SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

I. GENERAL INFORMATION

Device Generic Name: serafilcon A soft contact lens

Device Trade Name: Precision7™; Precision7™ for Astigmatism; Precision7™ Multifocal; Precision7™ Multifocal Toric (serafilcon A) Soft Contact Lenses

Device Procode: LPM

Applicant's Name and Address: Alcon Laboratories, Inc.
6201 South Freeway
Fort Worth, TX 76134-2099, USA

Date(s) of Panel Recommendation: None

Premarket Approval Application (PMA) Number: P220007

Date of FDA Notice of Approval: April 25, 2023

II. INDICATIONS FOR USE

Precision7™ (serafilcon A) spherical soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic and aphakic persons with non-diseased eyes with up to approximately 1.50 diopters (D) of astigmatism that does not interfere with visual acuity.

Precision7™ for Astigmatism (serafilcon A) toric soft contact lenses are indicated for the optical correction of refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may have up to 6.00 diopters (D) of astigmatism.

Precision7™ Multifocal (serafilcon A) soft contact lenses are indicated for the optical correction of presbyopia with or without refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may require a reading addition of +3.00 diopters (D) or less and who may have up to approximately 1.50 diopters of astigmatism that does not interfere with visual acuity.

Precision7™ Multifocal Toric (serafilcon A) soft contact lenses are indicated for the optical correction of presbyopia with or without refractive ametropia (myopia and hyperopia) in phakic or aphakic persons with non-diseased eyes who may require a

reading addition of +3.00 diopters (D) or less and who may have up to 6.00 diopters (D) of astigmatism.

The lenses are to be prescribed for extended wear for up to 6 continuous nights with removal for disposal, or cleaning and disinfection (chemical, not heat) prior to reinsertion, as recommended by the eye care professional. Lenses should be discarded and replaced with a new pair each week, or more often, if recommended by the eye care professional.

III. CONTRAINDICATIONS

Do not use serafilcon A contact lenses when any of the following exists:

- Inflammation or infection of the anterior chamber of the eye
- Active disease, injury or abnormality affecting the cornea, conjunctiva, or eyelids
- Microbial infection of the eye
- Insufficiency of lacrimal secretion (dry eye) that interferes with contact lens wear
- Corneal hypoesthesia (reduced corneal sensitivity)
- Use of any medication that is contraindicated or interferes with contact lens wear, including eye medications
- Any systemic disease that may be exacerbated by or interferes with contact lens wear
- Allergic reactions or irritation of the ocular surfaces or adnexa that may be caused by or exacerbated by the wearing of contact lenses
- Patient history of recurring eye or eyelid infections, adverse effects associated with contact lens wear, intolerance or abnormal ocular response to contact lens wear
- If eyes become red or irritated

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the Precision7™, Precision7™ for Astigmatism, Precision7™ Multifocal, Precision7™ Multifocal Toric (serafilcon A) Soft Contact Lenses labeling.

V. DEVICE DESCRIPTION

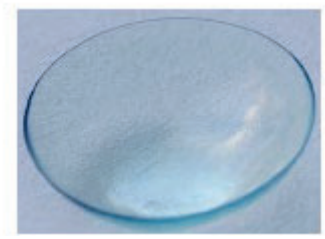

Figure 1. Photo of Precision7™ (serafilcon A) soft contact lens (not to scale, contains reflections)

Precision7™, Precision7™ for Astigmatism, Precision7™ Multifocal, Precision7™ Multifocal Toric (serafilcon A) Soft Contact Lenses are composed of 55% water and 45% serafilcon A material. The serafilcon A material is an amphiphilic copolymer of silicone containing monomer, silicone containing macromer, hydrophilic monomers, and a cross linker. The lenses are tinted for visibility with Reactive Blue 247, a color additive that conforms to 21 CFR 73.3100. In addition, lenses contain two benzotriazole monomers to block UVA and UVB radiation, and additionally, reduce transmittance in the range of 380 nm to 450 nm. In its hydrated state, the Precision7™, Precision7™ for Astigmatism, Precision7™ Multifocal, Precision7™ Multifocal Toric (serafilcon A) Soft Contact Lenses, when placed on the cornea, act as a refracting medium to focus light rays on the retina.

LENS PARAMETERS

The lens designs include spherical, toric, multifocal, and multifocal toric lenses in the following parameter ranges:

Diameter	13.0mm to 15.0mm
Center Thickness	0.08mm @ -3.00 D (varies with power)
Base Curve	8.0mm to 9.2mm
Power Range	+20.00D to -20.00D
Cylinder Power (Toric)	-0.25D to -10.00D
Cylinder Axis (Toric)	001 to 180°
Add Power (Multifocal)	LO, MED, HI

The Precision7™, Precision7™ for Astigmatism, Precision7™ Multifocal, Precision7™ Multifocal Toric (serafilcon A) Soft Contact Lenses have the following physical properties:

Refractive Index:	1.402
Light Transmittance:	≥ 90% (@ 640 nm, -3.00 D)
Water Content:	55% by weight in normal saline
Oxygen Permeability:	119 ± 24 barrer @ 35°C (polarographic method)
UV Transmittance:	The transmittance characteristics are less than 1% in the UVB range of 280 nm to 315 nm and less than 10% in the UVA range of 316 to 380 nm for the entire power range.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of refractive ametropia (myopia, hyperopia, and astigmatism) and presbyopia in aphakic and/or not-aphakic persons with non-diseased eyes. The currently available alternate practices and procedures for vision correction are commercially available daily disposable contact lenses, commercially available daily wear contact lenses, other commercially available contact lenses approved for extended wear, spectacles, refractive keratoplasty, laser-assisted in-situ keratomileusis

(LASIK), and corneal implants. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

VII. MARKETING HISTORY

Since December 28, 2021, Alcon Laboratories, Inc. has held US marketing clearance for (serafilcon A) soft contact lenses for daily wear under 510(k) K212806. Summary information about these lenses (Alcon™, Alcon™ for Astigmatism, Alcon™ Multifocal, Alcon™ Multifocal Toric (serafilcon A) soft contact lens) is available on the FDA website at: http://www.accessdata.fda.gov/cdrh_docs/pdf21/K212806.pdf. The lenses cleared under K212806 have not been marketed in the US or any foreign country.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

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

- Moderate to severe eye pain not relieved by removing the lens
- Foreign body sensation
- Excessive watering or other eye secretions including mucopurulent discharge
- Redness of the eyes
- Photophobia (light sensitivity)
- Burning, stinging or itching, or other pain associated with the eyes
- Poor visual acuity (reduced sharpness of vision)
- Blurred vision, rainbows or halos around objects
- Feeling of dryness

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

IX. SUMMARY OF NONCLINICAL STUDIES

A. Laboratory Studies

1. Biocompatibility

Non-clinical biocompatibility testing was conducted in accordance with FDA's *Premarket Notification 510(k) Guidance Document for Daily Wear Contact Lenses,* May 1994 and GLP regulation (21 CFR part 58) and applicable standards. The Applicant also determined that given the cumulative exposure from repeated use of the extended wear contact lenses, the permanent/long-term patient contact categorization would apply. Therefore, the Applicant performed a number of in

vitro and in vivo biocompatibility studies to support the safety of the subject final finished sterilized device serafilcon A contact lenses considering this permanent/long-term patient contact categorization.

Endpoints addressed according to the May 1994 Guidance referenced above include cytotoxicity, acute ocular irritation, guinea pig maximization skin sensitization, acute systemic toxicity, and -ocular irritation due to repeated wear of contact lenses (rabbit contact lens wear studies). In addition, the Applicant elected to perform additional endpoint testing not specified in the May 1994 Guidance, including genotoxicity testing (bacterial and chromosomal), as well as performing cytotoxicity testing by multiple different test methods to evaluate the lenses or lens extracts. In addition, the Applicant performed several different rabbit contact lens wear studies with different contact lens care products used for cleaning/disinfection, as well as different lens wearing paradigms, considering that the subject device is an extended wear contact lens.

The Applicant performed biocompatibility testing on the final finished sterilized contact lens and the primary packaging solution itself.

The Applicant also provided sufficient information/justification to support that historical biocompatibility testing on primary packaging (blister shell and foil lidding) would be applicable to the subject device, since the subject device uses the same primary packaging that is also used by the referenced US marketed Alcon soft contact lenses.

The non-clinical testing performed includes the following referenced biocompatibility standards: ISO 10993-5:2009, ISO 10993-10:2010, ISO 10993-11:2017, ISO 9394:2012, ISO 18189:2016, ISO 10993-3:2014.

All test results met the pre-established acceptance criteria.

The testing performed on the Precision7™ (serafilcon A) extended wear soft contact lenses demonstrates that the lens is safe.

Table 1: Biocompatibility – Contact Lens

Test	Purpose	Acceptance Criteria	Results
Cytotoxicity-Elution Method	Evaluates cellular toxicity potential of serum supplemented media-contact lens extract on cultured cells.	Non-cytotoxic	Pass
Cytotoxicity-Direct Contact	Evaluates the cellular toxicity potential of the contact lens through direct placement of contact lens on cultured cell layer	Non-cytotoxic	Pass
Cytotoxicity-Cell Growth Inhibition	Evaluates the potential for serum supplemented media-contact lens extract to impair cell growth	Non-cytotoxic	Pass
Cytotoxicity-contact lens in combination with contact lens care solution	Evaluates the cellular toxicity potential, considering interactions between the contact lens used in combination with the evaluated lens care product solution	Non-cytotoxic	Pass
Acute ocular irritation	Evaluates the potential of a single exposure to polar or non-polar contact lens extracts to cause acute eye irritation in rabbits	Not irritating to the eyes of New Zealand White rabbits through 72 hours after instillation	Pass
28 Day Contact Lens Wear using CLEARCARE®	Evaluates the potential of contact lenses to cause eye irritation in rabbits when worn daily for 28 days. 6 New Zealand White rabbits were used. Control lenses were CooperVision Biofinity® (comfilcon A), worn in the opposite eye. Test and control contact lenses were worn for 8 hours a day. New lenses (directly from final finished packaging) were used on days 1, 8, 15, and 22. On	No trends of worsening ocular irritation response. No slit lamp findings on day 1, 8, 15, 21, and 28. Conjunctival congestion was observed at similar sporadic levels in test and control eyes and did not show any trends of worsening over time. Histological results did not raise concerns. Restraint harness was used during the first few days of the study only and animals were	Pass

