SUMMARY OF SAFETY AND EFFECTIVENESS (SSED)

I. GENERAL INFORMATION

Device Generic Name: Monofocal Posterior Chamber Foldable Intraocular Lens (IOL)

Device Trade Name: The Advanced Vision Science (AVS), Inc. XACT® Foldable Hydrophobic Acrylic Ultraviolet (UV) Light-Absorbing Posterior Chamber Intraocular Lens (IOL), [Model X-60 and Model X-70]

Applicant's Name and Address: Advanced Vision Science Inc.
5743 Thornwood Drive
Goleta, CA 93117

Date of Panel Recommendation: Not Applicable

Premarket Approval Application (PMA) Number: P080021

Date of FDA Notice of Approval: February 02, 2009

Expedited: Not Applicable

II. INDICATIONS FOR USE

The Advanced Vision Science (AVS), Inc. XACT® Foldable Hydrophobic UV Light-Absorbing Posterior Chamber Intraocular Lens is indicated for primary implantation for the visual correction of aphakia in adult patients in whom the cataractous lens has been removed by an extracapsular cataract extraction method. The lens is intended for placement in the capsular bag.

III. CONTRAINDICATIONS

None Known

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions for the XACT® Foldable Hydrophobic UV Light-Absorbing Posterior Chamber Intraocular Lens can be found in the instructions for use packaged with the device.

V. DEVICE DESCRIPTION

The AVS, Inc. XACT® Foldable Hydrophobic UV Light-Absorbing Posterior Chamber Intraocular Lens (IOL), is a three-piece foldable acrylic posterior chamber intraocular lens with a biconvex optic made from a proprietary high refractive index soft acrylic material, allowing the device to be folded and inserted though an incision smaller than

of the optic. The supporting haptics are made from polyvinylidene fluoride (PVDF) monofilament.

Model X-60 has a 6.0 mm optic and an overall diameter of 12.75 mm.
Model X-70 has a 7.0 mm optic and an overall diameter of 13.2 mm.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

There are several other alternatives for the correction of aphakia after cataract surgery. Each alternative has its own advantages and disadvantages. A patient should fully discuss these alternatives with his/her physician to select the method that best meets expectations and lifestyle.

1. Other approved IOLs may be used for visual correction after cataract surgery.
2. The following are non-surgical alternatives to implantation of an intraocular lens following cataract extraction:
   i. Spectacles: Spectacles, or eyeglasses, are the safest means for improving vision after cataract surgery. However, they are rarely used after modern cataract surgery as the lenses are required to be thick, which causes distorted vision and may be uncomfortable or cosmetically unappealing to the patient.
   ii. Contact lenses: Contact lenses are rarely prescribed for patients after cataract extraction, although they may provide excellent vision. Contact lenses have risks associated with their use including infection.

VII. MARKETING HISTORY

The XACT® Foldable Hydrophobic UV Light-Absorbing Posterior Chamber IOL, is approved for distribution in the European Union (CE Marked) and in Japan. The device has not been withdrawn from any market for reasons relating to the safety and effectiveness of the device, or for any other reason.

Several cases of toxic anterior segment syndrome (TASS) (8 eyes) were associated with implantation of the AVS IOL in Europe. Manufacturing changes and supplemental endotoxin testing were implemented to prevent endotoxin contamination, which was believed to be the source of the clinically observed inflammation.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

Potential adverse events and complications accompanying cataract or implant surgery may include, but are not limited to the following: corneal endothelial damage, infection (including endophthalmitis), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, cyclitic membrane, iris prolapse, hypopyon, transient or persistent glaucoma, acute corneal decompensation, TASS, and secondary surgical intervention.

Secondary surgical interventions include, but are not limited to, lens repositioning (due to decentration, subluxation, or corneal touch), lens exchange (due to residual refractive

error or severe inflammation), vitreous aspirations or iridectomy for pupillary block, wound leak repair, retinal detachment repair, and corneal transplantation.

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

IX. SUMMARY OF PRECLINICAL STUDIES

Optical and Mechanical Testing

Optical and mechanical testing has been performed on the AVS XACT® Foldable IOL in accordance with ISO 11979-2 and ISO 11979-3, respectively.

