SUMMARY OF SAFETY AND EFFECTIVENESS (SSED)

I. GENERAL INFORMATION

Device Generic Name:	comfilcon A soft (hydrophilic) contact lens
Device Trade Names:	BIOFINITY® (comfilcon A) soft contact lens Aquaclear™ (comfilcon A) soft contact lens SiH48 (comfilcon A) soft contact lens
Applicant's Name and Address:	COOPERVISION, INC. 6140 Stoneridge Mall Rd. Suite 500 Pleasanton, CA 94588
Date(s) of Panel Recommendation:	None
Premarket Approval Application (PMA) Number:	P080011
Date of FDA Notice of Approval:	November 19, 2008
Expedited:	Not Applicable

II. INDICATIONS FOR USE

BIOFINITY® (comfilcon A) Sphere and Asphere soft contact lenses are indicated for the correction of ametropia (myopia and hyperopia) in aphakic and non-aphakic persons with non-diseased eyes in powers from -20.00 to +20.00 diopters. The lenses may be worn by persons who exhibit astigmatism of 2.00 diopters or less that does not interfere with visual acuity

BIOFINITY® (comfilcon A) Toric soft contact lenses are indicated for the correction of ametropia (myopia or hyperopia with astigmatism) in aphakic and non-aphakic persons with non-diseased eyes in powers from -20.00 to +20.00 diopters and astigmatic corrections from -0.25 to -5.00 diopters.

BIOFINITY® (comfilcon A) Multifocal soft contact lenses are indicated for the correction of refractive ametropia (myopia and hyperopia) and emmetropia with presbyopia in aphakic and non-aphakic persons with non-diseased eyes in powers from -20.00 to +20.00 diopters with add powers from +0.50 to +3.00 diopters. The lenses may be worn by persons who exhibit astigmatism of 2.00 diopters or less that does not interfere with visual acuity.

The BIOFINITY® (comfilcon A) Contact Lenses may be prescribed for Extended Wear for up to 6 nights and 7 days of continuous wear. It is recommended that the contact lens wearer be first evaluated on a Daily Wear schedule prior to overnight wear. The lenses may be prescribed for either one week disposable wear or for frequent replacement with cleaning, disinfection and scheduled replacement. When prescribed

for frequent replacement, the lenses must be cleaned and disinfected using a chemical disinfection system only.

III. CONTRAINDICATIONS

Product instructions specify to not use this product when any of the following conditions exist:

- Acute and subacute inflammation or infection of the anterior chamber of the eye.
- Any eye disease, injury, or abnormality that affects the cornea, conjunctiva, or eyelids.
- Severe insufficiency of lacrimal secretion (dry eyes).
- Corneal hypoesthesia (reduced corneal sensitivity), if not aphakic.
- Any systemic disease that may affect the eye or be exaggerated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa that may be induced or exaggerated by wearing contact lenses or use of contact lens solutions.
- Allergy to any ingredient, such as mercury or thimerosal, in a solution, which is to be used to care for any BIOFINITY® lens.
- Any active corneal infection (bacterial, fungal, or viral).
- If eyes become red or irritated.
- The patient is unable to follow lens care regimen or unable to obtain assistance to do so.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the BIOFINITY® (comfilcon A) Soft Contact Lens package insert labeling (attached).

V. DEVICE DESCRIPTION

BIOFINITY® (comfilcon A) soft contact lenses are available as spheric, aspheric, toric and multifocal lens designs in powers from -20.00 D to + 20.00 D. Toric lenses are available in cylinders from -0.25 D to -5.00 D. Add powers are available from +0.50 D to +3.00 D.

The lenses are made from a material containing 48% water and 52% comfilcon A, a silicone-containing hydrogel. The lenses have a blue tint added to make the lens more visible for handling.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Alternative options to using the BIOFINITY® extended wear contact lens include wearing other contact lenses approved for extended wear, spectacles, refractive keratoplasty (e.g., laser-assisted in-situ keratomileusis (LASIK), and corneal implants.

VII. MARKETING HISTORY

The BIOFINITY® (comfilcon A) Soft Contact Lens is available for daily wear in the United States, South America, Taiwan, Hong Kong, Australia, Malaysia and Singapore.

