

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

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### **I. GENERAL INFORMATION**

<b>Device Generic Name:</b>	AMD implant or AMD device
<b>Device Trade Name:</b>	Implantable Miniature Telescope IMT (by Dr. Isaac Lipshitz)
<b>Applicant's Name and Address:</b>	VisionCare Ophthalmic Technologies, Inc. 14395 Saratoga Ave., Suite 150 Saratoga, CA 95070 (408) 872-9393 (phone) (408) 872-9395 (fax)
<b>Date(s) of Panel Recommendation:</b>	TBD
<b>PMA Number:</b>	TBD
<b>Date of Good Manufacturing Practice Inspection:</b>	TBD
<b>Date of Notice of Approval to Applicant:</b>	TBD

### **II. INDICATIONS FOR USE**

The IMT (by Dr. Isaac Lipshitz; hereafter "AMD implant or AMD device") is indicated for use in adult patients with bilateral, stable, untreatable moderate to profound central vision impairment due to macular degeneration.

### **III. CONTRAINDICATIONS, WARNINGS AND PRECAUTIONS**

#### **A. Contraindication**

Implantation of the AMD implant is contraindicated in patients with:

- Evidence of active CNV on fluorescein angiography or treatment for CNV within the past six months
- Any ophthalmic pathology that compromises the patient's peripheral vision in the fellow eye
- Significant communication impairments or severe neurological disorders
- Previous intraocular or corneal surgery of any kind in the operative eye, including any type of surgery for either refractive or therapeutic purposes.
- Prior or expected ophthalmic related surgery within 30 days preceding AMD device implantation

- A history of steroid-responsive rise in intraocular pressure, uncontrolled glaucoma, or preoperative IOP >22 mm Hg.
- Pregnancy or lactation.
- The planned operative eye has:
  - ◆ Myopia > 6.0 D
  - ◆ Hyperopia > 4.0 D
  - ◆ An axial length < 21 mm
  - ◆ Endothelial cell density < 1600 cells/mm<sup>2</sup>
  - ◆ A narrow angle, i.e., < Schaffer grade 2
  - ◆ Cornea stromal or endothelial dystrophies or disorders
  - ◆ Inflammatory ocular disease
  - ◆ Zonular weakness/instability of crystalline lens, or pseudoexfoliation
  - ◆ Diabetic retinopathy
  - ◆ Untreated retinal tears
  - ◆ Retinal vascular disease
  - ◆ Optic nerve disease
  - ◆ A history of retinal detachment
  - ◆ Intraocular tumor
  - ◆ Retinitis pigmentosa
  - ◆ An ocular condition that predisposes the patient to eye rubbing

#### **B. Warning and Precautions**

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

#### **IV. DEVICE DESCRIPTION**

VisionCare's Implantable Miniature Telescope, or IMT™ (by Dr. Isaac Lipshitz) is a visual prosthetic device which, when combined with the optics of the cornea, constitutes a telephoto lens for improvement of visual acuity in patients with bilateral moderate to profound macular degeneration. The AMD device is surgically implanted in the posterior chamber of the eye, in place of the eye's crystalline lens and is held in position by haptic loops.

The AMD device contains two micro lenses, which magnify objects in the central visual field, allowing the patient to see without the need for external low-vision aids. A magnified image is projected by the AMD implant onto the retina, enabling the patient to recognize and identify objects that could not otherwise be seen. The AMD device is available in two models: Wide Angle (WA) 2.2X, and Wide Angle (WA) 3.0X, which provide nominal magnification of ×2.2 and ×2.7, respectively.

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Both models are designed predominantly for the restoration of intermediate to far vision (increasing the ability to view objects several meters away from the patient). The addition of conventional spectacles provides correction for near vision activities.

The AMD device is implanted in one eye only. The implanted eye provides central vision, while the fellow eye continues to be used for peripheral vision.

The AMD implant is composed of three primary components; a fused silica capsule that contains optical elements, a clear polymethylmethacrylate (PMMA) carrier, and a blue PMMA light restrictor. The optical component is snap-fitted into the carrier. All materials are biocompatible for long-term ocular implantation per ISO 10993. One of the internal components (not in contact with body fluids or tissue) of the AMD implant contains stainless steel, which may interfere with the safe use of Magnetic Resonance Imaging (MRI). Until MRI compatibility of the AMD implant has been established, the use of MRI is contraindicated. The AMD implant is assembled and packaged in a controlled environment and is sterilized by ethylene oxide. Table 4-1 below compares the finished product specifications of the two device models.

Each AMD implant is packaged in a protective polycarbonate case with cap, which assures that the device is held firmly during handling and transportation. The protective case containing the AMD device is placed in a Polyethylene (PETG) blister, which is sealed with a Tyvek<sup>®</sup> lid. Following ethylene oxide sterilization, the blister is placed in a unit box with labels and product information. The expiration date appears on the outside of the Tyvek<sup>®</sup> lid and on the outside of the box (the shelf-life is 2-years from the date of manufacture).

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**TABLE 4-1**  
**FINISHED PRODUCT SPECIFICATIONS OF THE IMT**  
**(BY DR. ISAAC LIPSHITZ) MODELS**

FEATURE	MODEL WA 2.2X	MODEL WA 3.0X
Magnification	x 2.2 ± 10%	x 2.7 ± 10%
Depth of Field	1.5 to 10 m	1.5 to 10 m
Optimal Focusing Distance	3 m	3 m
Field of View	Full field: 24° (Nominal), 52.8° on the retina Center (High Resolution): 9°, 20° on the retina	Full field: 20° (Nominal), 54° on the retina Center (High Resolution): 6°, 16.2° on the retina
Optical Transmission (visible Spectrum)	T > 80% in the eye T > 70% in air	T > 80% in the eye T > 70% in air
<b>DIMENSIONS</b>		
Overall Diameter	13.5 mm	13.5 mm
Clear Aperture	3.2 mm	3.2 mm
Telescope Diameter	3.6 mm	3.6 mm
Axial Length	4.4 mm	4.4 mm
Haptic Angulation	12.7°	12.7°
<b>WEIGHT</b>		
Air	115 mg ± 10%	115 mg ± 10%
Aqueous	60 mg ± 10%	60 mg ± 10%

**V. ALTERNATIVE PRACTICES OR PROCEDURES**

Alternative, corrective interventions currently available are vision aids such as special spectacles and head-mounted or hand-held telescopes, which magnify images onto the retina.

