SUMMARY OF SAFETY AND EFFECTIVENESS DATA (SSED)

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I. GENERAL INFORMATION

Device Generic Names: oprifocon A rigid gas permeable contact lenses

Device Trade Names: Euclid Systems Orthokeratology (oprifocon A) Contact Lenses for Overnight Wear

Applicant's Name and Address: Euclid Systems Corporation
2810 Towerview Road
Herndon VA 20171

Premarket Approval Application (PMA) Number: P010062

Panel Recommendation: None

Date of Notice of Approval to Applicant: June 7, 2004

II. INDICATIONS FOR USE

Euclid Systems Orthokeratology (oprifocon A) Contact Lenses for Overnight Wear are indicated for use in the reduction of myopic refractive error in non-diseased eyes. The lenses are indicated for overnight wear for the temporary reduction of myopia up to 5.00 diopters with eyes having astigmatism up to 1.50 diopters. The lenses may only be disinfected using a chemical disinfection system.

Note: To maintain the Orthokeratology effect of myopia reduction, overnight lens wear must be continued on a prescribed schedule. Failure to do so can affect daily activities (e.g., night driving), visual fluctuations and changes in intended correction.

III. CONTRAINDICATIONS

Euclid Systems Orthokeratology (oprifocon A) Contact Lenses for Overnight Wear should not be used when any of the following conditions exist:

- Acute and subacute inflammations 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 tears (dry eyes).
- Corneal hypoesthesia (reduced corneal sensitivity).

- Any systemic disease that may affect the eye or be exacerbated by wearing contact lenses.
- Allergic reactions of ocular surfaces or adnexa which 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 contact lenses.
- Any active corneal infection (bacterial, fungal or viral).
- If eyes become red or irritated.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the labeling for the device labeling.

V. DEVICE DESCRIPTION

Euclid Systems Orthokeratology (oprifocon A) Contact Lenses are lathe cut contact lenses with spherical posterior surfaces in blue, green, red and yellow tinted versions. The posterior curve is selected to properly fit an individual eye for orthokeratology and the anterior curve is selected to provide the necessary optical power for a temporary reduction of myopia. A peripheral curve system on the posterior surface allows tear exchange between the lens and the cornea.

Euclid Systems Orthokeratology (oprifocon A) Contact lenses are made from Boston® Equalens®II (oprifocon A) polymer with a water content of less than 1 percent. The material contains an ultraviolet absorber, Uvinul D-49. The blue tinted lenses contain D&C Green No.6 as a color additive. The green tinted lenses contain D&C Green No.6 and D&C Yellow No.18. The red tinted lenses contain D&C Red No.17 as a color additive. The yellow tinted lenses contain D&C Yellow No.18 as a color additive.

LENS PARAMETERS AVAILABLE

Chord Diameter	9.6mm to 11.6mm
Center Thickness	0.20mm to 0.32mm
Base Curve	7.30mm-10.15mm
Reverse Curve	5.00 to 9.00 mm. Steeper than the base curve in proportion to the amount of correction
Alignment curve 1	7.00 to 9.00 mm. Steeper than the base curve but flatter than the Reverse curve. Generally equal to the Flat K of the cornea being fit.
Alignment curve 2	7.25 to 9.25 mm. Steeper than the base curve but flatter than AC1 and Reverse curve
Peripheral curves	9.00mm to 15.00mm
Back Vertex Power	+1.50 to –5.00 Diopters

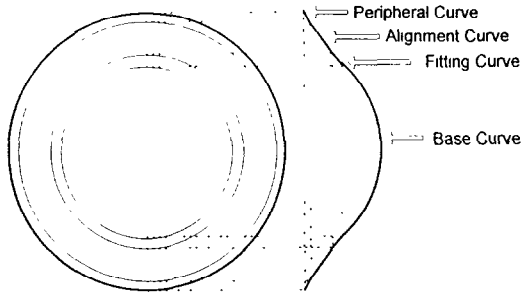

Figure 1: Representation of the reverse geometry lens design.

PHYSICAL PROPERTIES

The physical properties of oprifocon A

Refractive index 1.423

Light Absorbance (absorbance units/inch)

Blue (640nm)	10.0
Green (640nm)	4.8
Yellow (420nm)	10.3
Red (525nm)	2.5

Wetting Angle	30 degrees by Captive Bubble
Specific Gravity	1.24
Hardness	114 Rockwell
Water Content	less than 1%
Oxygen Permeability	85 by Iso/Fatt

VI. ALTERNATIVE PRACTICES OR PROCEDURES

The alternative practices and procedures to the temporary treatment of myopia using overnight reverse-geometry contact lenses include: the temporary treatment of myopia using daily wear contact lenses in a reverse geometry design, the permanent treatment of myopia with corrective surgeries such as LASIK, the compensation for myopia by wearing spectacles, daily or extended wear RGP, or soft (hydrophilic) contact lenses.

VII. MARKETING HISTORY

The device has not been marketed for this indication.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse effects on health associated with overnight wear contact lenses include eye problems such as corneal ulcers, epithelial microcysts, infiltrates and endothelial

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

Please refer to Section X. C Safety Data Analysis and Results of this document for information on adverse events observed in this clinical study.

