SUMMARY OF SAFETY AND EFFECTIVENESS DATA

I. GENERAL INFORMATION

Generic Name of Device: Collagen Glaucoma Drainage Device

Device Trade Name: AquaFlow™ Collagen Glaucoma Drainage Device, Model CGDD-20

Applicant's Name and Address: STAAR Surgical Company
1911 Walker Avenue
Monrovia, CA. 91016

Premarket Approval Application Number: P000026

Date of Panel Recommendation: November 8, 2000

Dates of Good Manufacturing Practice Inspection: March 12 – 14, 2001

Date of Notice of Approval to Applicant:
JUL 12 2001

II. INDICATIONS FOR USE

The AquaFlow™ is indicated for the maintenance of a sub-scleral space following non-penetrating deep sclerectomy used to facilitate aqueous outflow for the reduction of intraocular pressure in patients with open angle glaucoma where intraocular pressure remains uncontrolled while on maximally tolerated medical therapy.

III. CONTRAINDICATIONS

The AquaFlow™ is contraindicated under the following circumstances or conditions:

1. Known allergic reaction to porcine-derived products.
2. Known allergic reaction to collagen
3. In eye(s) with angle closure glaucoma

IV. WARNINGS AND PRECAUTIONS

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

V. DEVICE DESCRIPTION

The STAAR AquaFlow™ Collagen Glaucoma Drainage Device is designed to maintain a sub-scleral space following non-penetrating deep sclerectomy. After placement in the sub-scleral space and exposure to ocular fluids, the device swells by absorbing aqueous. Subsequently, the device dissolves slowly and is completely resorbed within 6-9 months. The AquaFlow™ is sterilized using gamma radiation. The AquaFlow™ device has a cylindrical shape; it is 4.0 mm long by 0.5 mm wide (when dry) and is composed entirely of lyophilized, cross-linked porcine collagen. Tensile strength is 25×10^5 N/m^2, specific gravity (when hydrated) is1.001 g/cm^2.

VI. ALTERNATIVE PRACTICES AND PROCEDURES

Currently, medication (i.e., local eye drops or systemic pressure reducing drugs) is usually the first form of treatment for glaucoma. Adverse side effects, which are sometimes severe, are to be expected, as well as the realization that the medication regimen may change in the future because of an acquired tolerance level, or the availability of new drugs. Also, the cost of medical glaucoma control over a lifetime can be prohibitive for some patients. Today the most common glaucoma treatments, after use of medications, are an argon-laser trabeculectomy (ALT) or a manual filtering surgical procedure such as a trabeculectomy, which removes part of the trabecular meshwork to increase the outflow of aqueous humor from the eye. Complications of a trabeculectomy include hyphema, cells in the anterior chamber, a flat or shallow anterior chamber with or without choroidal detachments, endophthalmitis, hypotony and suprachoroidal hemorrhage. Trabeculectomies generally fail at some point as the eye heals itself; and, have been known to be less successful in young eyes and those who produce large amounts of fibrous tissue. In the case of a failed filtration surgery, repeat operations can be performed with decreasing success as the sclera can support only a limited number of surgical insults.

In the event of failed trabeculectomy, third line therapy utilizes the placement of glaucoma drainage devices (setons) that act as shunts that relieve pressure by diverting intraocular fluid into an extraocular space (bleb). Examples of such drainage devices are the Molteno, Baerveldt, Krupin and White shunts. These function via placement of a tube directly into the anterior chamber with a space-maintaining plate secured in a sub-scleral space. Relatively good rates of success have been demonstrated. However, their design and placement technique contribute to increased risks for serious and irreversible complications. Hyphema, hypotony, cells in the anterior chamber, a slightly shallow or flat anterior chamber with or without choroidal detachments, endophthalmitis, suprachoroidal hemorrhage and corneal decompensation are complications often reported with the use of setons. The effect of these devices can be temporary as the implant becomes clogged with inflammatory or pigmentary debris.