CooperVision BIOFINITY® soft contact lenses bear the CE mark and were introduced outside the United States for use up to 29 nights of extended wear. The lens is marketed in over 19 countries. The CooperVision BIOFINITY® lens has not been withdrawn from market for any reason relating to the safety or effectiveness of the device.

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.

- Corneal ulcers
- Epithelial microcysts
- Permanent decrease in visual acuity
- Corneal infiltrates
- Endothelial polymegathism

The risk of corneal ulcer has been shown to be greater among users of extended wear lenses than among users of daily wear lenses. The risk among extended wear users increases with the number of days that the lenses are worn between removals, beginning with the first overnight use. In addition, smoking increases the risk of corneal ulcer for contact lens users, especially when the lenses are worn overnight or while sleeping. Strict compliance with the proper care regimen and wearing schedule is essential in minimizing risk.

Please see Section X below for a description of the specific adverse events that occurred in the primary clinical study.

IX. SUMMARY OF PRECLINICAL STUDIES

Preclinical tests were conducted to ensure initial safety of the device prior to human clinical studies. Tests included analysis of extractable residual components, lens care solution compatibility and preservative interaction, characterization of physical and chemical properties, toxicology, microbiology and shelf life stability. A summary of test results is shown below.

A. Laboratory Studies

Lens care solution compatibility ..... Studies conducted per BS EN ISO 11981:1999 as described in the May, 1994 Premarket Notification 510(k) Guidance Document for Daily Wear Contact lenses "PASS" indicates the testing demonstrated that lens handling, cleaning and disinfection procedures, with representative lens care solutions, do not alter the optical and performance characteristics of	PASS

the lens.	
Lens care solution preservative uptake/release ..... Studies conducted per ISO-11986:2001 as described in the May, 1994 Premarket Notification 510(k) Guidance Document for Daily Wear Contact lenses. Uptake and release of Polyquaternium-1 (Polyquad) and Polyaminopropyl Biguanide (PAPB) were measured. "PASS" indicates the amounts of preservative contained and released are considered inconsequential.	PASS PAPB < 0.1 ppm Polyquad < 1.3 ppm
Physical and chemical properties	
Refractive index ..... Studies conducted per EN ISO 9914:1997	1.40
Oxygen permeability, Dk, 34 ° C ($(cm^2/sec)(ml\ O_2/ml*mmHg)*10^{-11}$) Studies conducted based on ANSI Z80.20:2004 and BS EN ISO 9913-2:2000, adapted for correction of a boundary layer (BS EN ISO 9913-1:1998).	128
Oxygen transmissibility, Dk/t, -3.00D, 34 ° C $((cm/sec)(ml\ O_2/ml*mmHg)*10^{-11}$	160
Water content @ 20° C (%) ..... Studies conducted per BS EN ISO 10339:1999 gravimetric method.	48
Light transmittance (%) ..... Studies conducted per BS EN ISO 8599:1997	≥ 97
Shelf Life ..... Shelf life studies for parameter stability over time indicate no change to measured parameters from baseline over the storage period. Shelf life studies for sterility over time at 25°C tested using Direct Inoculation per USP <71> showed no growth (sterile) for all samples tested.	3 years
Toxicology Cytotoxicity (ISO agarose overlay) ..... Studies conducted per BS EN ISO 10993-5:1999 PASS indicates no evidence of cell lysis or toxicity	PASS

B. <u>Animal Studies</u>

Systemic Toxicity Study Studies conducted per BS EN ISO 10993-11:1996 PASS indicates no mortality or evidence of toxicity.	PASS

ISO Ocular Irritation Study Studies conducted per BS EN ISO 10993-10:2002 PASS indicates no evidence of significant irritation. Not considered an irritant.	PASS
22 Day Ocular Irritation Test Studies conducted per BS EN ISO 9394:1998 PASS indicates no evidence of effects, no ocular irritation.	PASS

C. **Additional Studies**

Overnight pachymetry study

1. Purpose

   To assess the overnight physiological response to the BIOFINITY® (comfilcon A) contact lens in comparison with the CIBA Vision NIGHT & DAY® (lotrafilcon A) contact lens in a group of neophytes.