TABLE 1: OPTICAL AND MECHANICAL TESTING

LABORATORY TESTING	RESULT
Optical Testing	
Dioptric power	Pass
Image quality	Acceptable
Spectral transmittance	Acceptable
Mechanical Testing	
Dimensions	Acceptable
Optic decentration	Pass
Optic tilt	Pass
Dynamic fatigue durability	Pass
Fold/recovery test	Acceptable
Surface and bulk homogeneity	Acceptable

Biocompatibility Testing

The biocompatibility of the AVS XACT® Foldable IOL lens materials was evaluated in a battery of *in vivo* and *in vitro* acute and chronic toxicity tests. Biocompatibility testing was performed in accordance with ISO 11979-5, and the relevant sections of ISO 10993.

TABLE 2: BIOCOMPATIBILITY TESTING

TEST	RESULTS
OPTIC MATERIAL	
Cytotoxicity	
Agarose Overlay Method (Solid)	No significant cell lysis or toxicity; slightly cytotoxic
Agarose Overlay Method (Extraction – Saline)	No cell lysis or toxicity; Non-cytotoxic
Agarose Overlay Method (Extraction - Cottonseed Oil)	No cell lysis or toxicity; Non-cytotoxic
Inhibition of Cell Growth (One Point)	Non-inhibitory
MEM Elution Method	No cell lysis or toxicity; Non-cytotoxic
Sensitization Test in Guinea Pigs (Maximization)	No evidence of delayed dermal contact sensitization; Non-sensitizing
Muscle Implantation Study (30 days)	No significant macroscopic reaction; Non-irritating
Genotoxicity	
Ames Mutagenicity (Saline and DMSO Extracts)	No mutagenic changes induced in *S. typhimurium*; Non-mutagenic
Chromosome Aberrations (Extraction)	No aberrations induced in human lymphocytes in culture; Non-genotoxic
Mouse Bone Marrow Micronucleus Study	No micronuclei present in mouse bone marrow cells; Non-genotoxic
HAPTIC MATERIAL	
Cytotoxicity	
ISO Agarose Overlay Method (Solid)	No cell lysis or toxicity; Non-cytotoxic
ISO Agarose Overlay Method (Extraction – MEM)	No cell lysis or toxicity; Non-cytotoxic
ISO Sensitization Test in Guinea Pigs (Maximization)	No evidence of delayed dermal contact sensitization; Non-sensitizing
Genotoxicity	
Ames Mutagenicity (Saline and DMSO Extracts)	No mutagenic changes induced in *S. typhimurium*; Non-mutagenic

Chromosome Aberrations (Extraction)	No aberrations induced in human lymphocytes in culture; Non-genotoxic
Mouse Bone Marrow Micronucleus Study	No micronuclei present in mouse bone marrow cells; Non-genotoxic
COMPLETE IOL	
Intraocular Implant Study (1 year)	No signs of significant irritation or toxicity to ocular tissues; well-tolerated and biocompatible
Extracts from Nd:YAG Laser Compatibility Test	No cell lysis or toxicity; Non-cytotoxic
Extractables and Hydrolytic Stability	No significant extractables
Photostability	No significant residual extracted
Insoluble inorganic residuals (for residual alumina determination)	Acceptable level of residual alumina

Sterilization, Packaging, Shelf-Life and Transport Stability

Sterilization, packaging, shelf life and transport testing were performed to establish the microbiological profile for the AVS XACT® Foldable IOL. Testing performed and study results are summarized in Table 3.

TABLE 3: STERILIZATION, PACKAGING, SHELF-LIFE AND TRANSPORT STABILITY

STERILIZATION VALIDATION	TEST RESULTS
The product is sterilized by gamma irradiation. Sterilization dose was set and the dosage validated in accordance with ANSI/AAMI/ISO 11137:1995 *Sterilization of Healthcare Products – Requirements for Validation and Routine Control – Radiation Sterilization (Method 1).*	All test samples from the validation were sterile, demonstrating that the sterilization process delivers a minimum Sterility Assurance Level (SAL) of $10.^{-6}$ Acceptability of the sterilization dose is verified by quarterly dose audit.
Bacteriostasis/fungistasis	No bacteriostatic or fungistatic characteristics
Bacterial endotoxin testing	Endotoxin levels are below the limits for implantable medical devices, in accordance with the USP.
PACKAGE INTEGRITY TESTS	**TEST RESULTS**
Distribution/shipping simulation (stress test)	Test results are acceptable.
Bubble leak test (whole package integrity) Testing was performed in accordance with ASTM F 2096-01, "*Standard test method for detecting gross leaks in porous medical packaging by internal pressurization (Bubble test)*"	Test results are acceptable.

