SUMMARY OF SAFETY AND EFFECTIVENESS (SSED)

I. GENERAL INFORMATION

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

Device Trade Name: iSpheric™ Model YA-60BB Intraocular Lens

Applicant's Name and Address: Hoya Surgical Optics
14768 Pipeline Avenue
Chino Hills, CA 91709

Date(s) of Panel Recommendation: Not Applicable

Premarket Approval Application (PMA) Number: P080004

Date of FDA Notice of Approval: September 26, 2008

Expedited: Not applicable

II. INDICATIONS FOR USE

The Hoya iSpheric™ Model YA-60BB Intraocular Lens is indicated for primary implantation in the capsular bag of the eye for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed.

III. CONTRAINDICATIONS

No absolute contraindications are known.

IV. WARNINGS AND PRECAUTIONS

The warnings and precautions can be found in the iSpheric™ Model YA-60BB Intraocular Lens labeling.

V. DEVICE DESCRIPTION

The Hoya iSpheric™ Model YA-60BB Intraocular Lens (IOL), is an ultraviolet absorbing posterior chamber intraocular lens designed to be implanted posterior to the iris where the lens will replace the optical function of the natural crystalline lens. However, accommodation will not be replaced. The lens has a foldable UV-absorbing acrylic optic with a 6.0 mm diameter. The acrylic optic material blocks approximately 95% of ultraviolet light and has an additional yellow tint added to absorb most visible blue light. The optic thus has a characteristically yellowish tint. The haptics of the Hoya iSpheric™ Model YA-60BB IOL are made from polymethylmethacrylate (PMMA) which has been bonded to the optic. The haptics are tinted blue to make them easier for the surgeon to visualize during surgery and have a 5° angulation. The overall diameter of the lens is 12.5 mm. The lens is provided in a Tyvek pouch which has been sterilized using

ethylene oxide gas. In the U.S. IDE study all lenses were folded using forceps during surgery to allow insertion of the lens through a small incision following cataract extraction. The Hoya iSpheric™ Model YA-60BB Intraocular Lens is intended to be placed in the posterior chamber of the eye entirely within the capsular bag. The Hoya iSpheric™ Model YA-60BB will be marketed in 0.5 diopters (D) increments from 6.0 to 30.0 D.

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 iSpheric™ Model YA-60BB IOL was introduced into the European Union in 2003 and into Japan in 2004. The lens is also marketed in Korea, the Republic of China, Singapore, Thailand and Malaysia. The lens has not been withdrawn from any market for reasons related to safety and effectiveness of the device.

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 (endophthalmitis), retinal detachment, vitritis, cystoid macular edema, corneal edema, pupillary block, cyclitic membrane, iris prolapse, hypopyon, transient or persistent glaucoma and secondary surgical intervention. Secondary surgical interventions include, but are not limited to, lens repositioning, lens replacement, vitreous aspirations or iridectomy for pupillary block, wound leak repair, and retinal detachment repair. Amongst those directly related to the IOL are decentering and subluxation, precipitates on the surface of the IOL. Silicone oil, particularly when used in the surgical treatment of detached retina, may stick to the IOL if the posterior capsule of the crystalline lens is not intact.

Other potential adverse events which may accompany cataract or implant surgery include, but are not limited to, the following: nonpigmented precipitates, lens epithelial cell on-growth, vitreous wick syndrome, iris prolapse, acute corneal decompensation and pupillary membrane. No cases of acute corneal decompensation were reported in this study.

Potential secondary surgical interventions that have been associated with intraocular lenses include, but are not limited to, the following: Vitreous aspiration or iridectomy for pupillary block, wound leak repair, retinal detachment repair, lens repositioning due to corneal touch, corneal transplant, and lens replacement due to refractive error or severe inflammation.

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

IX. SUMMARY OF PRECLINICAL STUDIES

Hoya Surgical Optics performed non-clinical studies on this device in accordance with the ISO 11979 standards for intraocular lenses.

Biocompatibility Studies

Hoya conducted a battery of *in vivo* and *in vitro* acute and chronic toxicity tests that establish the biocompatibility of the lens materials. The biocompatibility studies were performed in accordance with the requirements in ISO 11979-5 to establish a complete profile for the IOL material. The ocular implantation study was waived because of existing human clinical trial data with the IOL material. Summaries of the biocompatibility tests conducted are listed in Table 1.