2. Methods

   This was a contralateral, non-dispensing, randomized, overnight wear study in which corneal thickness was measured via pachymetry prior to overnight wear and the morning following overnight wear for two hours in 20 subjects.

3. Endpoints

   Corneal thickness (swelling)

4. Results

	BIOFINITY®	NIGHT & DAY®
corneal swelling (mean %)	4.1 ± 1.9	4.0 ± 1.7
range (%)	1.1 – 7.3	1.1 – 7.2

5. Conclusions

   Overnight central corneal swelling induced by the BIOFINITY® contact lens was not significantly different from the swelling induced by NIGHT & DAY® contact lenses.

X. SUMMARY OF PRIMARY CLINICAL STUDY

The applicant performed a clinical study in the US under IDE # G050172 to establish a reasonable assurance of safety and effectiveness of BIOFINITY® (comfilcon A) soft contact lens when worn for up to 7 days Extended Wear with a monthly planned replacement regimen, as compared to the Johnson & Johnson VISTAKON® ACUVUE® 2™ (etafilcon A) control lenses worn for up to 7 days extended wear with a weekly planned replacement regimen. 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 March 31, 2006 and November 8, 2007. The database for this PMA reflected data collected from March 31, 2006 through November 8, 2007, and included 455 dispensed subjects. There were 23 investigational sites.

The study was an open-label, bilateral, multi-center, and randomized, concurrent-control study. The control contact lens was a legally marketed alternative with similar indications for use.

Eligible subjects were assigned either the test (BIOFINITY® (comfilcon A)) or the control (ACUVUE® 2™ (etafilcon A)) contact lenses based upon randomization tables provided to the investigators. The test subjects followed a 1-month planned replacement regimen, and the control subjects followed a weekly planned replacement regimen.

The sponsor employed a Clinical Research Organization (CRO) with regard to the data management and data analysis of the clinical study data.

1. Clinical Inclusion and Exclusion Criteria

   a. Inclusion Criteria
   Study enrollment limitations included that subjects were at least 18 years of age as of the date of initial evaluation, required lens powers between -0.50 and –6.00 diopters sphere with no more than 1.00 diopter 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.

   b. Exclusion Criteria
   Subjects were not permitted to enroll if they were previously unsuccessful with contact lens wear, wore rigid gas permeable contact lenses within the past 12 months, 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, lids, or associated structures, 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.

2. Follow-up Schedule

   The study subjects were examined at the Initial Visit to determine eligibility and to determine the lens parameters required. Test and control lenses were dispensed to subjects at the Dispensing Visit and all subjects were instructed to wear the lenses on a Daily Wear (DW) schedule for 2 weeks.

   The eligibility of subjects to move into Extended Wear (EW) was evaluated at the 2-Week visit and, if eligible, study subjects began Extended Wear.

   Extended wear Follow-up Visits were performed at 24 hours, 1 week, 1 month, 2 months, 3 months, 6 months, 9 months and 12 months after starting Extended Wear.

The subject's visual acuity, slit lamp findings, symptoms, average wear time, keratometry changes, adverse events, reasons for discontinuation, lens wear and lens replacement data were monitored at the follow-up visits.

3. Clinical Endpoints
   a. Primary Safety

      The primary safety variable was the frequency of serious and significant adverse events per patient defined as a composite of corneal infiltrates of higher than grade 2, symptomatic infiltrative events, neovascularization, peripheral ulcers, the loss of two or more lines of visual acuity at any time during the trial and other serious or significant events (as defined in the clinical study protocol), with the exception of papillary conjunctivitis. The primary safety hypothesis was that the per patient rate of composite serious and significant adverse events in the population dispensed with the test lens (BIOFINITY®) was not inferior to the rate of serious and significant adverse events with the control lens (ACUVUE® 2™).

   b. Secondary Safety

      Secondary safety parameters included protocol-defined adverse events not included in the primary safety analysis (e.g., conjunctivitis, papillary conjunctivitis, corneal infiltrates, and superficial punctate keratitis), discontinuations, slit lamp findings, symptoms; and keratometric and refractive changes.

   c. Effectiveness

      There were two primary effectiveness variables: wearing time and contact lens visual acuity.