	other study days, CLEAR CARE® was used for daily cleaning/disinfection of the lenses.	acclimated to the use of restraint harness prior to study start. Lens retention, which was checked every hour, was high (≥ 95%) for both test and control lenses.	
28 Day Contact Lens Wear using Opti-Free® Replenish®	Evaluates the potential of contact lenses to cause eye irritation in rabbits when worn daily for 28 days. 6 New Zealand White rabbits were used. Control lenses were CooperVision Biofinity® (comfilcon A), worn in the opposite eye. Test and control contact lenses were worn for 8 hours a day. New lenses (directly from final finished packaging) were used on days 1, 8, 15, and 22. On other study days, Opti-Free® Replenish® was used for cleaning/disinfection of the lenses.	No trends of worsening ocular irritation response. No slit lamp findings on day 1, 8, 15, 21, and 28. Conjunctival congestion and conjunctival discharge was observed at similar sporadic levels in test and control eyes and did not show any trends of worsening over time. Histological results did not raise concerns. Restraint harness was used for the majority of the study days, and animals were acclimated to the use of restraint harness prior to study start. Overall, lens retention, which was checked every hour, was ≥88% for test and control lenses.	Pass
7-Day 'Closed Eye' Contact Lens Wear	Evaluates the potential of contact lenses to cause eye irritation in rabbits when worn daily for 7 days using a 'closed-eye' model. 6 New Zealand White rabbits were used. Control lenses were CooperVision Biofinity® (comfilcon A), worn in the opposite eye. Test and control lenses were worn for 8 hours a day for the 7 day study period. Each	Slit lamp exams performed at pre-screen, 1 day, 3 days, and 7 days did not raise concerns. Scores for conjunctival congestion were minimal to moderate, seen in both test and control eyes, and therefore not specific to the test article lens. Conjunctival discharge scores were none to minimal that was considered a general	Pass

	day, new lenses were taken from the final finished packaging. Restraint devices were used throughout the study. After contact lens insertion, eyes were gently closed and a specific procedure was used to physically maintain eye closure for 8 hours each day.	response to contact lens wear and not specific to the test article lens. There were no trends toward worsening ocular irritation results over the course of the study. Histology was not performed as part of this study.	
Acute systemic injection	Evaluates the systemic toxicity potential of the contact lens extracts (polar and non-polar) in mice	Not systemically toxic based on daily weight measurements and observation for adverse clinical signs over 72 hours after administration.	Pass
Guinea pig maximization	Evaluates the potential of the contact lens extracts (polar and non-polar) to cause skin sensitization.	Does not cause a skin sensitization response in Hartley guinea pigs. Historical positive control and concurrent negative control yielded expected results.	Pass
Genotoxicity-Bacterial Reverse Mutation	Evaluates mutagenic potential of the contact lens extracts	Non-mutagenic	Pass
Genotoxicity-Chromosome Aberration	Evaluates the clastogenic (large scale genetic damage) potential of the contact lens extracts	Non-genotoxic	Pass

Table 2: Biocompatibility – Primary Packaging Solution

Test	Purpose	Acceptance Criteria	Results
Cytotoxicity-Modified Elution Method	Evaluates cellular toxicity potential of the neat packaging solution (combined with serum supplemented media) on cultured cells.	Non-cytotoxic	Pass
Acute ocular irritation	Evaluates the potential of a single exposure to neat packaging solution to cause acute eye irritation in rabbits.	Not irritating to the eyes of New Zealand White rabbits through 72 hours after instillation	Pass
Guinea pig maximization	Evaluates the potential of the neat primary packaging solution to cause skin sensitization.	Does not cause a skin sensitization response in Hartley guinea pigs.	Pass
Genotoxicity-Bacterial Reverse Mutation	Evaluates mutagenic potential of the primary packaging solution	Non-mutagenic	Pass
Genotoxicity-Chromosome Aberration	Evaluates the clastogenic (large scale genetic damage) potential of the primary packaging solution	Non-genotoxic	Pass

Table 3: Biocompatibility- Primary Packaging (Blister Shell/Foil Lidding)

Test	Purpose	Acceptance Criteria	Results
Cytotoxicity-Elution Method	Evaluates cellular toxicity potential of serum supplemented media-blister shell extract on cultured cells.	Non-cytotoxic	Pass
Cytotoxicity-Elution Method	Evaluates cellular toxicity potential of serum supplemented media-foil lidding extract on cultured cells.	Non-cytotoxic	Pass
Cytotoxicity- Direct Contact	Evaluates the cellular toxicity potential of foil lidding through direct placement of the lidding on cultured cell layer	Non-cytotoxic	Pass

Cytotoxicity-Cell Growth Inhibition	Evaluates the potential for serum supplemented media-blister shell extract to impair cell growth	Non-cytoxic	Pass
Acute ocular irritation	Evaluates the potential of a single exposure to blister shell extracts (polar and non-polar) to cause acute eye irritation in rabbits	Not irritating to the eyes of rabbits through 72 hours after instillation	Pass
Acute ocular irritation	Evaluates the potential of a single exposure to foil lidding extracts (polar and non-polar) to cause acute eye irritation in rabbits	Not irritating to the eyes of rabbits through 72 hours after instillation	Pass
Acute systemic injection	Evaluates the systemic toxicity potential of blister shell extracts (polar and non-polar) in mice	No biologically significant weight loss or adverse clinical/behavioral signs through 72 hours after extract administration	Pass
Acute systemic injection	Evaluates the systemic toxicity potential of foil lidding extracts (polar and non-polar) in mice	No biologically significant weight loss or adverse clinical/behavioral signs through 72 hours after extract administraiton	Pass

2. Physicochemical Tests

Physicochemical tests were performed to demonstrate long term safety and stability of the properties of the material used to manufacture the Precision7™ (serafilcon A) lens. See the following table for a summary of results.

Table 4. Physicochemical Tests

Test	Purpose	Acceptance Criteria	Results
Preservative Uptake and Release	To determine the preservative uptake and release of the contact lens material	N/A	No significant uptake of polyquaternium-1 (POLYQUAD®), ALDOX® myristamidopropyl dimethylamine (ALDOX®), polyhexamethylene biguanide (PHMB), or Alexidine.
Compatibility with Lens Care Products	To determine compatibility of contact lens care products with contact lenses	After 7-cycles[1], contact lens parameters should be within the tolerance[2] of the initial parameters before cycling	Pass
Extractables – Leachability	To determine if any monomer, initiator, or tint leached out during extraction with water	N/A	No detectable levels of monomers, initiator, or tint were found in any of the phosphate buffered saline (PBS) leachate.
Extractables - Soxhlet Extraction	The quantity of extractables from the Soxhlet extraction	N/A	The extractables ranged from 0% - 0.5% for water and 1.6% - 2.2% for 2-propanol

[1] 7-cycles were accepted as Precision 7™ (serafilcon A) contact lenses are indicated for continuous wear up to 6 nights.

[2] Contact lens tolerances per ISO 18369-2: Ophthalmic optics – Contact lenses – Part 2: Tolerances.

3. Sterilization, Bioburden, and Shelf Life

Finished contact lenses in buffered saline are provided sterile and individually packaged in sealed blister packs (blister shell and lidding). The packaged lenses are steam sterilized in a validated autoclave. Blister pack containers are labeled with variable information such as the lens parameters, lot number, and product expiration date. The expiration date has been established through stability studies that have assessed the chemical and physical stability of the lens and package integrity.

Routine bioburden testing is performed prior to sterilization every week during lens production. This testing provides an assessment of the cleanliness of the devices being manufactured and the facility in general. The bioburden test method was validated in accordance with ISO Standard 11737-1:2006, "Sterilization of health care products – Microbiological methods – Part 1: Determination of the population of microorganisms on product."

The contact lenses are terminally sterilized by subjecting the finished device to moist heat sterilization. The moist heat sterilization cycle was validated using the overkill method (partial cycle approach) in accordance with Annex D of ISO Standard 17665-1:2006, "Sterilization of health care products –Moist heat – Part 1: Requirements for the development, validation and routine control of sterilization process for medical devices." The sterilization process for the device was validated to achieve a Sterility Assurance Level (SAL) of 10^{-6}.

Shelf-life studies have been conducted to verify that the packaging for the subject contact lenses maintains a sterile barrier and adequately protects the device through the expiration date on the package label, which is 7 years from the date of sterilization. Shelf-life testing has also been conducted to verify that device physical and optical properties satisfy the requirements of the engineering drawings and product specification document through the 7-year labeled expiration date. All test samples satisfied all acceptance criteria (see **Table 4**).

Table 5: Sterility, Bioburden, and Shelf Life

Test	Purpose	Acceptance Criteria	Results
Bioburden Testing	Evaluate the cleanliness of the devices being manufactured and facility in general	Vegetative growth: Alert: ≤ 600 CFU (colony forming units)/device Action: ≤ 1,000 CFU/device Spores: Alert: ≤ 10 CFU/device Action: ≤ 20 CFU/device	Pass
Moist Heat Sterilization Validation	Evaluate the efficacy of the sterilization process	No growth is detected in the internal process challenge device/biological indicators	Pass
Package Evaluation Validated Container Closure Integrity Testing (CCIT: Vacuum Decay)	Evaluate whole package integrity	No evidence of vacuum-based leak	Pass
Validated Sterility Testing	Evaluate sterility	Negative for growth	Pass
Shelf-life	To establish the expiration date	Finished Product Specifications	7 years

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the Alcon Precision7™ (serafilcon A) soft contact lenses when worn for up to 7 days of extended wear for the optical correction of refractive ammetropia and presbyopia in persons with non-diseased eyes in the US under IDE #G190046. 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

Patients were treated between October 11, 2019 and March 26, 2021. The database for this PMA reflected data collected through March 26, 2021 and included 608 enrolled patients (1216 eyes). There were 35 primary cohort investigational sites. Among those patients enrolled, 27 subjects (54 eyes) were screen failures, and 581 subjects (1162 eyes) were dispensed study lenses.