IX. SUMMARY OF PRECLINICAL STUDIES

The application includes by reference the preclinical data in P860022 and related supplements. The application contains appropriate written authorization from Polymer Technology to reference its information and data for the Equalens II (oprifocon A) Contact Lens for Extended Wear. The PMA (P860022) was approved by FDA on November 30, 1987. The buttons used by Polymer Technology to manufacture the Equalens II are the same as those provided to the sponsor to manufacture the subject device. The Summary of Safety and Effectiveness (SSED) for P860022 is available via Docket Number 87M-0395. Written requests should be sent to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, Rockville, MD 20852.

X. SUMMARY OF CLINICAL STUDIES

The application also includes by reference the clinical data in P860022 and related supplements for the Equalens II (oprifocon A) Contact Lens for Extended Wear. The applicant references the clinical data in P860022 as a historical control which was compared to the safety information in this study such as positive slit lamp findings and patient symptoms.

A. Objectives

The main objective of this study was to assess the safety and effectiveness of the Euclid Systems Orthokeratology (oprifocon A) Contact Lenses in the temporary reduction of myopia, when worn overnight.

1. Study Design

This investigation was a multi-center study consisting of 9 investigational sites which included 14 investigators participating. The study was initiated on September 21, 1998 and ended on June 2, 2000. There were 191 patients (378 eyes) enrolled into the study including 4 monocular subjects. There were 4 ineligible eyes enrolled but not dispensed lenses. The subjects were at least 18 years old.

Clinical investigators and investigational sites were selected in an effort to provide sufficient diversity in geographic access, climate and elevation, and

urban and rural living for a resultant study population that represents the intended population to be treated. The study period was 9 months.

a. Safety Endpoints:

The primary endpoints used to evaluate the safety of the treatment were:

a) Corneal ulcer
b) Deep Neovascularization greater than 2 m (Grade 3 or worse).
c) Persistent stromal edema (Grade 3 or worse).
d) Best corrected VA is reduced by one line or more for longer than seven days (Snellen acuity).
e) Any degree of corneal scarring or corneal opacification.
f) Significant central corneal staining (Grade 3 or worse).
g) Gross distortion in keratometer reading.
h) Any eye infection.
i) Epiphora lasting more than one-half hour after lens insertion after the first two nights of lens wear.
j) Significant or unusual discharge from the eye or persistent inflammation of the lids.

b. Effectiveness Endpoints:

The effectiveness endpoints are used to profile the overall effectiveness of the treatment of myopia and myopia with astigmatism with the subject device.

The primary effectiveness endpoint was:

Improvement in uncorrected distance Snellen Visual acuity of at least two lines together with better than or equal to 20/40 unaided distance Snellen visual acuity (with age appropriate near visual acuity) that is stable throughout the day.

2. Eligibility Criteria

a. Inclusion Criteria

1. Have need of optical correction for myopia, from -1.00 to -4.00 diopters (D). Subjects whose refractive errors exceed -4.00 D may be enrolled in order to collect data, but this data will be used in order to make claims of safety only.
2. Have a refractive astigmatism of less than -1.50 D.
3. Have a minimum Best Spectacle Corrected Visual Acuity (BSCVA) of 20/40 or better.
4. Have reasonable expectations of improvement in visual acuity with the Euclid Orthokeratology Lens of 20/40 or better after overnight wear without corrective aids.
5. Have normal healthy eyes without the use of ocular medications. A normal eye is defined as one having the following characteristics:
   - No evidence of active infection involving the conjunctiva, lids or adnexa.
   - No evidence of structural abnormalities of the lids, conjunctiva or adnexal tissue considered significant by the investigator to include minimum levels (Grade 2 or less) of tarsal – conjunctival abnormalities.
   - A cornea which is clear with no edema, no staining, no opacities, and no corneal neovascularization greater than a trace amount (i.e. All vessels extending less than 1.5 mm from the limbus); all as observed on slit lamp examination.
   - Have no iritis.
   - Have no herpes keratitis (recurrent or otherwise) or other active ocular disease that would contraindicate lens wear or lessen attainability of VA sought in this study (20/40 or better).
   - Have no evidence of severe dry eye condition based on a Shirmer test (without anesthetic) of 5 mm wetting or less in five minutes, or significant Rose Bengal staining, or significant Fluorescein staining.
   - Be at least 18 years old to give informed consent.

b. Exclusion criteria:

1. Do not meet inclusion criteria stated above.
2. Unable or unwilling to give informed consent.
3. On questioning probably will have great difficulty in attaining the follow-up schedule (transportation problems, possibility of moving, etc.).
4. Are pregnant, lactating, or women who are planning to become pregnant during the course of this study.
5. Are individuals who are participating in another clinical trial, ophthalmic or otherwise, that may interfere with this investigation.

3. Assessment of Subjects

The clinical trial was conducted under an approved clinical protocol. The protocol detailed the procedures and methods for the initial examination, dispensing and all scheduled and non-scheduled follow up visits. Clinical investigators provided patient keratometry readings and refractive measurements to the applicant. The applicant used these numbers in an equation to determine the lens parameters needed for the patients.

4. Accountability and Demographic Data

FDA determined that the data needed to be audited prior to filing the PMA. Upon filing the PMA, FDA noted discrepancies between data in the audit and data in the PMA. Because of these discrepancies, the PMA was amended to include the data from the audit and to separate the study population into two groups, core and adjunct. Core subjects are defined as those subjects with more complete effectiveness data. Adjunct subjects are defined as those subjects for which incomplete efficacy data was collected but there was enough data provided to include in the evaluation of the safety of the device.