Table 1: Biocompatibility Testing

Test Description	Item Tested	Results and Conclusions
Cytotoxicity – Colony formation, direct and indirect	Optic	No significant cell lysis or toxicity; Noncytotoxic
Cytotoxicity –Colony formation, direct and indirect	Haptic	Cell lysis and toxicity; mildly cytotoxic
Cytotoxicity – Agar diffusion, indirect contact	Optic	No significant cell lysis or toxicity; Noncytotoxic
Cytotoxicity – Agar diffusion, indirect contact	Haptic	No significant cell lysis or toxicity; Noncytotoxic
Cytotoxicity – MEM elution	IOL	No significant cell lysis or toxicity; Noncytotoxic
Cytotoxicity – Inhibition of cell growth	IOL	14% growth inhibition; Mild inhibitor of cell growth

Test Description	Item Tested	Results and Conclusions
Genotoxicity – Ames Bacterial Reverse Mutation Assay	Optic	Did not cause a positive increase in the mean number of revertants per plate; Nonmutagenic
Genotoxicity – Ames Bacterial Reverse Mutation Assay	Haptic	Did not cause a positive increase in the mean number of revertants per plate; Nonmutagenic
Genotoxicity –Chromosomal aberration	Optic	Induced no clastogenic activity in the in vitro human lymphocyte metaphase analysis; nongenotoxic
Genotoxicity –Chromosomal aberration	Haptic	Induced no clastogenic activity in the in vitro human lymphocyte metaphase analysis; nongenotoxic
Maximization Sensitization	Optic	The extractants showed no evidence of causing sensitization in guinea pigs; Nonsensitizing
Maximization Sensitization	Haptic	The extractants showed no evidence of causing sensitization in guinea pigs; Nonsensitizing
Nonocular implantation – 7 and 28 days	Optic	Tissue reaction; mild irritant (mild)
Nonocular implantantion – 7 and 28 days	Haptic	Tissue reaction; mild irritant (mild)
Ocular implantation		Waived – Human evidence of IOL material and ocular tissue tolerance
Nd:YAG Laser Cytotoxicity	IOL	No cytotoxicity or leachables; Noncytotoxic
Test Extractable and Hydrolytic Stability	IOL	No significant extractables; No defects by scanning electron microscopy
Test Extractables by Exhaustive Extraction	IOL	0.35% extraction rate; Low extraction rate
Photostability Cytotoxicity (F-05-108)	IOL	No significant residual extracted; photostable
Cytotoxicity – Growth inhibition (04Z099)	IOL	No significant cell lysis or toxicity; noncytotoxic
Cytotoxicity – Direct contact (F-05-177)	Haptic	No significant cell lysis or toxicity; noncytotoxic
Cytotoxicity – Elution (F-05-178)	Haptic	No significant cell lysis or toxicity; noncytotoxic

Test Description	Item Tested	Results and Conclusions
Cytotoxicity – Direct contact (Y5J110G)	IOL	No significant cell lysis or toxicity; noncytotoxic
Cytotoxicity – Direct contact (Y6G054G)	IOL	No significant cell lysis or toxicity; noncytotoxic
Cytotoxicity – MEM elution (Y6G053G)	IOL	No significant cell lysis or toxicity; noncytotoxic
IOL Extraction in Saline and Acetone	IOL	0.25% extraction rate; Low levels of extractables from acetone
Optic Extraction Rate in Organic Solvent	Optic	From 0.10 to 0.44%; Low extraction rate
Haptic Extraction Rate in Organic Solvent	Haptic	From 0.10 to 0.44%; Low extraction rate
Cytotoxicity – Colony formation	AVBAA	Cell inhibition at 0.3mg/kg
Acute Ocular Irritation	AVBAA	No significant reaction; Nonirritant
Genotoxicity – Ames Bacterial Reverse Mutation Assay	AVBAA	2 wells/dose
Genotoxicity – Ames Bacterial Reverse Mutation Assay	AVBAA	Normal growth and colony number; nonmutagenic
Maximization Sensitization	AVBAA	No significant reaction; Nonsensitizing
Acute Oral Toxicity	AVBAA	No death, no signs; No oral toxicity

IOL – intraocular lens
AVBAA = aniline vinylbenzile anthraquinone

Laboratory Studies and Manufacturing

Data from engineering analyses demonstrate the suitability of the material and overall device design for use in intraocular lenses; these studies are summarized in Table 2. 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 inspections.