The study was a prospective, multi-center, parallel group, randomized, stratified (by corneal curvature radius), double-blinded, 12-month clinical study. Subjects were randomized in 1:1 ratio to one of the two study groups. There were 290 subjects (580 eyes) randomized to the Alcon serafilcon A investigational group and 291 subjects (582 eyes) to the CooperVision® Biofinity® (comfilcon A) control group. Both test and control lenses were replaced weekly, after each week of extended wear, throughout the duration of study participation. For the purposes of this study, extended wear meant that lenses were to be applied and worn around the clock, including during sleep. Weekly extended wear meant at the end of any six (6) consecutive nights of extended wear, the subject had to remove the lens for one night prior to beginning a new cycle of lens wear.

The primary safety endpoint was the proportion of ocular serious and significant non-serious adverse device effects (ADEs). The primary safety analysis was based on noninferiority, with a predefined margin of 0.05. The null hypothesis stated that the difference in this proportion between serafilcon A lens group and comfilcon A lens group (serafilcon A minus comfilcon A) was 0.05 (5%) or more. The alternative hypothesis stated that the difference in this proportion was less than 0.05. Therefore, rejection of the null hypothesis supports noninferiority of serafilcon A compared to comfilcon A. A generalized linear model with a logit link function was used, and a one-sided 95% upper confidence limit (UCL) was calculated for the difference in proportions between two lens groups.

The primary effectiveness endpoint was high contrast distance visual acuity (VA) with study lenses, obtained at the Screening/Dispensing Visit, and at each of the follow-up visits. Scores were recorded as the number of letters correctly identified in the eye examination. VA was converted to the Log10 of the Minimum Angle of Resolution (logMAR). Counts and percentages on the Snellen categories were displayed, and descriptive statistics (number of observations, mean, standard

deviation, median, minimum, and maximum) for the converted logMAR values were provided for each lens group, at each scheduled visit and all unscheduled visits combined.

For all remaining endpoints collected, continuous data were summarized using descriptive statistics: n, mean, median, standard deviation (SD), minimum, and maximum. Categorical data were presented by the total counts for each category and corresponding percentages.

Sample size calculation was based on the primary safety endpoint. Assuming that the expected difference between serafilcon A and comfilcon A was 0 and that the proportion in comfilcon A was 0.045, a sample size of 213 per group provided 80% power to reject the null hypothesis of inferiority in serafilcon A compared to comfilcon A, with a noninferiority margin of 0.05 (5%). Taking into consideration the long exposure/study duration of 12 months, a total of 568 subjects were planned to be randomized (284 test and 284 control) to compensate for approximately 25% drop-out rate.

Alcon representatives monitored all study site locations to assess the data, quality, and study integrity in a manner consistent with applicable health authority regulations and the procedures adopted by Alcon. Monitoring visits and telephone consultations occurred as necessary, or per the monitoring plan, to verify that the rights and well-being of subjects were protected, the conduct of the investigation was in compliance with the currently approved protocol, the integrity of the data was maintained, the facilities remained acceptable, and test article accountability was ensured.

The control group was an active control; the control treatment, CooperVision® Biofinity® (comfilcon A) Contact Lenses, is a legally marketed alternative with similar indications for use.

1. Clinical Inclusion and Exclusion Criteria

Enrollment in the study was limited to patients who met the following key inclusion criteria: at least 18 years of age as of the date of initial evaluation, required lens powers between requiring contact lens sphere power from +0.50 to +4.00 diopters sphere or -0.50 to -6.00 diopters sphere, with at least one eye requiring contact lens sphere power greater than or equal to ±1 diopters sphere with no more than 0.75D diopters of refractive astigmatism and were willing to wear lenses in both eyes, and were correctable to visual acuities of at least 20/25 in each eye with spectacles, and as specified otherwise in the study protocol.

Patients were not permitted to enroll in the study if they met any of the following key exclusion criteria: if they had participated in a clinical trial within the previous 30 days or were participating at the time of this study, had previous refractive surgery or current or previous orthokeratology treatment, had clinically significant (grade 3 or 4) anterior segment abnormalities or any infection of the eye, had ocular or systemic disease or need for medication

which might interfere with contact lens wear, or had slit lamp findings that would contraindicate contact lens wear, or were pregnant or breast feeding, or were monovision contact lens wearers, and as specified in the study protocol.

2. Follow-up Schedule

All patients were scheduled to return for follow-up examinations at baseline/dispense, 24 hours, 1 week, 1 month, 2 months, 3 months, 6 months, 9 months and 12 months during the study.

All subjects were evaluated at Baseline/Dispense and followed up according to the visit schedule below (**Table 6**).

Table 6: Study Visit Schedule

Visit	Description	Target	Visit Window
1	Baseline/Dispense	Day 1	N/A
2	24-Hour follow-up	Day 2	± 4 hours
3	1-Week follow-up	Day 7	± 2 days
4	1-Month follow-up	Day 30	± 4 days
5	2-Month follow-up	Day 60	± 7 days
6	3-Month follow-up	Day 90	± 7 days
7	6-Month follow-up	Day 189	-7 / + 14 days
8	9-Month follow-up	Day 270	± 14 days
9	12-Month follow-up	Day 365	± 14 days

At the screening/dispensing visit, a slit lamp biomicroscope examination was conducted, a spherocylindrical refraction (and best spectacle corrected visual acuity (BCVA)) was measured, and keratometry was performed. Following the contact lens fitting, symptoms/complaints were assessed, distance high contrast visual acuity was measured, contact lens over-refraction and visual acuity were measured, and lens wettability, deposits, centration and movement were assessed.

Follow-up visits were scheduled for 24 hours, 1 week, and 1-, 3-, 6-, 9-, and 12- months after starting extended wear. At follow-up visits, the slit lamp examination was repeated, high contrast visual acuity, symptoms/complaints, average wear time, keratometry changes, adverse events,

reasons for discontinuation, lens wettability, deposits and lens fit (movement and centration), lens wear and lens replacement data were assessed. Adverse events and device deficiencies were recorded at all visits.

Contact lenses were replaced weekly. At scheduled visits, randomized subjects were given enough lenses to last until the next study visit, allowing for scheduled and unplanned lens replacements. If a subject visit occurred between any regularly scheduled visits, this visit was documented as an Unscheduled Visit.

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

3. Clinical Endpoints

With regards to safety, the primary safety endpoint was the proportion of ocular serious and significant non-serious adverse device effects (ADEs) during the study.

Serious adverse events are those events that may result in death, or have potential to cause, either permanent impairment of an ocular function or damage to an ocular structure,and may necessitate medical or surgical intervention.

Serious adverse events may include any hazardous, sight-threatening conditions occurring after exposure to the study lenses, including the following:

- An ocular infection including a presumed infectious ulcer with any of the characteristics including central or paracentral location, penetration of Bowman's membrane, infiltrates > 2 mm diameter, iritis, increase in intraocular pressure, culture positive for microorganisms, increasing size or severity at subsequent visits);
- Any central or paracentral corneal event (such as neovascularization) that results in permanent opacification;
- Hypopyon, hyphema, or neovascularization within the central 6 mm of the cornea;
- Permanent vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that fails to resolve;
- Uveitis (anterior, intermediate, or posterior);
- Corneal abrasion affecting ≥ 50% of corneal surface area.

A significant nonserious AE was defined as a device-related, non-sight threatening AE that warrants discontinuation of any contact lens wear for greater than or equal to 2 weeks due to

- Peripheral non-progressive non-infectious ulcers;
- All symptomatic corneal infiltrative events;
- Corneal staining score greater than or equal to Grade 3;

- Temporary vision loss as defined by loss of 2 or more lines of BCVA from enrollment visit that persists for 2 or more weeks;
- Neovascularization score greater than or equal to Grade 2.

The primary safety analysis was to demonstrate that the proportion of serious and significant non-serious adverse device effects in eyes dispensed with the test lens (serafilcon A) was not inferior to the proportion of serious and significant non-serious adverse device effects with the control lens (comfilcon A).

Other safety parameters included protocol-defined adverse events not included in the primary safety analysis (e.g., ocular non-serious non-significant AEs, other SAEs and non-serious AEs determined to be not related to study device), discontinuations, and biomicroscopy findings.

With regards to effectiveness, the primary effectiveness endpoint was high contrast, distance visual acuity (VA) measured with study lenses. No hypothesis testing on the primary effectiveness endpoint was planned.

For the primary and each of the supportive effectiveness endpoints, separate summaries were prepared, when applicable, for the Completed and the Discontinued analysis sets as follows: Completed Control (eyes/subjects), Completed Test (eyes/subjects), Discontinued Control (eyes/subjects), Discontinued Test (eyes/subjects). Safety analyses was conducted using the safety analysis set on a treatment-emergent basis, and effectiveness endpoints were analyzed using the Eligible Dispensed population.

With regards to success/failure criteria, the applicant did not define any specific study success criteria beyond the safety and effectiveness endpoints.

B. Accountability of PMA Cohort

At the time of database lock, of the 608 subjects enrolled in the PMA study, all data (100%, 608 subjects) were available for analysis at the completion of the study; the 12-month safety and effectiveness data based on enrolled dispensed serve as the basis for approval of the PMA submission.

Of the 608 subjects enrolled, 27 (54 eyes) were ineligible at baseline. Of the 608 enrolled subjects, 581 subjects (1162 eyes) were dispensed lenses in the PMA study, 513 (88.3%) eligible subjects (1,026 eyes) completed the 12-month visit, 68 (11.7%) eligible subjects (136 eyes) were discontinued. Subject accountability is presented in **Table 7**. Reasons for subject discontinuations is presented in **Table 8**.