Two hundred and ten (210) core eyes and 168 adjunct eyes underwent baseline evaluation in the study with lenses dispensed to all but 4 adjunct eyes. Of the 374 eyes dispensed lenses for 191 subjects, there were 210 eyes included in the core group. The adjunct group consisted of 54 completed eyes, 4 ineligible eyes, and 110 discontinued eyes.

There were 63 males and 128 females in the study. The mean age of subjects was 40 years (ranging from 18 to 62 years) for the core group and 40.5 years (ranging from 17 to 64 years) for the adjunct group which included one protocol deviation where a 17 year old was enrolled. There were 15 % of the subjects in the core group and 18 % in the adjunct group with no previous lens wear experience. The ratio of women to men enrolled was consistent with the contact lens wearing population. Table 1 presents demographic information for all patients analyzed for safety. The pre-treatment refractive characteristics of the core eyes are represented in Table 2.

Table 1
Demographic Information of All Enrolled and Treated Subjects
Core N=113, (210 Eyes Treated) – Adjunct N=90, (164 Eyes Treated)

Category	Classification	Core n	% Eyes	Adjunct* n	% Eyes
Gender	Male	39	35%	26	29%
	Female	74	65%	64	71%
Current CL History	None	32	15%	30	18%
	Rigid	59	28%	25	15%
	Hydrophilic	112	53%	86	52%

	Hydrophilic and RGP	2	1%	0	0%
	Unknown	5	2%	23	14%
Age (in Years)	Average	40		40.5	
	Minimum	18		17	
	Maximum	62		64	

*12 subjects had one eye in the Core group and one eye in the Adjunct group and are therefore counted in both groups. Four subjects in the Core group were fit monocularly. Additionally, 4 ineligible eyes were enrolled but not dispensed.

Table 2 Pretreatment Refractive Cylinder Stratified by Pretreatment Sphere All Core Eyes (N=210)								
	Pretreatment Sphere (DS)							
Pretreatment Refractive Cylinder (DC)	≤ 1.0D	>1.00 to 2.00D	>2.00 to 3.00D	>3.00 to 4.00D	>4.00 to 5.00D	>5.00 to 6.00D	>6.00 to 7.00D	Total
	n %	n %	n %	n %	n %	n %	n %	n %
0.00	4	22	28	10	3	1	0	68
	2%	11%	13%	5%	1%	<1%	0%	32%
0.12 to 0.50	0	23	23	11	9	1	1	68
	0%	11%	11%	5%	4%	<1%	<1%	32%
0.62 to 1.00	1	14	20	7	10	0	0	52
	<1%	7%	10%	3%	5%	0%	0%	25%
1.12 to 1.50	1	4	5	6	3	3	0	22
	<1%	2%	2%	3%	1%	1%	0%	11%
Total	6	63	76	34	25	5	1	210
	3%	30%	36%	16%	12%	2%	<1%	100%

5. Discontinued Subjects

The discontinued rate of the study population was 29 %, all of which were analyzed in the adjunct group. Table 3 reports the subjects that were discontinued prior to the nine-month visit and the reason for discontinuation.

Table 3 Reasons for Discontinuation		
Clinical Reason*	# eyes	% of all eyes
Unacceptable vision	52	14%
Lack of Comfort	28	8%
Unacceptable physiology	12	3%
Non-clinical Reasons		
Lost-to-follow-up	38	10%
Other**	10	3%

*Several subjects reported more than 1 reason for discontinuation, without giving any priority to the reasons.

prior uncorrected near vision (2 eyes), financial (2 eyes), and could not maintain visit schedule (2 eyes).

B. Effectiveness Data Analysis and Results

1. Analysis of Uncorrected Visual Acuity (UCVA)

Table 4 presents the UCVA of core eyes available for efficacy analysis following 9 months of treatment. The UCVA results are stratified by pretreatment Manifest Refraction Spherical Equivalent (MRSE).

Table 4
Uncorrected Visual Acuity (UCVA) at the 9 Month Visit Stratified by Pre-treatment MRSE
Core Eyes (N=210)

Post treatment UCVA)	Pre Treatment Myopia (MRSE)							
	≤ 1.0D	>1.00 to 2.00D	>2.00 to 3.00D	>3.00 to 4.00D	>4.00 to 5.00D	>5.00 to 6.00D	>6.00 to 7.00D	Total N %
20/15 or better	2	16	15	7	5	0	0	45
	1%	8%	7%	3%	2%	0%	0%	21%
20/20or better	6	50	57	24	15	2	0	154
	3%	24%	27%	11%	7%	1%	0%	73%
20/25or better	6	53	67	29	18	3	0	176
	3%	25 %	32%	14%	9%	1%	0%	84%
20/30 or better	6	59	70	34	20	4	1	194
	3%	28%	33%	16%	10%	2%	<1%	92%
20/40or better	6	60	72	34	22	5	1	200
	3%	29%	34%	16%	11%	2%	<1%	95%
20/60 or better	6	61	75	34	23	5	1	205
	3%	29%	36%	16%	11%	2%	<1%	98%
20/70 or better	6	62	75	34	23	5	1	207
	3%	30%	36%	16%	11%	2%	<1%	99%
20/100 or better	6	62	76	34	23	5	1	207
	3%	30%	36%	16%	11%	2%	<1%	99%
20/200 or better	6	63	76	34	23	5	1	208
	3%	30%	36%	16%	11%	2%	<1%	99%
20/400 or better	6	63	76	34	25	5	1	210
	3%	30%	36%	16%	12	2%	<1%	100%

The analysis of eyes targeted for emmetropia is valuable for profiling the number of eyes that achieved 20/40 or better. In this trial, 95% of eyes (200/210) achieved 20/40 or better at nine months of treatment.