Table 2: Laboratory Studies

Laboratory Studies	**Test and Results**
Optical	Clear Optic Diameter, Dioptric Power (at 0° and 90°), resolution efficiency (at 0° and 90°), and spectral transmittance passed the acceptance criteria
Optical: Modulation Transfer Function (MTF)	All lenses had an MTF of 0.34 or better at 100 lp/mm.

Laboratory Studies	Test and Results
Mechanical: Dimensions	Overall diameter, sagitta, vault height, optic body diameter. All dimensions were within the designed acceptance criteria
Mechanical: Optic decentration	At a 10mm compression diameter, all lenses had a decentration of 0.42mm or less
Mechanical: Optic Tilt	The average optic tilt of a 20.0D lens at the compressed diameter was 0.63°
Mechanical: Loop pull strength	The force to pull the haptics exceeded 1N.
Mechanical: Fold and Recovery Testing	Lenses were free of cosmetic defects and any permanent changes to the optical or mechanical properties of the lens when held in a folded state in the Hoya – IS Injector System for a minimum of 3 minutes.
Mechanical: Surface and Bulk homogeneity	No lenses exhibited cosmetic defects

Sterilization, Packaging, Shelf Life and Transport Stability

The objective of the sterilization, shelf-life, and transport stability studies was to establish a complete microbiological profile for the iSpheric Lens.

Table 3 summarizes the tests conducted to establish the microbiological profile of the packaged iSpheric Lens.

Table 3: Sterilization, Packaging, Shelf Life & Transport Tests

Sterilization Validation	Test Conclusions
Sterilization Revalidation: Recommissioning of Ethylene Oxide Gas Sterilizer Requalification: Evaluation of Physical and Microbiological Qualification of Sterilizer	The recommissioning and requalification was performed according to ISO 11135-1: 1994, "Medical devices – Validation and routine control of ethylene oxide sterilization" and were within acceptable limits.
Sterilant Residuals: Ethylene Chlorohydrin (ECH)	The report of residual EO and ECH analysis was within acceptable limits in accordance with ISO 10993-7: 1995/R(2001), "Biological evaluation of medical devices, Part 7: Ethylene oxide sterilant residuals."
Ethylene Oxide (EO)	The report of residual EO analysis was within acceptable limits in accordance with ISO 11135-1: 1994, "Medical devices – Validation and routine control of ethylene oxide sterilization."
Bacterial Endotoxin Testing	Endotoxin levels are below normal limits as set by the Agency for medical devices and according to USP.

Bacteriostasis and Fungistasis Testing	No antimicrobial activity was exhibited with testing performed according to USP.
Package Integrity Tests	Test Conclusions
Environmental and Microbial Challenge	The results are deemed acceptable.
Seal Integrity Tests	Testing was performed according to ASTM F88-00, "Standard Test Method for Seal Strength of Flexible Barrier Materials" and the results are deemed acceptable.
Dye Penetration Tests	Testing was performed according to ASTM F 1929-98, "Standard Test Method for Detecting Seal Leaks in Porous Medical Packaging by Dye Penetration" and the results are deemed acceptable.
Burst and Creep Tests	Testing was performed according to ASTM F 1140-00, "Standard Test Methods for Internal Pressurization Failure Resistance of Unrestrained Packages" and the results are deemed acceptable.
Shelf Life and Transport Stability Tests	**Test Conclusions**
Aging Studies	Testing was performed according to ISO 11979-6, "Ophthalmic implants-Intraocular lenses-Part 6: Shelf-life and transport stability" and was acceptable for a 60 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 STUDY

The applicant performed a clinical study to establish a reasonable assurance of safety and effectiveness of IOL implantation with the Hoya iSpheric™ Model YA-60BB IOL in the US under IDE # G030239. Data from this clinical study were the basis for the PMA approval decision. A summary of the clinical study is presented below.

A. Study Design

The objective of this clinical study was to assess the safety and effectiveness of the Hoya iSpheric™ Model YA-60BB IOL for the visual correction of aphakia in adult patients in whom a cataractous lens has been removed. The clinical study was conducted in a single phase. A total of 617 eyes (412 were primary eyes and 205 were secondary eyes) were enrolled by and followed through 12 months postoperative after which their results were assessed by FDA.