Table 7: Subject Accountability (All Enrolled Subjects)

	Status	Serafilcon A number of subjects	Comfilcon A number of subjects	Overall number of subjects
Screen Failures				**27**
Enrolled Dispensed				
	Completed	**257**	**256**	**513**
	Discontinued	**33**	**35**	**68**
	Total Dispensed (Visit Attended)			
	Dispense	290	291	581
	24-Hour Follow-up	290	288	578
	1-Week Follow-up	287	283	570
	1-Month Follow-up	277	276	553
	2-Month Follow-up	264	270	534
	3-Month Follow-up	270	275	545
	6-Month Follow-up	263	268	531
	9-Month Follow-up	259	259	518
	12-Month Follow-up	257	256	513
Enrolled Not Dispensed				**27**
Total Enrolled				**608**

Table 8: Subject Disposition (All Enrolled Subjects)

	Serafilcon A n (%)	Comfilcon A n (%)	Overall n (%)
Total enrolled			608
Screen failures			27
Discontinued prior to randomization			0
Randomized	290	291	581
As Treated			
Enrolled Dispensed	290	291	581
Completed the study	257 (88.6)	256 (88.0)	513 (88.3)
Discontinued from study	33 (11.4)	35 (12.0)	68 (11.7)
Adverse Event	7 (2.4)	8 (2.7)	15 (2.6)
Lost to Follow Up	2 (0.7)	7 (2.4)	9 (1.5)
Physician Decision	1 (0.3)	0 (0.0)	1 (0.2)
Pregnancy	1 (0.3)	0 (0.0)	1 (0.2)
Withdrawal by Subject	16 (5.5)	15 (5.2)	31 (5.3)
Other	6 (2.1)	5 (1.7)	11 (1.9)

Percentages calculated as (n/Enrolled Dispensed) * 100
Total enrolled = Total number of subjects consented.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for a randomized, prospective, multi-center clinical study performed in the United States.

Table 9 presents the demographic data for the serafilcon A test group vs. the comfilcon A control group. Subject demographics were similar between the two lens groups. The mean age was 34.1

and 33.5 years for the test lens group and control lens group, respectively. Females represented more than half of both lens groups, and majority of subjects in both lens groups were white.

Table 9: Demographic Characteristics (Enrolled Dispensed Subjects)

	Serafilcon A (N = 290)	**Comfilcon A (N = 291)**	**Overall (N = 581)**
Age (Years)			
n	290	291	581
Mean (SD)	34.1 (9.6)	33.5 (8.4)	33.8 (9.0)
Median	33.5	33.0	33.0
(Min, Max)	(18, 69)	(18, 61)	(18, 69)
Sex, n (%)			
Male	112 (38.6)	113 (38.8)	225 (38.7)
Female	178 (61.4)	178 (61.2)	356 (61.3)
Ratio (Females/Males)	1.6	1.6	1.6
Race, n (%)			
White	262 (90.3)	254 (87.3)	516 (88.8)
Black or African American	15 (5.2)	22 (7.6)	37 (6.4)
American Indian or Alaska Native	1 (0.3)	1 (0.3)	2 (0.3)
Asian	3 (1.0)	3 (1.0)	6 (1.0)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)
Other	9 (3.1)	8 (2.7)	17 (2.9)
Multi-racial	0 (0.0)	3 (1.0)	3 (0.5)

Ethnicity, n (%)			
Hispanic or Latino	32 (11.0)	28 (9.6)	60 (10.3)
Not Hispanic or Latino	257 (88.6)	263 (90.4)	520 (89.5)
Not Reported	1 (0.3)	0 (0.0)	1 (0.2)

Percentages calculated as (n/N) * 100

D. Safety and Effectiveness Results

1. Safety Results

The analysis of safety was based on the enrolled dispensed cohort of 581 patients/procedures, etc. available for the 12 month evaluation. The key safety outcomes for this study are presented below in **Table 10**. Adverse effects are reported in **Tables 11 to 14.**

The study investigators were required to report all adverse events by diagnosis and by severity. Adverse events were graded as Serious, Significant and Non-Significant based on the definitions provided in the study protocol. The safety analysis was based on the 1162 enrolled dispensed eyes (581 subjects): 580 eyes (290 subjects) in serafilcon A and 582 eyes (291 subjects) in comfilcon A. The key safety outcomes for this study is presented below in **Table 10**.

a. Primary safety

The primary safety endpoint was proportion of ocular serious and significant non-serious adverse device effects (ADEs). Noninferiority of test to control for primary safety was met using a predetermined threshold of 0.05 (5.0%).

There were no serious adverse events (SAE) reported for the test group. There were 3 ocular device-related SAEs in the control group in 3 eyes (3 ulcerative keratitis). All three events resolved, and 1 subject discontinued from the study due to the SAE.

Overall, 1.0% (6/580) of the test eyes experienced significant non-serious ADEs during the study, compared to 2.1% (12/582) of the control eyes. In the test group, there were 6 device-related events in 6 eyes (4 corneal infiltrates, 2 ulcerative keratitis). In the control group, there were 12 device-related events in 12 eyes (6 corneal infiltrates, 3 giant papillary conjunctivitis, 3 ulcerative keratitis). The incidence rates of eyes with ocular device-related serious, and significant non-serious adverse events are presented in **Table 10**.

Table 10: Incidence of Ocular Serious and Significant Non-serious Adverse Device Effects (Enrolled Dispensed Eyes)

	Serafilcon A (N = 580)		Comfilcon A (N = 582)	
Preferred Term	**n**	**(%)**	**n**	**(%)**
Serious				
Any Adverse Event	0	(0.0)	3	(0.5)
Ulcerative keratitis	0	(0.0)	3	(0.5)
Significant Non-serious				
Any Adverse Event	6	(1.0)	12	(2.1)
Corneal infiltrates	4	(0.7)	6	(1.0)
Giant papillary conjunctivitis	0	(0.0)	3	(0.5)
Ulcerative keratitis	2	(0.3)	3	(0.5)

n = Number of eyes reporting specified adverse event.
Percentages calculated as (n/N) * 100

b. Other adverse events (non-primary safety AEs)

The majority of the AEs in the study were assessed as non-serious and non-significant. The overall rate of other ocular AEs were similar between groups. There were a total of 97 ocular adverse events in the test group, of which 35 events (29 eyes) were related to the device (5% of total 580 eyes dispensed). The two most frequently reported device-related AE in the test group were dry eye (8 events) and GPC (6 events). In the control group, there were a total of 102 events, of which 25 events were device-related in 24 eyes (4.1% of total 582 eyes dispensed). Commonly observed related AEs in the control group included corneal infiltrates, corneal edema, and eye irritation (n= 3 events each). **Table 11** summarizes the outcomes for Other Adverse Events.

Table 11: Incidence of Other Treatment-Emergent Adverse Events (Enrolled Dispensed Eyes)

	Related						Not Related						Overall					
	Serafilcon A (N = 580)			Comfilcon A (N = 582)			Serafilcon A (N = 580)			Comfilcon A (N = 582)			Serafilcon A (N = 580)			Comfilcon A (N = 582)		
Preferred Term	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**
Any Adverse Event	29	(5.0)	35	24	(4.1)	25	59	(10.2)	62	65	(11.2)	77	81	(14.0)	97	84	(14.4)	102
Allergic keratitis	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	1	(0.2)	1	1	(0.2)	1	1	(0.2)	1
Blepharitis allergic	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0
Chalazion	0	(0.0)	0	0	(0.0)	0	3	(0.5)	4	1	(0.2)	1	3	(0.5)	4	1	(0.2)	1
Chemical burns of eye	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0
Ciliary hyperaemia	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2
Conjunctival disorder	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2
Conjunctival haemorrhage	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	2	(0.3)	2	2	(0.3)	2	2	(0.3)	2
Conjunctival hyperaemia	0	(0.0)	0	2	(0.3)	2	1	(0.2)	1	1	(0.2)	1	1	(0.2)	1	3	(0.5)	3
Conjunctival oedema	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	4	(0.7)	4	0	(0.0)	0	4	(0.7)	4
Conjunctivitis	0	(0.0)	0	0	(0.0)	0	3	(0.5)	3	4	(0.7)	4	3	(0.5)	3	4	(0.7)	4
Conjunctivitis allergic	0	(0.0)	0	0	(0.0)	0	5	(0.9)	6	4	(0.7)	4	5	(0.9)	6	4	(0.7)	4
Conjunctivitis viral	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Contact lens acute red eye	2	(0.3)	2	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0
Corneal abrasion	1	(0.2)	1	0	(0.0)	0	2	(0.3)	2	2	(0.3)	2	3	(0.5)	3	2	(0.3)	2

Corneal epithelial microcysts	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1
Corneal epithelium defect	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Corneal infiltrates	1	(0.2)	1	3	(0.5)	3	4	(0.7)	4	2	(0.3)	2	5	(0.9)	5	5	(0.9)	5
Corneal oedema	0	(0.0)	0	3	(0.5)	3	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	5	(0.9)	5
Corneal scar	0	(0.0)	0	2	(0.3)	2	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2	2	(0.3)	2
Curetting of chalazion	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0
Dry eye	8	(1.4)	8	2	(0.3)	2	7	(1.2)	7	5	(0.9)	5	13	(2.2)	15	7	(1.2)	7
Episcleritis	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Eye allergy	2	(0.3)	2	0	(0.0)	0	3	(0.5)	3	0	(0.0)	0	5	(0.9)	5	0	(0.0)	0
Eye discharge	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2
Eye irritation	3	(0.5)	3	3	(0.5)	3	5	(0.9)	5	7	(1.2)	8	8	(1.4)	8	10	(1.7)	11
Eye pain	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2
Eye pruritus	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0
Eyelid disorder	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Eyelid erosion	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Eyelid injury	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Eyelid pain	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0
Facial paralysis	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Foreign body in eye	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	3	(0.5)	3	1	(0.2)	1	3	(0.5)	3
Foreign body sensation in eyes	0	(0.0)	0	1	(0.2)	1	1	(0.2)	1	4	(0.7)	4	1	(0.2)	1	5	(0.9)	5
Giant papillary conjunctivitis	6	(1.0)	6	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2	6	(1.0)	6	4	(0.7)	4
Hordeolum	0	(0.0)	0	0	(0.0)	0	4	(0.7)	4	2	(0.3)	2	4	(0.7)	4	2	(0.3)	2
Hypopyon	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Keratitis	1	(0.2)	1	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	1	(0.2)	1	2	(0.3)	2
Keratitis bacterial	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0

Muscle twitching	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Ocular discomfort	2	(0.3)	2	2	(0.3)	2	0	(0.0)	0	4	(0.7)	4	2	(0.3)	2	6	(1.0)	6
Ocular hyperaemia	0	(0.0)	0	0	(0.0)	0	3	(0.5)	3	0	(0.0)	0	3	(0.5)	3	0	(0.0)	0
Punctate keratitis	3	(0.5)	3	1	(0.2)	1	1	(0.2)	1	3	(0.5)	3	4	(0.7)	4	4	(0.7)	4
Superficial injury of eye	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Swelling of eyelid	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0
Ulcerative keratitis	1	(0.2)	1	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	1	(0.2)	1	2	(0.3)	2
Vision blurred	3	(0.5)	3	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	3	(0.5)	3	1	(0.2)	1
Visual acuity reduced	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0	2	(0.3)	2
Visual impairment	2	(0.3)	2	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(0.3)	2	0	(0.0)	0
Vital dye staining cornea present	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0
Vitreoretinal traction syndrome	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1
Vitreous floaters	0	(0.0)	0	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0	1	(0.2)	1	0	(0.0)	0

n = Number of eyes reporting specified adverse event; E = Number of events
Percentages calculated as (n/N) * 100
If an eye had multiple occurrences of an adverse event, the eye is presented only once in the respective eye count column (n), and each occurrence is counted each time in the event (E) column.