Seal integrity test Testing was performed in accordance with ASTM F 88-00, *"Seal Strength of flexible barrier materials"*, and	Test results are acceptable.
SHELF LIFE AND TRANSPORT STABILITY	**TEST RESULTS**
Aging studies Testing is performed in accordance with ISO 11979-6, *"Ophthalmic Implants- Intraocular lenses –Part 6: Shelf life and transport stability"*	Test results support a 36 month shelf-life.

Conclusions:
The overall results of the preclinical tests were acceptable from biocompatible, physiochemical, optical, mechanical and microbiological perspectives.

X. SUMMARY OF PRIMARY CLINICAL STUDIES

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of the XACT® Foldable Hydrophobic Acrylic IOL (Model X-60) for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed, in the U.S. under IDE # G020048. The Model X-70 is a minor design modification of the Model X-60 (i.e., the optic and overall diameters are slightly different), and was therefore not studied in the clinical study. Data from this clinical study, along with two other studies, one performed in Japan and one the Dominican Republic and Germany were the basis for the PMA approval decision. A summary of the clinical studies is presented below.

U.S. IDE Study

A. Study Design

Patient enrollment into the pivotal clinical trial was initiated in May 2002, with the first IOL implanted on May 5, 2002; Enrollment was completed on April 25, 2005, with the last lens implantation. The last patient was seen on February 28, 2008 for the 3-year visit, and the final database lock was on December 30, 2008. There were 14 investigational sites.

The study was a prospective, multi-center, one-arm, non-randomized, open label, clinical study. Patients were followed for three years, but primary analysis of major endpoints took place at one year postoperatively. Results were compared to literature controls, namely the "FDA Grid" of cataract surgery results, published in ISO 11979-7 (2006) to determine if statistically significant differences existed. A binomial exact test was used to compare the observed effectiveness rate and observed adverse event rates against the "FDA Grid." The level of significance for all statistical evaluations was $p = 0.05$.

Therefore, any comparisons of the study data to the literature controls in which the level of significance was less than or equal to 0.05 were considered statistically significant.

1. Clinical Inclusion and Exclusion Criteria
   Enrollment in the IDE study, G020048, was limited to patients who met the following inclusion/exclusion criteria.

   a. Inclusion Criteria
      i. Undergoing primary intraocular lens implantation for the correction of aphakia following cataract extraction by an extracapsular method (e.g., small incision phacoemulsification).
      ii. At least 40 years of age at the time of cataract surgery.
      iii. Able and willing to sign a written Informed Consent form.
      iv. Able to return for scheduled follow-up examinations.

   b. Exclusion Criteria
      i. Any anterior segment pathology (chronic uveitis, iritis, iridocyclitis, rubeosis iridis, corneal dystrophy, etc.) in the operative eye.
      ii. Uncontrolled glaucoma or under current treatment for glaucoma in either eye.
      iii. Previous retinal detachment or retinal pathology in the operative eye.
      iv. Proliferative diabetic retinopathy in either eye.
      v. Congenital bilateral cataracts.
      vi. Marked microphthalmos or aniridia in either eye.
      vii. Only one eye with potentially good vision.
      viii. Previous ocular surgery in the operative eye.
      ix. Previously received an AVS Foldable IOL in the fellow eye.
      x. Poorly dilated pupil in the operative eye.
      xi. Participation in a concurrent clinical trial, or participated in a clinical trial within 30 days prior to the date of cataract surgery.
      xii. More than 1.5 diopters of corneal astigmatism.
      xiii. Any other serious ocular pathology, serious ocular complications at the time of cataract extraction, or underlying serious medical conditions, based on the investigator's medical judgment.