**VI. MARKETING HISTORY**

The VisionCare Ophthalmic Technologies, Inc. IMT<sup>by Dr. Isaac Lipshitz</sup> devices are available for sale in the USA. The VisionCare Ophthalmic Technologies, Inc. IMT<sup>by Dr. Isaac Lipshitz</sup> devices have not been withdrawn from marketing for any reason relating to the safety and effectiveness of the device.

**VII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH**

Potential adverse events associated with AMD device implantation include:

- Anterior synechiae
- Choroidal detachment
- Corneal transplant
- Cystoid macular edema
- Endophthalmitis
- Hyphema
- AMD implant dislocation
- Inflammatory deposits on AMD implant
- Iris atrophy
- Iritis
- Pigment deposits on AMD implant
- Pupillary block
- Repeat iridectomy
- Retinal detachment
- Uveitis/Vitritis
- Vitreous in anterior chamber
- Wound leak
- Corneal decompensation
- Corneal edema
- Cyclitic membrane
- Distorted pupil
- Flat anterior chamber
- Hypopyon
- Increased IOP requiring treatment
- Intraocular inflammation
- Iris transillumination defects
- Optic atrophy
- Posterior synechiae
- Removal of AMD implant
- Repositioning of AMD implant
- Retinal vascular occlusion
- Vitrectomy/vitreous aspiration
- Vitreous incarceration in incision

**VIII. SUMMARY OF PRECLINICAL STUDIES**

Preclinical studies were performed on the AMD implant that are consistent with the FDA draft guidance document for refractive implants dated August 1, 2000. The applicant conducted a battery of *in vivo* and *in vitro* acute and chronic toxicity tests that establish the biocompatibility of the AMD implant materials. These studies, combined with data from chemistry and engineering analyses, demonstrate the suitability of the materials and overall device design for use as an intraocular implant. The adequacy of the manufacturing processes, including sterilization, was established through review of the manufacturing information in the PMA as well as through on-site inspection. Preclinical testing demonstrates safety and effectiveness of the AMD device from the microbiology, toxicology, engineering, and manufacturing perspectives.

**IX. SUMMARY OF CLINICAL STUDIES**

**A. Objectives**

The objective of this study was to demonstrate the safety and effectiveness of the Implantable Miniature Telescope (IMT™ by Dr. Isaac Lipshitz) for the improvement of visual acuity in patients with bilateral moderate to profound central vision impairment due to age-related macular degeneration.

**B. Study Design**

The data for this report were gathered from a prospective, multicenter clinical evaluation of the use of the AMD implant in subjects with bilateral, stable, untreatable moderate to profound central vision impairment due to age-related macular degeneration. The study was conducted in the U.S. under an approved IDE. A total of 218 consecutive patients were enrolled and 206 patients were implanted and evaluated at 28 clinical sites. At the time of database closure, 194 eyes had reached the 12-month follow-up, 180 eyes had reached the 18-month follow-up examination and 148 eyes had reached 24-month follow-up.

**C. Inclusion and Exclusion Criteria**

In order to be enrolled in the study, patients needed to meet these conditions: bilateral, stable, untreatable central vision disorders (untreatable AMD or Stargardt's macular dystrophy) as determined by fluorescein angiography, and cataract; distance BCVA between 20/80 and 20/800, and adequate peripheral vision in one eye (the non-targeted eye) to allow navigation; achievement of at least a five-letter improvement on the ETDRS chart in the eye scheduled for surgery, with the external telescope; anterior chamber depth of  $\geq 2.5$ mm in the operative eye; available for the study duration of approximately 24 months and willing to return for all visits for training and evaluation; alert, mentally competent, and able to understand and comply with the requirements of the clinical trial, and be personally motivated to abide by the requirements and restrictions of the clinical trial; at least 55 years of age; and provide written informed consent.

Patients not meeting the above inclusion criteria were excluded from the study. In addition, subjects who exhibited any of the following conditions were excluded: evidence of active CNV on fluorescein angiography or treatment for CNV within the past six months; anticipated need for cataract extraction and intraocular lens implantation during the first 12 months following AMD device implantation in the fellow eye [if cataract extraction was anticipated, this procedure had to be performed at least 30 days prior to enrollment in the clinical study]; ophthalmic related surgery within the 30 days preceding implantation of the AMD device; any of the following conditions in the operative eye: myopia  $> 6.0$  D, hyperopia  $> 4.0$  D, axial length  $< 21$  mm, endothelial cell density  $< 1600$  cells/mm<sup>2</sup>, narrow angle [i.e., less than Schaffer grade 2], cornea stromal or endothelial dystrophies or disorders, inflammatory ocular disease, zonular weakness/instability of crystalline

lens, pseudoexfoliation, diabetic retinopathy, untreated retinal tears, retinal vascular disease, optic nerve disease, history of retinal detachment, retinitis pigmentosa or any intraocular tumor and medical or ophthalmic condition that in the opinion of the Investigator rendered the subject unsuitable for participation in the study; any ophthalmic pathology that compromised the patient's peripheral vision in the fellow eye; any ocular condition that predisposed the patient to eye rubbing; significant communication impairments or severe neurological disorders that prevented or interfered with the study requirements; previous intraocular or corneal surgery of any kind in the operative eye(s), including any type of surgery for either refractive or therapeutic purposes; history of steroid-responsive rise in intraocular pressure, uncontrolled glaucoma, or preoperative IOP >22 mm Hg; known sensitivity to planned study concomitant medications; and participation in any other ophthalmic drug or device clinical trial during the time of this clinical investigation.

**D. Study Plan, Patient Assessments and Efficacy Criteria**

All subjects were expected to return for follow-up examinations at 1 day, 1 week, 1 month, 3 month, 6 months, 9 months, 12 months, 18 months and 24 months postoperatively. In addition, subjects were required to return for vision training at week 1, 2, 4, 6, 10 and 12.

Preoperatively, the subjects' medical and ocular histories were recorded. The clinical parameters measured during the study included: best corrected visual acuity (distance and near), manifest refraction, intraocular pressure, slit lamp examination, fundus examination, endothelial cell count, and activities of daily life questionnaire/VFQ-25.

The primary efficacy variable for this study was an improvement of 2 lines or greater in either near or distance best corrected acuity in 50% of the implanted eyes at 12 months post implantation. Quality of Life questionnaires were used as secondary measurements of procedure success.

Safety outcomes included preservation of best corrected visual acuity (i.e., no more than 10% of implanted eyes were to experience a loss of more than 2 lines in either near or distance BCVA without a corresponding improvement [gain of 2 or more lines] in the other BCVA), endothelial cell loss and the occurrence of adverse events and complications.