Patients were enrolled in the clinical study in a non-randomized fashion at 11 clinical sites with their results compared to literature controls, namely the FDA "Grid" of cataract surgery results. In Stark et al. Ophthalmology, 90(4):311-317), FDA published a grid of historical clinical data established from review of 45,543 eyes implanted with IOLs PMA-approved before 1982. FDA adopted the *Grid* which includes adverse reaction rates, sight-threatening complication rates and visual acuity results, for comparison to new lens models. Based on the analysis of the detailed data presented in the PMA, it was determined that the clinical performance of the Hoya iSpheric™ Model YA-60BB Intraocular Lenses compares acceptably with the grid of historical data. A medical monitor, contract research organization (CRO), and IRB oversight were utilized in this study. The study began on February 25, 2004 and the final patient was enrolled/implanted on July 20, 2005.

Statistical Analysis Plan

Study sample outcomes have been stratified and mean values for effectiveness and adverse event parameters evaluated to examine intra-study variations. Furthermore, the overall study data has been compared to the FDA Grid values using parametric Chi-Square Goodness of Fit testing to determine if statistically significant differences exist. The level of significance for all statistical evaluations will be P=0.05. Therefore, any within-groups comparisons or comparisons of the study data to the literature controls in which the level of significance is less than or equal to 0.05 are considered statistically significant.

1. Clinical Inclusion and Exclusion Criteria

- Inclusion Criteria:
    - Adult patients with cataract who were eligible for phacoemulsification cataract extraction of the lens through an incision of approximately 4 mm, and primary implantation of a posterior chamber intraocular lens
    - Patients must have had no pre-existing ocular conditions that preclude the ability of the treated eye to achieve best-corrected visual acuity (BCVA) of 20/40 or better after IOL implantation.
    - Patients must have been at least 21 years of age.
    - Patients must have signed a written informed consent form.
    - Patients must have been able and willing to return for scheduled follow-up examinations after surgery throughout the 36 month study.

- Exclusion Criteria:
    - Patients with a history of/or clinical signs of any of the following sight-threatening conditions:
        - Previous Retinal Detachment or retinal pathology in operative eye, only
        - Macular Degeneration in either eye
        - Macular Edema in either eye
        - Persistent Iritis/Uveitis in operative eye, only
        - Uncontrolled Glaucoma or under current treatment for glaucoma in either eye
        - Significant Corneal Disease in operative eye, only
        - Proliferative Diabetic Retinopathy in either eye
    - Patients who had previous ocular surgery, of any kind, within the last 6 months or patients who have had previous ocular surgery at any time

and who did not have potential BCVA after cataract extraction/IOL implantation of 20/40 or better
- Patients who had best corrected vision worse than 20/200 in the fellow eye.
- Patients with serious (i.e., life threatening) non-ophthalmic disease which may have precluded study completion.
- Patients who had undergone previous cataract extraction and intraocular lens implantation.
- Patients unwilling or unable to sign the IRB-approved informed consent document for the study or who could not or would not complete the study's examination schedule.
- Patients who were currently enrolled in another clinical trial, or who exited a clinical trial within the last 30 days.

2. Follow-up Schedule

All patients were scheduled to return for postoperative follow-up examinations at 1-2 days, 7-14 days, 30-60 days, 120-180 days, and 330 to 420 days postoperatively.

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 Best Corrected distance visual acuity (BCDVA), manifest refraction, intraocular pressure measurements, and slit-lamp ophthalmic evaluations to determine adverse events or postoperative complications. A sub-study to address the potential for diminution of color vision due to the yellow tint of the IOL optic was conducted on 50 patient eyes. A Farnsworth D-15 Color Vision assessment, which involves a timed test to arrange color-coded disks, was performed preoperatively and at two postoperative exams to detect any color vision abnormalities

Adverse events and complications were recorded at all visits. The key time points are shown below in the tables summarizing safety and effectiveness.

3. Clinical Endpoints

The major endpoints are as discussed in the FDA draft Intraocular Lens Guidance Document dated October 14, 1999.

- Safety:
  - Adverse Events (Cumulative and Persistent) as categorized and evaluated by the FDA grid.
- Effectiveness:
  - Best Spectacle Corrected Visual Acuity (BSCVA) - % of primary eyes (All eyes)≥ 20/40,

- BSCVA -- % of primary eyes ("Best Case" eyes) ≥20/40, as described by FDA draft Intraocular Lens Guidance Document (and ISO 1197907:2001(E)) and compared to FDA grid.