2. Follow-up Schedule
   All patients were scheduled to return for postoperative follow-up examinations as shown below. Preoperatively, patients scheduled to undergo cataract extraction and intraocular lens implantations were screened for eligibility, and eligible patients were evaluated to obtain a medical history and to establish a baseline for ocular condition. Postoperatively, patients underwent a complete ophthalmic evaluation at regularly scheduled intervals to assess the condition of their eyes and visual function for 12 months after their cataract surgery. Adverse events and complications were recorded at all visits. Clinical evaluations included distance best corrected visual acuity (BCVA), manifest refraction, intraocular pressure

measurements, and slit-lamp ophthalmic evaluations to determine adverse events or postoperative complications.

i.	(Form P)	Preoperative Exam
ii.	(Form O)	Operative Report
iii.	(Form 1)	Postoperative days 1-2
iv.	(Form 2)	Postoperative days 7-14
v.	(Form 3)	Postoperative days 30-60
vi.	(Form 4)	Postoperative days 120-180
vii.	(Form 5)	Postoperative days 330-420
viii.	(Form 6)	Postoperative days 695-795
ix.	(Form 7)	Postoperative days 1060-1130

3. Clinical Endpoints

With regards to safety, the primary endpoint was the incidence of adverse events (as defined by the "FDA Grid") evaluated at one year postoperatively.

With regards to effectiveness, the primary endpoint was the percentage of patients (overall and best case) achieving best corrected distance visual acuity of 20/40 or better at one year.

With regard to study success, these rates (for both safety and effectiveness endpoints) were compared to those in the "FDA Grid."

B. Accountability of PMA Cohort

The study was conducted at 14 geographically diverse investigational sites in the United States. A total of 383 patients were implanted and 367 patients were examined at one year, the protocol-defined time of evaluation for safety and effectiveness endpoints. For this study, there is only one dataset of patients to analyze: "all patients enrolled." Only unilateral implantation was performed, so the number of patients and eyes are the same. The number of patients enrolled and "attempt-to-treat patients" are the same. At one year ten patients were discontinued due to death, voluntary withdrawal or other assignable causes. Two patients were missing but were seen at a later visit. Four patients were lost to follow-up.

At two and three years, 312 and 281 patients were examined, respectively.

TABLE 4
ACCOUNTABILITY BY VISIT: ALL PATIENTS ENROLLED

Total Patients (N) = 383		Form 1	Form 2	Form 3	Form 4	Form 5	Form 6	Form 7
Available for Analysis	**n/N (%)**	380/383 (99.2%)	381/383 (99.5%)	381/383 (99.5%)	375/383 (97.9%)	367/383 (95.8%)	312/383 (81.5%)	281/383 (73.4%)
Discontinued[1]	**n/N (%)**	1/383 (0.3%)	1/383 (0.3%)	1/383 (0.3%)	3/383 (0.8%)	10/383 (2.6%)	15/383 (3.9%)	22/383 (5.7%)
Deceased	**n/N (%)**	1/383 (0.3%)	1/383 (0.3%)	1/383 (0.3%)	3/383 (0.8%)	9/383 (2.3%)	14/383 (3.7%)	19/383 (5.0%)
Explant	**n/N (%)**	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	1/383 (0.3%)	1/383 (0.3%)	3/383 (0.8%)
Active (Not yet eligible for the interval)	**n/N (%)**	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)
Lost to Follow-up[2]	**n/N (%)**	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	1/383 (0.3%)	4/383 (1.0%)	28/383 (7.3%)	53/383 (13.8%)
Missed Visit[3]	**n/N (%)**	2/383 (0.5%)	1/383 (0.3%)	1/383 (0.3%)	4/383 (1.0%)	2/383 (0.5%)	1/383 (0.3%)	0/383 (0.0%)
Completed Per Protocol[4]	**n/N (%)**	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	0/383 (0.0%)	27/383 (7.0%)	27/383 (7.0%)
% Accountability = Available for Analysis ÷ (Enrolled - Discontinued - Not yet eligible - Completed per protocol)		380/382 (99.5%)	381/382 (99.7%)	381/382 (99.7%)	375/380 (98.7%)	367/373 (98.4%)	312/341 (91.5%)	281/334 (84.1%)

N = Total number of patients enrolled.