Of the 210 core eyes targeted for emmetropia, 73% of the eyes (154/210) demonstrated 20/20 UCVA at 9 months.

2. Primary Effectiveness Endpoint

The primary efficacy endpoint for the core group was the number of eyes achieving at least 2 lines of improvement in uncorrected visual acuity with at least 20/40 vision. For the 210 Core eyes available at 9 months, 199 eyes (95%) met these criteria of success, while 11 eyes did not achieve this successful outcome. Table 5 summarizes the primary effectiveness endpoint data.

Table 5
PRIMARY EFFICACY ENDPOINT AT 9 MONTHS
STRATIFIED BY PRE-TREATMENT MYOPIA
CORE EYES (210)

		PRETREATMENT MYOPIA (MRSE)						
	0 to -1.00D*	<-1.00 to -2.00D	<-2.00 to -3.00D	<-3.00 to -4.00D	<-4.00 to -5.00D	<-5.00 to -6.00D	<-6.00 to -7.00D	Total
	n	n	n	n	n	n	n	n
A. #eyes at 9 months with 2 lines improvement and 20/40 or better	5	60	72	34	22	5	1	199
B. #eyes at 9 months not meeting above criteria, data available	1	3	4	0	3	0	0	11
C. #eyes enrolled and available at 9 months	6	63	76	34	25	5	1	210
% eyes at visit with Acuity "Success" (A/Dx100)	83	95	95	100	88	100	100	95
MRSE Mean	0.21	-0.15	-0.13	-0.22	-0.57	-0.68	-1.25	
Std. Dev.	0.17	0.64	0.50	0.51	1.14	0.68	0.0	

*only 1 eye had an MRSE <-1.00 (0.63)

3. Analysis of MRSE

The analysis of the reduction in MRSE at the nine- month visit provides an endpoint to assist in profiling the effectiveness of the treatment. Table 6 reports the refractive change in diopters of the MRSE from the baseline to the nine-month post dispensing follow-up visits stratified by pretreatment MRSE for core eyes.

Table 6
Refractive Change in Diopters from Baseline to Month 9
Stratified by Pretreatment MRSE
9 Month Core Eyes (N = 210)

Change at 9 Months (DSE)	Pretreatment Myopia (MRSE)							
	≤ 1.0D	>1.00 to 2.00D	>2.00 to 3.00D	>3.00 to 4.00D	>4.00 to 5.00D	>5.00 to 6.00D	>6.00 to 7.00D	Total
	n	n	n	n	n	n	n	n
	%	%	%	%	%	%	%	%
Decrease								
>0.00 to 0.50	0	5	0	0	2	0	0	7
	0%	2%	0%	0%	1%	0%	0%	3%
>0.50 to 1.00	3	2	1	0	0	0	0	6
	1%	1%	<1%	0%	0%	0%	0%	3%
>1.00 to 1.50	3	23	3	0	0	0	0	29
	1%	11%	1%	0%	0%	0%	0%	14%
>1.50 to 2.00	0	25	11	1	0	0	0	37
	0%	12%	5%	<1%	0%	0%	0%	18%
>2.00 to 2.50	0	5	31	2	0	0	0	38
	0%	2%	15%	1%	0%	0%	0%	18%
>2.50 to 3.00	0	1	25	8	1	0	0	35
	0%	<1%	12%	4%	<1%	0%	0%	17%
>3.00 to 3.50	0	1	4	12	5	0	0	22
	0%	<1%	2%	6%	2%	0%	0%	11%
>3.50 to 4.00	0	0	0	11	5	2	0	18
	0%	0%	0%	5%	2%	1%	0%	9%
>4.00 to 4.50	0	0	0	0	5	0	0	5
	0%	0%	0%	0%	2%	0%	0 %	2%
>4.50 to 5.00	0	0	0	0	6	0	1	7
	0%	0%	0%	0%	3%	0%	<1%	3%
>5.00 to 5.50	0	0	0	0	0	3	0	3
	0%	0%	0%	0%	0%	1%	0%	1%
>5.50	0	0	0	0	1	0	0	1
	0%	0%	0%	0%	<1%	0%	0%	<1%
Increase								
0.00 to 0.50	0	0	1	0	0	0	0	1
	0%	0%	<1%	0%	0%	0%	0%	<1%
>0.50 to 1.00	0	0	0	0	0	0	0	0
	0%	0%	0%	0%	0%	0%	0%	0%
>1.00 to 1.50	0	1	0	0	0	0	0	1
	0%	<1%	0%	0%	0%	0%	0%	<1%
Total	6	63	76	34	25	5	1	210
	3%	30%	36%	16%	12%	2%	<1%	100%

At the 9 month visit for core eyes, 99% of eyes (2 08/210) demonstrated a reduction in the MRSE of pretreatment myopia. The trend is present for a corresponding increase in the refractive error reduction with greater pretreatment MRSE. Sixteen eyes, 8% (16/210) demonstrated a reduction in MRSE of greater than 4.00 D.

4. Analysis of Predictability (Targeted vs. Achieved)

Table 7 provides the accuracy of treatment of the core eyes at the 9-month follow up visit.

