month and 6 Months (5 Degrees Increment) (Rotation Analysis Set)

		(N =141)	
Visit	**Category**	**n**	**(%)**
6 Months	Total	129	
	0-5 degrees	127	(98.4)
	>5-10 degrees	2	(1.6)
	>10-15 degrees	0	(0.0)
	>15-20 degrees	0	(0.0)
	>20-30 degrees	0	(0.0)
	>30 degrees	0	(0.0)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

Table 40: Categorical Statistics for Absolute Change in IOL Axis Between 1 Month and 6 Months (10 Degrees Increment) (Rotation Analysis Set)

		(N =141)	
Visit	**Category**	**n**	**(%)**
6 Months	Total	129	
	Less than 10 degrees	129	(100.0)
	Less than 20 degrees	129	(100.0)
	Less than 30 degrees	129	(100.0)
	Greater than 30 degrees	0	(0.0)

N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data

Percentages are calculated as (n/Total) * 100

3. Subgroup Analyses

The following preoperative characteristics were evaluated for potential association with outcomes:

- BCDVA by age (<65 years vs. ≥65 years)
- BCDVA by gender
- BCDVA by investigative site
- BCDVA by adverse event (study eyes with ocular adverse events vs. study eyes without ocular adverse events)
- BCDVA by preoperative ocular pathology (study eyes with preoperative ocular pathology vs. study eyes without preoperative ocular pathology)

The results showed similar mean BCDVA values in each subgroup.

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 16 investigators of which none were full-time or part-time employees of the sponsor and 2 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: 2
- 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. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

Bench studies demonstrated equivalent optical performance between the previously approved marketed AcrySof™ Toric IOL and the Clareon™ Toric IOL. Accordingly, the data presented in the AcrySof™ Toric IOL SSEDs for PMA P930014/S015 and P930014/S045, which are available on the CDRH website and are incorporated by reference here, is applicable to both AcrySof™ and Clareon™ Toric IOLs. An overview of the AcrySof™ Toric IOL studies is as follows:

> A multicenter, subject-masked, randomized, prospective clinical study was previously performed in the US to evaluate the safety and effectiveness of AcrySof™ Toric IOL (Models SA60T3-SA60T5, collectively referred to as SA60TT, N=211) compared to Model SA60AT as control lens (N=210). Results achieved by the subjects followed for 6 months postoperatively (120 to 180 days after second eye implant) provide reasonable assurance that the AcrySof™ Toric IOL is safe and effective for visual correction of aphakia and pre-existing corneal astigmatism following cataract surgery. A clinical study was also conducted to investigate rates of spatial distortions related to axial misalignment of the AcrySof™ Toric Posterior Chamber High Cylinder Power IOLs (Models SN60T6-SN60T9). The results in patients followed to six months (Visit 5A) demonstrate that the AcrySof™ Toric High Cylinder Power IOL models are safe and effective for the visual correction of aphakia to significantly reduce pre-existing corneal astigmatism with excellent rotational stability following implantation in the capsular bag.

For this submission for the Clareon™ IOLs, consideration was also given to the following additional comparative analysis provided to evaluate lens rotational stability in support of approval of the Indication for Use claims for the Clareon™ Toric IOL (i.e., "improved uncorrected distance vision" and "reduction of residual refractive cylinder") consistent with the approved AcrySof™ Toric IOL upon which the Clareon™ Toric IOL Indications for Use language is leveraged.

The mean absolute change in IOL axis orientation (from the operative visit to 6 months) and absolute change in IOL axis rotation (from the operative visit to 6 months) between the AcrySof™ Toric (P930014/S015) (for all cylindrical powers, SA60, and for the lowest cylindrical power, SA60T3) and Clareon™ IOLs was assessed. The Clareon™ IOL provides superior rotational stability to the AcrySof™ Toric IOL (**Tables 41-44**). These analyses support leveraging the AcrySof™ data to support the Clareon™ Toric Indication for Use statement with respect to reduction of residual refractive cylinder and improved uncorrected distance vision.

