BAUSCH + LOMB

TotalVisc™

viscoelastic system

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For Intraocular Use
Please Read Carefully And Keep This Package Insert For Future Reference.

Device Description And Physical Characteristics

TotalVisc™ viscoelastic system is designed to provide two viscoelastic products with different physicochemical characteristics that can be used in combination to perform specific tasks during the cataract procedure. TotalVisc viscoelastic system consists of ClearVisc™ dispersive and StableVisc™ cohesive ophthalmic viscosurgical devices (OVDs). The combination of the products utilizes the different physiochemical properties of the products in order to facilitate the complete cataract surgical procedure.

ClearVisc and StableVisc are sterile solutions of highly purified, medium molecular weight sodium hyaluronate. The sodium hyaluronate is prepared from the culture of Streptococcus pyogenes.

ClearVisc is a dispersive OVD, which contains 25 mg/mL of sodium hyaluronate and 40 mg/mL of sorbitol, dissolved in physiological sodium chloride phosphate, tromethamine buffered solution with a pH of 6.8 to 7.6. The viscosity is 40 Pa.s at 25°C (77°F) and a shear rate of 1 s^{-1} (**FIG. 1**). The average molecular weight of the sodium hyaluronate is 750,000 Daltons. The osmolality is approximately 330 mOsm/Kg. ClearVisc is offered in a 1 mL glass syringe with a 25-gauge thin wall blunt cannula.

StableVisc is a cohesive OVD, which contains 10 mg/mL of sodium hyaluronate and 40 mg/mL of sorbitol, dissolved in physiological sodium chloride phosphate, tromethamine buffered solution with a pH 6.8 to 7.6. The viscosity is 50 ± 15 Pa.s at 25°C (77°F) at a shear rate of 1 s^{-1} (**FIG. 1**). The average molecular weight of the sodium hyaluronate is 2,100,000 Daltons. The osmolality is approximately 340 mOsm/Kg. StableVisc is offered in a 1 mL glass syringe with a 27-gauge blunt cannula.

For both ClearVisc and StableVisc, the cannula is attached to the syringe by a standard Luer fitting and is used to inject the solution into the eye. It also includes a polypropylene retention clip, which helps to maintain standard Luer connection between the syringe and cannula.

Intended Purpose

TotalVisc is intended for use in cataract surgery to maintain the anterior chamber space, re-inflate the capsular bag for intraocular lens (IOL) insertion, and protect the corneal endothelium from surgical instruments and ultrasonic energy. TotalVisc includes both ClearVisc dispersive OVD and StableVisc cohesive OVD. Dispersive OVDs have a lower viscosity and are often chosen for their ability to coat intraocular structures during surgery and selectively isolate segments within the eye during surgery. Cohesive OVDs have a higher viscosity and are often chosen for their ability to offer structural stability in

the eye and create space in the chamber during surgery. The cohesive properties facilitate ease of removal from the eye.

Indications For Use
TotalVisc is indicated for use as a surgical aid in ophthalmic anterior segment procedures including:

- Extraction of a cataract
- Implantation of an intraocular lens (IOL)

Contraindications
There are no contraindications to the use of TotalVisc when used as a surgical aid in ophthalmic anterior segment procedures.

Applications
Cataract Surgery And IOL Implantation
The required amount of OVD is infused through a needle or cannula into the anterior chamber. The protective effect of TotalVisc as an aid is optimized when the injection is performed prior to cataract extraction and insertion of the IOL and is effective for phacoemulsification cataract procedures. Additional OVD can be injected as required to facilitate surgical procedures (see **Precautions**).

Directions For Use
- Prior to opening, visually inspect for breaches of packaging integrity. Using sterile opening technique, open tray and transfer sterile syringe onto sterile field.

- Remove the tip cap (**FIG. 2**) and attach the sterile cannula. Make sure the cannula is tightly connected with the Luer Lock tip of the syringe (**FIG. 3**). Cannulas are color coded to correspond gauge with product (gray=StableVisc, blue=ClearVisc).

- After the cannula is attached to the syringe (**FIG. 4** and **FIG. 5**), insert the syringe/cannula assembly through the rounded end of the retention clip (**FIG. 6**) until the retention clip is fully seated against the cannula hub. The syringe flange snaps into the “wings” of the retention clip (**FIG. 7**).

Precautions
Precautions normally considered during anterior segment procedures are recommended. Pre-existing glaucoma may place patients at risk for increases in intraocular pressure from the OVD during the early postoperative period.

Warnings
The following warnings should be considered when using TotalVisc:

- Do not use if the sterile barrier has been breached. Sterility cannot be guaranteed, and the patient will be at increased risk for infection.

- Do not use TotalVisc OVD in subjects with known allergies to any of its components.

- An excess quantity of OVD should not be used. Excess OVD can cause increased intraocular pressure.

- The OVD should be removed from the anterior chamber at the end of surgery to prevent or minimize postoperative intraocular pressure increases (spikes). OVD remaining in the eye can cause increased intraocular pressure.

- If the postoperative intraocular pressure increases above expected values, corrective therapy should be administered. Increased intraocular pressure may lead to inflammation or vision loss.

- Do not re-use the cannula. Even after cleaning and rinsing, resterilized cannula could release particulate matter as the OVD is injected. It is recommended that a single-use disposable cannula be used when administering the OVD. Re-use may cause eye inflammation.

- If any particulate matter is observed, it should be removed by irrigation and/or aspiration. Particulate matter left in the eye may cause increased intraocular pressure (IOP) or light scattering/obstruction.

- Store at 2° to 8°C (36° to 46°F). Protect from freezing. The shelf life of TotalVisc is not guaranteed if it is not properly stored.

Adverse Reactions
Sodium hyaluronate is a natural component of tissues within the body and is generally well tolerated in human eyes. Transient postoperative inflammatory reactions and increases in intraocular pressure have been reported. Inflammation may result from increased intraocular pressure caused by use of the OVD. Intraocular inflammation, i.e., toxic anterior segment syndrome (TASS), has been attributed to OVDs. Furthermore, vision loss may be possible as a result of increased intraocular pressure and inflammation.

Adverse Reaction Reporting
Adverse reactions and/or potentially sight-threatening complications that may be reasonably regarded as TotalVisc related should be reported to Bausch & Lomb Incorporated at 1-800-338-2020.

How Supplied
Both TotalVisc OVDs (ClearVisc and StableVisc) are sterile viscoelastic preparations supplied in a disposable glass syringe delivering 1.0 mL of sodium hyaluronate, sorbitol and dual buffering system dissolved in USP water for injection (WFI). ClearVisc and StableVisc are sterile filtered and aseptically transferred to syringes. The filled syringes are sealed and the final package sterilized using ethylene oxide (EO). Contents of unopened and undamaged pouches are sterile. Do not use if package is opened or damaged. Refrigerated ClearVisc and StableVisc should be allowed to reach room temperature (approximately 20 to 45 minutes) prior to use.

Disposal
Dispose of the unused or contaminated equipment and/or packaging by following applicable safe disposal procedures and in accordance with applicable laws and regulations regarding the disposal of biohazardous materials.

Storage Conditions
Store at 2° to 8°C (36° to 46°F). Protect from freezing.

Medical Device Re-Use Statement
If this product is reprocessed and/or re-used, Bausch + Lomb cannot guarantee the functionality, material structure, cleanliness or sterility of the product. Re-use could lead to illness, infection and/or injury to the patient or user and, in extreme incidents, death. This product is labeled as “single-use” which is defined as a device intended to be used once only for a single patient.

ClearVisc Clinical Trial
A clinical study was performed to establish a reasonable assurance of safety and effectiveness of ClearVisc OVD for use as a surgical aid in patients undergoing ophthalmic anterior segment procedures in the United States under IDE # G170265. A summary of the clinical study is presented below.

A. Study Design
Subjects were treated between April 25, 2018 and December 28, 2018. The database for this PMA reflected data collected through the last postoperative visit on April 1, 2019 and the database lock on April 30, 2019 and included 372 subjects. There were 16 investigational sites.

The study was a prospective, multi-center, active control, two-armed, randomized, partially masked, comparative clinical trial. Eligible subjects were randomized 1:1 at the time of planned cataract surgery

with posterior chamber IOL implantation to receive either the investigational device (ClearVisc OVD) or the control OVD (VISCOAT OVD). Randomization was stratified by site, age group, and cataract severity. Only one eye of each subject was included in the study. Subjects were followed for 90 days postoperatively (Visit 5).

VISCOAT OVD (Alcon) is a legally marketed alternative with similar indications for use and similar properties (i.e., dispersive) as the ClearVisc OVD. Although the investigators were not masked at the time of surgery as to which OVD was used, a delegated examiner at each site who was masked to the randomized assignment of each patient performed all postoperative assessments.
Noninferiority statistical hypothesis testing for safety and effectiveness endpoints was pre-specified.

1. Clinical Inclusion And Exclusion Criteria
Enrollment in the ClearVisc OVD study was limited to subjects who met the following inclusion criteria:

- The subject must have been at least 45 years old and had a clinically documented diagnosis of age-related non-complicated cataract that was considered amenable to treatment with standard phacoemulsification cataract extraction and IOL implantation.

- The subject must have had the capability to provide written informed consent on the Institutional Review Board (IRB) approved Informed Consent Form (ICF) and provide authorization as appropriate for local privacy regulations.

- The subject must have been willing and able to return for all scheduled follow-up examinations through 90 days following surgery.

- The subject must have had clear intraocular media other than the cataract in the operative eye.

Patients were not permitted to enroll in the ClearVisc OVD study if they met any of the following exclusion criteria:

- The subject had participated in any drug or device clinical investigation within 30 days prior to entry into this study and/or during the period of study participation.

- The subject had any corneal pathology (e.g., significant scarring, guttata, inflammation, edema, dystrophy, etc.) in the operative eye.

- The subject had anterior segment pathology likely to increase the risk of an adverse outcome for phacoemulsification cataract surgery (e.g., pseudoexfoliation syndrome, synechiae, iris atrophy, inadequate dilation, shallow anterior chamber, traumatic cataract, lens subluxation) in the operative eye.

- The subject had any condition that prevented reliable specular microscopy in the operative eye.

- The subject had a congenital ocular anomaly (e.g., aniridia, congenital cataract) in the operative eye.

- The subject had a baseline ECD<1500 cells/mm^2 in the operative eye.

- The subject had a Grade 4+ nuclear cataract density in the planned operative eye.

- The subject had glaucoma or ocular hypertension (IOP>24 mmHg) in the operative eye.

- The subject had any abnormality that prevented reliable Goldmann applanation tonometry in the operative eye.

- The subject had a known allergy to any of the components of the test or control OVDs.

- The subject was using any topical or systemic medications known to interfere with visual performance or complicate cataract surgery within 30 days of enrollment or during the study.

- The subject was scheduled to undergo other combined intraocular procedures during the cataract/IOL implantation surgery in the operative eye.

NOTE: A relaxing keratotomy was allowed.

- The subject had diabetic retinopathy, wet age-related macular degeneration, or other retinal pathology that might limit postoperative visual acuity or predisposed the subject to postoperative retinal complications in the operative eye.

- The subject's fellow eye was already participating in this study.

- The subject had a history of chronic or recurrent inflammatory eye disease (e.g., iritis, scleritis, uveitis, iridocyclitis, rubeosis iridis) in the operative eye.

- The subject had a best-corrected distance visual acuity of logarithm of the minimum angle of resolution (LogMAR) 1.0 (20/200, 6/60) or worse in the fellow eye.

- The subject had previous corneal surgery in the planned operative eye.

- The subject had a previous retinal detachment in the operative eye.

- Females of childbearing potential (those who were not surgically sterilized or not postmenopausal for at least 12 months) were excluded from participation in the study if they met any one of the following conditions:

    - they were currently pregnant;

    - they planned to become pregnant during the study; and/or

    - they were breastfeeding.

2. Follow-Up Schedule
All subjects were scheduled for follow-up examinations at 6 hours ± 2 hours, 24 hours ± 4 hours, 7 days ± 2 days, 30 days ± 7 days, and 90 days ± 14 days postoperatively.

Table 1 includes the parameters measured preoperatively and postoperatively. Adverse events and complications were recorded at all visits.