4. Summary of Statistical Methods

   The clinical study was designed and powered as a non-inferiority trial on the primary safety variable, the frequency of serious and significant adverse events. The analysis was done per subject and the hypothesis is presented below.

   $$H_0: P_t - P_c \geq \delta \quad \text{Versus} \quad H_a\ P_t - P_c < \delta$$

   Where P_t is the per patient rate observed in the test lens group, P_c is per patient rate observed in the control lens group, and δ defines the region of indifference. For the purposes of this trial the value of δ was 0.05. This non-inferiority hypothesis was tested with a one-sided level 0.05 test.

   The sample size was estimated from the formula given by Blackwelder (1982).

   Using estimated rates of serious and significant adverse events from the literature, a value of 3.3% was assumed and it was used for the estimate for both the test and control arms. The computation resulted in a sample size of 161 per arm and increased to 202 per group to account for a possible loss to follow-up of about 20%. In negotiations with FDA, the list of serious and significant adverse events was expanded. To account for a possible increase in event rates that

would increase sample size, the sample size was recomputed. Using an increased rate of events of 3.8% per arm, the sample size necessary for 80% power was 184 per arm and to account for a possible 20% loss to follow-up resulted in a sample size of 230 per group.

A univariate analysis of the primary safety endpoint in the intention to treat and completed cases populations was done with Blackwelder's test. For subjects who had no follow-up, imputation was done by propensity score to provide an endpoint and the imputation was done 10 times. The overall p-value from the 10 imputations was obtained by the method of Rubin (1987).

If the computed statistic was less than z_α, the null would have been rejected in favor of the alternative hypothesis and the test lens would have been said to be non-inferior to the control lens with respect to the frequency of serious or significant adverse events. The univariate analysis was to be followed by a multivariate non-inferiority analysis by the method of Mehrotra and Railkar (2000). This analysis could not be completed as planned, however, because the small number of adverse events left several strata with no events to be adjusted. An analysis by eye was done to substitute for this multivariate analysis.

The primary effectiveness variables were the wearing time and visual acuity. These variables were presented descriptively by study visit.

Secondary safety and effectiveness variables were presented descriptively providing mean, standard deviation, median, minimum and maximum for quantitative variables, and rate with exact 95% confidence limits for qualitative variables.

(The z_α is the standard normal value associated with the one-sided probability of a Type I error, a=0.05. For the purposes of this trial, z_α is -1.645.)

B. Accountability of PMA Cohort

At the time of database lock, 455 subjects were dispensed lenses in the PMA study, 366 (80%) of subjects were available for analysis at study completion at the 12 month visit. Subject enrollment and follow-up are summarized in **Table 1**.

Table 1
Subject Accountability

	Subjects	Eyes
Subjects Recruited	463	926
Not Enrolled	3	6
Not Dispensed, After Enrolled	5	10
Total Dispensed	455	910

	Test			Control		
	Subjects	**Eyes**	**% of Dispensed**	**Subjects**	**Eyes**	**% of Dispensed**
Enrolled	229	458		231	462	
Dispensed	227	454		228	456	
Discontinued	46	92	20.3%	43	86	18.9%
Completed	181	362	79.7%	185	370	81.1%

Discontinuations

Four hundred sixty-three (463) subjects were recruited into this clinical study. Of the 460 subjects enrolled, 2 test and 3 control subjects respectively were not dispensed study lenses. Of the 455 dispensed subjects, 89 subjects (19.6%) were discontinued over the study duration for a variety of reasons.

A slightly larger percentage of dispensed test cohort subjects discontinued from the study (46 subjects/20.3%) as compared to the control cohort (43 subjects/18.9%).

The primary reasons for discontinuation were Protocol Violation and Subject Decision for both the test and the control cohorts, accounting for 44.2% (19/43) of the control cohort discontinuations and 45.7% (21/46) of the test cohort discontinuations. **Table 2** presents the reasons for discontinuation for each of the cohorts.