1 Discontinued = Exited due to explant (n = 3), or death (n = 19).

2 Lost to follow-up: Eyes were not examined at the Form-7 visit, and were not considered active or discontinued.

3 Missed visit: Eyes were not examined at the scheduled visit, however, were examined or may have been examined at a subsequent visit. It should be noted that, since the study is still on-going, the Missed Visit row includes records which have not been entered in the database. These records will be updated in the next report.

4 Patients completed the study and were exited from the study per study protocol prior to the protocol amendment.

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an intraocular lens study performed in the U.S. The inclusion/exclusion criteria for the clinical trial did not include criteria for selecting patients on the basis of gender or race, or gender or race-related pathologies. All willing patients meeting the inclusion/exclusion criteria were included in the study.

Females comprised 60.3% percent of the patients enrolled. At the time of surgery, 11.2% of patients were less than 60 years old; 27.2% were 60 to 69 years old; 46.2% were 70 to 79 years old and 15.4% were at least 80 years old. Caucasians comprised 97.4% of the study population; 2.1% were African American and 0.5% were Hispanic.

TABLE 5
DEMOGRAPHICS

	n	%
Number of Patients	383	100.0%
Gender		
Male	152	39.7%
Female	231	60.3%
Race		
Black	8	2.1%
Caucasian	373	97.4%
Hispanic	2	0.5%
Age		
< 60	43	11.2%
60 to <70	105	27.2%
70 to <80	177	46.2%
≥ 80	58	15.4%
Mean ± SD	71.0 (9.11)	
Range (Min , Max)	45, 93	

D. Safety and Effectiveness Results

1. Safety Results

The primary safety analysis was based on the 383 enrolled patients (1 patient died 1 day post surgery and was excluded from analysis) and the 367 patients available at the one year postoperative evaluation. Sight threatening adverse events are defined and categorized by the "FDA Grid" [published in ISO 11979-7 (2006)] as either cumulative (occurring at any time up to one year) and persistent (present at one year). The key safety outcomes for this study are presented below in Table 3. The rates of FDA defined adverse events that occurred in the clinical trial at 1 year were compared to the "FDA Grid" of Historical Controls and were found to be less, except for the rate for retinal detachment. The observed retinal detachment rate was not greater than the "FDA Grid" rate at a level that was statistically significant ($p = 0.105$).

Adverse effects that occurred in the PMA clinical study:

No historical control exists for FDA defined adverse events which occur after one year; however, the rates of FDA defined adverse events that occurred in the clinical trial after one year were evaluated and found to be acceptably low.

TABLE 6
FDA DEFINED CUMULATIVE AND PERSISTENT ADVERSE EVENTS

Adverse Events	1 Year		FDA Grid 1 Year	2 Years		3 Years	
Cumulative Safety Events Number of Eyes with Postop Visits=382	n/N[1-3]	%	%	n/N[1-2,4]	%	n/N[1-2,5]	%
Endophthalmitis	0/382	0.0%	0.1%	0/382	0.0%	0/382	0.0%
Hyphema	0/382	0.0%	2.2%	0/382	0.0%	0/382	0.0%
Hypopyon	0/382	0.0%	0.3%	0/382	0.0%	0/382	0.0%
IOL Dislocation	0/382	0.0%	0.1%	0/382	0.0%	0/382	0.0%
Cystoid Macular Edema	3/376	0.8%	3.0%	3/377	0.8%	3/377	0.8%
Pupillary Block	0/382	0.0%	0.1%	0/382	0.0%	0/382	0.0%
Retinal Detachment	3/376	0.8%	0.3%	4/377	1.1%	4/377	1.1%
Secondary Surgical Intervention	1/382[6]	0.3%	0.8%	1/382	0.3%	3/382[7,8]	0.8%
Persistent Safety Events	n/N[1-3]	%	%	n/N[1-2,4]	%	n/N[1-2,5]	%
Number of Eyes Available at the Visit	367			312		281	
Corneal Edema	0/366	0.0%	0.3%	0/312	0.0%	0/281	0.0%
Iritis	1/366	0.3%	0.3%	0/312	0.0%	0/281	0.0%
Cystoid Macular Edema	0/364	0.0%	0.5%	0/309	0.0%	0/280	0.0%
Raised IOP Requiring Treatment	0/366	0.0%	0.4%	0/312	0.0%	0/281	0.0%