Table 1: Study Visit Schedule And Parameters Evaluated At Each Study Visit

Procedure/Assessments	Preop Visit Day -60 to Day -1	Op Visit Day 0	Postop Visit 6 Hours ± 2 Hours Postop	Postop Visit 2 24 Hours ± 4 Hours Postop	Postop Visit 3 7 Days ± 2 Days Postop	Postop Visit 4 30 Days ± 7 Days Postop	Postop Visit 5 90 Days ± 14 Days Postop
Informed Consent	X						
Demographic Data	X						
Medical History	X						
Urine Pregnancy Test	X	X			X	X	X
Eligibility Criteria	X	X					
Randomization		X					
Fellow Eye Status	X						

Surgical Procedure		X					
Manifest Subjective Refraction	X						X
Uncorrected Distance VA	X		X	X	X	X	X
Best-Corrected Distance VA	X						X
Cataract Classification	X						
Slit Lamp Examination	X		X	X	X	X	X
IOP (Goldmann Tonometry)	X		X	X	X	X	X
Dilated Fundus Examination	X						X
Ultrasound Pachymetry	X			X			X
ECD via Specular Microscopy of the Central Cornea	X						X
Concomitant Medications	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X

ABBREVIATIONS: ECD=endothelial cell density, IOP=intraocular pressure, VA=visual acuity

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

3. Clinical Endpoints

With regard to safety, the primary safety endpoint was evaluated by a noninferiority test of the proportion of subjects who experienced at least one IOP measurement ≥30 mmHg in the study eye at any follow-up visit. Following Markov chain Monte Carlo (MCMC) imputation of missing IOP data, a one-sided upper 95% confidence interval (CI) for the difference between the test and control groups (i.e., test – control) in the proportion of subjects with at least one IOP measurement ≥30 mmHg in the study eye at any follow-up visit was constructed using the normal approximation to test the null hypothesis for the primary safety endpoint that the upper confidence limit of the 95% CI for the difference was ≥0.117. If the upper confidence limit was less than 0.117, then the null hypothesis of inferiority was rejected in favor of the alternative hypothesis of noninferiority.

With regard to effectiveness, the primary effectiveness endpoint was a test for noninferiority of the test OVD (ClearVisc OVD) when compared to the control OVD (VISCOAT OVD) in mean percent change in endothelial cell density (ECD) from baseline to Postoperative Visit 5 (90 Days ± 14 days) in the study eye. Following MCMC imputation of missing cell density data, a one-sided upper 95% confidence limit for the mean difference (test – control) in percent change between the test and comparator OVDs was constructed. If the upper confidence limit was less than 5%, then the null hypothesis of inferiority for the primary effectiveness endpoint was rejected in favor of the alternative hypothesis of noninferiority. Therefore, both the primary safety endpoint and the primary effectiveness endpoint needed to be met in order for the trial to be considered a success.

B. Accountability Of PMA Cohort

At the time of database lock, of 372 subjects randomized to treatment in the PMA trial, 99.2% (n=369) of subjects were available for analysis at the completion of the study, the 3-month postoperative visit (Visit 5; **Table 2**). Of the 369 subjects that completed the study, 182 subjects (98.9%) and 187 subjects (99.5%) were in the ClearVisc and VISCOAT groups, respectively (**Table 3**).

Table 2: Subject Accountability - All Treated Subjects

Subject Status (n, %)	Preop Visit (N=372)	Op Visit Day 0 (N=372)	Postop Visit 1 (N=372)	Postop Visit 2 (N=372)	Postop Visit 3 (N=372)	Postop Visit 4 (N=372)	Postop Visit 5 (N=372)

Available for analysis	372 (100%)	372 (100%)	367 (98.7%)	368 (98.9%)	368 (98.9%)	370 (99.5%)	369 (99.2%)
Discontinued	0	0	0	1 (0.3%)	2 (0.5%)	2 (0.5%)	2 (0.5%)
Lost to follow-up	0	0	0	0	0	0	1 (0.3%)
Missing	0	0	5 (1.3%)	3 (0.8%)	2 (0.5%)	0	0
Percent Accountability[1]	100%	100%	98.7%	99.2%	99.5%	100%	99.7%

ABBREVIATIONS: N=number of subjects in total, Op=operative, Preop=preoperative, Postop=postoperative
[1] Percent Accountability by Visit=[(# Available for Analysis) / (# Enrolled - # Discontinued - # Active)]*100

Table 3: Subject Accountability By Treatment Assignment - All Treated Subjects

Treatment Group		Preop Visit	Op Visit Day 0	Postop Visit 1	Postop Visit 2	Postop Visit 3	Postop Visit 4	Postop Visit 5
ClearVisc (N=184; n, %)	Available for analysis	184 (100%)	184 (100%)	180 (97.8%)	181 (98.4%)	183 (99.5%)	183 (99.5%)	182 (98.9%)
	Discontinued	0	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.5%)
	Lost to follow-up	0	0	0	0	0	0	1 (0.5%)
	Missing	0	0	4 (2.2%)	3 (1.6%)	0	0	0
	Percent Accountability[1]	100%	100%	97.8%	98.4%	100%	100%	99.5%
VISCOAT (N=188; n, %)	Available for analysis	188 (100%)	188 (100%)	187 (99.5%)	187 (99.5%)	185 (98.4%)	187 (99.5%)	187 (99.5%)
	Discontinued	0	0	0	1 (0.5%)	1 (0.5%)	1 (0.5%)	1 (0.5%)
	Lost to follow-up	0	0	0	0	0	0	0
	Missing	0	0	1 (0.5%)	0	2 (1.1%)	0	0
	Percent Accountability[1]	100%	100%	99.5%	100%	98.9%	100%	100%

ABBREVIATIONS: N=number of subjects in total, n=number of subjects per treatment group, Op=operative, Preop=preoperative, Postop=postoperative
[1] Percent Accountability by Visit=[(# Available for Analysis) / (# Enrolled - # Discontinued - # Active)]*100

The demographics of the trial population (**Table 4**) are slightly atypical for a cataract study performed in the US, since there is a slightly higher proportion of Asian subjects. However, the demographics of this population are reasonably representative of the US intended-use population for an OVD.

Table 4: Demographics - Safety Population

	ClearVisc	VISCOAT	Total

	(N=184)	(N=188)	(N=372)
Age (years), n	184	188	372
Mean (SD)	69.6 (6.76)	69.2 (7.37)	69.4 (7.07)
Median	70.0	69.0	70.0
Min, Max	47, 86	45, 86	45, 86
Sex, n (%)			
Male	73 (39.7%)	68 (36.2%)	141 (37.9%)
Female	111 (60.3%)	120 (63.8%)	231 (62.1%)
Ethnicity, n (%)			
Hispanic or Latino	20 (10.9%)	33 (17.6%)	53 (14.2%)
Not Hispanic or Latino	164 (89.1%)	155 (82.4%)	319 (85.8%)
Race, n (%)[1]			
American Indian/Alaska Native	2 (1.1%)	2 (1.1%)	4 (1.1%)
Asian	39 (21.2%)	43 (22.9%)	82 (22.0%)
Black/African American	20 (10.9%)	7 (3.7%)	27 (7.3%)
Native Hawaiian/Other Pacific Islander	0	0	0
White	124 (67.4%)	138 (73.4%)	262 (70.4%)
Other	1 (0.5%)	0	1 (0.3%)

ABBREVIATIONS: Max=maximum, Min=minimum, N=number of subjects per treatment group, n=number of subjects per category, SD=standard deviation
[1] Four subjects self-identified as two races: 1 White + Black/African American and 3 White + American Indian/Alaskan Native

The baseline ocular characteristics are summarized in **Table 5**. Baseline ocular characteristics were fairly similar between treatment groups.

Table 5: Baseline Ocular Characteristics - Safety Population

	ClearVisc (N=184)	VISCOAT (N=188)	Total (N=372)
Study Eye, n (%)			
OD	91 (49.5%)	110 (58.5%)	201 (54.0%)
OS	93 (50.5%)	78 (41.5%)	171 (46.0%)
Cataract Classification, n (%) Type			
Nuclear	75 (40.8%)	72 (38.3%)	147 (39.5%)
Cortical	4 (2.2%)	4 (2.1%)	8 (2.2%)
Posterior Subcapsular	1 (0.5%)	2 (1.1%)	3 (0.8%)
Combination	104 (56.5%)	110 (58.5%)	214 (57.5%)
Density			
Slight (1+)	9 (4.9%)	4 (2.1%)	13 (3.5%)
Moderate (2+)	86 (46.7%)	102 (54.3%)	188 (50.5%)
Dense (3+)	88 (47.8%)	82 (43.6%)	170 (45.7%)
Very Dense (4+)	1 (0.5%)	0	1 (0.3%)
Fellow Eye Status, n (%)			
Normal	0	0	0
Cataract	97 (52.7%)	89 (47.3%)	186 (50.0%)
Aphakic	0	0	0
Pseudophakic	87 (47.3%)	99 (52.7%)	186 (50.0%)

ABBREVIATIONS: N=number of subjects per treatment group, n=number of subjects per category, OD=oculus dexter (right eye), OS=oculus sinister (left eye)

C. Safety And Effectiveness Results

1. Safety Results

The analysis of safety was based on the Safety Population of all 372 eyes that were exposed to either the ClearVisc OVD or VISCOAT OVD (control). The key safety outcomes for this study are presented below in **Tables 6** to **11**. Adverse effects are reported in **Table 12**.

The results of the analysis of the primary safety endpoint are presented in **Table 6**. For this analysis, missing data for eight subjects in the ClearVisc arm and four subjects in the control arm were imputed by the MCMC method and the calculated proportion was based on the average of 20 imputed datasets. By this method, the proportion of subjects with postoperative IOP ≥30 mmHg (IOP spike) at any follow-up visit was 0.174 for the ClearVisc group and 0.203 for the VISCOAT group. The upper confidence limit of the estimated difference in proportions was 0.038, which is less than the noninferiority margin of 0.117 (p=0.0002). Therefore, the primary safety endpoint of noninferiority of the proportion of subjects who experienced at least one IOP spike at any follow-up visit in the ClearVisc group when compared with the VISCOAT group was met.

Table 6: Proportion Of Subjects With Postoperative Intraocular Pressure ≥30 mmHg At Any Follow-Up Visit - Safety Population

	ClearVisc (N=184)	VISCOAT (N=188)	Difference In Proportions (ClearVisc - VISCOAT)[1]	
			Estimate (90% CI)	P-value
IOP ≥30 mmHg at any follow-up visit	32.05/184=0.174	38.25/188=0.203	-0.029 (-0.096, 0.038)	0.0002

ABBREVIATIONS: CI=confidence interval, IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group

NOTES:

- Missing IOP values at follow-up visits are imputed using Markov chain Monte Carlo methods. The calculated proportion is based on the average of 20 imputed datasets.
- Subjects experiencing one or more IOP spikes are counted only once.
- In the ClearVisc treatment arm, 8 subjects have imputed data for this table. In the VISCOAT treatment arm, 4 subjects have imputed data for this table.

[1] The estimated difference in proportions between the treatment groups and the 90% confidence interval is constructed using the normal approximation. An upper confidence limit less than 0.117 favors the hypothesis of noninferiority of ClearVisc as compared to VISCOAT and the one-sided p-value at a 0.050 significance level is presented for this noninferiority test.

Similar proportions were seen using only observed data (**Table 7**). Thirty-one (31) of 184 subjects (0.168) in the ClearVisc arm and 38 of 187 subjects in the VISCOAT arm (0.203) had at least one postoperative IOP spike; one subject in the control group had no postoperative IOP data.

Table 7: Proportion Of Subjects With Postoperative Intraocular Pressure ≥30 mmHg At Any Follow-Up Visit (Observed Data) – Safety Population

	ClearVisc (N=184)	VISCOAT (N=188)	Difference In Proportions (90% CI)
IOP ≥30 mmHg at any follow-up visit	31/184=0.168	38/187=0.203	-0.035 (-0.101, 0.032)

ABBREVIATIONS: CI=confidence interval, IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category

The timepoint of subjects' first IOP spikes were similar for the two groups with the majority of spikes occurring at <6 hours postoperatively (**Table 8**).

Table 8: Percentage Of Subjects Who Had Their First IOP ≥30 mmHg By Visit - Safety Population

Subjects With First IOP Spike Occurring At Each Visit Timing Of Measurement	ClearVisc (N=184)	VISCOAT (N=187)
Visit 1 (n/N, %)	25/180 (13.9%)	34/186 (18.3%)
Measurement Obtained <6 hours postoperatively	19	25
Measurement Obtained ≥6 hours postoperatively	6	9
Visit 2 (n/N, %)	6/181 (3.3%)	4/187 (2.1%)

ABBREVIATIONS: IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category
NOTE: The denominator consists of all subjects that had an IOP measurement at that visit.
NOTE: There were no subjects who had their first IOP spike at Visits 3, 4, or 5.

The proportion of subjects in each group at each postoperative visit with a first IOP increase in the study eye of ≥10 mmHg from baseline is presented in **Table 9** stratified by whether this degree of increase raised the IOP to ≥30 mmHg (qualified as an "IOP spike"). The proportions of subjects at each postoperative visit with their first IOP increase of ≥10 mmHg from baseline are fairly similar between groups with the proportions of these increases at each visit that qualified as IOP spikes also being fairly similar between groups.