B. Accountability of PMA Cohort

For this PMA, the 446 patient eyes (300 primary eyes and 146 fellow eyes) that completed the Form 5 exam in adherence with the study protocol exam windows were used to assess the safety and effectiveness of the IOL. The Primary Cohort excludes 148 "Incomplete" patients who had missed a follow-up visit or were seen outside of the protocol-specified windows (full data sets are provided for these patients). All but 9 of these "Incomplete" eyes had a Form 5 visit on record. Separate effectiveness analysis of these 148 eyes demonstrates that that there was no selection bias regarding BCVA results at each study site with respect to classification of patients as Incomplete. The safety analysis included all 616 patients (including the "incomplete patients"). Table 4 provides a summary of patient accountability.

Table 4: Accountability by Post-operative Visit
Total Eyes

		Total Number (% enrolled) [% accountability]						
Patient Status	Enrolled 617	Form 1 1-2 days	Form 2 1-2 weeks	Form 3 1-2 months	Form 4 4-6 months	Form 5 11-14 months	Form 6 22-36 months	Form 7 33-39 months
Available		614 (99.5%) [614/616 = 99.7%]	615 (99.7%) [615/616 = 99.8%]	610 (98.9%) [610/616 = 99.0%]	604 (97.9%) [604/613 = 98.5%]	584 (94.7%) [584/595 = 98.2%]	531 (86.1%) [531/566 = 93.8%]	506 (82.0%) [506/521 = 97.1%]
Missing patients:								
Discontinued		1 (0.2%)	1 (0.2%)	1 (0.2%)	4 (0.6%)	22 (3.6%)	51 (8.3%)	96 (15.6%)
Missing at scheduled visit but seen later		0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	2 (0.3%)	1 (0.2%)
Not seen but accounted for		2 (0.3%)	1 (0.2%)	4 (0.6%)	9 (1.5%)	11 (1.8%)	28 (4.5%)	3 (0.5%)
Lost to follow-up		0 (0.0%)	0 (0.0%)	1 (0.2%)	0 (0.0%)	0 (0.0%)	5 (0.8%)	11 (1.8%)
Active		0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)

Discontinued patients are those who have a Study Exit form.
Patients who are missing at a scheduled visit have a later follow-up/unscheduled form.
Patients who are not seen but accounted for have a form which indicates patient is unavailable but continuing in the study.
Patients lost to follow-up do not have a form, are past due for the visit, and the date of their latest form is before the new window.
Active patients are those who have not reached the time associated with the form.
Percent accountability is the number available/(Enrolled – discontinued – active).

C. Study Population Demographics and Baseline Parameters

The demographics of the study population are typical for an IOL study performed in the US. The population at risk for developing visually-disabling cataracts and needing cataract surgery is typically elderly; the elderly population generally has a higher proportion of females to males. The average age for the 617 patients enrolled in this study was approximately 70 years at the time of surgery and 62.7% of the enrolled patients were female with 37.3% being male. The study population did not exclude patients on the basis of gender or gender-related pathology. The study

population was approximately 93% Caucasian or Hispanic; 4.2% were African-American, 2.9% were Asian. All patients who met the Inclusion criteria and received the study IOL were included in the study analyses. One patient did not get included in the analyses after enrollment because the patient did not receive the study IOL due to rupture of the posterior capsule before IOL implantation was attempted. Table 5 provides a summary of population demographics and baseline parameters.