**E. Study Period and Investigational Sites**

Subjects were implanted with the AMD device between December 2002 and November 2003. The database for this PMA reflected data collected through June 20, 2005. Twelve of the 218 eyes enrolled were excluded from further analyses. Reasons for exclusion included one subject who canceled surgery, 5 eyes in which the AMD device was not implanted due to surgical complications, and 6 eyes in which the AMD device was removed at the time of surgery. Consequently, a total of 206 eyes were successfully implanted at 28 US clinical sites. Of the 206 eyes, 115 eyes were implanted with the 2.2X WA and 91 eyes were implanted with the 3.0X WA device.

**F. Data Analysis and Results**

**1. Demographics**

Presented in Table 9-1 are the demographic characteristics for all eyes implanted with AMD device. As anticipated, this is an elderly study population (mean age at surgery was 75.4 years [S.D. 7.2, range 55 – 93 years]). The cohort consists primarily of Caucasians.

**TABLE 9-1  
DEMOGRAPHIC INFORMATION  
ALL AMD DEVICE IMPLANTED EYES**

<b>206 EYES OF 206 ENROLLED &amp; IMPLANTED SUBJECTS</b>			
		<b>NUMBER</b>	<b>PERCENTAGE</b>
<b>Gender</b>	Female	98	47.6%
	Male	108	52.4%
<b>Race</b>	Caucasian	198	96.1%
	Black	3	1.5%
	Hispanic	4	1.9%
	Asian	1	0.5%
	Other	0	0.0%
<b>Eye Implanted</b>	Right	98	47.6%
	Left	108	52.4%
<b>Age (In Years)</b>	Mean	75.4	
	Standard Deviation	7.2	
	Minimum	55	
	Maximum	93	

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**2. Preoperative Characteristics**

Presented in Table 9-2 are the preoperative parameters for all eyes implanted with AMD device.

**TABLE 9-2  
PREOPERATIVE PARAMETERS  
ALL AMD DEVICE IMPLANTED EYES**

206 Eyes of 206 Enrolled & Implanted Subjects		
	Number	Percentage
<b>Anterior Chamber Depth</b>		
Mean	3.145	
Standard Deviation	0.374	
1st Quartile, Median, 3rd Quartile	2.89, 3.11, 3.34	
Range	2.48, 4.74	
<b>Axial Length</b>		
Mean	23.739	
Standard Deviation	0.927	
1st Quartile, Median, 3rd Quartile	23.1, 23.6, 24.4	
Range	21.53, 26.14	
<b>Type of AMD</b>		
Geographic atrophy (GA)	78	37.9%
Drusen	3	1.5%
Disciform scar	91	44.2%
GA & Drusen	7	3.4%
GA & Disciform scar	8	3.9%
Drusen & Disciform scar	12	5.8%
GA & Drusen & Disciform scar	7	3.4%
<b>Cataract Type</b>		
Nuclear	147	71.4%
Cortical	1	0.5%
Posterior subcapsular (PSC)	2	1.0%
Nuclear & Cortical	41	19.9%
Nuclear & PSC	12	5.8%
Nuclear & Cortical & PSC	3	1.5%
<b>Best-corrected Visual Acuity</b>		
Mean BCDVA (Range)	20/312 (20/328, 20/120)	
Mean BCNVA @ 8" (Range)	20/315 (20/360, 20/80)	
Mean BCNVA @ 16" (Range)	20/262 (20/300, 20/100)	

1 eye canceled surgery. 5 eyes were reported with an aborted implantation. 6 eyes were reported with IMT removal at surgery. These eyes were excluded from analyses, but their safety data will be discussed separately.

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### 3. Post-operative Characteristics and Results

#### a. Accountability

Accountability for all successfully implanted subjects at the time of database closure across the study visit schedule is presented in Table 9-3.

**TABLE 9-3**  
**ACCOUNTABILITY AS OF DATABASE LOCK ON 20 JUNE 2005**  
**(N = 206 EYES SUCCESSFULLY IMPLANTED WITH AMD DEVICE)**

TOTAL SUBJECTS (N) = 206		1 Month	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months
Available for Analysis	n/N (%)	206/206 (100.0%)	201/206 (97.6%)	202/206 (98.1%)	196/206 (95.1%)	194/206 (94.2%)	180/206 (87.4%)	148/206 (71.8%)
Discontinued	n/N (%)	0/206 (0.0%)	3/206 (1.5%)	4/206 (1.9%)	5/206 (2.4%)	9/206 (4.4%)	10/206 (4.9%)	16/206 (7.8%)
Deceased	n/N (%)	0/206 (0.0%)	2/206 (1.0%)	3/206 (1.5%)	4/206 (1.9%)	7/206 (3.4%)	8/206 (3.9%)	10/206 (4.9%)
IMT Removed*	n/N (%)	0/206 (0.0%)	1/206 (0.5%)	1/206 (0.5%)	1/206 (0.5%)	2/206 (1.0%)	2/206 (1.0%)	6/206 (2.9%)
Active (Not yet eligible for the interval)	n/N (%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	35/206 (17.0%)
Lost to Follow-up†	n/N (%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	0/206 (0.0%)	1/206 (0.5%)	3/206 (1.5%)	6/206 (2.9%)
Missed Visit‡	n/N (%)	0/206 (0.0%)	2/206 (1.0%)	0/206 (0.0%)	5/206 (2.4%)	2/206 (1.0%)	13/206 (6.3%)	1/206 (0.5%)
% Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible)		206/206 (100.0%)	201/203 (99.0%)	202/202 (100.0%)	196/201 (97.5%)	194/197 (98.5%)	180/196 (91.8%)	148/155 (95.5%)

DB was locked for data entry on 06/20/2005. However, it was reopened for necessary data revision and was frozen on 07/18/2005 for PMA.

010-202's office chart was lost and no 24-month data could be collected. The subject was included in the "Missed Visit" row.

N = Total number of enrolled eyes with a device. One eye canceled surgery. Five eyes were reported with an aborted implantation. Six eyes were reported with device removal at surgery.

N = Total number of enrolled eyes with device.

\* Eight eyes were reported with device removal postoperatively at the time of DB closure. Six of these eight eyes have been exited from the study.

† Lost to follow-up: Eyes were not examined at the visit interval, and were not considered active or discontinued.

‡ Missed visit: Eyes were not examined at the scheduled visit, however were examined or may have been examined at a subsequent visit.

#### b. Summary of Visual Acuity Outcomes

Table 9-4 presents the effectiveness and safety endpoints in visual acuity for all implanted eyes.