Table 2

Reasons for Discontinuation
Dispensed Subjects

	Test		Control	
Reasons for Discontinuation	**Freq**	**Order**	**Freq**	**Order**
Protocol Violation	11	23.9%	7	16.3%
Subject Decision	10	21.7%	12	27.9%
Comfort Related	6	13.0%	7	16.3%
Lost to Follow-up	5	10.9%	6	14.0%
Adverse Event	4	8.7%	2	4.7%
Other Reasons	4	8.7%	0	0.0%
Treatment Failure	3	6.5%	6	14.0%
Unacceptable Visual Acuity	2	4.3%	1	2.3%
Positive Slit Lamp Finding	1	2.2%	2	4.7%
Total Subjects	46		43	

The top four reasons for discontinuation for both cohorts were the same: Protocol Violation, Subject Decision, Comfort Related and Lost to Follow-up. These reasons accounted for 74.4% of the control cohort subject and 69.9% of the test cohort subjects. Protocol Violations included 9 subjects who were discontinued for having missed two extended wear visits.

The "Other" reasons for discontinuation for the test cohort were type II diabetes, pregnancy, non-contact lens related allergies and subject accidentally exited early prior to 12 month visit.

C. Study Population Demographics and Baseline Parameters of Enrolled Subjects

The ratio of females to males was lower in the test cohort when compared to the control cohort. The test cohort gender ratio was 1.7 to 1 (144 female/85 male) versus the control cohort ratio of 2.2 to 1 (159 female/72 male). The mean age for the test cohort was 34.9 years and the mean for the control cohort was 33.1 years.

The distribution of ethnicity in the study was similar for dispensed subjects between the two cohorts with greater than 72% of the subjects reported as white, more than 15% of the subjects reported as Japanese and the remaining 9% relatively evenly distributed between African-American, Asian and Hispanic ethnicities/races.

The 460 subjects reporting previous vision correction included 39 subjects (8.5%) who entered the study wearing spectacles and 421 subjects (91.3%) who were wearing soft contact lenses. Four hundred and fifty (450) subjects reported previous soft contact lens wear with 66.7% reporting previous daily wear and 33.3% reporting previous extended wear. There were no statistically significant differences between the test and control groups with regard to previous contact lens wear.

The comparison of baseline symptoms between the two cohorts also showed no statistically significant differences.

The study was balanced in baseline characteristics of study subjects.

D. Safety and Effectiveness Results

1. Safety Results

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 descriptions provided in the study protocol. Among observed adverse events, serious adverse events were 3.2% (test) vs. 2.2% (control), Significant Adverse Events were 31.7% (test) vs. 21.7% (control) and Non-Significant adverse events were 65.1% (test) vs. 76.1% (control).

In the literature, papillary conjunctivitis has been reported at a higher incidence associated with the wear of silicone-hydrogel contact lenses (Dumbleton, K., 2003). Of the adverse events reported by the investigators in the current study, 9 of the significant events (1 control/8 test) were reported as papillary conjunctivitis.

a. Primary Safety

The primary safety variable for statistical analysis was defined as the frequency of serious and significant adverse events defined as a composite of infiltrates of higher than grade 2, symptomatic infiltrative events, neovascularization, peripheral ulcers, the loss of two or more lines of visual acuity at any time during the trial and other serious or significant events listed in the protocol with the exception of papillary conjunctivitis.

The primary analysis was done on a per patient basis. The data were imputed 10 times for the intention to treat (ITT) analysis.

The overall p-value for the hypothesis of non-inferiority combining the results of the 10 imputations was 0.0335, which indicates that the test group was non-inferior to the control group for serious and significant adverse events within a non-inferiority margin of 0.05 (5%).

Table 3 below presents the proportion of subjects in each study arm who completed the trial and had at least one composite primary endpoint adverse event (as defined above).

Table 3
The Number and Proportion of Completed Study Subjects with Serious and Significant Adverse Events by Lens Group

	Test n/N (%)	**Control n/N (%)**	**Total**
Adverse Event	11 (5.1)	8 (3.7)	**19**
No Adverse Event	206 (94.9)	210 (96.3)	**416**
Total[1]	**217**	**218**	**435**

[1]To provide a conservative analysis of adverse events, the subjects included were those enrolled (229 test and 231 control subjects) minus those withdrawn at the 24 hour visit (12 test and 13 control subjects). This leaves 217 test and 218 control subjects at risk for adverse events with extended exposure to the lens.