Table 5: Patient Population Demographics and Baseline Parameters

	All Eyes N = 617	Primary Eyes N = 412	Fellow Eyes N = 205
Gender:	**N (%)**	**N (%)**	**N (%)**
Female	387 (62.7%)	256 (62.1%)	131 (63.9%)
Male	230 (37.3%)	156 (37.9%)	74 (36.1%)
Age (years)	**Mean (S.D.) Range**	**Mean (S.D.) Range**	**Mean (S.D.) Range**
Overall	70.5 (9.3) 38.2 – 89.8	70.4 (9.4) 38.2 – 89.8	70.7 (9.1) 38.2 – 88.9
Female	70.5 (9.0) 40.4 – 89.8	70.5 (9.3) 40.4 – 89.8	70.4 (8.5) 41.7 – 88.9
Male	70.5 (9.6) 38.2 – 88.3	70.2 (9.4) 38.2 – 88.2	71.2 (10.0) 38.2 – 88.3
Patients by Age	**N (%)**	**N (%)**	**N (%)**
<50	17 (2.8%)	11 (2.7%)	6 (2.9%)
50-59	66 (10.7%)	47 (11.4%)	19 (9.3%)
60-69	186 (30.2%)	125 (30.3%)	61 (29.8%)
70-79	266 (43.1%)	172 (41.8%)	94 (45.9%)
≥ 80	82 (13.3%	57 (13.8%)	25 (12.2%)
Ethnicity	**N (%)**	**N (%)**	**N (%)**
Hispanic/Latino	32 (5.2%)	22 (5.3%)	10 (4.9%)
Not Hispanic/Latino	585 (94.8%)	390 (94.7%)	195 (95.1%)
Race	**N (%)**	**N (%)**	**N (%)**
Asian	18 (2.9%)	11 (2.7%)	7 (3.4%)
Black/African American	26 (4.2%)	20 (4.9%)	6 (2.9%)
White	573 (92.9%)	381 (92.5%)	192 (93.7%)

D. Safety and Effectiveness Results

1. Safety Results

Safety was evaluated with regards to specific cumulative adverse event rates and persistent adverse events rates as specified in the FDA Intraocular Lens Guidelines, 1996 and ISO 11979-7 (Ophthalmic implants - Intraocular lenses - Part 7: Clinical investigations). Primary safety analyses are based on data from all enrolled patients with follow-up to at least one-year post implantation. The FDA historical control is derived from weighted averages of the data from 13 large clinical investigations of IOLs (anterior and posterior chamber) between March 1988 and June 1991. The pooled sample size for these clinical investigations was 5162 adverse events.

Cumulative adverse events are those which occurred at any time during the patient's postoperative course, through Form 7 (approximately 3 years post-operatively). Although cumulative adverse events were tabulated if they were

reported at any time through Form 7, the FDA Grid rates for persistent complications are listed for events that are present at the 12 month exam (Form 5).

The adverse event rates were not statistically significantly different from the historical FDA grid control population rate for all of the listed cumulative and persistent adverse events.

The key safety outcomes, cumulative and persistent adverse events, for this study are presented below in Tables 6 and 7.

Table 6: Cumulative Ocular Adverse Events for all Enrolled Eyes Compared to FDA Grid (N=616) †

Adverse Events	**Hoya YA-60BB**	**FDA Grid**
	N (%)	N (%)
Cumulative Endophthalmitis	2 (0.3%)	0.1%*
Cumulative Hyphema	0 (0%)	2.2%
Cumulative Hypopyon	1 (0.2%)	0.3%
Cumulative Lens Dislocation	2 (0.3%)	0.1%*
Cumulative Macular Edema	24 (3.9%)	3.0%*
Cumulative Pupillary Block	1 (0.2%)	0.1%*
Cumulative Retinal Detachment	2 (0.3%)	0.3%
Cumulative Secondary Surgical Intervention	9 (1.5%)	0.8%*
Lens repositioning	2 (0.3%)	
Lens removal (any reason)	2 (0.3%)	

*Differences are not statistically significant

†One patient was enrolled in the study but did not receive the study IOL due to surgical problems before lens implantation.

Table 7: Adverse Events Reported at 12 Months Postoperative

Adverse Events	**Hoya YA-60BB**	**FDA Grid**
	N (%)	N (%)
Persistent Corneal Edema	(0%)	0.3%
Persistent Iritis	(0.2%)	0.3%
Persistent Macular Edema	(0.8%)**	0.5%
Persistent Raised IOP Requiring Treatment	(0%)	0.4%

**** Persistent macular edema occurred at a rate of 0.8% which was statistically insignificant from the FDA Grid rate ($X^2 = 0.46$, $P>0.05$).**

The adverse event rates were not statistically significantly different from the historical FDA grid control population rate for all of the listed cumulative and persistent adverse events. Of note, is that during the IDE, there were two cases of endophthalmitis (one culture positive and the other "sterile"). With two cases of endophthalmitis reported among the 616 total implanted patients (inclusive of the 22 "discontinued patients" and 148 "incomplete patients"), the rate is 2/616 (0.3%). The FDA grid has a rate of 0.1% for comparison but a Chi-Square analysis ($X^2= 0.73$, $P>0.05$) indicates this difference is not statistically significant. These cases are not believed to be device related.