Overall success rate was achieved by 89.1% of eyes at 6 months, by 89.7% at 9 months, 90.1% at 12 months and remained generally stable at 87.2% at 18 months and 85.7% at 24 months. The binominal exact p-value for the alternative hypothesis testing success rate > 50% was < 0.001 at each time point

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indicating that the results significantly surpassed the effectiveness endpoint defined in the protocol.

The proportion of eyes that showed a gain of at least 2 lines in both BCDVA **and** BCNVA (at either 8 inches or 16 inches) underscores the effectiveness of the AMD implant, with approximately 70% of eyes achieving an improvement of 2 or more lines in both near and distance acuity.

The safety parameter of preservation of best corrected visual acuity established in the study protocol consisted of a limit of  $\leq 10\%$  of implanted eyes with a loss of  $>2$  lines of either near (8" and 16") or distance BCVA without a corresponding improvement or with a loss in the other measure of acuity.

Per protocol, the safety parameter of preservation of best corrected visual acuity established in the study protocol consisted of a limit of  $\leq 10\%$  of implanted eyes with a loss of  $>2$  lines of either near or distance BCVA without a corresponding improvement (gain of 2 lines or more) in BCVA (a gain of 2 or more lines of near BCVA in eyes with loss of  $>2$  lines distance BCVA, and vice versa). The binominal exact p-value for the alternative hypothesis testing safety rate  $<10\%$  was  $<0.05$  at the 6, 9, 12 and 18 month follow-up visits, and nearly significant ( $p=0.0696$ ) at the 24 month visit as well.

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**TABLE 9-4**  
**SUMMARY OF EFFECTIVENESS AND SAFETY ENDPOINTS IN VISUAL ACUITY**  
**ALL AMD DEVICE IMPLANTED EYES**

BCVA Endpoints	6 Months n (%) % CI	9 Months n (%) % CI	12 Months n (%) % CI	18 Months n (%) % CI	24 Months n (%) % CI
<b>Effectiveness (N=)</b>	201	195	192	179	147
<b>Overall Effectiveness Endpoint (Success Rate)</b>	<b>179</b>	<b>175</b>	<b>173</b>	<b>156</b>	<b>126</b>
<i>(Success Rate)</i>	<i>(89.1%)</i>	<i>(89.7%)</i>	<i>(90.1%)</i>	<i>(87.2%)</i>	<i>(85.7%)</i>
<b>≥2 lines gain of BCDVA or BCNVA*</b>	<b>84.7%, 92.5%</b>	<b>85.4%, 93.1%</b>	<b>85.8%, 93.4%</b>	<b>82.3%, 91.1%</b>	<b>80.1%, 90.2%</b>
<b>Binomial exact p-value for Ha: success rate &gt; 50%</b>	<b>&lt;.0001</b>	<b>&lt;.0001</b>	<b>&lt;.0001</b>	<b>&lt;.0001</b>	<b>&lt;.0001</b>
<b>≥2 lines gain of BCDVA and BCNVA*</b>	138 (68.7%) 62.8%, 74.1%	134 (68.7%) 62.8%, 74.2%	141 (73.4%) 67.7%, 78.6%	127 (70.9%) 64.9%, 76.5%	99 (67.3%) 60.4%, 73.7%
Not reported/IMT removal	1	1	2	1	1
Total	202	196	194	180	148
<b>Safety (N=)</b>	201	195	193	179	147
<b>Overall Safety Rate</b>					
<b>&gt;2 lines loss of BCDVA and no change/loss of BCNVA or &gt;2 lines loss of BCNVA and no change/loss of BCDVA†</b>	<b>9 (4.5%) 2.4%, 7.7%</b>	<b>9 (4.6%) 2.4%, 7.9%</b>	<b>10 (5.2%) 2.8%, 8.6%</b>	<b>8 (4.5%) 2.2%, 7.9%</b>	<b>9 (6.1%) 3.2%, 10.4%</b>
<b>Binomial exact p-value for Ha: safety rate &lt; 10%</b>	<b>0.0033</b>	<b>0.0048</b>	<b>0.0120</b>	<b>0.0055</b>	<b>0.0696</b>
<b>&gt;2 lines loss of BCDVA and BCNVA‡</b>	2 (1.0%) 0.2%, 3.1%	4 (2.1%) 0.7%, 4.6%	2 (1.0%) 0.2%, 3.2%	2 (1.1%) 0.2%, 3.5%	2 (1.4%) 0.2%, 4.2%
<b>&gt;2 lines loss of BCDVA and no change in BCNVA§</b>	1 (0.5%) 0.0%, 2.3%	2 (1.0%) 0.2%, 3.2%	1 (0.5%) 0.0%, 2.4%	1 (0.6%) 0.0%, 2.6%	0 (0.0%) 0.0%, 2.0%
<b>&gt;2 lines loss of BCNVA and no change of BCDVA§</b>	6 (3.0%) 1.3%, 5.8%	3 (1.5%) 0.4%, 3.9%	7 (3.6%) 1.7%, 6.7%	5 (2.8%) 1.1%, 5.8%	7 (4.8%) 2.3%, 8.8%
Not reported/IMT removal	1	1	1	1	1
Total	202	196	194	180	148

For effectiveness, N = number of records with non-missing BCDVA and BCNVA changes from preop. The records with BCDVA gain ≥2 lines and BCNVA missing and the records with BCNVA gain ≥2 lines and BCDVA missing were counted as successful events.

For safety, N = number of records with non-missing BCDVA and BCNVA changes from preop. The records with BCDVA loss > 2 lines and BCNVA missing and the records with BCNVA loss > 2 lines and BCDVA missing were counted as safety events.

Not reported = number of records with missing BCDVA and/or BCNVA changes from preop.

IMT removal = number of treated eyes with IMT removal at the visit. Records after IMT removal were excluded and reported separately.

Total = number of treated eyes that returned for the visit.

% =  $n \div N \times 100$ . %CI = **90%** confidence interval for %. It was calculated based on Clopper Pearson method.

\* BCNVA gain ≥2 lines means that either BCNVA at 8" or BCNVA at 16" gained ≥2 lines.

† No gain in BCNVA means that both BCNVA at 8" and BCNVA at 16" did not gain ≥2 lines. No gain in BCDVA means that BCDVA did not gain ≥2 lines.

‡ >2 lines loss in BCNVA means that one BCNVA (8" or 16" lost > 2 lines without the other BCNVA (8" or 16") gaining ≥2 lines.

§ No change = within a loss of 2 lines to a gain of <2 lines. For BCNVA, it means that both BCNVA at 8" and BCNVA at 16" are within a loss of 2 lines to a gain of <2 lines.