Table 9: Percentage Of Subjects Who Had Their First IOP Change From Baseline Of ≥10 mmHg By Visit And IOP Measurement Level - Safety Population

Percentage Of Subjects With First IOP Change From Baseline Of ≥10 mmHg At Each Visit	ClearVisc (N=184)	VISCOAT (N=187)
Visit 1 (n/N, %)	84/180 (46.7%)	85/186 (45.7%)
IOP measurement <30 mmHg	59/84 (70.2%)	51/85 (60.0%)
IOP measurement ≥30 mmHg	25/84 (29.8%)	34/85 (40.0%)
Visit 2 (n/N, %)	11/181 (6.1%)	7/187 (3.7%)
IOP measurement <30 mmHg	8/11 (72.7%)	5/7 (71.4%)
IOP measurement ≥30 mmHg	3/11 (27.3%)	2/7 (28.6%)
Visit 3 (n/N, %)	0/183 (0.0%)	1/185 (0.5%)
IOP measurement <30 mmHg	0	1/1 (100.0%)
IOP measurement ≥30 mmHg	0	0

ABBREVIATIONS: IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category

NOTE: There were no subjects who had their first IOP change from baseline ≥10 mmHg at Visits 4 or 5.

The mean, median, minimum, and maximum of observed IOP measurements at each specified study visit and change from baseline at each specified postoperative study visit are presented in **Table 10** stratified by treatment arm. The mean changes in IOP from baseline were similar between the two groups at each of the specified postoperative visits.

Table 10: Intraocular Pressure - Summary By Visit - Safety Population

Visit	ClearVisc (N=184)		VISCOAT (N=188)	
	Observed Value	Change From Baseline	Observed Value	Change From Baseline
Baseline[1]				
n	184		188	
Mean (SD)	15.3 (2.84)		15.2 (2.73)	
Median	16.0		15.0	
Min, Max	9, 22		9, 24	
Postop Visit 1 (6 ± 2 hours)				
n	180	180	186	186
Mean (SD)	24.7 (7.97)	9.4 (7.60)	25.2 (9.00)	10.0 (8.92)
Median	24.0	9.0	24.0	9.0
Min, Max	10, 62	-10, 43	5, 65	-12, 53
Postop Visit 2 (24 ± 4 hours)				
n	181	181	187	187
Mean (SD)	19.4 (5.81)	4.1 (5.72)	19.0 (5.18)	3.8 (4.98)
Median	19.0	3.0	19.0	4.0
Min, Max	10, 42	-10, 25	8, 37	-10, 19
Postop Visit 3 (7 ± 2 days)				
n	183	183	185	185
Mean (SD)	15.2 (3.42)	-0.1 (3.50)	15.6 (3.43)	0.5 (3.89)
Median	15.0	0.0	15.0	0.0
Min, Max	8, 28	-9, 14	8, 26	-11, 17
Postop Visit 4 (30 ± 7 days)				
n	183	183	187	187
Mean (SD)	14.6 (3.17)	-0.7 (3.25)	15.0 (3.01)	-0.1 (3.30)
Median	14.0	-1.0	15.0	0.0
Min, Max	8, 27	-10, 9	10, 24	-14, 11
Postop Visit 5 (90 ± 14 days)				
n	182	182	187	187
Mean (SD)	13.9 (2.95)	-1.3 (3.22)	14.2 (2.76)	-0.9 (2.87)
Median	14.0	-1.0	14.0	-1.0
Min, Max	6, 27	-10, 7	6, 23	-16, 9

ABBREVIATIONS: Max=maximum, Min=minimum, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device, Postop=postoperative, SD=standard deviation

NOTE: No subjects have imputed data for this table. Only observed data is used.
[1] Baseline is defined as the last available measurement prior to OVD exposure.

In addition, the distributions of the changes in IOP from baseline were fairly similar between the two groups at each postoperative visit. These results are shown through Visit 2 (the 24-hour postoperative visit) in **Table 11**.

Table 11: Categorical Change From Baseline In IOP Measurement (mmHg) By Visit Through Visit 2 - Safety Population

Visit Change From Baseline Category (n, %)	ClearVisc (Total N=184)	VISCOAT (Total N=187)

Number of subjects with both Baseline[1] and Interim between operative and Visit 1 IOP Measurements	N=0	N=0
Number of subjects with both Baseline[1] and Visit 1 IOP Measurements	N=180	N=186
Visit 1		
-15 to -11	0 (0.0%)	1 (0.5%)
-10 to -6	3 (1.7%)	1 (0.5%)
-5 to -1	8 (4.4%)	12 (6.5%)
0 to 4	32 (17.8%)	39 (21.0%)
5 to 9	53 (29.4%)	48 (25.8%)
10 to 14	55 (30.6%)	41 (22.0%)
15 to 19	13 (7.2%)	21 (11.3%)
20 to 24	6 (3.3%)	10 (5.4%)
25 to 29	8 (4.4%)	7 (3.8%)
30 to 34	1 (0.6%)	3 (1.6%)
35 to 39	0 (0.0%)	2 (1.1%)
40 to 44	1 (0.6%)	0 (0.0%)
50 to 54	0 (0.0%)	1 (0.5%)
Number of subjects with both Baseline[1] and Interim between Visit 1 and Visit 2 IOP Measurements	N=24	N=33
Interim between Visit 1 and Visit 2		
-10 to -6	2 (8.3%)	2 (6.1%)
-5 to -1	1 (4.2%)	0 (0.0%)
0 to 4	2 (8.3%)	5 (15.2%)
5 to 9	5 (20.8%)	8 (24.2%)
10 to 14	9 (37.5%)	11 (33.3%)
15 to 19	4 (16.7%)	6 (18.2%)
20 to 24	0 (0.0%)	1 (3.0%)
30 to 34	1 (4.2%)	0 (0.0%)
Number of subjects with both Baseline[1] and Visit 2 IOP Measurements	N=181	N=187
Visit 2		
-10 to -6	7 (3.9%)	6 (3.2%)
-5 to -1	30 (16.6%)	27 (14.4%)
0 to 4	71 (39.2%)	72 (38.5%)
5 to 9	40 (22.1%)	64 (34.2%)
10 to 14	27 (14.9%)	13 (7.0%)
15 to 19	4 (2.2%)	5 (2.7%)
20 to 24	1 (0.6%)	0 (0.0%)
25 to 29	1 (0.6%)	0 (0.0%)

ABBREVIATIONS: IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device

NOTE: For multiple interim visits that occurred within the same interim time period, the largest (most positive) change from baseline is summarized.
[1] Baseline is defined as the last available measurement prior to OVD exposure.

Adverse Effects That Occurred In The PMA Pivotal Clinical Trial:
Intraoperative:
Two of 184 (1.1%) treated subjects in the ClearVisc group and five of 188 (2.7%) treated subjects in the VISCOAT control group had intraoperative complications in the study eye. A torn posterior capsule was reported for one ClearVisc group subject and five VISCOAT group subjects. Two of these events in the control group were considered serious; both resulted in vitreous loss and retained lens material and one

required pars plana vitrectomy with lensectomy and membrane stripping. Hyphema was reported as an intraoperative adverse event (AE) for another subject in the ClearVisc group.

Postoperative:
There was one non-ocular postoperative AE considered related to the device. This was headache, which occurred in a ClearVisc group subject. There were a total of 96 ocular postoperative AEs that occurred in the study eyes of 63 (34.2%) of the 184 treated ClearVisc subjects and 110 ocular postoperative AEs that occurred in the study eyes of 80 (42.6%) of the 188 treated VISCOAT subjects. The ocular postoperative AEs that occurred in each arm are summarized in **Table 12**.

Table 12: Postoperative Ocular Adverse Events (AEs) – Safety Population

Event	ClearVisc (N=184)		VISCOAT (N=188)	
	# Of Events	# (%) Of Subjects, n	# Of Events	# (%) Of Subjects, n
TOTAL	**96**	**63 (34.2%)**	**110**	**80 (42.6%)**
Increased IOP	**34**	**31 (16.8%)**	**38**	**38 (20.2%)**
Intraocular Inflammation	**13**	**11 (6.0%)**	**7**	**7 (3.7%)**
Iritis	6	6 (3.3%)	5	5 (2.7%)
Rebound inflammation	3	3 (1.6%)	2	2 (1.1%)
Macular edema/cystoid macular edema	3	3 (1.6%)	0	0
Macrophage deposits	1	1 (0.5%)	0	0
Corneal Edema Related AEs	**6**	**5 (2.7%)**	**5**	**5 (2.7%)**
Corneal edema	2	2 (1.1%)	1	1 (0.5%)
Corneal wound edema/inflammation	0	0	3	3 (1.6%)
Descemet's folds	3	3 (1.6%)	0	0
Decrease in endothelial cell density from baseline (of 55% to 922 cells/mm^2 at Visit 5)	0	0	1	1 (0.5%)
Increase in pachymetry from baseline (of 429 µ at Visit 2)	1	1 (0.5%)	0	0
Other Corneal AEs	**20**	**19 (10.3%)**	**18**	**17 (9.0%)**
Punctate keratitis	17	17 (9.2%)	13	13 (6.9%)
Corneal abrasion	2	2 (1.1%)	3	3 (1.6%)
Herpes simplex keratitis	1	1 (0.5%)	1	1 (0.5%)
Foreign body - metallic at wound	0	0	1	1 (0.5%)
Conjunctiva	**5**	**5 (2.7%)**	**8**	**8 (4.3%)**
Conjunctival/subconjunctival hemorrhage	4	4 (2.2%)	4	4 (2.1%)
Ocular hyperemia	1	1 (0.5%)	0	0
Conjunctivitis bacterial	0	0	1	1 (0.5%)
Conjunctivitis allergic	0	0	3	3 (1.6%)
Other Ocular Surface Disorders/Lids & Lashes	**7**	**7 (3.8%)**	**9**	**8 (4.3%)**
Eye irritation	1	1 (0.5%)	2	2 (1.1%)
Foreign body sensation	2	2 (1.1%)	3	2 (1.1%)
Dry eye/meibomian gland dysfunction/ blepharitis/chalazion	4	4 (2.2%)	3	3 (1.6%)
Upper lid tenderness	0	0	1	1 (0.5%)
Lens	**7**	**7 (3.8%)**	**8**	**8 (4.3%)**
Posterior capsule opacification	7	7 (3.8%)	6	6 (3.2%)
Halo vision	0	0	1	1 (0.5%)
Negative dysphotopsia	0	0	1	1 (0.5%)

Retina	**3**	**3 (1.6%)**	**8**	**7 (3.7%)**
Epiretinal membrane (ERM)	1	1 (0.5%)	2	2 (1.1%)
Retinal hemorrhage	1	1 (0.5%)	1	1 (0.5%)
Chorioretinal scar	1	1 (0.5%)	0	0
Age-related macular degeneration	0	0	1	1 (0.5%)
Macular drusen	0	0	1	1 (0.5%)
Retinal pigment epithelial changes	0	0	1	1 (0.5%)
Paramacular pigmentary changes – around arcade	0	0	1	1 (0.5%)
Retinal tear	0	0	1	1 (0.5%)
Vitreous	**1**	**1 (0.5%)**	**7**	**7 (3.7%)**
Floaters/degeneration/detachment	1	1 (0.5%)	6	6 (3.2%)
Flashes	0	0	1	1 (0.5%)
Decrease in Vision - Indeterminate	**0**	**0**	**2**	**1 (0.5%)**

ABBREVIATIONS: IOP=intraocular pressure, N=number of subjects per treatment group, n=number of subjects per category

The most frequently reported AE was IOP increase (16.8% and 20.2% of eyes for ClearVisc and VISCOAT groups, respectively). None of the ocular postoperative AEs were reported as serious AEs (SAEs).

2. Effectiveness Results

The analysis of effectiveness was based on the Intent-to-Treat (ITT) Population of all 372 study eyes randomized to treatment and was performed at the 3-month postoperative timepoint (Visit 5). Key effectiveness outcomes are presented in **Tables 13** to **15**.

The results of the analysis of the primary effectiveness endpoint are presented in **Table 13**. For the ITT Population with missing data imputed using MCMC methods, mean percent change in ECD from baseline to Visit 5 was 8.4% loss for the ClearVisc group and 6.8% loss for the VISCOAT control group. The upper confidence limit for the least square mean difference (LSMD) in the percent change in ECD between groups was 3.6%, which is less than the pre-specified noninferiority margin of 5% (p=0.0032). Therefore, the primary effectiveness endpoint of noninferiority of mean percent change in ECD from baseline to postoperative Visit 5 (90 days ± 14 days) in the study eye for the ClearVisc group when compared to the control group was considered met.