Biomicroscopy findings for each enrolled dispensed eye, assessed at the Screening/ Dispensing Visit (baseline) and all follow-up visits, were graded for severity on a scale from 0 (No Finding) to 4 (Severe Finding). Over All Follow-up Visits, ≥ Grade 2 findings were noted in 152 (26.2%) eyes in the test group and 154 (26.6%) eyes in the control group. **Table 12** provides summary for each group for eyes with slit lamp findings ≥ Grade 2.

Table 12: Graded Slit Lamp Findings Over All Follow-up Visits, Eyes with Findings ≥ Grade 2 (Enrolled Dispensed Eyes)

Finding		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Any Finding	Absent	428 (73.8)	424 (73.4)
	Present	152 (26.2)	154 (26.6)
Limbal Hyperemia	Absent	550 (94.8)	554 (95.8)
	Present	30 (5.2)	24 (4.2)
Bulbar Hyperemia	Absent	537 (92.6)	544 (94.1)
	Present	43 (7.4)	34 (5.9)
Corneal Staining	Absent	547 (94.3)	526 (91.0)
	Present	33 (5.7)	52 (9.0)
Conjunctival Staining	Absent	525 (90.5)	520 (90.0)
	Present	55 (9.5)	58 (10.0)
Palpebral Conjunctival Observations	Absent	504 (86.9)	508 (87.9)
	Present	76 (13.1)	70 (12.1)
Corneal Epithelial Edema	Absent	577 (99.5)	574 (99.3)
	Present	3 (0.5)	4 (0.7)
Corneal Stromal Edema	Absent	579 (99.8)	575 (99.5)
	Present	1 (0.2)	3 (0.5)
Corneal Vascularization	Absent	579 (99.8)	576 (99.7)
	Present	1 (0.2)	2 (0.3)
Corneal Infiltrates	Absent	580 (100.0)	574 (99.3)
	Present	0 (0.0)	4 (0.7)

Other Findings	Absent	564 (97.2)	566 (97.9)
	Present	16 (2.8)	12 (2.1)

Percentages calculated for each category use total non-missing as denominator
Present = finding ≥ grade 2 for category at least once across all follow-up visits.

Table 13 presents Eyes with device-related Medically Treated serious and significant non serious Adverse Events. There were 6 (1.0%, 6/580) Serafilcon A test lens related events compared to 14 (2.4%, 14/582) Comfilcon A control lens related events that were medically treated.

Table 13: Eyes with Medically Treated Serious and Significant Non-serious Adverse Device Effects (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	**Comfilcon A (N = 582) n (%)**
Eyes with medically treated serious or significant non-serious ADEs	Yes	6 (1.0)	14 (2.4)
	No	574 (99.0)	568 (97.6)
	Total	**580**	**582**

N = Number of eyes in each lens; n = Number of eyes in specified category
Total = Number of eyes with non-missing response; Percentages calculated as (n/Total) * 100

Ungraded slit lamp findings were marked as either present or absent for each eye. Over All Follow-up Visits, for conjunctival compression or chemosis, there were 104 (17.9%) eyes in the serafilcon A test group, and 124 (21.5%) eyes in the comfilcon A control group with these slit lamp findings.

Table 14 presents the ungraded slit lamp findings for the Test and Control groups, based upon all enrolled dispensed eyes across all follow-up visits.

Table 14: Ungraded Slit Lamp Findings (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Baseline	Absent	570 (98.3)	575 (98.8)
	Present	10 (1.7)	7 (1.2)
Over All Follow-up Visits	Absent	476 (82.1)	454 (78.5)
	Present	104 (17.9)	124 (21.5)
24-Hour Follow-up	Absent	545 (94.0)	549 (95.3)
	Present	35 (6.0)	27 (4.7)
1-Week Follow-up	Absent	525 (93.1)	542 (95.8)
	Present	39 (6.9)	24 (4.2)
1-Month Follow-up	Absent	490 (93.5)	499 (94.5)
	Present	34 (6.5)	29 (5.5)
2-Month Follow-up	Absent	469 (94.2)	479 (94.3)
	Present	29 (5.8)	29 (5.7)
3-Month Follow-up	Absent	489 (97.0)	500 (95.4)
	Present	15 (3.0)	24 (4.6)
6-Month Follow-up	Absent	496 (95.8)	494 (93.2)
	Present	22 (4.2)	36 (6.8)
9-Month Follow-up	Absent	494 (95.4)	481 (93.6)
	Present	24 (4.6)	33 (6.4)
12-Month Follow-up	Absent	484 (94.2)	479 (93.6)
	Present	30 (5.8)	33 (6.4)
Unscheduled Visits	Absent	186 (93.9)	174 (92.6)

	Present	12 (6.1)	14 (7.4)

Percentages calculated for each category use total non-missing as denominator
Present = conjunctival compression/indentation or chemosis present at visit
A subject may contribute more than one unscheduled visit

High contrast distance best spectacle corrected visual acuity (BCVA) was obtained at the Screening/Dispensing Visit (baseline) and again at the Exit Visit. VA was collected in the Snellen scale and converted to the logMAR scale based on the number of letters correctly identified. An eye was considered to have worsened 2 or more Snellen lines if the difference in logMAR VA ≥ 0.2 (exit BCVA – baseline BCVA). Over All Follow-up Visits, there were no eyes in either group with a 2 or more line decrease in BSCVA from baseline to exit (refer to **Table 15**).

Table 15: Change from Baseline in Best Spectacle Corrected Visual Acuity: Baseline BCVA vs Final BCVA (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	**Comfilcon A (N = 582) n (%)**
Change from Baseline	Absent	554 (100.0)	548 (100.0)
	Present	0 (0.0)	0 (0.0)

Percentages calculated for each category use total non-missing as denominator
Present = 2 or more line decrease in BCVA.

Symptoms, problems and complaints were noted at each study visit for each eye. Subject responses were binary (absent or present). Each of the symptoms were reported by the subject on their own accord, and responses were reviewed by the investigator during the visit. The proportion of the eyes that reported ‘absent’ or ‘present’ for each of the symptoms over the duration of the study was similar between the test and the control groups and is presented in **Table 16**.

Table 16: Summary of Symptoms, Problems, and Complaints (SPC) Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Burning/Stinging	Absent	543 (93.6)	537 (92.9)
	Present	37 (6.4)	41 (7.1)
Itching	Absent	507 (87.4)	522 (90.3)
	Present	73 (12.6)	56 (9.7)
Lens Awareness	Absent	474 (81.7)	471 (81.5)
	Present	106 (18.3)	107 (18.5)
Dryness	Absent	246 (42.4)	279 (48.3)
	Present	334 (57.6)	299 (51.7)
Discomfort	Absent	473 (81.6)	444 (76.8)
	Present	107 (18.4)	134 (23.2)
Blurred Vision	Absent	484 (83.4)	512 (88.6)
	Present	96 (16.6)	66 (11.4)
Fluctuating/Variable Vision	Absent	538 (92.8)	549 (95.0)
	Present	42 (7.2)	29 (5.0)
Halo	Absent	574 (99.0)	558 (96.5)
	Present	6 (1.0)	20 (3.5)
Lens needs cleaning	Absent	523 (90.2)	527 (91.2)
	Present	57 (9.8)	51 (8.8)
Redness	Absent	525 (90.5)	526 (91.0)
	Present	55 (9.5)	52 (9.0)

Excessive Tearing	Absent	560 (96.6)	557 (96.4)
	Present	20 (3.4)	21 (3.6)
Secretions	Absent	536 (92.4)	530 (91.7)
	Present	44 (7.6)	48 (8.3)
Photophobia	Absent	563 (97.1)	560 (96.9)
	Present	17 (2.9)	18 (3.1)
Other	Absent	540 (93.1)	549 (95.0)
	Present	40 (6.9)	29 (5.0)

Percentages calculated for each category use total non-missing as denominator
Present = SPC reported at least once across all follow-up visits.

Table 17 summarizes keratometry changes from baseline to Exit Visit for enrolled dispensed eyes. There were 12 eyes (2.2%) in the test group and 15 eyes (2.7%) in the control group with a change in keratometry (absolute value of >1.00 D), of which 16 were a decrease in at least 1 meridian (9 test and 7 control); none was considered clinically significant. For the majority of all eyes with change in keratometry values, the reasons were indicated by the investigator as erroneous measurements, no apparent reason, visits conducted shortly after lens removal, or movement during measurements. No apparent association to the study lens was noted for all except 1 eye in the test group, however, study lens VA for this eye was 20/15 at all visits, and lens fit was optimal at all follow-up visits. No AEs related to keratometry change were reported.

Table 17: Keratometry Change (Absolute Value) from Baseline to Final Visit (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	**Comfilcon A (N = 582) n (%)**
Maximum Absolute	0.00 to 1.00 D	540 (97.8)	541 (97.3)
	1.01 to 1.50 D	5 (0.9)	5 (0.9)
	1.51 to 2.00 D	3 (0.5)	3 (0.5)

	> 2.00 D	4 (0.7)	7 (1.3)
	Not Reported	28	22
	Total	**552 (100.0)**	**556 (100.0)**
	Mean (SD)	0.30 (0.39)	0.36 (0.42)
	Median	0.25	0.25
	(Min, Max)	(0.00, 5.13)	(0.00, 4.18)

Percentages calculated as (n/Total) * 100
Based on the absolute change from baseline to final visit
Maximum Absolute = maximum of the absolute change of the horizontal and vertical components
Baseline = Visit 1; Final = Last attended visit

Table 18 summarizes spherocylindrical refraction changes from baseline to Exit Visit for all enrolled dispensed eyes. There were 0 eyes (0.0%) in the test group and 1 eye (0.2%) in the control group with a change in refraction of > 1.00 D.