[1]n = number of eyes reported with the corresponding event. For cumulative event, N = number of implanted eyes. For persistent event, N = number of eyes returned for the corresponding examination with non-missing response for the corresponding adverse event. A patient could be reported with more than one AE.
[2]One patient died one day post surgery and was excluded from analysis.
[3]For 6 patients, case report form fields were not completed for cystoid macular edema and retinal detachment at or before one year; these 6 patients were excluded from the cumulative calculation for these adverse events. For 1 patient, case report form fields were not completed for corneal edema and iritis at one year; this patient was excluded from the persistent calculation for these adverse events. Three patients did not have case report form fields completed for cystoid macular edema at one year and were excluded from the persistent calculation for this adverse event. One patient did not have the case report form fields completed for corneal edema, iritis, and raised IOP requiring treatment at one year and was excluded from the persistent calculation for this adverse event.
[4]Five patients did not have case report form fields completed for cystoid macular edema and retinal detachment at or before two years and were excluded from the cumulative calculation for these adverse events. Three patients did not have case report form fields completed for cystoid macular edema at two years and were excluded from the persistent calculation for this event.
[5]Five patients did not have case report form fields completed for cystoid macular edema and retinal detachment at or before three years and were excluded from the cumulative calculation for these adverse events. One patient did not have a case report form field completed for cystoid macular edema at three years and was excluded from the persistent calculation for this event.
[6]IOL was exchanged due to patient complaint of blurred vision, despite good BCVA. Investigator suspected glistenings might be related, however only modest improvement of vision was achieved after IOL exchange.
[7]IOL with glistenings was exchanged during retinal surgery to improve fundus visualization by the surgeon. Loss of vision was the result of retinal pathology and was not associated with the IOL.
[8]IOL was exchanged due to patient complaint of blurred vision. Investigator suspected glistenings might be related, however vision did not improve after IOL exchange. Since vision did improve after subsequent Nd:Yag capsulotomy, the complaint of blurred vision was not associated with the IOL.

Other Findings

In the IDE clinical trial, "glistenings" were observed in some cases. Glistenings, known to sometimes occur in some other hydrophobic acrylic IOLs, are microscopic vacuoles within the optic of the IOL that are visible through the slit lamp as multiple small refractile specks. Analysis of Japanese (see below) and US clinical data found no significant correlation with visual function.

The AVS IOL was originally hydrated and packaged in a solution of 10.0% saline. After implantation the osmotic differential between the IOL and aqueous humor could cause water to be absorbed into the IOL optic creating points of refractive index differential at the water/polymer interface, resulting in the appearance of glistenings. The manufacturer changed the hydration and packaging solution to 0.9% saline to eliminate this effect.

Testing established that glistenings were eliminated by a change in the IOL hydration solution from 10.0% saline to 0.9% saline. This was confirmed in an additional clinical trial conducted in the Dominican Republic and Germany (see below).

2. Effectiveness Results

The primary safety analysis was based on the 367 patients with best corrected visual acuity measurements available at the one year postoperative evaluation. Nearly all (98.9%) patients implanted with the device and examined at one year achieved Best Corrected Visual Acuity (BCVA) of 20/40 or better, which exceeded the FDA Grid of Historical Controls ("All Patients" analysis). At two and three years, BCVA continued to be acceptably good, with 94.5% and 94.6% of patients achieving 20/40 or better, respectively.

TABLE 7
Best Corrected Visual Acuity (All Patients)

	1 Year		2 Years		3 Years	
Visual Acuity	**n**	**%**	**n**	**%**	**n**	**%**
20/20 or better	229	62.4	183	58.8	182	67.8
20/25 or better	311	84.7	246	79.1	231	84.1
20/30 or better	349	95.1	274	88.1	253	91.2
20/40 or better	363	98.9	294	94.5	264	94.6
FDA Grid for % of 20/40 or better	92.5%		N/A		N/A	
Total	367		312		280*	

*BCVA not available for 1 patient

Patients without significant pre-operative pathologies or macular degeneration at any time during the trial ("Best Cases") were analyzed separately for BCVA. There were 320 patients available for this analysis at one year. In the best case population, nearly all (99.1%) patients implanted with the device and examined at one year achieved BCVA of 20/40 or better, which met the FDA Grid of Historical Controls. At two and three years, BCVA continued to be acceptably good, with 94.4% and 95.1% of patients achieving 20/40 or better, respectively.