Two patient eyes had the Hoya lens explanted during the study; both of these were primary eyes (0.3%). One was explanted due to acute inflammation and the other was explanted when the patient went to a non-study surgeon and requested explant; no reason for explantation was provided by explanting surgeon.

Two cases of lens dislocation apparently related to iatrogenic causes were reported.

A total of 9/616 (1.5%) of enrolled eyes implanted with the study IOL eyes underwent a secondary surgical procedure after implantation with four of these cases being patients outside of the PMA Primary Cohort. None of the secondary surgical interventions can be directly related to the study IOL.

Fifty seven (57) of 616 eyes (9.3%) underwent an Nd:YAG posterior capsulotomy for Posterior Capsular Opacification through three-years of postoperative follow-up.

Postoperative Inflammation in PMA Primary Cohort Eyes

Non-routine postoperative inflammation was defined as:

- Form 2 – Cells, flare or iritis is considered routine if not rated moderate or severe; regardless of whether patient is on steroids or NSAIDs.

- Form 3 – Trace cells, flare or iritis is considered routine if patient is receiving steroids or non-steroidal anti-inflammatory drugs NSAIDs. If patient is no longer on steroids or NSAIDs, patient may have mild cell, flare or iritis. Any report of cells, flare or iritis that is moderate or severe is not routine, regardless of medication status.

- Form 4 or later – Cells, flare or iritis should be absent. Should be zero by Form 4.

Form 2: 1.6% reported non-routine postoperative inflammation.
None of these eyes reported macular edema or other adverse events. 100% achieved 20/40 or better BCVA at Form 5.

Form 3: 0.7% reported non-routine postoperative inflammation. One of these eyes (06-044B) represented a case of bacterial endophthalmitis approximately six weeks postoperative, but 100% achieved 20/40 or better BCVA at Form 5.

Form 4: No eyes met the criteria for non-routine inflammation at Form 4.

Form 5: No eyes met the criteria for non-routine inflammation at Form 5.

2. Effectiveness Results

Results for distance Best Corrected Visual Acuity (BCVA) are shown in Table 3. Of the 446 patient eyes, 98.7% reported a BCVA of 20/40 or better one year after surgery and 52.8% reported a BCVA of 20/20 or better. Table 8 contains a summary of BCVA results.

Table 8: Best Corrected Visual Acuity, (300 primary eyes and 146 fellow eyes)

	Pre-Op (N=446)	Form 1 (N=445) Pinhole VA	Form 2 (N=443)	Form 3 (N=445)	Form 4 (N=445)	Form 5 (N=445)
BCVA						
20/15	1 (1.4%)	13 (2.9%)	31 (7.0%)	32 (7.2%)	35 (7.9%)	29 (6.5%)
20/20	33 (7.4%)	90 (20.2%)	211 (47.6%)	246 (55.3%)	260 (58.4%)	235 (52.8%)
20/25	58 (13.0%)	106 (23.8%)	107 (24.2%)	102 (22.9%)	101 (22.7%)	110 (24.7%)
20/30	108 (24.2%)	93 (20.9%)	56 (12.6%)	42 (9.4%)	38 (8.5%)	47 (10.6%)
20/40	117 (26.2%)	81 (18.2%)	26 (5.9%)	17 (3.8%)	7 (1.6%)	18 (4.0%)
Total 20/40 or better	317 (71.1%)	383 (86.1%)	431 (97.3%)	439 (98.7%)	441 (98.7%)	439 (98.7%)
Total worse than 20/40	129 (28.9%)	62 (13.9%)	12 (2.7%)	6 (1.3%)	4 (1.3%)	6 (1.3%)
Total	446	445	443	445	445	446

Table 9 shows best corrected visual acuity for primary eyes.