Table 18: Refractive Changes (Absolute Value) from Baseline to Final Visit (Enrolled Dispensed Eyes)

Refractive Changes		**Serafilcon A (N = 580) n (%)**	**Comfilcon A (N = 582) n (%)**
	0.00 to 1.00 D	556 (100.0)	549 (99.8)
	1.12 to 1.50 D	0 (0.0)	1 (0.2)
	1.62 to 2.00 D	0 (0.0)	0 (0.0)
	Not Reported	24	28
	Total	**556 (100.0)**	**550 (100.0)**
	Mean (SD)	0.10 (0.15)	0.11 (0.17)

	Median	0.00	0.00
	(Min, Max)	(0.00, 0.88)	(0.00, 1.25)

Percentages calculated as (n/Total) * 100
Based on the absolute change from baseline to final visit in spherical equivalent
Spherical equivalent = sphere + 1/2 cylinder
Baseline = Visit 1; Final = Last attended visit

At the start of each follow-up visit, as part of the worn lens evaluation, the subject was asked whether they used rewetting drops. The frequency (count and percent) of subjects using rewetting drops is provided with percent based on the total non-missing responses over all follow-visits, for each lens group (**Table 19**).

Table 19: Rewetting Drop Usage Over All Follow-up Visits (Enrolled Dispensed Subjects)

		Serafilcon A (N = 290) n (%)	Comfilcon A (N = 291) n (%)
Rewetting Drop Usage	Absent	50 (17.2)	75 (26.0)
	Present	240 (82.8)	214 (74.0)

Percentages calculated for each category use total non-missing as denominator
Present = subject reported rewetting drop use at least once across all follow-up visits

2. Effectiveness Results

The analysis of effectiveness was based on the 581 enrolled, dispensed evaluable patients at the 12-month time point. Key effectiveness outcomes are presented in **Tables 20 and 21**.

Visual Acuity

The primary effectiveness endpoint was high contrast, distance visual acuity (VA) with dispensed lenses over the 12-month exposure duration. All enrolled dispensed eyes were included in the analysis under the actual treatment received. High contrast distance lens VA was obtained at the Screening/ Dispensing Visit, and at each follow-up visit. Scores were recorded as the numbers of letters correctly identified in the eye examination. VA was converted to the Log10 of the Minimum Angle of Resolution (logMAR) by using the score (number of letters).

Visual acuity (VA) with the study lenses was measured at each Extended Wear Follow-up visits. For completed eyes, the test group proportion of eyes (all follow-up visits combined) achieving Snellen VA of 20/20 or better was 98.1% (3952/4027) versus the proportion of control eyes

reporting 20/20 or better (99.0% or 3982/4024). Conversely, the proportion of VAs of 20/40 or worse reported over the duration of the extended wear segment of the study were 0.0% for the test and control groups (**Table 20**).

Overall, the distribution of study lens VA was similar between the test and control eyes. Approximately 99.9% (4247/4253) of enrolled dispensed eyes (completed + discontinued eyes) in the clinical study achieved at least 20/25 with the serafilcon A test contact lens over all follow-up visits.

Table 20: Distribution for Snellen Study Lens Visual Acuity Over All Follow-up Visits By Cohort and Status

	Completed Eyes		**Discontinued Eyes**	
	Serafilcon A (N = 514) n (%)	**Comfilcon A (N = 512) n (%)**	**Serafilcon A (N = 66) n (%)**	**Comfilcon A (N = 70) n (%)**
≥20/20	3952 (98.1)	3982 (99.0)	211 (93.4)	261 (99.6)
≥20/25	70 (1.7)	38 (0.9)	14 (6.2)	1 (0.4)
≥20/30	5 (0.1)	4 (0.1)	0 (0.0)	0 (0.0)
≤20/40	0 (0.0)	0 (0.0)	1 (0.4)	0 (0.0)
Total	**4027**	**4024**	**226**	**262**

Percentages calculated for each category use total non-missing as denominator.

VA was converted to the Log10 of the Minimum Angle of Resolution (logMAR) by using the score (number of letters) correctly identified. As shown in **Table 21**, mean logMAR VA was comparable between the two lens groups in the enrolled dispensed eyes over all follow-up visits.

Table 21: Descriptive Statistics for logMAR Study Lens Visual Acuity Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580)	Comfilcon A (N = 582)
Visual Acuity	**Total**	**4253**	**4286**
	Mean (SD)	-0.05 (0.07)	-0.06 (0.06)
	Median	0.00	0.00
	(Min, Max)	(-0.20, 0.30)	(-0.30, 0.18)

SD = Standard Deviation; Min = Minimum; Max = Maximum
Analyses are based on the number of dispensed eyes with non-missing scores in each treatment group

With regard to the line change in visual acuity from baseline over all follow-up visits, 9 (1.6%, 9/578) eyes in the test group and 5 (0.9%, 5/576) eyes in the control group experienced a worsening of 2 lines or more from Dispensing Lens VA at any time point. **Table 22** presents the line change in visual acuity from baseline over all follow-up visits.

Table 22: Study Lens Distance VA Line Change: Screening/Dispensed Lens VA versus Follow-up Lens VA Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Line Change from Dispense	-3	3 (0.5)	1 (0.2)
	-2	6 (1.0)	4 (0.7)
	-1	139 (24.0)	106 (18.4)
	No Change	421 (72.8)	460 (79.9)
	1	9 (1.6)	5 (0.9)
	Total	**578**	**576**

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits
Negative line change indicates worsened visual acuity; positive indicates improved visual acuity

Supportive Effectiveness Endpoints

Extended lens wear was reported by subjects using the eDiary. For each week of participation in the study, subjects indicated the number of consecutive nights the lenses were worn during the week. The percentage of diary entries where subjects reported at least six consecutive nights of lens wear per week during the study is shown in **Table 23**. In the test group, majority of diary entries (91.7%, 19582/21360) indicated that the subjects were able to wear lenses for 6 consecutive nights. Similarly, in the control group, majority of diary entries (92.0%, 20549/22326) indicated that the subjects were able to wear lenses for 6 consecutive nights during the study.

Table 23: Number of Nights Lenses Worn (Enrolled Dispensed Eyes)

Diary entries post dispense visit	**Serafilcon A N = 580**		**Comfilcon A N = 582**	
	n	%	n	%
Total number of observations	21360	100	22326	100
6 nights of lens wear	19582	91.7	20549	92

Percentages calculated as (n/Total) * 100

Front surface lens wettability was assessed at the Screening/Dispensing Visit on the newly dispensed lens and at each follow-up visit, using a 5-point scale (0 = a smooth uniformly reflecting surface, 1 = a coarse hazy surface which seems resolved momentarily with each blink and becomes exacerbated with staring, 2 = one stable dry (non-wetting) area of some magnitude, 3 = more than one stable dry (non-wetting) area of some magnitude, 4 = non-wettable lens surface). Over All Follow-up Visits, the majority of eyes (Test 96.5% (558/578 eyes); and Control 96.9% (558/576 eyes) were assessed with Grade 0 or 1 front surface wettability, and frequency of lenses with Grade 2 were similar between groups (**Table 24**). There were 2 lenses with grade 3 in the test group. **Table 24** presents lens wettability over all follow-up visits.

Table 24: Lens Wettability Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Front Surface Wettability	0	342 (59.2)	372 (64.6)
	1	216 (37.4)	186 (32.3)
	2	18 (3.1)	18 (3.1)
	3	2 (0.3)	0 (0.0)
	4	0 (0.0)	0 (0.0)
	Total	**578**	**576**

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits

Front surface deposits were assessed at the Screening/Dispensing Visit on the newly dispensed lens and at each follow-up visit, using a 5-point scale (0 = absent, clean surface, 1 = very slight, only visible after tear film drying, 2 = slight, visible deposits easily removable, 3 = moderate, deposits adherent and not removable, 4 = severe, non-removable deposits and comfort affected).

Over All Follow-up Visits, the majority of the test and control lenses were assessed with Grade 0 or 1 front surface deposits (**Table 25**). Grade 2 or higher front surface deposits were observed at a similar rate between the test and control lenses; a few were assessed higher than Grade 2. One (1) lens in each of the test and control group was assessed with Grade 4 deposits.

Table 25: Front Surface Lens Deposits Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Front Surface Deposits	0 (Absent)	318 (55.0)	304 (52.8)
	1 (Very Slight)	203 (35.1)	211 (36.6)
	2 (Slight)	51 (8.8)	52 (9.0)
	3 (Moderate)	5 (0.9)	8 (1.4)
	4 (Severe)	1 (0.2)	1 (0.2)
	Total	**578**	**576**
Moderate/Severe Lens Deposits	Absent	572 (99.0)	567 (98.4)
	Present	6 (1.0)	9 (1.6)

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits
Present = lens deposits graded 3 or 4 at least once across all follow-up visits

Back surface deposits were assessed at the Screening/Dispensing Visit on the newly dispensed lens and at each follow-up visit, using a 5-point scale (0 = absent, clean surface, 1 = very slight, 3 spots or less of moving particles, 2 = slight, up to 10 spots of moving particles, 3 = moderate, 3 or less non-moving deposits adherent to lens, 4 = severe, 4 or more deposits adherent to the lens and/or corneal indentation). Over All Follow-up Visits, the majority of the test and control lenses in the enrolled dispensed eyes were assessed with Grade 0 or 1 back surface deposits (**Table 26**). The rates of lenses with Grade 2 or 3 assessments were low across the study visits in both groups (2.1% test (12/578), 3.1% control (18/576)).

Table 26: Back Surface Lens Deposits Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Back Surface Deposits	0 (Absent)	485 (83.9)	450 (78.1)
	1 (Very Slight)	81 (14.0)	108 (18.8)
	2 (Slight)	9 (1.6)	16 (2.8)
	3 (Moderate)	3 (0.5)	2 (0.3)
	4 (Severe)	0 (0.0)	0 (0.0)
	Total	**578**	**576**
Moderate/Severe Lens Deposits	Absent	575 (99.5)	574 (99.7)
	Present	3 (0.5)	2 (0.3)

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits
Present = lens deposits graded 3 or 4 at least once across all follow-up visits

Contact lens centration was assessed at the Screening/Dispensing Visit on the newly dispensed lens and at each follow-up visit.