Table 13: Change From Baseline In Endothelial Cell Density (ECD; Cells/mm^2) At 90 Days – Intent-to-Treat Population

	ClearVisc (N=184)		**VISCOAT (N=188)**	
Time Point	**Observed Value**	**Percent Loss[1]**	**Observed Value**	**Percent Loss[1]**
Baseline[2]				
n	183		188	
Mean (SD)	2508.8 (363.68)		2487.4 (373.14)	
Median	2498.0		2492.0	
Min, Max	1238, 3404		1242, 3396	
Postop Visit 5 (90 ± 14 days)				
n	168	168	178	178
Mean (SD)	2280.2 (443.03)	8.4 (12.19)	2309.4 (467.84)	6.8 (12.54)
Median	2313.5	3.8	2375.5	2.4
Min, Max	1102, 3574	-10, 55	777, 3467	-11, 63
LSM (SE)[2]	2291.6 (48.49)	8.3 (1.26)	2311.9 (48.94)	6.7 (1.26)
LSMD (ClearVisc - VISCOAT) (SE)[3]		1.6 (1.25)		
90% CI of LSMD[3]		-0.5, 3.6		

P-value[3]		0.0032		
Superiority Test:				
95% CI of LSMD[4]		-0.9, 4.0		
P-value[4]		0.1021		

ABBREVIATIONS: CI=confidence interval, ECD=endothelial cell density, ITT=Intent-to-Treat, LSM=least square mean change from baseline, LSMD=least square mean difference between treatment groups, Max=maximum, Min=minimum, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device, Postop=postoperative, SD=standard deviation, SE=standard error

NOTE: Missing ECD values are imputed using Markov chain Monte Carlo methods. Descriptive statistics are presented with observed data only.

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.
[2] Baseline is defined as the last available measurement prior to OVD exposure.
[3] Estimates of the LSM and LSMD between treatment groups are based on a statistical model with percent loss as the dependent variable, and treatment group and investigator as fixed factors. An upper confidence limit less than 5% favors the hypothesis of noninferiority of ClearVisc as compared to VISCOAT and the one-sided p-value at a 0.050 significance level is presented for this noninferiority test of difference in percent loss.
[4] A two-sided 95% confidence interval is constructed around the LSMD in percent loss between treatment groups and a one-sided p-value is presented. A p-value <0.025 favors the secondary effectiveness hypothesis of superiority of ClearVisc as compared to VISCOAT if the primary endpoints are met.

Similar results were obtained for the Complete-Case analysis that included only those study eyes from the ITT Population which had both observed preoperative and postoperative Visit 5 ECD measurements available (**Table 14**).

Table 14: Endothelial Cell Density (Cells/mm^2) And Percent Loss Sensitivity Analysis: Complete Case - Intent-to-Treat Population

	ClearVisc (N=184)		VISCOAT (N=188)	
Time Point	**Observed Value**	**Percent Loss[1]**	**Observed Value**	**Percent Loss[1]**
Baseline[2]				
n	168		178	
Mean (SD)	2490.5 (357.20)		2476.4 (375.88)	
Median	2483.0		2479.0	
Min, Max	1238, 3404		1242, 3396	
Postop Visit 5 (90 ± 14 days)				
n	168	168	178	178
Mean (SD)	2280.2 (443.03)	8.4 (12.19)	2309.4 (467.84)	6.8 (12.54)
Median	2313.5	3.8	2375.5	2.4
Min, Max	1102, 3574	-10, 55	777, 3467	-11, 63
LSM (SE)[3]	2272.4 (48.99)	8.5 (1.26)	2301.9 (49.23)	6.8 (1.26)
LSMD (ClearVisc - VISCOAT) (SE)[3]		1.7 (1.25)		
90% CI of LSMD[3]		-0.3, 3.8		
P-value[4]		0.0046		

ABBREVIATIONS: CI=confidence interval, ECD=endothelial cell density, ITT=Intent-to-Treat, LSM=least square mean change from baseline, LSMD=least square mean difference between treatment groups, Max=maximum, Min=minimum, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device, Postop=postoperative, SD=standard deviation, SE=standard error

NOTE: Complete case analysis includes only subjects with both Preoperative and Postoperative Visit 5 ECD measurements.

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.
[2] Baseline is defined as the last available measurement prior to OVD exposure.
[3] Estimates of the LSM and LSMD between treatment groups are based on a statistical model with percent loss as the dependent variable, and treatment group and investigator as fixed factors. An upper confidence limit less than 5% favors the hypothesis of noninferiority of ClearVisc as compared to VISCOAT.
[4] The one-sided p-value at a 0.050 significance level is presented for the noninferiority test of difference in percent loss.

The distribution of the percent loss in ECD from baseline at Visit 5 (with negative (-) values indicating gain) in each arm is shown in **Table 15**. The distributions are fairly similar between groups, although there is a trend for slightly higher frequencies of percent losses at higher ECD percent levels with the ClearVisc OVD than the control.

Table 15: Categorical Percent Loss In Endothelial Cell Density (Cells/mm^2) At Visit 5: Complete Case – Intent-to-Treat Population

Visit Percent Loss	ClearVisc (N=184)	VISCOAT (N=188)
Number of subjects with both Baseline[1] and Postoperative Visit 5 ECD Measurements	n=168	n=178
Postoperative Visit 5 (90 days +/- 14 days)		
>-15 to -10%	1 (0.6%)	1 (0.6%)
>-10 to -5%	4 (2.4%)	4 (2.2%)
>-5 to 0%	34 (20.2%)	50 (28.1%)
>0 to 5%	56 (33.3%)	51 (28.7%)
>5 to 10%	24 (14.3%)	31 (17.4%)
>10 to 15%	13 (7.7%)	16 (9.0%)
>15 to 20%	6 (3.6%)	5 (2.8%)
>20 to 25%	11 (6.5%)	4 (2.2%)
>25 to 30%	5 (3.0%)	5 (2.8%)
>30 to 35%	7 (4.2%)	3 (1.7%)
>35 to 40%	2 (1.2%)	3 (1.7%)
>40 to 45%	1 (0.6%)	0
>45 to 50%	2 (1.2%)	0
>50 to 55%	2 (1.2%)	1 (0.6%)
>55 to 60%	0	3 (1.7%)
>60 to 65%	0	1 (0.6%)

ABBREVIATIONS: ECD=endothelial cell density, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device
[1] Baseline is defined as the last available measurement prior to OVD exposure.

3. Subgroup Analyses
The following characteristics were evaluated for potential association with outcomes:

Subgroup Analyses Concerning Study Sites:
Subgroup analysis concerning study sites was conducted as an assessment of data poolability across sites for both primary safety and effectiveness endpoints.

For the primary safety endpoint, poolability of results (observed data only) across study sites was assessed by performing a Cochran-Mantel-Haenszel test between the treatment groups stratified by study site. The p-value for the Breslow-Day test for homogeneity of odds ratios across study sites was compared to a critical value of 0.15. The resulting p-value is 0.4866. Based on these results summarized in **Table 16** below, it is reasonable to assume that there is minimal site effect on device safety performance.

Table 16: Proportion Of Subjects With Postoperative Intraocular Pressure ≥30 mmHg At Any Follow-Up Visit By Study Center - Safety Population

	ClearVisc (N=184)	**VISCOAT (N=188)**
Site 1	n=24	n=25
IOP ≥30 mmHg at any follow-up visit	0	0
Site 2	n=11	n=12
IOP ≥30 mmHg at any follow-up visit	0	0
Site 3	n=27	n=28
IOP ≥30 mmHg at any follow-up visit	4/27=0.148	4/28=0.143
Site 4	n=14	n=16
IOP ≥30 mmHg at any follow-up visit	6/14=0.429	10/16=0.625
Site 5	n=21	n=23
IOP ≥30 mmHg at any follow-up visit	4/21=0.190	10/23=0.435
Site 6	n=25	n=25
IOP ≥30 mmHg at any follow-up visit	5/25=0.200	2/25=0.080
Site 7	n=6	n=7
IOP ≥30 mmHg at any follow-up visit	2/6=0.333	3/7=0.429
Site 8	n=7	n=7
IOP ≥30 mmHg at any follow-up visit	1/7=0.143	1/7=0.143
Site 9	n=17	n=15
IOP ≥30 mmHg at any follow-up visit	4/17=0.235	3/15=0.200
Site 10	n=2	n=3
IOP ≥30 mmHg at any follow-up visit	1/2=0.500	1/3=0.333
Site 11	n=12	n=12
IOP ≥30 mmHg at any follow-up visit	2/12=0.167	2/12=0.167
Site 12	n=1	n=0
IOP ≥30 mmHg at any follow-up visit	0	
Site 13	n=6	n=4
IOP ≥30 mmHg at any follow-up visit	1/6=0.167	0
Site 15	n=7	n=6
IOP ≥30 mmHg at any follow-up visit	0	1/6=0.167
Site 16	n=3	n=3

IOP ≥30 mmHg at any follow-up visit	1/3=0.333	0
Site 17	n=1	n=2
IOP ≥30 mmHg at any follow-up visit	0	1/2=0.500
P-value[1]	0.4866	
P-value[2]	0.6610	

ABBREVIATIONS: CMH=Cochran-Mantel-Haenszel, IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category

NOTES:
- Subjects experiencing one or more IOP spikes are counted only once.
- No subjects have imputed data for this table. Only observed data is used.

[1] The p-value comparing treatment groups is based on a CMH test stratified by study center.
[2] The p-value for the Breslow-Day test for homogeneity of odds ratios across study sites is compared to a critical value of 0.15.

For the primary effectiveness endpoint, poolability across study sites was evaluated by modeling ECD loss (%) as a function of the fixed class variables of treatment and investigator including their interaction using the available data for the ITT Set. Poolability is assessed by comparing the p-value for the interaction to a critical value of 0.15. Based on the results summarized in **Table 17** below, the p-value for the interaction term is 0.3984. Therefore, it is believed that a possible site effect on device effectiveness is reasonably low.

Table 17: Endothelial Cell Density (Cells/mm^2) And Percent Loss By Study Center – Intent-to-Treat Population

	ClearVisc (N=184)		VISCOAT (N=188)	
Time Point	**Observed Value**	**Percent Loss[1]**	**Observed Value**	**Percent Loss[1]**
Baseline[2]				
n	183		188	
Mean (SD)	2508.8 (363.68)		2487.4 (373.14)	
Median	2498.0		2492.0	
Min, Max	1238, 3404		1242, 3396	
Postop Visit 5 (90 ± 14 days)				
n	168	168	178	178
Mean (SD)	2280.2 (443.03)	8.4 (12.19)	2309.4 (467.84)	6.8 (12.54)
Median	2313.5	3.8	2375.5	2.4
Min, Max	1102, 3574	-10, 55	777, 3467	-11, 63
LSM (SE)[3]	2272.4 (34.20)	8.5 (0.88)	2301.9 (34.37)	6.8 (0.88)
LSMD (ClearVisc - VISCOAT) (SE)[3]		1.7 (0.87)		
90% CI of LSMD[3]		0.3, 3.2		
P-value[4]		0.3984		

ABBREVIATIONS: CI=confidence interval, LSM=least square mean change from baseline, LSMD=least square mean difference between treatment groups, Max=maximum, Min=minimum, N=number of subjects per treatment group, n=number of subjects per category, OVD=ophthalmic viscosurgical device, Postop=postoperative, SD=standard deviation, SE=standard error

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.
[2] Baseline is defined as the last available measurement prior to OVD exposure.

[3] Estimates of the LSM and LSMD between treatment groups are based on a statistical model with difference in percent loss as the dependent variable, and treatment group, investigator, and the interaction term as fixed factors.
[4] A p-value for the interaction term (treatment*investigator)>0.15 indicates poolability across sites.

Subgroup analyses concerning IOP-reducing intervention:
A subgroup analysis was conducted concerning the primary safety endpoint according to the following categorization:

- Subjects who received IOP-reducing intervention; and
- Subjects who did not receive IOP-reducing intervention.

The results are presented in **Table 18** below.

Table 18: Proportion Of Subjects With Postoperative Intraocular Pressure ≥30 mmHg At Any Follow-Up Visit By IOP Intervention - Safety Population

	ClearVisc (N=184)	VISCOAT (N=188)	Difference In Proportion (ClearVisc - VISCOAT)[1]	
			Estimate (95% CI)	P-value
Subjects who received IOP-reducing intervention	n=34	n=39		
IOP ≥30 mmHg at any follow-up visit	28/34=0.824	35/39=0.897	-0.074 (-0.208, 0.060)	0.0095
Subjects who did not receive IOP-reducing intervention	n=150	n=149		
IOP ≥30 mmHg at any follow-up visit	4.05/150=0.027	3.25/149=0.022	0.005 (-0.026, 0.036)	<0.0001

ABBREVIATIONS: CI=confidence interval, IOP=intraocular pressure, mmHg=millimeters of mercury, N=number of subjects per treatment group, n=number of subjects per category

NOTES:
- Missing IOP values at follow-up visits are imputed using Markov chain Monte Carlo methods. The calculated proportion is based on the average of 20 imputed datasets.
- Subjects experiencing one or more IOP spikes are counted only once.
- In the ClearVisc treatment arm, 8 subjects have imputed data for this table. In the VISCOAT treatment arm, 4 subjects have imputed data for this table.