**c. Quality of Life**

The VFQ-25 is a validated version of the National Eye Institute Vision Function Questionnaire (VFQ) which measures vision-targeted health status for persons with chronic eye diseases including macular degeneration. The VFQ-25 consists of a base set of 25 vision-targeted questions representing 11 vision-related constructs, plus an additional single-item general health rating question which is an independent component and not part of the composite or individual subscales. The maximum score is 100 points and 0 is the lowest possible score. A five (5) point difference in subscale and/or composite scores may be interpreted as clinically significant.

Table 9-5 shows the change in VFQ score from baseline for all eyes implanted with the AMD device. At 12 months, the VFQ-25 subscales of general vision, near activities, and distance activities improved by clinically significant levels. Additionally clinically significant improvements across all vision specific subscales (social functioning, mental health, role difficulties, and dependency) were noted. In subscales where no improvement or a decline in performance was expected (color vision, driving and peripheral vision), performance was stable or declined.

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**TABLE 9-5**  
**CHANGE IN VFQ-25 SCORE FROM BASELINE**  
**ALL AMD DEVICE IMPLANTED EYES**

<b>Change in VFQ-25</b>	<b>3 Months</b>	<b>6 Months</b>	<b>9 Months</b>	<b>12 Months</b>
<b>General Vision</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	17.99 (20.60)	16.90 (21.23)	15.10 (20.47)	14.09 (21.99)
95% confidence interval for mean*	15.11, 20.87	13.94, 19.86	12.22, 17.99	10.97, 17.22
Median	20.00	20.00	20.00	20.00
Range	-40.00, 60.00	-40.00, 80.00	-20.00, 60.00	-40.00, 60.00
<b>Near Activities</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	12.63 (17.91)	12.10 (19.35)	11.93 (18.68)	11.16 (19.28)
95% confidence interval for mean*	10.12, 15.13	9.41, 14.80	9.30, 14.56	8.42, 13.90
Median	8.34	8.34	8.34	8.34
Range	-33.33, 58.34	-33.34, 58.34	-33.33, 75.00	-25.00, 100.00
<b>Distance Activities</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	11.56 (22.09)	11.04 (22.44)	9.99 (23.58)	7.90 (24.68)
95% confidence interval for mean*	8.47, 14.65	7.91, 14.17	6.67, 13.31	4.40, 11.41
Median	8.34	8.34	8.33	8.33
Range	-41.67, 75.00	-50.00, 75.00	-37.50, 83.34	-50.00, 83.34
<b>Social Functioning</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	11.68 (27.90)	11.13 (25.64)	8.86 (27.42)	8.61 (26.63)
95% confidence interval for mean*	7.78, 15.58	7.55, 14.70	5.00, 12.73	4.83, 12.39
Median	12.50	12.50	12.50	0.00
Range	-75.00, 100.00	-62.50, 87.50	-87.50, 75.00	-75.00, 75.00
<b>Mental Health</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	9.83 (23.24)	9.81 (22.81)	9.15 (22.83)	9.29 (22.54)
95% confidence interval for mean*	6.58, 13.08	6.63, 12.99	5.94, 12.37	6.09, 12.49
Median	6.25	6.25	6.25	6.25
Range	-50.00, 87.50	-50.00, 87.50	-62.50, 81.25	-50.00, 81.25
<b>Role Difficulties</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	9.30 (24.52)	7.88 (26.62)	9.25 (29.41)	7.25 (26.13)
95% confidence interval for mean*	5.87, 12.72	4.16, 11.59	5.10, 13.39	3.54, 10.96
Median	12.50	0.00	0.00	0.00
Range	-75.00, 75.00	-75.00, 87.50	-62.50, 87.50	-62.50, 87.50
<b>Dependency</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	10.64 (27.99)	9.83 (26.81)	9.40 (26.87)	10.02 (27.53)
95% confidence interval for mean*	6.72, 14.55	6.10, 13.57	5.61, 13.18	6.11, 13.93
Median	8.33	8.33	8.33	8.33
Range	-66.67, 83.33	-58.33, 100.00	-41.67, 91.67	-66.67, 100.00

N = number of treated eyes returned for the visit with a non-missing change in VFQ-25 assessment. Records after device removal were excluded.

Per protocol, VFQ-25 was performed at baseline, and the 1, 3, 6, 9, and 12 months follow-up visits.

\* Normal distribution approach was used for mean. CI for % was calculated based on Clopper Pearson method.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

**TABLE 9-5 (CONTINUED)**  
**CHANGE IN VFQ-25 SCORE FROM BASELINE**  
**ALL AMD DEVICE IMPLANTED EYES**

<b>Change in VFQ-25</b>	<b>3 Months</b>	<b>6 Months</b>	<b>9 Months</b>	<b>12 Months</b>
<b>Driving</b>	<b>N = 187</b>	<b>N = 185</b>	<b>N = 184</b>	<b>N = 179</b>
Mean (SD)	-0.82 (7.49)	0.12 (6.69)	-0.29 (6.29)	-0.52 (7.00)
95% confidence interval for mean*	-1.90, 0.26	-0.85, 1.09	-1.21, 0.63	-1.55, 0.51
Median	0.00	0.00	0.00	0.00
Range	-60.00, 35.00	-45.00, 35.00	-45.00, 35.00	-45.00, 40.00
<b>Peripheral Vision</b>	<b>N = 197</b>	<b>N = 197</b>	<b>N = 194</b>	<b>N = 190</b>
Mean (SD)	-1.90 (30.82)	-2.66 (33.06)	-1.42 (31.81)	-5.92 (30.99)
95% confidence interval for mean*	-6.23, 2.43	-7.31, 1.98	-5.92, 3.09	-10.36, -1.49
Median	0.00	0.00	0.00	0.00
Range	-75.00, 100.00	-100.00, 100.00	-75.00, 100.00	-75.00, 100.00
<b>Color Vision</b>	<b>N = 190</b>	<b>N = 190</b>	<b>N = 189</b>	<b>N = 185</b>
Mean (SD)	8.95 (26.83)	6.71 (27.78)	6.48 (27.43)	3.38 (24.56)
95% confidence interval for mean*	5.11, 12.79	2.74, 10.69	2.55, 10.42	-0.18, 6.94
Median	0.00	0.00	0.00	0.00
Range	-75.00, 100.00	-75.00, 100.00	-75.00, 100.00	-75.00, 75.00
<b>Ocular Pain</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	2.83 (16.78)	-0.44 (18.56)	1.08 (17.39)	0.58 (18.85)
95% confidence interval for mean*	0.48, 5.17	-3.03, 2.15	-1.37, 3.53	-2.09, 3.26
Median	0.00	0.00	0.00	0.00
Range	-50.00, 75.00	-50.00, 62.50	-62.50, 50.00	-75.00, 62.50
<b>Overall Composite</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	8.38 (13.42)	7.43 (13.90)	7.23 (14.16)	6.03 (14.41)
95% confidence interval for mean*	6.50, 10.25	5.49, 9.37	5.24, 9.23	3.98, 8.07
Median	6.56	5.89	4.57	5.34
Range	-20.46, 50.15	-19.73, 50.15	-19.43, 51.85	-31.29, 58.29
n & % of eyes with increase ≥5 points	107 ( 53.8%)	103 ( 51.5%)	94 ( 48.0%)	100 ( 51.8%)
95% confidence interval for %*	46.6%, 60.8%	44.3%, 58.6%	40.8%, 55.2%	44.5%, 59.0%
<b>General Health</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	-2.89 (20.75)	-3.38 (22.09)	-5.10 (21.32)	-5.05 (21.73)
95% confidence interval for mean*	-5.79, 0.01	-6.46, -0.29	-8.11, -2.10	-8.14, -1.97
Median	0.00	0.00	0.00	0.00
Range	-50.00, 50.00	-100.0, 75.00	-75.00, 50.00	-75.00, 50.00