Based on the statistical analysis, the test lens was considered to be non-inferior to the control lens with respect to serious and significant adverse events.

A list of the events and incidence rates in the Completed populations is contained in **Table 4** below. NOTE: if an eye had more than one adverse event, only the most severe event experienced is presented.

Table 4
Completed Subjects with Primary Safety Endpoint
Serious and Significant Adverse Events

	Test (n = 217)		Control (n = 218)	
Adverse Event	**n**	**%**	**n**	**%**
Serious				
Bacterial Keratitis	1	0.5	0	0
Iritis	1	0.5	0	0
Preseptal Orbital Cellulitis	0	0	1	0.5
Significant				
Corneal Infiltrates	4	1.8	5	2.3
Conjunctivitis (bacterial or unknown etiology)	2	0.9	0	0
Superficial Punctate Keratitis	1	0.5	0	0
Corneal Abrasion	1	0.5	0	0
Phlyctenulosis	0	0	1	0.5
Limbal and Bulbar Hyperemia	1	0.5	0	0
Temporary 2-line Loss of Visual Acuity	0	0	1	0.5
TOTAL	**11**	**5.1**	**8**	**3.7**

b. Secondary Safety

1) Other Adverse Events

The number and proportion of eyes (all randomized subjects) with secondary endpoint adverse events are presented by diagnosis in **Table 5** below based on the number of eyes for which lenses were dispensed. NOTE: eyes that had a recurrence of the same event in the same eye were only counted once.

Table 5

Eyes with Secondary Safety Endpoint Adverse Events

	Test (n = 454)		Control (n = 456)	
Adverse Event	**n**	**%**	**n**	**%**
Conjunctivitis: Bacterial, Viral, or Allergic	15	3.3	12	2.6
Other Non-significant Adverse Event	6	1.3	8	1.7
Papillary Conjunctivitis	11	2.4	1	0.2
Corneal Infiltrates	4	0.9	6	1.3
Superficial Punctate Keratitis	3	0.7	4	0.9
Blepharitis	2	0.4	3	0.7
Any Corneal Event Requiring Lens Removal (< 2 Weeks)	4	0.9	0	0
Localized Allergic Reactions	2	0.4	1	0.2
Meibomianitis	1	0.2	0	0
TOTAL	**48**	**10.6**	**35**	**7.6**

2) Slit Lamp Findings

At each visit the subject's eyes were examined using a biomicroscope (slit lamp). More than 90% of the examinations for both test and control cohorts for Edema (epithelial and stromal), Microcysts, Infiltrates, Limbal Hyperemia and "Other" resulted in Grade 0 (no findings). **Table 6** presents the proportion of reports of Grade 0 (no findings) for each finding over all completed and discontinued extended wear follow-up visits combined.

Table 6

Proportion of Slit Lamp Eye Examinations with Grade 0 (None) by Cohort and Finding over All Extended Wear Visits

Grade 0 (None) reports for:	Test	Control
Palpebral Conjunctivitis	78.20%	78.10%
Corneal Staining	79.00%	83.30%
Bulbar Hyperemia	84.30%	80.20%
Corneal Neovascularization	90.10%	84.20%
Limbal Hyperemia	92.80%	90.60%
Other Findings	95.70%	92.70%
Epithelial Edema	98.60%	95.40%
Epithelial Microcyst	99.20%	99.00%
Corneal Infiltrates	98.60%	99.60%
Stromal Edema	99.50%	99.50%

The most the frequently reported slit lamp findings were Palpebral Conjunctival findings, which were reported at more than 20% of the study examinations for both the test and the control cohorts. However, there were no clinically significant differences in either frequency or severity in the overall rate of Palpebral Conjunctival findings.

The completed control cohort eyes reported more epithelial edema (3.2% difference), neovascularization (5.9%), hyperemia (2.1% and 4.0% difference) and other findings (3.0% difference) over the duration of the extended wear portion of the study while the completed test subjects were reported with more staining (4.3% difference) and infiltrates (1.0% difference) during the extended wear portion of the study.