[1] The estimated difference in proportions between the treatment groups and the 90% confidence interval is constructed using the normal approximation. An upper confidence limit less than 0.117 favors the hypothesis of noninferiority of ClearVisc as compared to VISCOAT and the one-sided p-value at a 0.050 significance level is presented for this noninferiority test.

For both subgroups, the results demonstrated noninferiority for ClearVisc when compared with VISCOAT (p=0.0095 for subjects who received IOP-reducing intervention and p<0.0001 for subjects who did not receive IOP-reducing intervention).

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

D. 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 1 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: 1
- Proprietary interest in the product tested held by the investigator: 0
- Significant equity interest held by investigator in sponsor of covered study: 0

Bausch + Lomb has adequately disclosed the financial interest/arrangements with clinical investigators. The one investigator with a disclosable financial interest treated only 6 subjects out of 184 (3.3%) in the ClearVisc group and only 7 subjects out of 188 (3.7%) in the VISCOAT group. Given the results of the primary analyses, there is little concern that the results of these subjects significantly affected the outcomes of the trial. Therefore, the information provided does not raise any questions about the reliability of the data.

StableVisc Clinical Trial
The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of StableVisc OVD for use as a surgical aid in patients undergoing ophthalmic anterior segment procedures in the US under IDE # G190194. 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
Subjects were treated between December 12, 2019 and January 31, 2022. The database for this PMA reflected data collected through the last postoperative visit on January 31, 2022 and the database lock on March 25, 2022 and included 390 subjects. There were 22 investigational sites.

The study was a prospective, multi-center, active control, two-armed, randomized, partially masked, comparative clinical trial. Eligible subjects were randomized 1:1 at the time of planned cataract surgery with posterior chamber intraocular lens (IOL) implantation to receive either the investigational device (StableVisc OVD) or the control OVD (ProVisc® OVD). Randomization was stratified by site, age group, and cataract severity. Only one eye of each subject was included in the study. Subjects were followed for 90 days postoperatively (Visit 5).

ProVisc® OVD is a legally marketed alternative with similar indications for use and similar properties (i.e. cohesive) as the StableVisc OVD. Although the investigators were not masked at the time of surgery as to which OVD was used, a delegated examiner at each site who was masked to the randomized assignment of each patient performed all postoperative assessments.

Non-inferiority statistical hypothesis testing for safety and effectiveness endpoints were pre-specified.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the StableVisc OVD study was limited to subjects who met the following inclusion criteria:

- The subject must have been at least 45 years old and had a clinically documented diagnosis of age-related non-complicated cataract that was considered amenable to treatment with standard phacoemulsification cataract extraction and IOL implantation.

- The subject must have had the capability to provide written informed consent on the Institutional Review Board (IRB) approved Informed Consent Form (ICF) and provide authorization as appropriate for local privacy regulations.
- The subject must have been willing and able to return for all scheduled follow-up examinations through 90 days following surgery.
- The subject must have had clear intraocular media other than the cataract in the operative eye.

Patients were not permitted to enroll in the StableVisc OVD study if they met any of the following exclusion criteria:

- The subject had participated in any drug or device clinical investigation within 30 days prior to entry into this study and/or during the period of study participation.
- The subject had any corneal pathology (e.g., significant scarring, guttata, inflammation, edema, dystrophy, etc.) in the operative eye.
- The subject had anterior segment pathology likely to increase the risk of an adverse outcome for phacoemulsification cataract surgery (e.g., pseudoexfoliation syndrome, synechiae, iris atrophy, inadequate dilation, shallow anterior chamber, traumatic cataract, lens subluxation) in the operative eye.
- The subject had any condition which prevented reliable specular microscopy in the operative eye.
- The subject had a congenital ocular anomaly (e.g., aniridia, congenital cataract) in the operative eye.
- The subject had a baseline ECD < 1500 cells/mm^2 in the operative eye.
- The subject had a Grade 4+ nuclear cataract density in the planned operative eye.
- The subject had glaucoma or ocular hypertension (IOP > 24 mmHg) in the operative eye.
- The subject had any abnormality that prevented reliable Goldmann applanation tonometry in the operative eye.
- The subject had a known allergy to any of the components of the test or control OVDs.
- The subject was using any topical or systemic medications known to interfere with visual performance or complicate cataract surgery within 30 days of enrollment or during the study.
- The subject was scheduled to undergo other combined intraocular procedures during the cataract/IOL implantation surgery in the operative eye. NOTE: A relaxing keratotomy was allowed.
- The subject had diabetic retinopathy, wet age-related macular degeneration, or other retinal pathology that might limit postoperative visual acuity or predisposed the subject to postoperative retinal complications in the operative eye.
- The subject's fellow eye was already participating in this study.
- The subject had a history of chronic or recurrent inflammatory eye disease (e.g., iritis, scleritis, uveitis, iridocyclitis, rubeosis iridis) in the operative eye.
- The subject had a best corrected distance visual acuity of logarithm of the minimum angle of resolution (LogMAR) 1.0 (20/200, 6/60) or worse in the fellow eye.
- The subject had had previous corneal surgery in the planned operative eye.
- The subject had a previous retinal detachment in the operative eye.
- Females of childbearing potential (those who were not surgically sterilized or not postmenopausal for at least 12 months) were excluded from participation in the study if they met any one of the following conditions:
    - they were currently pregnant;
    - they planned to become pregnant during the study; and/or
    - they were breast-feeding.

2. Follow-up Schedule

All subjects were scheduled for follow-up examinations at 6 hours ± 2 hours, 24 hours ± 4 hours, 7 days ± 2 days, 30 days ± 7 days, and 90 days ± 14 days postoperatively.

Table 19 includes the parameters measured preoperatively and postoperatively. Adverse events and complications were recorded at all visits.

Table 19: Study visit schedule and parameters evaluated at each study visit.

PROCEDURE/ ASSESSMENTS	Preop Visit Day -60 to Day -1	Op Visit Day 0	Postop Visit 6 Hours ± 2 hours Postop	Postop Visit 2 24 Hours ± 4 hours Postop	Postop Visit 3 7 Days ± 2 days Postop	Postop Visit 4 30 Days ± 7 days Postop	Postop Visit 5 90 Days ± 14 days Postop
Informed Consent	X						
Demographic Data	X						
Medical History	X						
Urine Pregnancy Test	X	X			X	X	X
Eligibility Criteria	X	X					
Randomization		X					
Fellow Eye Status	X						
Surgical Procedure		X					
Manifest Subjective Refraction	X						X
Uncorrected Distance VA	X		X	X	X	X	X
Best Corrected Distance VA	X						X
Cataract Classification	X						
Slit Lamp Examination	X		X	X	X	X	X
IOP (Goldmann tonometry)	X		X	X	X	X	X
Dilated Fundus Examination	X						X
Ultrasound Pachymetry	X			X			X
ECD via specular microscopy of the central cornea	X						X
Concomitant Medications	X	X	X	X	X	X	X
Adverse Events	X	X	X	X	X	X	X

Abbreviations: ECD = endothelial cell density; IOP = intraocular pressure;VA = visual acuity

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

3. Clinical Endpoints

With regard to safety, the primary safety endpoint was evaluated by a non-inferiority test of the proportion of subjects who experienced at least one IOP measurement ≥ 30 mmHg in the study eye at any follow-up visit. A one-sided upper 95% confidence interval (CI) for the difference between the test and control groups (i.e., test – control) in the proportion of subjects with at least one IOP measurement ≥ 30 mmHg in the study eye at any follow-up visit was constructed using the normal approximation to test the null hypothesis for the primary safety endpoint. If the upper confidence limit was less than 5%, then the null hypothesis of inferiority for the primary effectiveness endpoint was rejected in favor of the alternative hypothesis of noninferiority.

With regard to effectiveness, the primary effectiveness endpoint was a test for noninferiority of the test OVD (StableVisc OVD) when compared to the control OVD (ProVisc®) in mean percent change in endothelial cell density (ECD) from baseline to Postoperative Visit 5 (90 Days ± 14 days) in the study eye. Following Markov chain Monte Carlo (MCMC) imputation of missing cell density data, a one-sided upper 95% confidence limit for the mean difference (test – control) in percent change between the test and comparator OVDs was constructed. If the upper confidence limit was less than 5%, then the null hypothesis of inferiority for the primary effectiveness endpoint was rejected in favor of the alternative hypothesis of noninferiority.

Therefore, both the primary safety endpoint and the primary effectiveness endpoint needed to be met in order for the trial to be considered a success.

B. Accountability of PMA Cohort

At the time of database lock, of 390 subjects randomized to treatment in the PMA trial, 97.4% (380/390) subjects were available for analysis at the completion of the study, the 3-month postoperative visit (Visit 5; **Table 20**). Of the 380 subjects that completed the study, 187 subjects and 193 subjects were in the StableVisc and ProVisc® groups, respectively (**Table 21**).

Table 20: Subject Accountability (All Enrolled Subjects)

	Preop Visit (N=388)	Op Visit Day 0 (N=388)	Postop Visit 1 (N=388)	Postop Visit 2 (N=388)	Postop Visit 3 (N=388)	Postop Visit 4 (N=388)	Postop Visit 5 (N=388)
Available for Analysis	388/388 (100%)	388/388 (100%)	387/388 (99.7%)	388/388 (100%)	385/388 (99.2%)	380/388 (97.9%)	381/388 (98.2%)
Discontinued	0	0	0	0	0	2/388 (0.5%)	3/388 (0.8%)
Lost to Follow-up	0	0	0	0	1/388 (0.3%)	1/388 (0.3%)	4/388 (1.0%)
Missing[a]	0	0	1/388 (0.3%)	0	2/388 (0.5%)	5/388 (1.3%)	0
Percent Accountability[b]	100%	100%	99.7%	100%	99.2%	98.4%	99.0%

Abbreviations: N = number of subjects in total, Op = operative, Preop = preoperative, Postop = postoperative
[a] Missing subjects were those who were not available for analysis, not active, discontinued, or lost to follow-up.
[b] Percent Accountability by Visit = [(# Available for Analysis)/(# Enrolled - # Discontinued - # Active)]*100.

Table 21: Subject Accountability by Treatment Assignment - All Treated Subjects

Treatment Group		Preop Visit	Op Visit Day 0	Postop Visit 1	Postop Visit 2	Postop Visit 3	Postop Visit 4	Postop Visit 5
StableVisc (N=192; n, %)	Available for analysis	192/192 (100%)	192/192 (100%)	192/192 (100%)	192/192 (100%)	192/192 (100%)	189/192 (98.4%)	187/192 (97.4%)
	Active[1]	0	0	0	0	0	0	0
	Discontinued	0	0	0	0	0	2/192 (1.0%)	3/192 (1.6%)
	Lost to Follow-up	0	0	0	0	0	0	2/192 (1.0%)
	Missing[2]	0	0	0	0	0	1/192 (0.5%)	0
	Percent Accountability[3]	100%	100%	100%	100%	100%	99.5%	98.9%
ProVisc® (N=196; n, %)	Available for analysis	196/196 (100%)	196/196 (100%)	195/196 (99.5%)	196/196 (100%)	193/196 (98.5%)	191/196 (97.4%)	194/196 (99.0%)
	Active[1]	0	0	0	0	0	0	0

Treatment Group	Preop Visit	Op Visit Day 0	Postop Visit 1	Postop Visit 2	Postop Visit 3	Postop Visit 4	Postop Visit 5
Discontinued	0	0	0	0	0	0	0
Lost to Follow-up	0	0	0	0	1/196 (0.5%)	1/196 (0.5%)	2/196 (1.0%)
Missing[2]	0	0	1/196 (0.5%)	0	2/196 (1.0%)	4/196 (2.0%)	0
Percent Accountability[3]	100%	100%	99.5%	100%	98.5%	97.4%	99.0%

Abbreviations: N = number of subjects in total, n = number of subjects per treatment group, Op = operative, Preop = preoperative, Postop = postoperative

[1] Active subjects are those still ongoing in the study.

[2] Missing subjects are those who are not available for analysis, not active, discontinued, or lost to follow-up.

[3] Percent Accountability by Visit = [(# Available for Analysis) / (# Enrolled - # Discontinued - # Active)]*100

The demographics of the trial population (**Table 22**) are representative of the US intended use population for an OVD. Demographics were similar between the treatment groups, with the exceptions of a higher percentage of Hispanic or Latino subjects in the StableVisc group compared with the ProVisc® group.