N = number of treated eyes returned for the visit with a non-missing change in VFQ-25 assessment. Records after device removal were excluded.

Per protocol, VFQ-25 was performed at baseline, and the 1, 3, 6, 9, and 12 months follow-up visits.

\* Normal distribution approach was used for mean. CI for % was calculated based on Clopper Pearson method.

## SUMMARY OF SAFETY AND EFFECTIVENESS DATA

The Activities of Daily Life (ADL) questionnaire is a modified version of the Activities of Daily Vision Scale (a questionnaire developed to provide a reliable and valid means of measuring the patient’s perception of visual function impairment in patients with cataract) to more appropriately address challenges facing individuals with end-stage macular degeneration. The scoring system in the ADL is consistent with the VFQ-25, 100 for a perfect score and 0 for the lowest possible score for subscale and composite analyses. Table 9-6 shows the change in ADL score from baseline for all eyes implanted with the AMD device. At 12 months, the total ADL score improved by 14.2 points, and the subcategories mobility, distance activities, and near activities improved by 12.0, 13.4 and 17.0 points respectively.

**TABLE 9-6**  
**CHANGE IN ADL SCORE FROM BASELINE**  
**ALL AMD DEVICE IMPLANTED EYES**

<b>Change in ADL</b>	<b>3 Months</b>	<b>6 Months</b>	<b>9 Months</b>	<b>12 Months</b>
<b>Mobility</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	15.82 (20.82)	14.00 (22.49)	12.90 (22.46)	11.97 (22.80)
95% confidence interval for mean*	12.91, 18.73	10.87, 17.14	9.73, 16.06	8.74, 15.21
Median	14.50	12.50	12.50	10.50
Range	-35.50, 75.00	-56.25, 81.25	-56.25, 87.50	-56.25, 100.00
<b>Distance Activities</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	17.37 (19.60)	15.29 (20.10)	15.29 (20.68)	13.36 (20.97)
95% confidence interval for mean*	14.63, 20.11	12.48, 18.09	12.38, 18.20	10.38, 16.34
Median	16.50	13.75	12.50	12.50
Range	-21.00, 87.50	-33.50, 66.75	-33.50, 71.00	-33.50, 100.00
<b>Near Activities</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	21.75 (21.55)	20.92 (22.22)	18.30 (23.10)	17.01 (22.27)
95% confidence interval for mean*	18.74, 24.76	17.82, 24.02	15.05, 21.55	13.85, 20.17
Median	20.75	20.75	20.00	16.50
Range	-40.00, 85.75	-35.00, 81.75	-54.25, 80.75	-46.00, 91.50
<b>Total</b>	<b>N = 199</b>	<b>N = 200</b>	<b>N = 196</b>	<b>N = 193</b>
Mean (SD)	18.49 (18.40)	16.99 (19.10)	15.82 (19.77)	14.15 (19.63)
95% confidence interval for mean*	15.91, 21.06	14.32, 19.65	13.04, 18.61	11.37, 16.94
Median	18.75	16.88	14.88	12.50
Range	-25.00, 76.75	-35.50, 68.75	-35.50, 69.75	-34.75, 81.25
n & % of eyes with increase ≥10 points	134 ( 67.3%)	128 ( 64.0%)	113 ( 57.7%)	110 ( 57.0%)
95% confidence interval for %*	60.3%, 73.8%	56.9%, 70.6%	50.4%, 64.7%	49.7%, 64.1%

N = number of treated eyes returned for the visit with a non-missing change in ADL assessment. Records after device removal were excluded.

Per protocol, ADL was performed at baseline, and the 1, 3, 6, 9, and 12 months follow-up visits.

\* Normal distribution approach was used for mean. CI for % was calculated based on Clopper Pearson method.

Statistical analyses revealed a statistically significant relationship between change in VFQ-25 composite score and change in ADL total score at each postoperative examination (p < 0.0001 at 3, 6, 9 and 12 month).

**d. Adverse Events**

Ocular adverse events reported for all eyes implanted with an AMD device are shown in Table 9-7 respectively for all regularly scheduled visits, including subject visits following AMD implant removal, and for all unscheduled interim visits. The cumulative incidence of each adverse event is displayed in Table 9-7.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