Table 7
Accuracy of Targeted Vs. Achieved Correction at 9 Month Visit
Stratified by Pretreatment Myopia
9 Month Core Eyes (N=210)

Targeted. vs. Achieved (DSE)	Pre Treatment Myopia (MRSE)							
	< 1.0D	>1.00 to 2.00D	>2.00 to 3.00D	>3.00 to 4.00D	>4.00 to 5.00D	>5.00 to 6.00D	>6.00 to 7.00D	Total
	%	%	%	%	%	%	%	%
±0.50 D	6	51	66	27	15	3	0	168
	3%	24%	31%	13%	7%	1%	0%	80%
±1.00 D	6	59	73	32	22	3	0	195
	3%	28%	35%	15%	10%	1%	0%	93%
±2.00 D	6	62	75	34	23	5	1	206
	3%	30%	36%	16%	11%	2%	<1%	98%
±3.00 D	6	62	76	34	23	5	1	207
	3%	30%	36%	16%	11%	2%	<1%	99%
> 4.00 D	6	63	76	34	24	5	1	209
	3%	30%	36%	16%	11%	2%	<1%	100%
>5.00 D	6	63	76	34	25	5	1	210
	3%	30%	36%	16%	12%	2%	<1%	100%
Overcorrected								
>+1.00 D	0	1	0	0	0	0	0	1
	0%	<1%	0%	0%	0%	0%	0%	<1%
Undercorrected								
<1.00 D	0	2	2	2	1	2	1	10
	0%	1%	1%	1%	<1%	1%	<1%	5%
<2.00 D	0	0	1	0	0	0	0	1
	0%	0%	<1%	0%	0%	0%	0%	<1%
<3.00 D	0	1	0	0	1	0	0	2
	0%	<1%	0%	0%	<1%	0%	0%	1%
<4.00 D	0	0	0	0	1	0	0	1
	0%	0%	0%	0%	<1%	0%	0%	<1%
Total	6	63	76	34	25	5	1	210

For core eyes, 80% demonstrate post treatment MRSE within 0.50 D of the attempted target the 9 month visit. More than 93% demonstrate accuracy within 1.00 D at 9 months.

5. Analysis of Stability

The analysis of the stability of the MRSE is presented as the number of eyes that manifest each level of dioptric change in MRSE measured in two consecutive visits (three month to six months and six month to nine months). Stability of outcome is evaluated for core eyes with refractive data at all "key visits" of 1, 3, 6, and 9 months (179 eyes).

Table 8 shows that from three to six months, 91% of eyes (162/179) demonstrated $\leq$ 1.00 D of difference in the MRSE while 97% of eyes (173/179) demonstrated less than or equal to 2.00 D of difference in the MRSE.

Table 8
Stability of MRSE from 3 Month to 6 Month Visit
Stratified by Pretreatment Dioptic Group
Core Eyes with 3, 6, and 9 month visits (N=179)*

Change in MRSE (DSE)	Pre Treatment Myopia (MRSE)							
	≤ 1.0D n %	>1.00 to 2.00D n %	>2.00 to 3.00D n %	>3.00 to 4.00D n %	>4.00 to 5.00D n %	>5.00 to 6.00D n %	>6.00 to 7.00D n %	Total n %
<0.00 to -1.00	1	11	20	11	5	2	0	50
	<1%	6%	11%	6%	3%	1%	0 %	28%
<-1.00 to -2.00	0	1	1	0	2	0	0	4
	0%	<1%	<1%	0%	1%	0%	0%	2%
<-2.00 to -3.00	0	0	0	1	0	0	0	1
	0%	0%	0%	<1%	0%	0%	0%	<1%
<-3.00 to -4.00	0	0	0	1	0	1	0	2
	0%	0%	0%	<1%	0%	<1%	0%	1%
No Change	3	21	22	6	3	1	1	57
	2%	12%	12%	3%	2%	<1%	<1%	32%
>0.00 to 1.00	2	17	18	9	8	1	0	55
	1%	10%	10%	5%	5%	<1%	0%	31%
>1.00 to 2.00	0	0	1	3	3	0	0	7
	0%	0%	<1%	2%	2%	<1%	0%	4%
>2.00 to 3.00	0	0	2	0	1	0	0	3
	0%	0%	1%	0 %	<1%	0%	0%	2%
Mean Difference	0.13	0.02	0.03	-0.11	0.22	-0.75	0.00	
SD	0.306	0.423	0.634	0.960	0.915	1.425		
n	6	50	64	31	22	5	1	179

*Eyes completing 9 months and having refractive data at 1, 3, 6 and 9 months = 179

Table 9 shows that from six to nine months, 94% of eyes (169/179) demonstrated less than 1.00 D of difference in the MRSE while 98% of eyes (176/179) demonstrated less than or equal to 2.00 D of difference in the MRSE.