Table 22: Demographics - Safety Population

	StableVisc (N=192)	ProVisc® (N=196)	Total (N=388)
Age[1]			
n	192	196	388
Mean (SD)	68.7 (7.78)	67.9 (8.24)	68.3 (8.01)
Median	70.0	68.0	69.0
Min, Max	46, 93	45, 88	45, 93
≤ 65 years	59 (30.7%)	65 (33.2%)	124 (32.0%)
> 65 years	133 (69.3%)	131 (66.8%)	264 (68.0%)
Sex			
Male	77 (40.1%)	69 (35.2%)	146 (37.6%)
Female	115 (59.9%)	127 (64.8%)	242 (62.4%)
Ethnicity			
Hispanic or Latino	33 (17.2%)	21 (10.7%)	54 (13.9%)
Not Hispanic or Latino	159 (82.8%)	175 (89.3%)	334 (86.1%)
Race			
American Indian / Alaska Native	0	0	0
Asian	26 (13.5%)	26 (13.3%)	52 (13.4%)
Black / African American	11 (5.7%)	19 (9.7%)	30 (7.7%)
Native Hawaiian / Other Pacific Islander	1 (0.5%)	2 (1.0%)	3 (0.8%)
White	154 (80.2%)	149 (76.0%)	303 (78.1%)

Abbreviations: Max = maximum, Min = minimum, N = number of subjects per treatment group, n = number of subjects per category, SD = standard deviation

[1] Age is calculated relative to the date of informed consent as described in the Statistical Analysis Plan

The baseline ocular characteristics are summarized in **Table 23**. Baseline ocular characteristics were similar between treatment groups, with the exception of the percentage of subjects with OD as the study eye (60.4% [116/192] vs 52.6% [103/196]) and the percentage of subjects with a cataract classification of nuclear or combination (35.9% [69/192] vs 42.3% [83/196] for nuclear and 63.5% [122/192] vs 55.1% [108/196] for combination) for the StableVisc group compared with the ProVisc® group, respectively.

Table 23: Baseline Ocular Characteristics - Safety Population

	StableVisc (N=192)	ProVisc® (N=196)	Total (N=388)
Study Eye			
OD	116 (60.4%)	103 (52.6%)	219 (56.4%)
OS	76 (39.6%)	93 (47.4%)	169 (43.6%)
Cataract Classification			
Type			
Nuclear	69 (35.9%)	83 (42.3%)	152 (39.2%)
Cortical	1 (0.5%)	2 (1.0%)	3 (0.8%)
Posterior Subcapsular	0	3 (1.5%)	3 (0.8%)
Combination	122 (63.5%)	108 (55.1%)	230 (59.3%)
Density			
Slight (1+)	17 (8.9%)	18 (9.2%)	35 (9.0%)
Moderate (2+)	119 (62.0%)	125 (63.8%)	244 (62.9%)
Dense (3+)	56 (29.2%)	53 (27.0%)	109 (28.1%)
Very Dense (4+)	0	0	0
Fellow Eye Status			
Normal	1 (0.5%)	2 (1.0%)	3 (0.8%)
Cataract	93 (48.4%)	87 (44.4%)	180 (46.4%)
Aphakic	0	0	0
Pseudophakic	98 (51.0%)	107 (54.6%)	205 (52.8%)

Abbreviations: N = number of subjects per treatment group, OD = oculus dexter (right eye), OS = oculus sinister (left eye)

C. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the Safety Population of all 388 eyes that were exposed to either the StableVisc OVD or ProVisc® OVD (control). The key safety outcomes for this study are presented below in **Tables 24** to **28**. Adverse effects are reported in **Table 29**.

The results of the analysis of the primary safety endpoint are presented in **Table 24**. For this analysis, the proportion of subjects with postoperative IOP ≥ 30 mmHg at any Follow-Up Visit was 0.052 for the StableVisc group and 0.082 for the ProVisc® group (difference estimate [test – control] = -0.030; 90% CI = -0.0711 to 0.0121). These results demonstrated that the study met its endpoint for noninferiority for StableVisc when compared with ProVisc® (p=0.0027). In this analysis, the null hypothesis was that the test was inferior to the control; therefore, a p-value of < 0.05 determines that this null hypothesis can be rejected and StableVisc can be considered noninferior to ProVisc®. This analysis as presented here does not evaluate, nor was it intended to evaluate, whether StableVisc was superior to ProVisc®.

Table 24: Proportion of Subjects with Postoperative Intraocular Pressure ≥30 mmHg at Any Follow-Up Visit - Safety Population

	StableVisc (N=192)	ProVisc® (N=196)	Difference in Proportion (StableVisc – ProVisc®)[a] Estimate (90% CI)	P-value
IOP ≥ 30 mmHg at any follow-up visit	10/192 = 0.052	16/196 = 0.082	-0.030 (-0.0711, 0.0121)	0.0027

Abbreviations: CI = confidence interval, IOP = intraocular pressure, mmHg = millimeters of mercury, N = number of subjects per treatment group

Notes: Subjects experiencing one or more IOP spikes were counted only once. No subjects had imputed data for this table. Only observed data were used.

[a] The estimated difference in proportions between the treatment groups and the 90% CI was constructed using the normal approximation z-test. An upper confidence limit less than 0.1 favored the hypothesis of noninferiority of StableVisc as compared to ProVisc® and the one-sided p-value at a 0.050 significance level was presented for this noninferiority test.

The timepoint of subjects' first IOP spikes were similar for the two groups with the majority of spikes occurring at < 6 hours postoperatively (**Table 25**).

Table 25: Percentage of Subjects Who Had Their First IOP ≥30 mmHg by Visit - Safety Population

Subjects with First IOP Spike Occurring at Each Visit Timing of Measurement	StableVisc (N=192)	ProVisc® (N=196)
Visit 1	7/191 (3.7%)	13/195 (6.7%)
Measurement Obtained <6 hours postoperatively	6	11
Measurement Obtained ≥6 hours postoperatively	1	2
Interim between Visit 1 and Visit 2	1/13 (7.7%)	0
Measurement Obtained <6 hours postoperatively	1	0
Measurement Obtained ≥6 hours postoperatively	0	0
Visit 2	2/192 (1.0%)	2/195 (1.0%)
Visit 3	1/192 (0.5%)	1/193 (0.5%)

Abbreviations: IOP = intraocular pressure, mmHg = millimeters of mercury, N = number of subjects per treatment group

Note: The denominator consists of all subjects that had an IOP measurement at that visit.

Note: There were no subjects who had their first IOP spike at Visits 4 or 5.

The proportion of subjects in each group at each postoperative visit with a first IOP increase in the study eye of ≥ 10 mmHg from baseline is presented in **Table 26** stratified by whether this degree of increase raised the IOP to ≥ 30 mmHg qualified as an "IOP spike"). The proportions of subjects at each postoperative visit with their first IOP increase of ≥ 10 mmHg from baseline are fairly similar between groups with the proportions of these increases at each visit that qualified as IOP spikes also being fairly similar between groups.

Table 26: Percentage of Subjects Who Had Their First IOP Change from Baseline of ≥10 mmHg by Visit and IOP Measurement Level - Safety Population

Percentage of Subjects with First IOP Change from Baseline of ≥10 mmHg at Each Visit	StableVisc (N=192)	ProVisc® (N=196)
Visit 1	25/191 (13.1%)	29/195 (14.9%)
IOP measurement <30 mmHg	18	17
IOP measurement ≥30 mmHg	7	12
Visit 2	12/192 (6.3%)	7/195 (3.6%)
IOP measurement <30 mmHg	10	5
IOP measurement ≥30 mmHg	2	2

Percentage of Subjects with First IOP Change from Baseline of ≥10 mmHg at Each Visit	StableVisc (N=192)	ProVisc® (N=196)
Interim between Visit 2 and Visit 3	1/9 (11.1%)	0
IOP measurement <30 mmHg	1	0
IOP measurement ≥30 mmHg	0	0
Visit 3	2/192 (1.0%)	2/193 (1.0%)
IOP measurement <30 mmHg	1	1
IOP measurement ≥30 mmHg	1	1

Abbreviations: IOP = intraocular pressure, mmHg = millimeters of mercury, N = number of subjects per treatment group
Note: The denominator consists of all subjects that had an IOP measurement at that visit.
Note: There were no subjects who had their first IOP change from baseline ≥ 10 mmHg at Visits 4 or 5.

The mean, median, minimum, and maximum of observed IOP measurements at each specified study visit and change from baseline at each specified postoperative study visit are presented in **Table 27** stratified by treatment arm. The mean changes in IOP from baseline were similar between the two groups at each of the specified postoperative visits.

Table 27: Intraocular Pressure - Summary by Visit - Safety Population

	StableVisc (N=192)		ProVisc® (N=196)	
Visit	Observed Value	Change from Baseline	Observed Value	Change from Baseline
Baseline[1]				
n	192		196	
Mean (SD)	15.7 (2.80)		15.8 (3.04)	
Median	16.0		16.0	
Min, Max	8, 22		8, 24	
Postop Visit 1 (6 ± 2 hours)				
n	191	191	195	195
Mean (SD)	19.5 (6.53)	3.8 (6.29)	20.0 (6.75)	4.2 (6.87)
Median	19.0	4.0	20.0	4.0
Min, Max	8, 48	-12, 31	6, 60	-11, 48
Postop Visit 2 (24 ± 4 hours)				
n	192	192	195	195
Mean (SD)	18.0 (4.70)	2.3 (4.57)	18.4 (4.78)	2.6 (4.73)
Median	18.0	2.0	18.0	2.0
Min, Max	10, 38	-7, 20	10, 36	-9, 19
Postop Visit 3 (7 ± 2 days)				
n	192	192	193	193
Mean (SD)	15.6 (3.76)	-0.1 (3.92)	15.7 (3.39)	-0.0 (3.49)
Median	15.0	0.0	16.0	0.0
Min, Max	9, 35	-8, 22	4, 30	-15, 11
Postop Visit 4 (30 ± 7 days)				
n	181	181	184	184
Mean (SD)	14.5 (3.05)	-1.2 (3.10)	15.0 (3.14)	-0.7 (3.32)
Median	14.0	-1.0	15.0	-1.0
Min, Max	8, 22	-10, 7	9, 26	-7, 9
Postop Visit 5 (90 ± 14 days)				
n	184	184	192	192
Mean (SD)	14.0 (2.85)	-1.7 (3.06)	14.1 (3.15)	-1.7 (3.11)
Median	14.0	-1.0	14.0	-1.0
Min, Max	8, 25	-11, 9	8, 24	-9, 6

Abbreviations: IOP= intraocular pressure, Max = maximum, Min = minimum, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device, SD = standard deviation;
Note: No subjects have imputed data for this table. Only observed data is used.
[1] Baseline is defined as the last available measurement prior to OVD exposure.

In addition, the distributions of the changes in IOP from baseline were fairly similar between the two groups at each postoperative visit. These results are shown through Visit 2 (the 24-hour postoperative visit) in **Table 28**.

Table 28: Categorical Change from Baseline in IOP Measurement (mmHg) by Visit through Visit 2 - Safety Population

Visit Change from Baseline Category (n, %)	StableVisc (N=192)	ProVisc® (N=196)
Number of subjects with both Baseline[1] and Interim between operative and Visit 1 IOP Measurements	N=0	N=0
Number of subjects with both Baseline[1] and Visit 1 IOP Measurements	n=191	n=195
Visit 1		
-15 to -11	3 (1.6%)	1 (0.5%)
-10 to -6	7 (3.7%)	7 (3.6%)
-5 to -1	28 (14.7%)	34 (17.4%)
0 to 4	75 (39.3%)	71 (36.4%)
5 to 9	53 (27.7%)	53 (27.2%)
10 to 14	19 (9.9%)	18 (9.2%)
15 to 19	3 (1.6%)	7 (3.6%)
20 to 24	1 (0.5%)	2 (1.0%)
25 to 29	0	1 (0.5%)
30 to 34	2 (1.0%)	0
45 to 49	0	1 (0.5%)
Number of subjects with both Baseline[1] and Interim between Visit 1 and Visit 2 IOP Measurements	n=8	n=11
Interim between Visit 1 and Visit 2		
-15 to -11	3 (37.5%)	1 (9.1%)
-10 to -6	1 (12.5%)	3 (27.3%)
-5 to -1	0	1 (9.1%)
5 to 9	1 (12.5%)	0
10 to 14	1 (12.5%)	4 (36.4%)
15 to 19	1 (12.5%)	2 (18.2%)
20 to 24	1 (12.5%)	0
Number of subjects with both Baseline[1] and Visit 2 IOP Measurements	n=192	n=195
Visit 2		
-10 to -6	3 (1.6%)	7 (3.6%)
-5 to -1	52 (27.1%)	35 (17.9%)
0 to 4	85 (44.3%)	95 (48.7%)
5 to 9	35 (18.2%)	41 (21.0%)
10 to 14	15 (7.8%)	15 (7.7%)
15 to 19	1 (0.5%)	2 (1.0%)
20 to 24	1 (0.5%)	0

Abbreviations: IOP = intraocular pressure, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device
Note: For multiple interim visits that occurred within the same interim time period, the largest (most positive) change from baseline is summarized.