**TABLE 9-7**  
**REPORTED OCULAR ADVERSE EVENTS**  
**ALL AMD DEVICE IMPLANTED EYES**

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Adverse Events	Operative N = 206	Day 1 N = 206	Day 7 N = 205	1 Month N = 206	3 Months N = 201	6 Months N = 202	9 Months N = 196	12 Months N = 194	18 Months N = 180	24 Months N = 148	Interim N = 109	Cumulative N = 206
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)
Anterior chamber inflammation > 30 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 1.5%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.0%)	3 ( 1.7%)	0 ( 0.0%)	3 ( 2.8%)	6 ( 2.9%)
Anterior ischemic optic neuropathy	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	1 ( 0.5%)
Choroidal neovascularization	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)	2 ( 1.0%)	1 ( 0.5%)	2 ( 1.1%)	2 ( 1.4%)	0 ( 0.0%)	5 ( 2.4%)
Conjunctivitis	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 2.8%)	4 ( 1.9%)
Corneal decompensation > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)	2 ( 1.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)
Corneal edema > 30 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 2.0%)	2 ( 1.8%)	6 ( 2.9%)
Cyclitic membrane > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Cystoid macular edema	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Decrease in visual acuity	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.1%)	3 ( 2.0%)	2 ( 1.8%)	4 ( 1.9%)
Device failure	1 ( 0.5%)	2 ( 1.0%)	2 ( 1.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)
Diplopia	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.0%)	2 ( 1.0%)	1 ( 0.6%)	1 ( 0.7%)	2 ( 1.8%)	3 ( 1.5%)
Distorted pupil	0 ( 0.0%)	1 ( 0.5%)	3 ( 1.5%)	3 ( 1.5%)	3 ( 1.5%)	5 ( 2.5%)	4 ( 2.0%)	4 ( 2.1%)	4 ( 2.2%)	2 ( 1.4%)	3 ( 2.8%)	7 ( 3.4%)
Dry eye	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	2 ( 1.0%)	2 ( 1.0%)	6 ( 3.1%)	4 ( 2.1%)	3 ( 1.7%)	1 ( 0.7%)	4 ( 3.7%)	10 ( 4.9%)
Entropion	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	3 ( 1.5%)
Exposed suture	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 2.8%)	3 ( 1.5%)
Eye pain	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)	2 ( 1.0%)	1 ( 0.6%)	1 ( 0.7%)	3 ( 2.8%)	3 ( 1.5%)
Flat anterior chamber > 21 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.6%)	1 ( 0.7%)	0 ( 0.0%)	1 ( 0.5%)
Floater	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.6%)	1 ( 0.7%)	1 ( 0.9%)	2 ( 1.0%)
Focal striae	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Foreign body sensation	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	2 ( 1.0%)	4 ( 2.0%)	4 ( 2.0%)	4 ( 2.1%)	4 ( 2.2%)	1 ( 0.7%)	7 ( 6.4%)	9 ( 4.4%)
Guttae	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	7 ( 3.5%)	8 ( 4.1%)	13 ( 6.7%)	11 ( 6.1%)	9 ( 6.1%)	3 ( 2.8%)	16 ( 7.8%)
AMD device dislocation	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)	2 ( 1.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	2 ( 1.0%)
AMD device removal	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	8 ( 7.3%)	8 ( 3.9%)
AMD device replacement	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	1 ( 0.5%)
Increased IOP requiring treatment > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	5 ( 2.4%)	2 ( 1.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.6%)	2 ( 1.4%)	3 ( 2.8%)	7 ( 3.4%)

% = n/N x100.

The same adverse event could have been reported for a subject at multiple visits.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

**TABLE 9-7 (CONTINUED)**  
**REPORTED OCULAR ADVERSE EVENTS**  
**ALL AMD DEVICE IMPLANTED EYES**

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Adverse Events	Operative	Day 1	Day 7	1 Month	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months	Interim	Cumulative
	N = 206	N = 206	N = 205	N = 206	N = 201	N = 202	N = 196	N = 194	N = 180	N = 148	N = 109	N = 206
	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)	n (%)					
Inflammatory deposits on AMD device	0 ( 0.0%)	2 ( 1.0%)	9 ( 4.4%)	2 ( 1.0%)	5 ( 2.5%)	18 ( 8.9%)	21 ( 10.7%)	25 ( 12.9%)	24 ( 13.3%)	10 ( 6.8%)	6 ( 5.5%)	51 ( 24.8%)
Inflammatory membrane	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.6%)	1 ( 0.7%)	1 ( 0.9%)	1 ( 0.5%)
Iridotomy > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.6%)	0 ( 0.0%)	1 ( 0.9%)	3 ( 1.5%)
Iris atrophy > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	4 ( 1.9%)	4 ( 2.0%)	4 ( 2.0%)	3 ( 1.5%)	6 ( 3.1%)	7 ( 3.9%)	7 ( 4.7%)	2 ( 1.8%)	7 ( 3.4%)
Iris transillumination defects > 21 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	5 ( 2.4%)	9 ( 4.5%)	9 ( 4.5%)	9 ( 4.6%)	8 ( 4.1%)	8 ( 4.4%)	6 ( 4.1%)	2 ( 1.8%)	11 ( 5.3%)
Iritis > 30 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 1.5%)	2 ( 1.0%)	1 ( 0.5%)	0 ( 0.0%)	4 ( 2.2%)	1 ( 0.7%)	7 ( 6.4%)	12 ( 5.8%)
Keratic precipitates on AMD device > 30 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.7%)	1 ( 0.9%)	2 ( 1.0%)
Obstructed iridectomy	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Ocular allergy	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	1 ( 0.5%)
Pigment deposits on AMD device	0 ( 0.0%)	1 ( 0.5%)	2 ( 1.0%)	1 ( 0.5%)	3 ( 1.5%)	4 ( 2.0%)	12 ( 6.1%)	12 ( 6.2%)	13 ( 7.2%)	7 ( 4.7%)	4 ( 3.7%)	23 ( 11.2%)
Pigment epithelium around the peripheral iridectomy > 30 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Posterior synechiae	0 ( 0.0%)	0 ( 0.0%)	4 ( 2.0%)	4 ( 1.9%)	7 ( 3.5%)	9 ( 4.5%)	8 ( 4.1%)	8 ( 4.1%)	7 ( 3.9%)	4 ( 2.7%)	4 ( 3.7%)	15 ( 7.3%)
Ptosis	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.6%)	0 ( 0.0%)	1 ( 0.9%)	2 ( 1.0%)
Secondary glaucoma	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.0%)
Subconjunctival hemorrhage	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	6 ( 5.5%)	9 ( 4.4%)
Subretinal hemorrhage	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.6%)	1 ( 0.7%)	1 ( 0.9%)	3 ( 1.5%)
Synechiae	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.5%)	1 ( 0.6%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Tearing	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	1 ( 0.5%)
Visual disturbance	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	1 ( 0.5%)
Vitreous flare	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)
Vitreous hemorrhage > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	2 ( 1.8%)	3 ( 1.5%)
Vitreous in anterior chamber > 7 days	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	3 ( 1.5%)	1 ( 0.5%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	0 ( 0.0%)	1 ( 0.9%)	4 ( 1.9%)

% = n/N x100.

The same adverse event could have been reported for a subject at multiple visits.

**e. Endothelial Cell Density**

To evaluate change in endothelial cell density over time, specular microscopy was performed preoperatively and at the Month 3, 6, 9, 12, 18 and 24 examinations in both the operated eyes and fellow eyes. Three images were obtained at each visit and sent to a central reading center for analysis.