Table 9
Stability of MRSE from 6 Month to 9 Month Visit
Stratified by Pretreatment Dioptic Group
Core Eyes with 3, 6, and 9 month visits (N=179)*

Change in MRSE (DSE)	Pre Treatment Myopia (MRSE)							
	≤ 1.0D n %	>1.00 to 2.00D n %	>2.00 to 3.00D n %	>3.00 to 4.00D n %	>4.00 to 5.00D n %	>5.00 to 6.00D n %	>6.00 to 7.00D n %	Total n %
<0.00 to -1.00	3	14	21	6	8	2	1	55
	2%	8%	12%	3%	5%	1%	<1%	31%
<-1.00 to -2.00	0	4	1	0	0	0	0	5
	0%	2%	<1%	0%	0%	0%	0%	3%
<-2.00 to -3.00	0	0	0	0	0	0	0	0
	0%	0%	0%	0%	0%	0%	0%	0%
<-3.00 to -4.00	0	1	0	0	0	0	0	1
	0%	<1%	0%	0%	0%	0%	0%	<1%
No Change	2	16	16	11	3	1	0	49
	1%	9%	9%	6%	2%	<1%	0%	27%
>0.00 to 1.00	1	15	26	13	9	1	0	65
	<1%	8%	15%	7%	5%	<1%	0%	36%
>1.00 to 2.00	0	0	0	0	1	1	0	2
	0%	0%	0%	0%	<1%	<1%	0%	1%
>2.00 to 3.00	0	0	0	1	1	0	0	2
	0%	0%	0%	<1%	<1%	0%	0%	1%
Mean Difference	-0.10	-0.20	0.00	0.21	0.18	0.20	-0.25	
SD	0.357	0.709	0.424	0.763	0.864	1.077		
n	6	50	64	31	22	5	1	179

*Eyes completing 9 months and having refractive data at 1, 3, 6 and 9 months = 179

The mean change between 3 and 6 months for these 179 eyes was a decrease (toward target) in MRSE of 0.01(±0.72) D.
The mean change between 6 and 9 months for these 179 eyes was 0.00 (±0.66) D.

6. Change in Corneal Cylinder

The reduction in refractive error and improvement in unaided visual acuity is the result in part of a change in the corneal radius as measured by keratometry. The keratometer measures the corneal curvature in the two principal meridians at a chord diameter slightly less than 3 millimeters. The keratometer does not provide data of the local curvature inside or outside of the location of its measurement.

14% of all treated eyes manifested more than one diopter of increase in corneal cylinder from baseline to the last visit. The core group contained of 26 eyes with greater than 1 D increase and the adjunct group contained of 24 eyes with greater than 1 D increase.

There were 7 eyes in the core group and 11 in the adjunct group that had increases (initial to patient's last visit) in corneal cylinder of >2 D. No eyes with cylinder increase >1 D had a BSCVA at exit worse than 20/30.

7. Change in the Flat Meridian Curvature as a Function of Pretreatment MRSE

Table 10 reports the change in the flat meridian at 9 months of treatment for all core eyes stratified by the pretreatment MRSE.

Table 10
Keratometry Change in the Flat Meridian at 9 Months
Stratified by Pretreatment Dioptric Group
9 Months Core Eyes (N=210)

K-Change (D)	0 – 1		>1 - 2		>2 - 3		>3 - 4		>4 - 5		>5 - 6		Increase >0 - 1		Total	
	n	%	n	%	n	%	n	%	n	%	n	%	n	%	n	%
>Flatter													1	<1	1	<1
>0.00 – 0.50	5	2	9	4	7	3	3	1	0	0	0	0	0	0	24	11
>0.50 – 1.00	2	2	28	13	12	6	4	2	1	<1	0	0	0	0	47	22
>1.00 – 1.50	0	0	18	9	22	11	6	3	0	0	0	0	0	0	46	22
>1.50 – 2.00	0	0	4	2	13	6	11	5	3	1	0	0	0	0	31	15
>2.00 – 2.50	0	0	1	<1	6	3	8	4	2	1	1	<1	0	0	18	9
>2.50 – 3.00	0	0	0	0	0	0	1	<1	5	2	3	1	0	0	9	4
>3.00 – 3.50	0	0	0	0	0	0	2	1	0	0	0	0	0	0	2	1
>3.50 – 4.00	0	0	0	0	0	0	1	<1	1	<1	0	0	0	0	2	1
No Change	2	1	0	0	2	1	0	0	0	0	0	0	0	0	4	2
Steeper																
0.00 - <0.50	3	1	0	0	2	1	0	0	0	0	0	0	0	0	5	2
Not Reported	0	0	0	0	0	0	0	0	0	0	0	0	0	0	21	10

Analysis of keratometry change in the flat meridian at 9 months post-treatment shows that 86% (180/210) eyes experienced some degree of change in the flat k meridian. There were 5 eyes experiencing an increase in k of less 0.5 D and 21 eyes for which data was not reported. Overall, there is a flattening of the flat k meridian with this treatment modality.

8. Analysis of Refractive and Keratometric Stability

The analysis indicates that the major portion of the treatment occurs within the first 3 months with continued reduction of the MRSE thereafter.

9. Analysis of Wearing Time

The subjects were instructed to apply their lenses within 30 minutes of going to sleep and to remove them within 30 minutes of awakening. The wearing time does not correspond to the expected distribution of sleep time per night. The average wear time during this study was 8 to 10 hours per night. There does not appear to be a relationship between length of wear and unaided visual acuity when measured shortly after removal in the morning.

10. Analysis of post Lens Removal UCVA Regression

The data collected during the study for the regression of UCVA following lens removal were incomplete. Please refer to Section XIII CDRH Decision for additional information involving regression.

C. Safety Data Analysis and Results

1. Change in Best Spectacle Corrected Visual Acuity (BSCVA) from Baseline

Table 11 provides the change in lines of BSCVA at the 9-month post- treatment interval for 210 completed core eyes in the study.