[1] Baseline is defined as the last available measurement prior to OVD exposure.

Adverse effects that occurred in the PMA pivotal clinical trial:

Intraoperative:
The only intraoperative complications reported for more than two subjects in either treatment group were the placement of a suture to seal the corneal incision (3 subjects [1.6%, 3/192] in the StableVisc group and 5 subjects [2.6%, 5/196] in the ProVisc® group) and the use of standard of care surgical medication with prophylactic IOP lowering treatments (7 subjects [3.6%, 7/192] in the StableVisc group and 8 subjects [4.1%, 8/196] in the ProVisc® group).

Postoperative:
There were no non-ocular postoperative adverse event (AE) considered related to the device. The ocular postoperative AEs that occurred in each arm are summarized in **Table 29**.

Table 29: **Postoperative Ocular Adverse Events (AEs) – Safety Population**

System Organ Class[1] / Preferred Term[1]	StableVisc (N=192)	ProVisc® (N=196)
Total Number of TEAEs	75	90
Subjects Reporting at Least One TEAE	62 (32.3%)	63 (32.1%)
Eye disorders	34 (17.7%)	33 (16.8%)
Corneal oedema	14 (7.3%)	10 (5.1%)
Dry eye	3 (1.6%)	3 (1.5%)
Punctate keratitis	1 (0.5%)	3 (1.5%)
Anterior chamber inflammation	3 (1.6%)	0
Conjunctival haemorrhage	1 (0.5%)	2 (1.0%)
Cystoid macular oedema	1 (0.5%)	2 (1.0%)
Foreign body sensation in eyes	2 (1.0%)	1 (0.5%)
Iritis	2 (1.0%)	1 (0.5%)
Photophobia	2 (1.0%)	1 (0.5%)
Posterior capsule opacification	1 (0.5%)	2 (1.0%)
Vitreous detachment	2 (1.0%)	1 (0.5%)
Vitreous floaters	2 (1.0%)	1 (0.5%)
Conjunctival hyperaemia	0	2 (1.0%)
Anterior chamber cell	0	1 (0.5%)
Astigmatism	1 (0.5%)	0
Blepharospasm	0	1 (0.5%)
Diabetic retinopathy	1 (0.5%)	0
Diplopia	0	1 (0.5%)
Eye disorder	0	1 (0.5%)
Eye inflammation	1 (0.5%)	0
Eye pain	0	1 (0.5%)
Hypotony of eye	0	1 (0.5%)
Macular fibrosis	0	1 (0.5%)
Meibomian gland dysfunction	1 (0.5%)	0
Neovascular age-related macular degeneration	0	1 (0.5%)
Photopsia	0	1 (0.5%)
Refraction disorder	0	1 (0.5%)
Retinal haemorrhage	0	1 (0.5%)
Scleral discolouration	1 (0.5%)	0
Uveitis	0	1 (0.5%)
Visual acuity reduced	0	1 (0.5%)
Investigations	14 (7.3%)	16 (8.2%)
Intraocular pressure increased	14 (7.3%)	16 (8.2%)

System Organ Class[1] / Preferred Term[1]	StableVisc (N=192)	ProVisc® (N=196)
Surgical and medical procedures	12 (6.3%)	9 (4.6%)
Cataract operation	11 (5.7%)	7 (3.6%)
Intra-ocular injection	0	1 (0.5%)
Intraocular lens repositioning	1 (0.5%)	0
Ptosis repair	0	1 (0.5%)
Injury, poisoning and procedural complications	5 (2.6%)	7 (3.6%)
Corneal abrasion	1 (0.5%)	3 (1.5%)
Posterior capsule rupture	2 (1.0%)	1 (0.5%)
Anterior capsular rupture	0	1 (0.5%)
Cataract operation complication	0	1 (0.5%)
Fall	0	1 (0.5%)
Femur fracture	0	1 (0.5%)
Joint dislocation	0	1 (0.5%)
Post procedural inflammation	1 (0.5%)	0
Procedural nausea	1 (0.5%)	0
Immune system disorders	2 (1.0%)	1 (0.5%)
Hypersensitivity	1 (0.5%)	1 (0.5%)
Seasonal allergy	1 (0.5%)	0
Infections and infestations	2 (1.0%)	1 (0.5%)
Conjunctivitis	1 (0.5%)	0
Endophthalmitis	1 (0.5%)	0
Hordeolum	0	1 (0.5%)
Metabolism and nutrition disorders	0	2 (1.0%)
Dehydration	0	1 (0.5%)
Hypokalaemia	0	1 (0.5%)
Hyponatraemia	0	1 (0.5%)
Congenital, familial and genetic disorders	0	1 (0.5%)
Corneal dystrophy	0	1 (0.5%)
Gastrointestinal disorders	0	1 (0.5%)
Abdominal pain	0	1 (0.5%)
Diarrhoea	0	1 (0.5%)
Nervous system disorders	0	1 (0.5%)
Visual field defect	0	1 (0.5%)
Renal and urinary disorders	0	1 (0.5%)
Acute kidney injury	0	1 (0.5%)
Vascular disorders	0	1 (0.5%)
Hypotension	0	1 (0.5%)

Abbreviations: N = number of subjects per treatment group, TEAE = treatment-emergent adverse event
Note: At each level of summarization (any event, system organ class, and preferred term), subjects reporting more than one adverse event are counted only once.
[1] Adverse events not related to a device are coded to System Organ Class and Preferred Term using the Medical Dictionary for Regulatory Activities (MedDRA), version 22.1.

The proportion of subjects reporting a TEAE at least once was similar across groups. Of the most common TEAEs, the most frequently reported ≥ 5% of subjects in either group) were corneal oedema 7.3% [14/192] and 5.1% [10/196] for StableVisc and ProVisc®, respectively), intraocular pressure increased (7.3% [14/192] and 8.2% [16/196] for StableVisc and ProVisc®, respectively), and cataract operation (5.7% [11/192] and 3.6% [7/196] for StableVisc and ProVisc®, respectively).

One Serious Adverse Event (SAE) was reported. One patient in the StableVisc group developed acute postoperative bacterial endophthalmitis which was severe, considered not related to StableVisc according to the surgeon, and was ongoing when the patient discontinued from the study.

2. Effectiveness Results

The analysis of effectiveness was based on the Intent-to-Treat (ITT) Population of all 390 study eyes randomized to treatment and was performed at the 3-month postoperative timepoint (Visit 5). Key effectiveness outcomes are presented in **Tables 30** to **32.**

The results of the analysis of the primary effectiveness endpoint are presented in **Table 30**. For the ITT Population with missing data imputed using MCMC methods, mean percent change in ECD from baseline to Visit 5 was 17.5% loss for the StableVisc group and 16.9% loss for the ProVisc® control group. The upper confidence limit for the least square mean difference (LSMD) in the percent change in ECD between groups was 2.9%, which is less than the pre-specified non-inferiority margin of 5% (p=0.0019). Therefore, the primary effectiveness endpoint of non-inferiority of mean percent change in ECD from baseline to postoperative Visit 5 (90 days ± 14 days) in the study eye for the StableVisc group when compared to the control group was considered met.

Table 30: Change from baseline in Endothelial Cell Density (ECD; cells/mm^2) at 90 days – Intent to Treat Population

	StableVisc (N=194)		ProVisc® (N=196)	
Time Point	Observed Value	Percent Loss[1]	Observed Value	Percent Loss[1]
Baseline[2]				
n	191		194	
Mean (SD)	2566.9 (344.77)		2511.3 (348.91)	
Median	2617.0		2520.0	
Min, Max	1644, 3381		1055, 3392	
Postop Visit 5 (90 ± 14 days)				
n	176	176	182	182
Mean (SD)	2121.7 (561.51)	17.5 (17.58)	2073.1 (533.61)	16.9 (18.73)
Median	2238.5	11.3	2159.5	9.6
Min, Max	660, 3166	-7, 71	546, 3103	-11, 81
LSM (SE)[2]	2117.1 (49.76)	18.2 (1.63)	2056.8 (49.16)	18.0 (1.60)
LSMD (StableVisc – ProVisc®) (SE)[3]		0.2 (1.65)		
90% CI of LSMD[3]		-2.5, 2.9		
P-value[3]		0.0019		

Abbreviations: CI = confidence interval, ECD = endothelial cell density, ITT = Intent-to-Treat, LSM = least square mean change from baseline, LSMD = least square mean difference between treatment groups, Max = maximum, Min = minimum, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device, Postop = postoperative, SD = standard deviation, SE = standard error

Note: Missing ECD values are imputed using Markov chain Monte Carlo methods. Descriptive statistics are presented with observed data only.

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.

[2] Baseline is defined as the last available measurement prior to OVD exposure.

[3] Estimates of the LSM and LSMD between treatment groups were based on a statistical model with percent loss as the dependent variable, and treatment group, baseline cataract severity, and Investigator as fixed factors, and age as a continuous covariate. An upper confidence limit less than 5% favored the hypothesis of noninferiority of StableVisc as compared to ProVisc® and the one-sided p-value at a 0.050 significance level was presented for this noninferiority test of difference in percent loss.

Similar results were obtained for the Complete-Case analysis that included only those study eyes from the ITT Population which had both observed preoperative and postoperative Visit 5 ECD measurements available (**Table 31**).

Table 31: Endothelial Cell Density (cells/mm^2) and Percent Loss Sensitivity Analysis: Complete Case – Intent to Treat Population

	StableVisc (N=194)		ProVisc® (N=196)	
Time Point	Observed Value	Percent Loss[1]	Time Point	Observed Value
Baseline[2]				
n	176		182	
Mean (SD)	2560.3 (349.97)		2505.5 (352.04)	
Median	2614.0		2514.0	
Min, Max	1644, 3381		1055, 3392	
Postop Visit 5 (90 ± 14 days)				
n	176	176	182	182
Mean (SD)	2121.7 (561.51)	17.5 (17.58)	2073.1 (533.61)	16.9 (18.73)
Median	2238.5	11.3	2159.5	9.6
Min, Max	660, 3166	-7, 71	546, 3103	-11, 81
LSM (SE)[3]	2103.2 (51.01)	18.6 (1.60)	2044.2 (49.84)	18.4 (1.56)
LSMD (StableVisc - ProVisc®) (SE)[3]		0.3 (1.59)		
90% CI of LSMD[3]		-2.3, 2.9		
P-value[4]		0.0016		

Abbreviations: CI = confidence interval, ECD = endothelial cell density, ITT = Intent-to-Treat, LSM = least square mean change from baseline, LSMD = least square mean difference between treatment groups, Max = maximum, Min = minimum, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device, Postop = postoperative, SD = standard deviation, SE = standard error

Note: Complete case analysis includes only subjects with both Preoperative and Postoperative Visit 5 ECD measurements.

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.
[2] Baseline is defined as the last available measurement prior to OVD exposure.
[3] Estimates of the LSM and LSMD between treatment groups are based on a statistical model with percent loss as the dependent variable, and treatment group and investigator as fixed factors. An upper confidence limit less than 5% favors the hypothesis of noninferiority of StableVisc as compared to ProVisc®.
[4] The one-sided p-value at a 0.050 significance level is presented for the noninferiority test of difference in percent loss.

The distribution of the percent loss in ECD from baseline at Visit 5 (with negative (-) values indicating gain) in each arm is shown in **Table 32**. The distributions are fairly similar between groups.