The following common sources of variability in specular microscopy were identified in the study protocol, a priori:

- difficulty in returning to same location on the cornea at each visit;
- poor image quality (less than 100 countable cells); and
- technician error

Table 9-8 shows ECD for all AMD device implanted eyes. Variability in ECD data increased sharply after baseline. This is likely a result of patient-to-patient variability in endothelial cell loss as well as the difficulty in obtaining high-quality specular images in AMD device-implanted eyes.

**TABLE 9-8**  
**ENDOTHELIAL CELL DENSITY (ECD)**  
**ALL AMD DEVICE IMPLANTED EYES**

<b>ECD</b>	<b>Preop</b>	<b>3 Months</b>	<b>6 Months</b>	<b>9 Months</b>	<b>12 Months</b>	<b>18 Months</b>	<b>24 Months</b>
N	206	192	198	190	186	180	144
Mean	2496.13	1996.87	1936.83	1890.82	1871.29	1878.11	1786.36
Standard Deviation	354.33	585.92	579.73	572.29	592.09	618.22	602.61
Median	2510.0	2026.3	2017.8	1938.8	1929.5	1977.5	1860.0
Range	1695.0, 3356.0	432.3, 3125.7	385.3, 2935.7	309.0, 3008.0	310.7, 2959.0	351.0, 2900.0	385.7, 2930.0

N = number of successful device implanted eyes returned for the visit with non-missing ECD.

% =  $n \div N \times 100$

Table 9-9 shows the percentage change in ECD from baseline for all implanted eyes.

SUMMARY OF SAFETY AND EFFECTIVENESS DATA

**TABLE 9-9**  
**PERCENTAGE CHANGE IN ENDOTHELIAL CELL DENSITY (ECD) FROM BASELINE**  
**ALL AMD DEVICE IMPLANTED EYES**

ECD % Change from Baseline	3 Months	6 Months	9 Months	12 Months	18 Months	24 Months
N	192	198	190	186	180	144
Mean	-20.0%	-22.4%	-24.4%	-25.3%	-25.2%	-28.2%
Standard Deviation	21.1%	20.9%	20.5%	21.3%	22.2%	22.5%
90% confidence interval for mean	-22.5%, -17.5%	-24.8%, -19.9%	-26.9%, -22.0%	-27.9%, -22.7%	-28.0%, -22.5%	-31.3%, -25.1%
Median	-13.0%	-17.0%	-19.2%	-20.9%	-21.3%	-24.2%
Range	-85.1%, 18.0%	-84.4%, 30.9%	-87.5%, 13.5%	-87.6%, 12.7%	-87.9%, 25.1%	-80.9%, 28.1%

N = number of successful device implanted eyes returned for the visit with non-missing ECD change from baseline.

Percentage change in ECD from baseline = (postop - baseline) ÷ baseline × 100.

% = n ÷ N × 100

Extensive statistical analyses showed that the most significant loss in ECD was observed from baseline to 3 months in the study cohort, with ECD loss tapering off after 3 months and stabilizing at the 9 month visit

Since the most significant loss in ECD occurred at 3 months, factors that may have contributed to early cell loss were evaluated. The final model identified that Day 1 corneal edema and surgeon specialty are the two factors that appear to affect the mean change in ECD from baseline to 3 months.

As shown in Table 9-10, based on the least square estimation, AMD device implanted eyes reported with normal cornea or 1+ corneal edema at postoperative Day 1 had a smaller mean percentage loss in ECD at 3 months than those with ≥ 2+ corneal edema on postoperative Day 1 (12.7% versus 35.2%; p<0.0001). Furthermore, study subjects implanted by cornea specialists had less endothelial cell loss at 3 months than non-cornea specialists (20.7% versus 27.2%; p=0.0336).

**TABLE 9-10**  
**ECD PERCENTAGE CHANGE AT 3 MONTHS FROM BASELINE**  
**MODELING ANALYSES — FINAL MODEL**  
**ALL AMD DEVICE IMPLANTED EYES & ECD CHANGE AT 3 MONTHS**

Factor Level	Least Square Means 95% CI	Comparison	P-value*
<b>Day-1 Corneal Edema</b>			
Normal/1+Edema	-12.74% (-15.97%, -9.51)	Normal/1+Edema vs. ≥2+Edema	<.0001
≥2+Edema	-35.18% (-40.76%, -29.61)		
<b>Surgeon's Specialty</b>			
Corneal	-20.72% (-26.23%, -15.21)	Corneal vs. Non-corneal	0.0336
Non-corneal	-27.20% (-30.48%, -23.93)		

\* Type III analysis of ANOVA for Day-1 Corneal Edema and Surgeon's Specialty.

The annual ECD percentage change was calculated for the 188 AMD device implanted eyes with at least one postoperative ECD percentage change at 9 months or later, the mean annual percent change in ECD from 9 months to 24 months is -0.5% (S.D. 28.6%; 90% CI -4.0% to 2.9%). The annual ECD percentage change for the 24-month consistent cohort, which consists of 130 AMD device implanted eyes, was -3.0% (S.D. 15.0%).

In order to compare the change in ECD after 3 months in the study cohort to a clinically relevant control group, the percentage change in ECD in pseudophakic fellow eyes was calculated. As would be anticipated, the change in ECD between visits in the pseudophakic fellow eyes was similar to that observed in the AMD implanted eyes.

**f. Replacements and AMD Device Failures**

The AMD implant was removed from eight eyes postoperatively after the initial implantation procedure. Four subjects requested removal of the AMD implant since they were dissatisfied with the device. The AMD device was also removed from two eyes due to condensation of the telescope portion of the AMD implant, and in two eyes that underwent corneal transplantation as a result of corneal decompensation.

A total of four AMD device failures have been reported in this 24-month study. Two failures involved a broken haptic, one case occurred prior to implantation and one occurred during implantation, requiring intraoperative AMD device replacement (see Table 9-7). The two other device failures consisted of condensation in the telescope portion of the AMD device, and resulted in postoperative AMD implant removal (see previous paragraph).

**X. CONCLUSIONS DRAWN FROM THE STUDIES**

The data in this application provides reasonable assurance that the AMD device is safe and effective when used in accordance with the directions for use.

**XI. 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 referred to the Ophthalmic Device Panel, and FDA advisory committee, for review of valid scientific evidence to provide reasonable assurance of the safety and effectiveness of the AMD implant under the prescribed indications for use.

**XII. CDRH DECISION**

CDRH issued an approval order on \_\_\_\_\_, 2006. The applicant's manufacturing facility was inspected on \_\_\_\_\_, 2005 and was found to be in compliance with the medical device Quality System Regulation.

**XIII. 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 labeling.

Post-approval requirements and restrictions: See Approval Order