Across all follow-up visits, all but one test and all control lenses in the study were reported with optimal or acceptable centration. The majority were assessed optimal (82.5% in the test and 87.8% in the control groups, **Table 27**).

Table 27: Lens Centration Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Lens Position	Optimal lens centration	477 (82.5)	506 (87.8)
	Acceptable decentration	100 (17.3)	70 (12.2)
	Unacceptable decentration	1 (0.2)	0 (0.0)
	Total	**578**	**576**

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits

Contact lens movement was assessed at the Screening/Dispensing Visit on the newly dispensed lens and at each follow-up visit. **Table 28** summarizes lens movement by lens group for enrolled dispensed eyes. In this Table, lens movement is categorized into 3 bins: optimal, acceptably loose or acceptably tight, and unacceptably tight or unacceptably loose. Over All follow-up visits, optimal or acceptable lens movement was reported for all except 1 test lens and 4 control lenses.

Table 28: Lens Movement Over All Follow-up Visits (Enrolled Dispensed Eyes)

		Serafilcon A (N = 580) n (%)	Comfilcon A (N = 582) n (%)
Lens Movement	Optimal fit/movement	378 (65.4)	371 (64.4)
	Acceptably tight/loose	199 (34.4)	201 (34.9)
	Unacceptably tight/loose	1 (0.2)	4 (0.7)
	Total	**578**	**576**
Unacceptable Lens Movement	Absent	577 (99.8)	572 (99.3)
	Present	1 (0.2)	4 (0.7)

Percentages calculated for each category use total non-missing as denominator
Over All Follow-up Visits summarizes the worst case over all follow-up visits
Present = unacceptably tight or unacceptably loose at least once across all follow-up visits

Contact lens subjective performance was assessed at each scheduled visit for a number of attributes (insertion comfort, insertion handling, overall vision, overall comfort, and removal handling), using a 1 (least favorable outcome) to 10 (most favorable outcome) point scale questionnaire. In the completed eyes, the mean subjective acceptance ratings were similar between the test and control lenses, with ratings ≥ 8.5 for each of the attributes assessed at the majority of scheduled study visits. In Discontinued eyes, there were no clinically relevant differences in mean subject acceptance ratings between test and control lenses.

Supplemental Clinical Information

The pivotal study protocol (under IDE G190046) also included a separate cohort of Asian patients, to assess in this cohort, the safety and performance of the serafilcon A test lens when worn in an extended wear modality (i.e., up to 6 nights of continuous wear) as compared to comfilcon A control lenses. A total of 67 patients were enrolled at 7 investigative sites in the US.

Of the 67 enrolled patients, 64 eligible patients were randomized and exposed to study lenses, of which 58 patients completed the study, and were evaluable. Twenty-nine (58 eyes) patients in each group completed the 12-month study. Lenses were replaced on a weekly basis. Data tables summarizing demographics and key safety data pertinent to Asian subjects from the 7 sites are presented in **Table 29** and **Table 30**. Overall mean age of subjects was 33.3 years, with 32.8% (21/64) male and 67.2% (43/64) female participants. Subjects self-identified predominantly as Asian Chinese and Not Hispanic or Latino ethnicity (100%, 64/64).

Table 29: Demographic Characteristics (Supplemental - Enrolled Dispensed Subjects)

	Control (N = 32)	Test (N = 32)	Overall (N = 64)
Age (Years)			
n	32	32	64
Mean (SD)	31.6 (7.4)	34.9 (8.5)	33.3 (8.1)
Median	31.5	34.0	33.0
(Min, Max)	(19, 52)	(18, 51)	(18, 52)
Sex, n (%)			
Male	8 (25.0)	13 (40.6)	21 (32.8)
Female	24 (75.0)	19 (59.4)	43 (67.2)
Ratio (Females/Males)	3.0	1.5	2.0
Race, n (%)			
White	0 (0.0)	0 (0.0)	0 (0.0)
Black or African American	0 (0.0)	0 (0.0)	0 (0.0)
American Indian or Alaska Native	0 (0.0)	0 (0.0)	0 (0.0)
Asian (Chinese)	32 (100.0)	32 (100.0)	64 (100.0)
Native Hawaiian or Other Pacific Islander	0 (0.0)	0 (0.0)	0 (0.0)
Other	0 (0.0)	0 (0.0)	0 (0.0)

Ethnicity, n (%)			
Hispanic or Latino	0 (0.0)	0 (0.0)	0 (0.0)
Not Hispanic or Latino	32 (100.0)	32 (100.0)	64 (100.0)

Control = Biofinity® (comfilcon A) soft contact lenses; Test = Mercury soft contact lenses
N = Number of subjects in each lens or overall; n = Number of subjects with non-missing response or in specified category
Percentages calculated as (n/N) * 100
SD = Standard Deviation; Min = Minimum; Max = Maximum

Primary effectiveness results indicated that for distance visual acuity, all eyes, whether with serafilcon A test or comfilcon A control lens, achieved VA of 20/25 or better throughout the duration of the study, and both lens groups performed similarly with respect to study lens VA.

For the primary safety endpoint, there were no reports of ocular serious, and significant non-serious adverse device effects in this cohort, for either lens group. There was 1 device-related non-serious non-significant AE (punctate keratitis) in the test group and no events in the control group (**Table 30**). There were no ocular Treatment-Emergent adverse events in the discontinued eyes.

Table 30: Incidence of All Ocular Non-serious Non-significant Treatment-Emergent Adverse Events (Supplemental -Completed Eyes)

	Related						**Not Related**						**Overall**					
	Control (N = 58)			**Test (N = 58)**			**Control (N = 58)**			**Test (N = 58)**			**Control (N = 58)**			**Test (N = 58)**		
Preferred Term	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**	**n**	**(%)**	**E**
Any Adverse Event	0	(0.0)	0	1	(1.7)	1	2	(3.4)	2	6	(10.3)	8	2	(3.4)	2	7	(12.1)	9
Conjunctivitis allergic	0	(0.0)	0	0	(0.0)	0	2	(3.4)	2	4	(6.9)	6	2	(3.4)	2	4	(6.9)	6
Eye allergy	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	2	(3.4)	2	0	(0.0)	0	2	(3.4)	2
Punctate keratitis	0	(0.0)	0	1	(1.7)	1	0	(0.0)	0	0	(0.0)	0	0	(0.0)	0	1	(1.7)	1

Control = Biofinity® (comfilcon A) soft contact lenses; Test = Mercury soft contact lenses
N = Number of eyes in each lens; n = Number of eyes reporting specified adverse event; E = Number of events
Percentages calculated as (n/N) * 100
Data summarized based on relatedness to the lensIf an eye had multiple occurrences of an adverse event, the eye is presented only once in the respective eye count column (n), and each occurrence is counted each time in the event (E) column.

Biomicroscopy findings for each enrolled dispensed eye, assessed at the Screening/ Dispensing Visit (baseline) and all follow-up visits, were graded for severity on a scale from 0 (No Finding) to 4 (Severe Finding). **Table 31** provides summary for each group for eyes with biomicroscopy findings ≥ Grade 2 compared to the baseline visit.

Table 31: Incidence of Increased Severity by 2 or More Grades in Biomicroscopy Findings (Supplemental- Completed Eyes)

Finding	Control (N = 58) n (%)	Test (N = 58) n (%)
Limbal Hyperemia	0 (0.0)	0 (0.0)
Bulbar Hyperemia	2 (3.4)	0 (0.0)
Corneal Staining	4 (6.9)	0 (0.0)
Conjunctival Staining	1 (1.7)	2 (3.4)
Palpebral Conjunctival Observations	2 (3.4)	2 (3.4)
Corneal Epithelial Edema	0 (0.0)	0 (0.0)
Corneal Stromal Edema	0 (0.0)	0 (0.0)
Corneal Vascularization	0 (0.0)	0 (0.0)
Corneal Infiltrates	0 (0.0)	0 (0.0)

Control = Biofinity® (comfilcon A) soft contact lenses; Test = Mercury soft contact lenses
N = Number of eyes in each lens; n = Number of eyes with increase of 2 or more grades; Percentages calculated as (n/N) * 100
Increase by 2 or more grades from baseline to any subsequent visit for the specific lens in the same eye
Baseline defined as Visit 1

It was concluded that the clinical performance of the serafilcon A test lens was similar to that of comfilcon A control lens when used for extended wear in these subjects, with respect to the variables which were assessed in this study.

3. Subgroup Analyses

The following demographic characteristics were evaluated for potential association with safety and effectiveness primary outcomes: gender, age, race and ethnicity.

Primary Safety Endpoint

To assess homogeneity of treatment effect across demographics subgroups with regards to the proportion of ocular serious and significant non-serious ADEs (primary safety endpoint), the following were conducted for each of the demographics characteristics (gender, age, race, and ethnicity):

1. Descriptive statistics (counts and proportions) for each treatment and treatment difference were reviewed.
2. Plots on the treatment difference (proportions) with the corresponding 95% CI was generated.
3. Homogeneity test was also performed using Breslow-Day (**Table 32**).

Since there was no pre-specified age categorization in the protocol, the observed median value of 33 in the study was used as the cutoff to define 2 age subgroups for assessing homogeneity: ≤33 years and >33 years. In subjects ≤33 years, there was an equal number of primary safety events (n=6 each) in the Control and Test groups, however, in subjects >33 years, there were no events in the Test group and 9 events in the Control group. The Breslow-Day test for homogeneity was significant (p-value=0.0107, **Table 32**).

Several changes to the ocular adnexa, tear film and ocular surface are known to occur with normal aging (Lakkis, 2006), and whether or not the Test lens provided any potential benefits to subjects >33 years cannot be deduced based on the primary safety data due to the paucity of primary safety events. Published reports have confirmed that subject age ≤ 25 years (late adolescence and early adulthood) is a risk factor for increased corneal infiltrative events that include serious eye infections (Wagner et al. 2014, Chalmers et al. 2014). In this study, overall, 5 (2 Test and 3 Control) of total 21 (23.8%, 5/21) primary safety events were reported in subjects ≤ 25 years, and the remaining 16 events (76.2%, 16/21) were reported in subjects >25 years (V-RIM-0052828, Sections 11.4.5.1 –11.4.5.3), a pattern consistent with the difference in enrollment proportions between the two age brackets. For the remaining demographics characteristics, there was no evidence to suggest potential heterogeneity of treatment effect.