Table 32: Categorical Percent Loss in Endothelial Cell Density (cells/mm^2) at Visit 5: Complete Case – Intent to Treat Population

Visit Percent Loss	StableVisc (N=194)	ProVisc® (N=196)
Number of subjects with both Baseline[1] and Postoperative Visit 5 ECD Measurements	n=176	n=182
Postoperative Visit 5 (90 days +/- 14 days)		
> -20 to -15%	0	0
> -15 to -10%	0	1 (0.5%)
> -10 to -5%	3 (1.7%)	2 (1.1%)
> -5 to 0%	11 (6.3%)	17 (9.3%)
> 0 to 5%	32 (18.2%)	41 (22.5%)
> 5 to 10%	34 (19.3%)	31 (17.0%)
> 10 to 15%	22 (12.5%)	18 (9.9%)
> 15 to 20%	14 (8.0%)	7 (3.8%)

Visit Percent Loss	StableVisc (N=194)	ProVisc® (N=196)
> 20 to 25%	14 (8.0%)	17 (9.3%)
> 25 to 30%	12 (6.8%)	11 (6.0%)
> 30 to 35%	4 (2.3%)	6 (3.3%)
> 35 to 40%	8 (4.5%)	7 (3.8%)
> 40 to 45%	5 (2.8%)	7 (3.8%)
> 45 to 50%	2 (1.1%)	1 (0.5%)
> 50 to 55%	6 (3.4%)	5 (2.7%)
> 55 to 60%	4 (2.3%)	4 (2.2%)
> 60 to 65%	2 (1.1%)	2 (1.1%)
> 65 to 70%	2 (1.1%)	4 (2.2%)
> 70 to 75%	1 (0.6%)	0
> 75 to 80%	0	0
> 80 to 85%	0	1 (0.5%)

Abbreviations: ECD = endothelial cell density, ITT = intent-to-treat, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device
[1] Baseline is defined as the last available measurement prior to OVD exposure.

3. Subgroup Analyses

The following characteristics were evaluated for potential association with outcomes:

Subgroup analyses concerning study sites:

Subgroup analysis concerning study sites was conducted as an assessment of data poolability across sites for both primary safety and effectiveness endpoints.

For the primary safety endpoint, poolability of results (observed data only) across study sites was assessed by performing a Cochran-Mantel-Haenszel test between the treatment groups stratified by study site. The p-value for the Breslow-Day test for homogeneity of odds ratios across study sites was compared to a critical value of 0.15. The resulting p-value is less than 0.4319. Based on these results summarized in **Table 33** below, it is reasonable to assume that there is minimal site effect on device safety performance.

Table 33: Proportion of Subjects with Postoperative Intraocular Pressure ≥30 mmHg at Any Follow-Up Visit by Study Center - Safety Population

	StableVisc (N=192)	ProVisc® (N=196)
Site 1	n = 16	n = 15
IOP ≥30 mmHg at any follow-up visit	0	0
Site 2	n = 8	n = 10
IOP ≥30 mmHg at any follow-up visit	0	0
Site 3	n = 15	n = 14
IOP ≥30 mmHg at any follow-up visit	1/15 = 0.067	3/14 = 0.214
Site 4	n = 7	n = 8
IOP ≥30 mmHg at any follow-up visit	1/7 = 0.143	0
Site 5	n = 10	n = 12
IOP ≥30 mmHg at any follow-up visit	0	1/12 = 0.083
Site 6	n = 15	n = 17
IOP ≥30 mmHg at any follow-up visit	3/15 = 0.200	6/17 = 0.353
Site 7	n = 15	n = 17
IOP ≥30 mmHg at any follow-up visit	0	1/17 = 0.059

	StableVisc (N=192)	ProVisc® (N=196)
Site 8	n = 16	n = 16
IOP ≥30 mmHg at any follow-up visit	1/16 = 0.063	3/16 = 0.188
Site 9	n = 6	n = 3
IOP ≥30 mmHg at any follow-up visit	0	0
Site 10	n = 2	n = 2
IOP ≥30 mmHg at any follow-up visit	0	0
Site 12	n = 17	n = 17
IOP ≥30 mmHg at any follow-up visit	1/17 = 0.059	0
Site 13	n = 17	n = 15
IOP ≥30 mmHg at any follow-up visit	0	0
Site 14	n = 19	n = 15
IOP ≥30 mmHg at any follow-up visit	1/19 = 0.053	0
Site 16	n = 3	n = 4
IOP ≥30 mmHg at any follow-up visit	0	0
Site 17	n = 5	n = 6
IOP ≥30 mmHg at any follow-up visit	0	0
Site 18	n = 7	n = 8
IOP ≥30 mmHg at any follow-up visit	0	0
Site 19	n = 6	n = 6
IOP ≥30 mmHg at any follow-up visit	2/6 = 0.333	1/6 = 0.167
Site 20	n = 1	n = 2
IOP ≥30 mmHg at any follow-up visit	0	0
Site 21	n = 5	n = 7
IOP ≥30 mmHg at any follow-up visit	0	0
Site 22	n = 2	n = 2
IOP ≥30 mmHg at any follow-up visit	0	1/2 = 0.500
P-value[1]	<0.2460	
P-value[2]	<0.4319	

Abbreviations: CMH = Cochran-Mantel-Haenszel, IOP = intraocular pressure, mmHg = millimeters of mercury, N = number of subjects per treatment group, n = number of subjects per category

Notes:

- Subjects experiencing one or more IOP spikes are counted only once.
- No subjects have imputed data for this table. Only observed data is used.

[1] The p-value comparing treatment groups is based on a CMH test stratified by study center.

[2] The p-value for the Breslow-Day test for homogeneity of odds ratios across study sites is compared to a critical value of 0.15.

For the primary effectiveness endpoint, poolability across study sites was evaluated by modeling ECD loss (%) as a function of the fixed class variables of treatment and Investigator including their interaction using the available data for the ITT Set. Poolability is assessed by comparing the p-value for the interaction to a critical value of 0.15. Based on the results summarized in **Table 34** below, the p-value for the interaction term is 0.7861. Therefore, it is believed that a possible site effect on device effectiveness is reasonably low.

Table 34: Endothelial Cell Density (cells/mm^2 and Percent Loss by Study Center – Intent to Treat Population

	StableVisc (N=194)		ProVisc® (N=196)	
Time Point	Observed Value	Percent Loss[1]	Observed Value	Percent Loss[1]
Baseline[2]				
n	191		194	
Mean (SD)	2566.9 (344.77)		2511.3 (348.91)	
Median	2617.0		2520.0	
Min, Max	1644, 3381		1055, 3392	
Postop Visit 5 (90 ± 14 days)				
n	176	176	182	182
Mean (SD)	2121.7 (561.51)	17.5 (17.58)	2073.1 (533.61)	16.9 (18.73)
Median	2238.5	11.3	2159.5	9.6
Min, Max	660, 3166	-7, 71	546, 3103	-11, 81
LSM (SE)[3]	2102.8 (44.56)	18.7 (1.41)	2056.5 (43.15)	18.0 (1.36)
LSMD (StableVisc - ProVisc®) (SE)[3]		0.8 (1.65)		
90% CI of LSMD[3]		-2.0, 3.5		
P-value[4]		0.7861		

Abbreviations: CI = confidence interval, ECD = endothelial cell density, ITT = Intent-to-Treat, LSM = least square mean change from baseline, LSMD = least square mean difference between treatment groups, Max = maximum, Min = minimum, mm2 = millimeters squared, N = number of subjects per treatment group, n = number of subjects per category, OVD = ophthalmic viscosurgical device, Postop = postoperative, SD = standard deviation, SE = standard error

[1] Percent loss is calculated as [(Baseline value - Visit 5 value)/Baseline value]*100.
[2] Baseline is defined as the last available measurement prior to OVD exposure.
[3] Estimates of the LSM and LSMD between treatment groups are based on a statistical model with difference in percent loss as the dependent variable, and treatment group, investigator, and the interaction term as fixed factors.
[4] A p-value for the interaction term (treatment*investigator) > 0.15 indicates poolability across sites.

Subgroup analyses concerning IOP-reducing intervention:

A subgroup analysis was conducted concerning the primary safety endpoint according to the following categorization:

- Subjects who received IOP-reducing intervention; and
- Subjects who did not receive IOP-reducing intervention.

The results are presented in **Table 35** below.

Table 35: Proportion of Subjects with Postoperative Intraocular Pressure ≥30 mmHg at Any Follow-Up Visit by IOP Intervention - Safety Population

			Difference in Proportion (StableVisc – ProVisc®)[a]	
	StableVisc (N=192)	ProVisc® (N=196)	Estimate (90% CI)[a]	P-value
Subjects who received IOP-reducing intervention, n	18	22	-	-

			Difference in Proportion (StableVisc – ProVisc®)[a]	
	StableVisc (N=192)	ProVisc® (N=196)	Estimate (90% CI)[a]	P-value
IOP ≥30 mmHg at any follow-up visit	8/18 = 0.444	13/22 = 0.591	-0.146 (-0.405, 0.112)	0.6162
Subjects who did not receive IOP-reducing intervention, n	174	174	-	-
IOP ≥30 mmHg at any follow-up visit	2/174 = 0.011	3/174 = 0.017	-0.006 (-0.027, 0.015)	<0.0001

Abbreviations: CI = confidence interval, IOP = intraocular pressure, mmHg = millimeters of mercury, N = number of subjects per treatment group

Notes:

- No subjects had imputed data for this table. Only observed data were used. Subjects experiencing one or more IOP spikes were counted only once.
- Subjects experiencing one or more IOP spikes were counted only once.

[a] The estimated difference in proportions between the treatment groups and the 95% CI was constructed using the normal approximation z-test. An upper confidence limit less than 0.1 favored the hypothesis of noninferiority of StableVisc as compared to ProVisc® and the one-sided p-value at a 0.050 significance level was presented for this noninferiority test.

For subjects who did not receive IOP-reducing intervention, the results demonstrated noninferiority for StableVisc when compared with ProVisc® (p <0.0001). For subjects who received IOP-reducing intervention, the results did not demonstrate noninferiority (p=0.6162) due to the small number of subjects receiving such intervention.

4. Pediatric Extrapolation

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

D. 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 22 investigators of which none were full-time or part-time employees of the sponsor and none 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:
- Significant payment of other sorts:
- Proprietary interest in the product tested held by the investigator:
- Significant equity interest held by investigator in sponsor of covered study:

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

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Rochester, NY 14609 USA

Manufactured by:
Lifecore Biomedical, LLC
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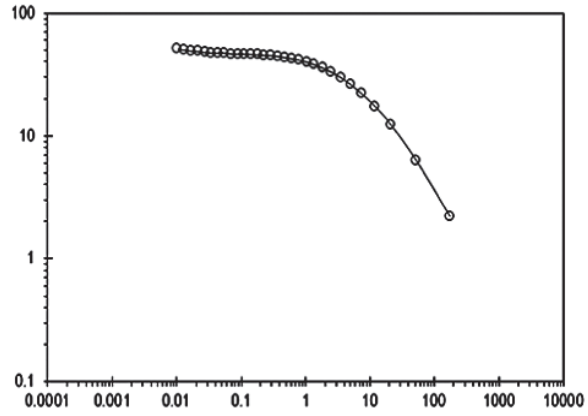
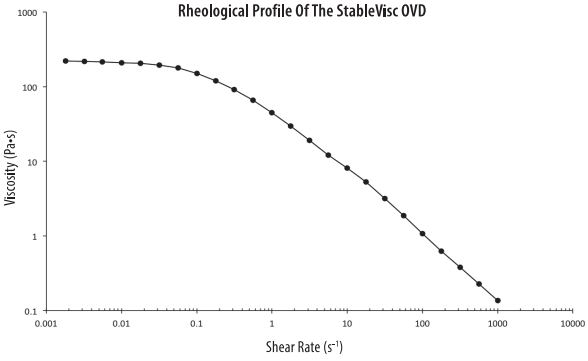
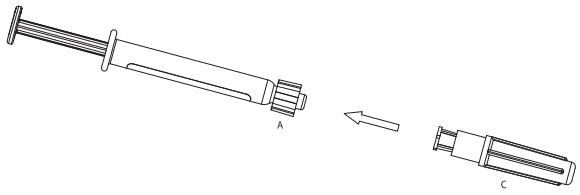




nnula and Sheath

FIG. 3



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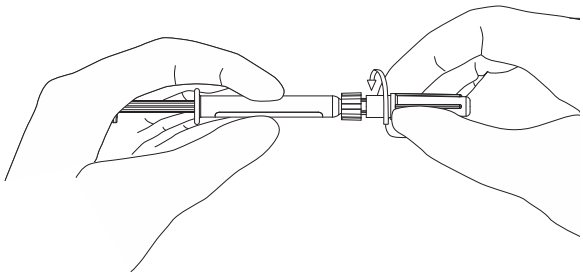

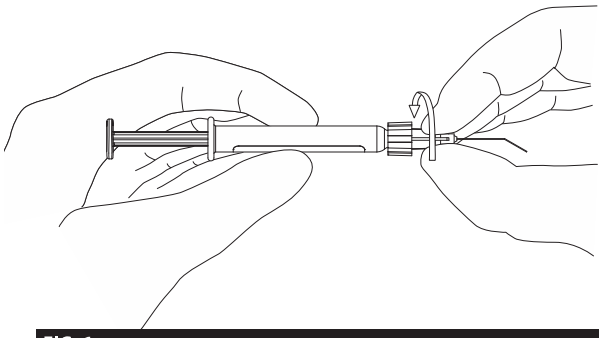

FIG. 6