Table 9: Best Corrected Visual Acuity, Primary Eyes by Form

	Pre-Op (N=308)	Form 1 (N=300) Pinhole VA	Form 2 (N=298)	Form 3 (N=299)	Form 4 (N=300)	Form 5 (N=300)
BCVA						
20/15	0 (0.7%)	7 (2.9%)	18 (5.9%)	18 (6.0%)	18 (6.0%)	17 (5.7%)
20/20	14 (25.7%)	55 (15.6%)	143 (45.3%)	166 (55.5%)	173 (57.7%)	156 (52.0%)
20/25	30 (22.7%)	74 (25.0%)	74 (28.0%)	64 (21.4%)	71 (23.7%)	73 (24.3%)
20/30	64 (23.0%)	55 (18.8%)	36 (11.7%)	35 (11.7%)	29 (9.7%)	35 (11.7%)
20/40	84 (17.3%)	59 (20.1%)	16 (4.9%)	13 (4.4%)	6 (2.0%)	15 (5.0%)
Total 20/40 or better	192 (89.3%)	250 (83.3%)	287 (96.3%)	296 (99.0%)	297 (99.0%)	296 (98.7%)
Total worse than 20/40	108 (10.7%)	50 (16.7%)	11 (3.7%)	3 (1.0%)	3 (1.0%)	4 (1.3%)
Total	300	300	298	299	300	300

Table 10 shows Best Corrected Visual Acuity Data for Best Case patients compared to FDA grid Best Case Patients. All the patients in the PMA Primary Cohort were Best Case Patients. Consequently, the Sponsor did not provide a separate clinical analyses for Best Case Patients in this PMA (no separate tables for Best Case patients) since they would be identical to the BCVA tables for all PMA Primary Cohort patients. Thus, the rate of 20/40 or better BCVA for Best Case patients is identical to the result for all PMA Primary Cohort patients, or 98.7% which compares acceptably with the FDA Grid for Best Case patients of 96.7%.

Table 10: Best Corrected Visual Acuity Data for Best Case patients

	<60 years (N = 51)	60-69 years (N = 144)	70-79 years (N = 198)	≥80 years (N = 53)	All patients (N = 445)
BCVA					
20/15	7 (13.73%)	15 (10.4%)	7 (3.6%)	0 (0.0%)	29 (6.5%)
20/20	31 (60.8%)	84 (58.3%)	94 (47.7%)	26 (49.1%)	235 (52.8%)
20/25	8 (15.7%)	31 (21.5%)	55 (27.9%)	16 (30.2%)	110 (24.7%)
20/30	2 (3.9%)	11 (7.6%)	27 (13.7%)	7 (13.2%)	47 (10.6%)
20/40	1 (2.03%)	1 (0.7%)	13 (6.6%)	3 (5.7%)	18 (4.0%)
Total 20/40 or better	49 (96.1%)	142 (98.6%)	196 (99.5%)	52 (98.1%)	439 (98.7%)
Total worse than 20/40	2 (3.9%)	2 (1.4%)	1 (0.5%)	1 (1.9%)	6 (1.3%)
Total	51	144	197*	53	445
FDA Grid	98.5%	96.5%	97.5%	94.8%	96.7%

*BCVA not reported for one patient

Only 6 patient eyes enrolled in the study failed to achieve BCVA of 20/40 or better at 12-14 months postoperative. All of those eyes were Best Case patients (i.e., patients with no preoperative ocular pathologies or macular degeneration at any time during the study).

3. Subgroup Analyses

For the purposes of the color vision sub-study, the sponsor assumed that a clinically significant level of post-op color vision defects with the Farnsworth D-15 would be 10% of patients. To obtain a confidence interval of ±7.5% at the 95% confidence level, they calculated a minimum sample size of 43. Allowing a small number of patients for loss to follow-up, a total of 52 eyes were enrolled in the color-vision sub-study and 44 of them met the protocol criteria and completed both the preoperative and postoperative testing.

None of the eyes that passed the test preoperatively and qualified for the sub-study also failed it both times postoperatively; 100% of these patient eyes passed the color vision test preoperatively and at least once postoperatively. None of the patients that received the Hoya IOL with yellow-tint requested explanation of the lens due to a color vision disturbance. These data indicate that the Hoya iSpheric™ Model YA-60BB Intraocular Lenses had no significant effect on color vision outcomes after implantation.

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 adverse events associated with the Hoya iSpheric™ Model YA-60BB IOL is comparable to or lower than the rates associated with the historical control population of IOLs.

B. Effectiveness Conclusions

The Hoya iSpheric™ Model YA-60BB IOL provides comparable or better distance visual acuity results compared to the rates associated with the historical control population of IOLs.

C. Overall Conclusions

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

XIII. CDRH DECISION

CDRH issued an approval order on September 26, 2008.

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.