Table 41: Mean absolute change in axis rotation from operative visit to 6 months (SA60) – continuous summary

Statistic	AcrySof Toric (SA60)	Clareon Monofocal
N	243	124
Mean	3.4	2.3
Std Dev	3.4	3.9

Min	0	0
Max	27	40

p-value based on a two-sided t-test = 0.0082

Table 42: Absolute change in axis orientation from operative visit to 6 months (SA60) – categorical summary

Category	AcrySof Toric (SA60)	Clareon Monofocal
0 – 5 degrees	196/243 (80.7%)	115/124 (92.7%)
>5 – 10 degrees	39/243 (16.0%)	7/124 (5.6%)
>10 – 15 degrees	7/243 (2.9%)	1/124 (0.8%)
>15 – 20 degrees	0/243 (0.0%)	0/124 (0.0%)
>20 – 30 degrees	1/243 (0.4%)	0/124 (0.0%)
>30 degrees	0/243 (0.0%)	1/124 (0.8%)

p-value based on a two-sided Mann-Whitney test = 0.0026
N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

Table 43: Mean absolute change in axis rotation from operative visit to 6 months (SA60T3) – continuous summary

Statistic	AcrySof Toric (SA60T3)	Clareon Monofocal
N	118	124
Mean	3.6	2.3
Std Dev	3.8	3.9
Min	0	0
Max	27	40

p-value based on a two-sided t-test = 0.0082

Table 44: Absolute change in axis orientation from operative visit to 6 months (SA60T3) – categorical summary

Category	AcrySof Toric (SA60T3)	Clareon Monofocal
0 – 5 degrees	95/118 (80.5%)	115/124 (92.7%)
>5 – 10 degrees	18/118 (15.3%)	7/124 (5.6%)
>10 – 15 degrees	4/118 (3.4%)	1/124 (0.8%)
>15 – 20 degrees	0/118 (0.0%)	0/124 (0.0%)
>20 – 30 degrees	1/118 (0.8%)	0/124 (0.0%)
>30 degrees	0/118 (0.0%)	1/124 (0.8%)

p-value based on a two-sided Mann-Whitney test = 0.0053
N = Number of eyes in the analysis set
n = Number of eyes in specified category
Total = Number of eyes with data
Percentages are calculated as (n/Total) * 100

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 Ophthalmics 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 effectiveness results of this study, including rotational stability, demonstrate that the Clareon™ IOL is effective for implantation in the capsular bag in the posterior chamber for the visual correction of aphakia. The co-primary effectiveness endpoint and secondary effectiveness endpoint targets were met, as well as for the supportive effectiveness endpoints, supporting a conclusion of device effectiveness in terms of IOL rotational stability and distance visual acuity:

- Co-Primary:
  - Proportion of subjects with monocular BCDVA 0.3 logMAR or better at 12 months (one-sided exact 95% UCL) was greater than ISO SPE rates, over 99.9% for all-implanted (AAS) and best-case (BAS) analysis sets.
- Secondary:
  - Absolute rotation <10 degrees at month 6 achieved for 98.4% of subjects (target >90%), and 99.2% had <20 degrees (target 95%).
  - Mean absolute rotation was 2.27 degrees (day of surgery to month 6).
  - Mean misplacement (intended vs actual orientation on day of surgery) was 5.12 degrees, with 85.5% of subjects as <10 degrees.
  - Mean misalignment (summation of rotation and misplacement) was 5.68 degrees, with 87% reported as <10 degrees at month 6.
- Supportive:
  - Proportion of subjects with monocular UCDVA 0.3 logMAR or better at month 12 was >95% (AAS and BAS).
  - Proportion of subjects with monocular BCDVA 20/20 or better at month 12 was 87%.
  - Proportion of subjects with monocular UCDVA 20/40 or better month 12 was 97%.