Primary Effectiveness Endpoint

To assess homogeneity of treatment effect across demographics subgroups with regards to distance VA with study lenses, the following were conducted for each of the demographics characteristics (gender, age, race, and ethnicity):

1. Descriptive statistics (mean, SD, median, min, and max) for each treatment and treatment difference were reviewed.
2. Forest plots on the treatment difference with the corresponding 95% CI was generated. All plots showed that the 95% CI were well within 1 Snellen line.
3. The effect of treatment-by-subgroup interaction was also evaluated with a post-hoc analysis by fitting a mixed effects repeated measures model for each of the demographics characteristics (**Table 33-36**; p-values>0.05 for all corresponding interaction terms).

There was no evidence to suggest potential heterogeneity of treatment effect for any of the demographics characteristics.

Table 32: Evaluation of Homogeneity of Treatment Effect Across Demographics Subgroups for Ocular Serious and Significant Non-Serious Adverse Device Effects (Enrolled Dispensed Eyes)

	Mantel-Haenszel Adjusted 95% CI for Difference in Proportions	Breslow-Day Test for Homogeneity p-value
Gender	(-0.0307, -0.0001)	0.5763
Age Group	(-0.0307, -0.0001)	0.0107
Race	(-0.0308, -0.0001)	0.5085
Ethnicity	(-0.0305, 0.0001)	0.4848

Control = Biofinity (comfilcon A) soft contact lenses; Test = Mercury soft contact lenses Difference = Test – Control Age Group defined as <=33 years and >33 years where 33 is the median value from the enrolled dispensed analysis set

Table 33: Evaluation of Homogeneity of Treatment Effect by Gender for Study Lens Visual Acuity (Enrolled Dispensed Eyes)

Effect	Num DF	Den DF	F Value	p-value
Treatment	1	578	0.34	0.5577
Visit	8	8460	4.83	<0.0001
Gender	1	577	0.35	0.5522
Treatment*Gender	1	578	1.16	0.2827

Num DF = Numerator Degrees of Freedom
Den DF = Denominator Degrees of Freedom
Results based on mixed effects repeated measures model

Table 34: Evaluation of Homogeneity of Treatment Effect by Age Group for Study Lens Visual Acuity (Enrolled Dispensed Eyes)

Effect	Num DF	Den DF	F Value	p-value
Treatment	1	578	0.74	0.3884
Visit	8	8460	4.83	<0.0001
Age Group	1	578	0.86	0.3538
Treatment*Age Group	1	578	0.49	0.4847

Num DF = Numerator Degrees of Freedom
Den DF = Denominator Degrees of Freedom
Results based on mixed effects repeated measures model
Age Group defined as <=33 years and >33 years where 33 is the median value from the enrolled dispensed analysis set

Table 35: Evaluation of Homogeneity of Treatment Effect by Race for Study Lens Visual Acuity (Enrolled Dispensed Eyes)

Effect	Num DF	Den DF	F Value	p-value
Treatment	1	577	0.19	0.6623
Visit	8	8459	4.83	<0.0001
Race	5	572	0.99	0.4249
Treatment*Race	4	573	0.09	0.9867

Num DF = Numerator Degrees of Freedom
Den DF = Denominator Degrees of Freedom
Results based on mixed effects repeated measures model

Table 36: Evaluation of Homogeneity of Treatment Effect by Ethnicity for Study Lens Visual Acuity (Enrolled Dispensed Eyes)

Effect	Num DF	Den DF	F Value	p-value
Treatment	1	576	0.24	0.6259
Visit	8	8444	4.84	<0.0001
Ethnicity	1	576	2.92	0.0878
Treatment*Ethnicity	1	576	0.00	0.9687

Num DF = Numerator Degrees of Freedom
Den DF = Denominator Degrees of Freedom
Results based on mixed effects repeated measures model

4. Pediatric Extrapolation

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

E. Financial Disclosure

The Financial Disclosure by Clinical Investigators regulation (21 CFR 54) requires applicants who submit a marketing application to include certain information concerning the compensation to, and financial interests and arrangement of, any clinical investigator conducting clinical studies covered by the regulation. The pivotal clinical study included 42 investigators of which 0 were full-time or part-time employees of the Applicant and 3 had disclosable financial interests/arrangements as defined in 21 CFR 54.2(a), (b), (c) and (f) and described below:

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

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

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

1. A one-night extended wear, single-site, prospective, randomized, controlled, double-masked, contralateral wear study was conducted at 1 investigative site in the US. The primary objective was to obtain initial insights to safety and performance of the serafilcon A test lens compared to the comfilcon A control lens following 1 night of extended wear. There were 4 study visits (Baseline/Dispense, Follow-up prior to sleeping on Day 1, Follow-up immediately upon awakening on Day 2, Follow-up 1 hour post awakening/Exit visit.

   A total of 12 subjects were enrolled. Of the 12 subjects enrolled, 1 subject screen failed, and the remaining 11 subjects were randomized, exposed to study lenses, completed the study, and were evaluable. Primary effectiveness results indicated that for distance visual acuity (Snellen), all eyes, whether with serafilcon A or comfilcon A soft contact lenses, achieved a VA of 20/30 or better during the study and 20/20 or better at the final study visit. The test lens and the control lens performed similarly with respect to VA.

   There were no reports of SAEs, nonocular AEs, clinically significant biomicroscopy findings, or device deficiencies in the study. There were 2 ocular ADEs reported by subjects, both in OS with comfilcon A, both mild and resolved. Based upon review of AEs, biomicroscopy findings, and device deficiencies, no safety concerns were identified for serafilcon A soft contact lenses when worn in an extended wear modality of 1 night.

   It was concluded that the clinical performance of the test lens was comparable to control lens when used for overnight wear, with respect to the variables which were assessed in this study.

2. A prospective, randomized, controlled, double-masked, contralateral clinical study was conducted to assess feasibility and initial safety and performance of the serafilcon A lens when worn in an extended modality (i.e., up to 6 nights of continuous wear) as compared to comfilcon A soft contact lens. Exposure duration was 1 week per subject, with 3 study visits (Baseline/Dispense, 24-hour and 1-week Follow-up visits). Two sites in the US enrolled and randomized 22 subjects. All subjects were exposed (22 serafilcon A eyes and 22 comfilcon A eyes) and completed the study. Mean subject age was 40.8 years. Primary effectiveness endpoint was distance visual acuity with study lenses. The majority of eyes achieved a distance VA of 20/20 or better during the study and all eyes had a study lens VA of 20/25 or better at the Exit Visit. A review of additional performance results including lens movement and position, surface deposits, wettability, ratings for overall comfort, vision, and handling were comparable for the two study lenses.

   There were no reports of SAEs, nonocular AEs, clinically significant biomicroscopy findings (greater than mild), or device deficiencies in the study. There were 2 treatment-emergent ADEs reported in 1 test eye ─ moderate blurred vision and mild mucous discharge, at the 24-hour follow-up visit, both mild or moderate and resolved, and subject completed the study wearing the same lens. Based on review of AEs, biomicroscopy

findings, and device deficiencies, no safety concerns were identified for test serafilcon A soft contact lenses when worn in an extended wear modality as studied.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Effectiveness Conclusions

The overall effectiveness of the Alcon serafilcon A contact lens was demonstrated based upon the results of the 12-month IDE clinical study.

The primary effectiveness endpoint was distance visual acuity (VA) with study lenses. Over All follow-up visits, mean LogMAR was -0.05 for the serafilcon A test lens and -0.06 for the comfilcon A control lens, indicating comparable outcomes. Approximately 99.9% (4247/4253) of enrolled dispensed eyes in the clinical study achieved at least 20/25 with the serafilcon A test contact lenses.

Supportive effectiveness and additional assessments showed similar clinical performance between the test and control lenses, with respect to the variables which were assessed in this study including lens movement and centration, lens surface performance, comfort, vision, handling, extended wear time, symptoms, problems, and complaints, when lenses were worn on an extended wear basis.

The effectiveness results from the PMA clinical trial provided evidence that the study outcomes met the acceptance criteria.

B. Safety Conclusions

The risks of the device are based on nonclinical laboratory studies as well as data collected in the pivotal clinical study conducted to support PMA approval as described above.

The primary safety endpoint was met. Noninferiority of serafilcon A to comfilcon A was demonstrated based on the noninferiority margin of 0.05 for the difference between groups in the proportion of ocular serious and significant nonserious ADEs.

There were no serious adverse events reported in the serafilcon A group, and 3 serious adverse events reported in the comfilcon A group. The rates of significant non-serious device related adverse events were comparable in both groups.

The safety results from the PMA clinical trial provided evidence that the study outcomes met the acceptance criteria.

C. Benefit-Risk Determination

The probable benefits of the device are based on data collected in a clinical study conducted to support PMA approval and other clinical studies as described above. The benefits of the device include vision correction, as well as the convenience of wearing contact lenses overnight, i.e., without removal, for up to 1 week.

The probable risks of the device are also based on data collected in a clinical study conducted to support PMA approval as described above. The risks of the devide include serious eye infection, ocular inflammation, and other ocular complications.

Additional factors to be considered in determining probable risks and benefits for serafilcon A contact lenses include:

- The results of the clinical study can be considered generalizable to the intended market or target patient population.
- Clinical data were collected using a study design that included randomized treatment and masking of subjects and evaluators.
- Adverse device effects observed for serafilcon A contact lenses in clinical studies are consistent with complications known with marketed extended wear contact lenses.

1. Patient Perspective
   This submission either did not include specific information on patient perspectives or the information did not serve as part of the basis of the decision to approve or deny the PMA for this device.

In conclusion, given the available information above, the data support that for the visual correction of refractive ametropia, the probable benefits of the serafilcon A soft contact lenses outweigh the probable risks.

D. Overall Conclusions

The data in this application support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use. The safety and effectiveness

endpoints of the study were met, demonstrating that the serafilcon A contact lens is as safe and effective as other approved extended wear contact lenses.

XIV. CDRH DECISION

CDRH issued an approval order on April 25, 2023.
The applicant's manufacturing facilities have been inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XV. APPROVAL SPECIFICATIONS

Directions for use: See device labeling.

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

Post-approval Requirements and Restrictions: See approval order.

XVI. REFERENCES

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