Table 11
Change in BSCVA Initial to Final
(Core Eyes, N=210)

Lines of Change	Pretreatment myopia						
	0-1.00	>1.00-2.00	>2.00-3.00	>3.00-4.00	>4.00-5.00	>5.00-6.00	>6.00-7.00
Increase > 2 Lines	0	0	1	0	0	0	1
Increase 2 Lines	0	1	0	0	0	0	0
Increase 1 Line	1	10	14	6	6	1	0
No Change	5	50	56	26	14	2	0
Decrease >1 Line	0	2	5	2	5	2	0
Total	6	63	76	34	25	5	1

- 73% of the eyes (153/210) had no change in BSCVA from baseline;
- 18% of the eyes (38/210) had a gain of 1 line;
- <1% of the eyes (1/210) had a gain of 2 lines; and,
- 1% of the eyes (2/210) had a gain of >2 lines in BSCVA as compared to baseline.

Concurrently, 8% of the eyes (16/210) had a loss of >1 line as compared to baseline. No core eyes had a loss of ≥2lines of BSCVA.

Table 12 provides the change in lines of BSCVA at the 9-month post-treatment interval for the 54 completed adjunct eyes.

Table 12
Change in BSCVA Initial to 9 Months
(Completed Adjunct Eyes, N=54)

Lines of Change	Pretreatment myopia						
	0-1.00	>1.00-2.00	>2.00-3.00	>3.00-4.00	>4.00-5.00	>5.00-6.00	>6.00-7.00
Increase > 2 Lines	0	0	0	0	0	0	0
Increase 2 Lines	0	0	0	0	0	0	0
Increase 1 Line	0	0	0	1	0	0	0
No Change	5	2	4	7	4	0	0
Decrease >1 Line	0	0	0	1	1	0	0
Not Reported	2	12	5	9	1	0	0
Total	7	14	9	18	6	0	0

- 41% of the eyes (22/54) had no change in BSCVA from baseline;
- <1% of the eyes (1/54) gained 1 line;
- 4% of the eyes (2/54) had a loss of 1 line in BSCVA; and,
- Data was not reported for 29 eyes.

There were a total of 42 incidents (in 34 eyes) of at least a temporary reduction of ≥2 lines of BSCVA during the course of the study for all eyes entered into the study. Only 12 of the 42 incidents occurred after 3 months. Duration of the vision loss was not accurately determined in all cases, but for incidents in which documentation and recovery was demonstrated, length of time to documented recovery varied from 1 day to 9 months. Thirty-three eyes had a duration of reduced vision of >7 days.

Four eyes in 3 patients showed a reduction of ≥2lines of BSCVA from initial visit to last study visit. All 4 eyes were discontinued; however, one of these eyes was subsequently documented to return to normal acuity. No significant ocular

abnormalities were observed in these eyes with biomicroscopy at the time of study exit.

2. Adverse Reactions

There were 12 significant lens-related adverse events reported by 10 subjects.

- Two eyes had bilateral grade 4 staining with significant decrease in vision to 20/80.
- One eye had grade 3 corneal staining secondary to a dislodged lens.
- One eye had significant corneal distortion with reduced vision to 20/200 and rippling on the cornea.
- Two eyes had bilateral iritis with trace cells and flare in both eyes.
- One eye had corneal infiltrates.
- Two eyes had abrasion (grade 3 staining).
- One eye had reduction of BSCVA to 20/50 secondary to a decentered lens.
- One eye had reduction of BSCVA to 20/60 due to central staining.
- One eye had reduction of BSCVA to 20/60 with no reason given.

All of these eyes that showed acuity reductions were documented as returning to normal vision, except two eyes of one subject with severe corneal staining showed $\geq$ 2 lines loss of BSCVA. The return to pretreatment VA was not recorded in the case report form of this subject although the subject returned to soft contact lens wear and verbally reported that vision was normal. Of the 10 subjects for which adverse events were reported, 4 subjects discontinued the study. All adverse events resolved without further complications.

3. Slit Lamp Findings

For 2,907 eye exams, there were 14 exams showing slit lamp findings greater than grade 2 which were reported as follows:

- Grade 3 for staining (3 incidents);
- Grade 4 for staining (2 incidents);
- Grade 3 for injection (2 incident);
- Grade 3 "other" (4 incidents); and,
- Ungraded (3 incidents: 2 staining and 1 tarsal abnormality).

All findings greater than grade 2 resolved without further complications. There were 5 slit lamp findings > Grade 2 or ungraded, in the Core, and 9 in the adjunct. The most significant of the > Grade 2 findings, were 3 Grade 3 Corneal Staining cases, 2 Grade 4 Corneal Staining cases, 1 case of Corneal Infiltrates (grade 3) and 2 Cases (2 eyes of 1 subject) of trace Iritis.

4. Symptoms, Problems and Complaints

Subjects were asked to report symptoms and complaints as part of the dispensing visit and each follow up visit. These complaints are tabulated in Table 13 as follows for 1,903 core eyes exams and 486 completed adjunct eye exams:

Table 13
Symptoms, Problems and Complaints
1,903 Core Eye Exams and 486 Completed Adjunct Eye Exams

	Core		Adjunct	
	n	%	n	%
Distance VA poor	290	15	99	20
Flaring/ghosting	167	9	49	10
Near VA poor	52	3	19	4
Excessive awareness/pain	29	2	14	3
Red eye	18	1	4	<1
Excessive discharge	18	1	2	<1
Photophobia	11	<1	8	2
Burning/itching	9	<1	4	<1

The report of distance VA poor and flaring/ghosting appears to fluctuate throughout the study.