Comparing the proportion of slit lamp findings of Grade 2 (Mild) or greater for Completed eyes, the control cohort eyes reported more grade 2+ epithelial edema (0.3% difference) and limbal hyperemia (0.2% difference) over the duration of the extended wear portion of the study. The completed test subjects were reported with more Grade 2+ stromal edema (0.1% difference), neovascularization (0.1% difference), corneal staining (1.0% difference), corneal infiltrates (0.4% difference), bulbar hyperemia (0.2% difference), palpebral conjunctival findings (1.2% difference) and other findings (0.1% difference) during the extended wear portion of the study.

When looking at the differences in the proportion of slit lamp findings graded 2 or higher only the findings of corneal staining (1.0%) and palpebral conjunctiva (1.2%) show a difference of more than a half of a percent.

The slit lamp findings reported during this clinical evaluation do not raise any questions as to the safety of the test lenses when compared to the control lenses.

3) Symptoms, Problems and Complaints

The proportion of the population that reported none for each of the symptoms over the duration of the study was similar between the test and the control cohorts and is presented in **Table 7.**

Table 7

Proportion of Exams with Symptoms Problems or Complaints Reported as None by Cohort over All Extended Wear Visits

Symptom, Problem Complaint reported as None	Test	Control
Dryness	77.30%	72.80%
Discomfort / Pain	94.70%	94.60%
Itch/ Burn	95.30%	95.20%
Blurred Vision	95.90%	94.80%
Other Symptoms*	96.10%	97.30%
Variable Vision	97.50%	96.00%
Photophobia	98.10%	97.80%
Halos	98.70%	97.60%
Tearing	97.90%	99.00%

* Other = any symptom not included in the defined categories of this table; Note all symptoms classified as other were transient and are not considered to demonstrate any clinically significant differences between the test and control lenses

The symptom reported most frequently was Dryness, reported at 27.2% of the control cohort examinations and at 22.7% of the test cohort examinations. All other symptoms were reported at low rates over the duration of the study.

The statistical analysis performed for the symptoms reported at the extended wear visits demonstrated statistical significant differences between the test and the control lenses for some symptoms. However, these differences were transient and are not considered to demonstrate any clinically significant differences between the test and control lenses. See **Table 8.**

Table 8

Statistically Significant Differences between Symptoms at Extended Wear Visits

Symptom	EW Visit	Test	Control
Dryness	12 Month	20.70%	30.30%
Blurred Vision	3 Month	3.70%	5.60%
Other	24 Hour	6.40%	2.10%
Other	3 Month	3.70%	1.40%
Tearing	2 Month	2.20%	0%

4) Keratometric Changes

Final keratometric readings remained relatively stable compared with baseline readings for both the control and test lens groups.

For the Completed subjects, 99.1% of the control and 99.3% of the test eye measurements (both meridians combined) were within 1.00D from the baseline to the final visit. The average changes (absolute value) were 0.30D for the control group and 0.28D for the test group. The control group maximum change (absolute value) was 2.87D, with 1.88D for the test group.

The test cohort demonstrated similar average changes in the final keratometry measurements as compared to the control cohort.

5) Refractive Changes

Final refractive error measurements remained relatively stable compared with baseline measurements for both the control and test lens groups.

For the Completed subjects, 99.2% of the control and 99.6% of the test eye measurements were within 1.00D from the baseline to the final visit. The control group maximum change was 2.25D, with 1.75D for the test group.

The test cohort demonstrated similar average changes in the final refraction measurements when compared to the control cohort.

2. Effectiveness Results

The analysis of effectiveness was based on the 366 evaluable subjects at the 12-month time point. Key effectiveness outcomes are described below and in Table 9.

a. Average Extended Wearing Time

During the extended wear portion of the study, subjects in the study were required to complete a wearing time questionnaire at each follow-up visit and record the number of removals of the lenses for sleep only, for sleep plus extended removal, and for any removal in the intervening period.