TABLE 8
Best Corrected Visual Acuity (Best Cases)

	1 Year		2 Years		3 Years	
Visual Acuity	**n**	**%**	**n**	**%**	**n**	**%**
20/20 or better	209	65.3	163	60.8	167	72.2
20/25 or better	275	85.9	215	80.2	203	86.3
20/30 or better	307	95.9	239	89.2	221	92.7
20/40 or better	317	99.1	253	94.4	229	95.1
FDA Grid for % of 20/40 or better	96.7%		N/A		N/A	
N	320		268		242	

3. Subgroup Analyses
   The following characteristics were evaluated for potential association with acuity outcomes: age, gender, site, and preoperative pathology. No significant relationships were found.

Japanese Clinical Study

The presence of glistenings in the AVS XACT® Foldable IOL was first reported to AVS by a clinical investigator during the course of a clinical trial of 40 eyes of 40 patients implanted with AVS XACT® Foldable IOLs being conducted for registration purposes in Japan.

The presence of glistenings was observed during fully dilated slit lamp examinations between one week and one month after implantation. The investigator described the glistenings as small, transparent in color, elliptical in shape, and sparsely dispersed throughout the lens. He also reported no loss of visual function related to glistenings and did not consider them a safety concern.

Contrast sensitivity was used as the measure of visual function because it is more sensitive than Snellen BCVA. Results of this analysis confirmed the clinical observation that the severity (count) of glistenings peaked early (at one month postoperatively) and decreased at every visit thereafter. There was no correlation between the number of glistenings and contrast sensitivity. Moreover, no differences were observed in contrast

sensitivity between study and control eyes, except for a clinically insignificant difference in contrast sensitivity detected in the highest spatial frequencies at one month.

Dominican Republic/ German Study
Enrollment in the US IDE clinical trial was already complete when the change of hydration/storage media from 10.0% to 0.9% saline was implemented, so clinical verification of the elimination of glistenings was conducted outside of the US, where the AVS XACT® Foldable IOL was commercially available under CE mark

Investigators were instructed to use a photographic grading scale that was used in the US IDE clinical trial. The primary endpoints of the study were the grades and incidence of glistenings. In this study, 172 eyes of 142 patients were examined at least once between 1 and 6 months, and 123 eyes of 101 patients were examined at least once between 6 months and 2 years. No glistenings were observed at any time.

XI. 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.

XII. CONCLUSIONS DRAWN FROM PRECLINICAL AND CLINICAL STUDIES

A. Safety Conclusions

The rates of "FDA Grid" adverse events associated with the XACT® Foldable Hydrophobic Acrylic UV Light-Absorbing Posterior Chamber IOL are comparable to, or lower than the rates associated with the historical IOL control population.

B. Effectiveness Conclusions

The rates of best corrected visual acuity of 20/40 or better that are provided by the XACT® Foldable Hydrophobic Acrylic UV Light-Absorbing Posterior Chamber IOL are comparable to, or better than, those associated with the historical IOL control population.

C. Overall Conclusions

The data contained in this application support the reasonable assurance of safety and effectiveness of the XACT® Foldable Hydrophobic Acrylic UV Light-Absorbing Posterior Chamber IOL, when used in accordance with the indications for use.

XIII. CDRH DECISION

The Center for Devices and Radiological Health (CDRH) reviewed the PMA and concluded that the PMA contained sufficient valid scientific evidence to provide reasonable assurance of the safety and effectiveness of the device under the prescribed indications for use. CDRH issued an approval order on February 02, 2009.

The applicant's manufacturing facility was inspected and found to be in compliance with the device Quality System (QS) regulation (21 CFR 820).

XIV. 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.