5. Device Replacements

The modality is designed as a single lens treatment. Investigators were permitted to retreat eyes and were allowed to reorder lenses. There were 199 lenses reordered for 210 core eyes, 47 lenses reordered for 54 adjunct eyes, and 89 lenses reordered for 110 discontinued eyes. Table 14 reports the number of lens reorders for all eyes after the original dispensing.

Table 14
Description and Number of Lens Reorders Completed Eyes
(N=374)

Reason for Replacement	Number of Lenses Replaced		
	Core	Adjunct	Disc.
Duplicate lenses	69	14	16
Increase overall diameter	64	17	27
Decrease overall diameter	11	3	11
Increase power	28	10	22
Decrease power	12	1	5
Other	15	2	8
TOTAL	199	47	89

Duplicates included a spare pair of lenses, lost lenses or broken lenses all of which did not involve any fit changes such as power, diameter or curve changes. To be included in the duplicate category, the lenses had to be the exact duplicate of the previous lenses.

Other included change in reverse curve, alignment curve, AOZ. Prescription, unspecified design changes, or changes to the original keratometry or refraction.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The results of the data provided from this clinical study revealed no major complications or slit lamp findings and 12 adverse events which resolved. Additionally, the results show that 95 % of the eyes completing the study in the core group achieved visual acuity of 20/40 or better at nine months and 99% demonstrated a reduction in pretreatment myopia. As shown in Table 15 the results of the clinical study provide reasonable assurance of the safety and effectiveness of the device for the subject population, refractive conditions and specified wearing modality.

Table 15
Summary of Key Safety and Effectiveness Variables

CRITERIA	9 Months Core n	%
Effectiveness	210	
UCVA 20/20 or better	154	73
UCVA 20/40 or better	199	95
MRSE Change of <0.00 D	2	1
MRSE Change of >0.0 to 0.50 D	7	3
MRSE Change of >0.50 to 1.00 D	6	3
MRSE Change of >1.00 to 1.50 D	29	14
MRSE Change of >1.50 to 2.00 D	37	18
MRSE Change of > 2.00 to 2.50 D	38	18
MRSE Change of > 2.50 to 3.00 D	35	17
MRSE Change of > 3.00 to 3.50 D	22	11
MRSE Change of > 3.50 to 4.00 D	18	9
MRSE Change of > 4.00 to 4.50 D	5	2
MRSE Change of > 4.50 to 5.00 D	7	3
MRSE Change of > 5.00 D	4	2
Accuracy MRSE ± 0.50 D	168	80
Accuracy MRSE ± 1.00 D	27	13
Accuracy MRSE ± 2.00 D	11	5
n	179*	
Stability; MRSE ≤0.00 Change 3 to 6 months	57	32
Stability; MRSE ≤ 1.00 Change 3 to 6 months	162	91
Stability; MRSE ≤2.00 Change 3 to 6 months	173	97
Stability; MRSE ≤ 3.00 Change 3 to 6 months	177	99
Stability; MRSE ≤ 4.00 Change 3 to 6 months	179	100
Stability; MRSE ≤0.00 Change 6 to 9 months	49	27
Stability; MRSE ≤1.00 Change 6 to 9 months	169	94
Stability; MRSE ≤2.00 Change 6 to 9 months	176	98
Stability; MRSE ≤3.00 Change 6 to 9 months	178	99
Stability; MRSE ≤ 4.00 Change 6 to 9 months	179	100

Safety	Combined for all subjects n	%	Core n	%	Adjunct n	%
Significant Adverse Events	12**	3	3	1	9**	3
Loss of ≥ 2 lines BSCVA†‡	4	1				
BSCVA worse than 20/40†	1	<1	0	0	1	2
Increase of > 1 D Refractive Cylinder†	12	3	4	2	8	5
Increase of > 1 D Corneal Cylinder†	50	14	26	12	24	16

*Stability results are for the 179 core eyes with refractive data at all key visits (1, 3, 6,& 9 months).
**Includes 4 discontinued subjects (6 eyes).
† from baseline to exit visit

‡ there were 42 incidents (in 34 eyes) of at least a temporary reduction of ≥2 lines of BSCVA during the course of the study. All except 4 discontinued eyes were documented as returning to normal during the study; one eye was documented to return to normal acuity after the study. No significant ocular abnormalities were observed in these eyes with biomicroscopy at the time of study exit.

FDA concludes that the benefits of these lenses – effective temporary reduction of myopia - are greater than the risk that may be associated with wearing these lenses in an overnight orthokeratology program. Therefore, FDA concludes that there is valid scientific evidence that provides reasonable assurance that the subject lenses are safe and effective when worn in accordance with the approved labeling.

XII. PANEL RECOMMENDATION

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. CDRH DECISION

CDRH issued a letter to Euclid Systems Corporation, Inc. on June 7, 2004, advising that its PMA was approved.

A postapproval study to evaluate the stability of treatment post lens removal was agreed to by the applicant as a condition of approval. Results of the study will be included in the product labeling.

The applicant's manufacturing facility was inspected on April 11, 2003, and was found to be in compliance with the Quality System Regulation (21 CFR 820).

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See CDRH Decision above and approval order.