The average wearing time based on removals, for sleep only, had a mean of 7.2 days with 95% confidence interval, (6.7, 7.8), for the test arm and 6.7 days with 95% confidence interval, (6.4, 7.0), for the control arm at 12 months. The average wearing time for sleep removals and other extended removals was for test, 6.9 days with 95% confidence interval, (6.3, 7.4), for the test arm and 6.2 days with 95% confidence interval, (6.0, 6.4), for the control arm. The average wearing time at 12 months for any removal was 6.6 days with 95% confidence interval, (6.0, 7.2), for the test arm and 5.9 days with 95% confidence interval, (5.5, 6.2), for the controls.

b. Visual Acuity

Visual acuity (VA) with the study lenses was measured at each Extended Wear study visit. For completed eyes, the test cohort proportion of eyes (all Extended Wear visits combined) achieving Snellen VA of 20/20 or better was 91.4% (2664/2914) versus the proportion of control eyes reporting 20/20 or better (89.5% or 2666/2978). Conversely, the proportion of VAs of 20/40 or worse reported over the duration of the extended wear segment of the study were 0.7% (21/2914) for the control cohort and 2.3% (67/2914) for the test cohort.

Table 9

Distribution of Snellen VA over All extended Wear Visits By Cohort and Status

	Completed		**Discontinued**	
Visual Acuity	Test	Control	Test	Control
≥20/20	91.40%	89.50%	91.90%	90.80%
≥20/25	5.20%	7.80%	6.00%	8.20%
≥20/30	1.10%	2.00%	0.60%	1.00%
≤20/40	2.30%	0.70%	1.50%	0

3. Subgroup Analyses

Not Applicable

XI. SUMMARY OF SUPPLEMENTAL CLINICAL INFORMATION

The device was tested outside the United States in a bilateral, open-label, randomized dispensing clinical study, in which subjects were treated between January 7, 2005 and March 29, 2006. 158 eligible subjects wore the CooperVision BIOFINITY® (comfilcon A) test lenses and the CIBA Vision® NIGHT & DAY™ (lotrafilcon A) control lenses for up to 30 Days, 29 nights of continuous wear. Lenses were replaced on a monthly basis. There were 6 investigational sites.

The purpose of the study was to test the hypothesis that the clinical performance of the BIOFINITY® test lens was non-inferior to the NIGHT & DAY™ control lens with respect to slit lamp variables, visual acuity, discontinuations and adverse events. Adverse events were graded as Serious, Significant and Non-Significant based on the descriptions provided in the study protocol.

Although the study results indicated that the incidence of adverse events was slightly higher for the test BIOFINITY® (comfilcon A) lenses (14% vs. 10% eyes), the difference was not statistically significant. The types of adverse events noted in this study have also been noted in other clinical trials of silicone hydrogel continuous wear lenses.

It was concluded that the clinical performance of the CooperVision BIOFINITY® (comfilcon A) was non-inferior to that of NIGHT & DAY™ when used for continuous wear, with respect to the variables which were assessed in this study.

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

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

XIII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The results of the preclinical studies (extraction, compatibility, preservative uptake/release, physicochemical properties and toxicology) and the pachymetry study demonstrate the safety of the CooperVision BIOFINITY® silicone-hydrogel contact lens. The adverse effects of the device are based on data collected in the clinical study conducted to support PMA approval as described above. The clinical evaluation primary endpoint outcomes indicate that the target safety criteria were met, and demonstrate the safety of the CooperVision BIOFINITY® silicone-hydrogel contact lens when worn for up to 7 days extended wear when compared to the Johnson & Johnson VISTAKON® ACUVUE® 2™ (etafilcon A) control lens worn for up to 7 days extended wear.

B. Effectiveness Conclusions

The clinical evaluation outcomes indicate that the effectiveness target criteria were met, and demonstrate the effectiveness of the CooperVision BIOFINITY® lenses as compared to the VISTAKON® ACUVUE® 2™ lenses.

C. Overall Conclusions

The results of the preclinical and clinical evaluations support the reasonable assurance of safety and effectiveness of this device when used in accordance with the indications for use.

XIV. CDRH DECISION

CDRH issued an approval order on November 19, 2008.

The applicant's manufacturing facilities were 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

A. Blackwelder, W. Proving the null hypothesis in clinical trials. *Controlled Clinical Trials* 3: 345-353, 1982.

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D. Dumbleton, K., Noninflammatory silicone hydrogel contact lens complications. *Eye & Cont Lens*, 2003. 29(1 Suppl): p. S186-9; discussion S190-1.