In addition, the effectiveness of the toric models in providing reduced postoperative residual refractive astigmatism is supported by the rotational stability data and the clinical data provided for the toric parent IOL in P930014/S015, which has a similar toric surface and mechanical design.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as data collected in a clinical study conducted to support PMA approval as described above. The results of the nonclinical laboratory testing and animal studies on the Clareon™ material and lens design support safety. The results of biocompatibility testing, dimensional, optical and mechanical testing, and chemical testing demonstrated conformance to applicable sections of ISO 10993-1, ISO 10993-5, ISO 10993-7, ISO 11979-2, ISO 11979-3, ISO11979-5 and internal product specifications. The 12-month results of the IDE clinical investigation of the Clareon™ IOL demonstrate the study safety endpoint was met, supporting conclusion of device safety, and no unanticipated risks were identified:

- Primary:
  - Cumulative and persistent AEs (one-sided 95% LCL) are within limits compared to ISO SPE rates.
- Other:
  - No device-related serious ocular AEs or SSIs.
  - Ocular SAEs <1%.
  - No IOL glistening, scratches, cracks, or surface haze, and no visible abnormalities on lens surface (haptics or optics).

The safety results of this study, including adverse events, provide reasonable evidence that the Clareon™ IOL is safe for implantation in the capsular bag in the posterior chamber for the visual correction of aphakia. No unanticipated risks associated with the Clareon™ IOL were identified.

C. Benefit-Risk Determination

The clinical data from the Clareon™ study provide reasonable assurance that the Clareon™ Intraocular Lens is safe and effective when used as intended and according to the instructions for use. The probable benefits of the device, as well as probable risks, are based on data collected in a clinical study conducted to support PMA approval, as described in Sections A and B, above. The data support that the probable benefits related to restoring vision secondary to cataract extraction outweigh the probable risks for the intended use of the device. The probable benefit is effective treatment of aphakia secondary to cataract removal surgery, of high probability and long duration. The probable risks are mainly based on the surgical procedure and are not anticipated to be greater than for other approved IOLs (e.g., unintended refractive outcomes, intraocular inflammation, bleeding, etc.) and are treated per clinical standard of care, the same as for other approved IOLs.

Additional factors considered in determining probable risks and benefits for the Clareon™ IOL device included the following. The uncertainty of this determination is relatively low based on the quality of clinical study design and conduct, and expected results are generalizable to the US cataract population. Based on clinical

experience and history of cataract surgery and IOL implantation in the US, patient tolerance for expected risks is acceptable. Alternative treatments for cataract are available (e.g., other approved monofocal and toric IOLs), however the applicant has provided data to support device approval with acceptable risk mitigation in labeling warnings, precautions, and instructions for use.

This submission did not include specific information on patient perspectives for this device.

In conclusion, given the available information summarized above, the data support that for the proposed Indications for Use, the probable benefits outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of Clareon™ and Clareon™ Toric Aspheric Hydrophobic Acrylic IOL when used in accordance with the indications for use. Study was conducted consistent with recognized ISO standard and typical enrollment criteria for an IOL study. Bias was minimized by inclusion and exclusion criteria, protocol-standardized clinical assessments and surgical procedure, safety and effectiveness performance criteria endpoints in accord with the ISO standard, and no subject discontinuations as result of adverse events or upon investigator advice. This was a single-arm, un-masked, prospective, multicenter, pivotal clinical study consisting of 350 implanted adult subjects with cataract requiring surgery, at 16 US sites. Success was based on protocol-specified safety and effectiveness endpoints. A sub-study to assess rotational stability (based on toric axis markings) was also conducted. Safety and effectiveness findings from the clinical study, summarized in Sections A and B above, support that a significant portion of the patient population will achieve clinically significant results. The benefits of using the device outweigh the risks, as summarized in Section C, above. The labeling appropriately presents key outcomes from the device description, the clinical study, benefits and risks, indications for use, warnings and precautions, and instructions for use. There are no unsubstantiated performance claims regarding haze or light scatter. Post-approval study (PAS) is not recommended since there are no outstanding clinical concerns.

XIV. CDRH DECISION

CDRH issued an approval order on January 7, 2020.

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

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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