Fibrinous tissue, or the formation of a collagen meshwork, is a natural healing process the body performs when there is a cut or incision. The collagen meshwork formation also plays a key role in healing a wound made during filtration surgery. As the collagen meshwork becomes progressively dense over time, resistance is created and the aqueous flow is subsequently reduced. Antimetabolites such as 5-Fluorouracil (5-FU) and Mitomycin-C (MMC), are then administered to inhibit fibroblast production and external scarring of the bleb. These medications are also used in conjunction with trabeculectomies to minimize scar formation in high-risk patients. The disadvantages with the use of 5-FU include corneal epithelial defects, globe perforation, wound leaks, and patient discomfort from repeated injections. Conversely, MMC can be given as a single application during surgery and since it appears to be stronger than 5-FU, it can provide a sustained effect on bleb preservation and intraocular pressure control. However, the use of MMC increases the risk of complications especially in the later postoperative period. Ocular complications of MMC use include prolonged wound leaks, late bleb breakdown, endophthalmitis, and excessive hypotony. MMC is toxic if administered systemically and is primarily used as an anti-tumor drug.

VII. MARKETING HISTORY

The STAAR AquaFlow™ Collagen Glaucoma Drainage received CE marking for distribution in 1997 and it is marketed in the following countries: All European Union Countries, Switzerland, New Zealand, Ireland, Romania, Czechoslovakia, Hong Kong, Chile, Singapore and South Africa.

VIII. POTENTIAL ADVERSE EFFECTS OF THE DEVICE ON HEALTH

This section provides a description of all reported surgical and postoperative adverse events. Under each individual postoperative adverse event heading, information is first presented regarding the results of the U.S. AquaFlow™ clinical study. Adverse events reported in papers located in a comprehensive search for all available unpublished and published peer reviewed papers of non-penetrating deep sclerectomy with AquaFlow™ papers are then presented. This provides an overall perspective on the safety of Deep Sclerectomy with Collagen Implant (DSCI) with the AquaFlow. Lastly, the AquaFlow™ U.S. clinical study results are compared to reports from peer reviewed trabeculectomy literature; the current gold standard for the treatment of medically controlled glaucoma.

Antimetabolite therapy was not administered during the AquaFlow™ U.S. clinical study.

Surgery-Related Adverse Events

Vitreous Hemorrhage*	1/194	(0.5%)
Microperforation of Descemet's Membrane With Iris to Sclerectomy Site**	1/194	(0.5%)

* Secondary to perforation with anesthesia needle at surgery

** 2 iris sweep procedures of sclerectomy site were performed postoperatively on same eye

Postoperative Adverse Events

Hypotony (IOP <5 mm Hg):

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
	Literature		
All 31.9%	(0-13%)	(0-53%)	(4.5-58.1%)

Hypotony Maculopathy:

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature	Trabeculectomy Literature
	Literature	No Antimetabolites	With Antimetabolites
All 0.0%	(0-1%)	(0-2%)	(0-18%)

Shallow Anterior Chamber:

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature	Trabeculectomy Literature
	Literature	No Antimetabolites	With Antimetabolites
All 11.3%	(0-10%- early)	(3-33%)	(3-28%)
≥1 Week 3.6%			

Flat Anterior Chamber:

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature	Trabeculectomy Literature
	Literature	No Antimetabolites	With Antimetabolites
All 0.5%	(0%)	(0-13.3%)	(0-12%)
≥1 Week 0.0%			

Hyphema:

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature	Trabeculectomy Literature
	Literature	No Antimetabolites	With Antimetabolites
All 10.3%	(2-8%)	(0-56%)	(0-27%)
≥1 Week 1.5%,			

Wound Leak:

PMA Cohort	DSCI (AquaFlow™)	Trabeculectomy Literature	Trabeculectomy Literature
	Literature	No Antimetabolites	With Antimetabolites
All 5.6%	(2%, 8%, 10%,	(0.3%, 1.3%, 6.6%, 6.7%,	(0%, 0%, 0%, 1.1%, 3%

≥1 Week	4.1%	10%-early, 11%)	6.7%, 9.3%, 11%-early, 12%)	3.5%, 3.9%, 7%, 8.1%, 9%, 10.2%, 11%-early, 11.1%, 40%)

Choroidal Effusion/Detachment/Drainage:

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All	4.1%	(5-11%)	(0-33%)	(2.8-36%)
≥1 Week	2.6%			

Corneal/Epithelial Problems (dellen, dry eye, punctate epitheliopathy):

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All	3.6%	(1-5.7%)	(0-65.6%)	(0-65.6%)
≥1 Week	2.0%			

Cataract Progression:

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All	20.6%	(0-23%)	(4-31%)	(0-30%)

Cataract Formation:

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All	0.0%	(0%)	(0-20%)	(0%)

Endophthalmitis:

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All	0.0%	(0%)	(0-2.3%)	(0-2.2%)

Iris Prolapse:

Iris prolapse into the deep sclerectomy site secondary to trauma was seen n 1 eye (0.7%) at the 12 month exam.

Serious Adverse Events

No AquaFlow™ related serious adverse events were reported during any postoperative visit during this U.S. clinical study.

Serious Adverse Events at ALL Postoperative Visits

-Endophthalmitis	0/194	0.0%
-Secondary Surgical Intervention to Remove AquaFlow	0/194	0.0%
-Sudden Loss of Vision (CRAO)	1/194	0.5%

A sudden loss of vision was observed in one study eye (0.5%) in a 76 year old male with a pre-existing cataract, two days after surgery that was determined to be unrelated to the AquaFlow™ implantation. This sudden loss of vision, (Central Retinal Artery Occlusion (CRAO) with delayed arterial filling), as communicated by the investigator was most likely a result of atherosclerosis, a history of deep vein thrombosis (DVT) and the discontinuation of anticoagulation (aspirin) therapy prior to surgery.

IX. SUMMARY OF PRECLINICAL STUDIES

Some of the preclinical testing was performed on the Aquaflow™ Collagen Glaucoma Drainage Devices from the original supplier and additional testing was performed on the device manufactured by STAAR. Equivalence of devices made by STAAR and the original supplier is evidenced by the identical results obtained from Fourier Transmission Infrared Spectroscopy (FTIR) and Differential Scanning Colorimetry (DSC) testing of samples from both processes.

In addition to the preclinical testing done for the Aquaflow™ Collagen Glaucoma Drainage Devices from the original supplier (Table 1), a second series of tests was performed on device material manufactured by STAAR (Table 2). The clinical study was performed using the devices manufactured by STAAR.

Table 1

Biological Tests Performed on the Aquaflow™ Collagen Glaucoma Drainage Device:

TEST	RESULT
CYTOTOXICITY MEM ELUTION	There was no evidence of lysis or cytopathic effects.
CYTOTOXICITY AGAR OVERLAY - DIRECT CONTACT	There was no evidence of cell lysis.
CYTOTOXICITY AGAR OVERLAY – EXTRACT	There was no evidence of cell lysis.
ACUTE SYSTEMIC TOXICITY	There were no signs of toxicity.

INTRACUTANEOUS TOXICITY	There was no evidence of significant irritation or toxicity.
INTRAMUSCULAR IMPLANTATION	Test sample reaction was not significant as compared to the USP negative control implant material.
HEMOLYSIS TEST - EXTRACT (IN VITRO)	After one hour there was no significant evidence of red blood cell lysis as determined spectrophotometrically.
HEMOLYSIS - DIRECT CONTACT (IN VITRO)	After one hour, there was no significant evidence of red blood cell lysis as determined spectrophotometrically.
INHIBITION OF CELL GROWTH - ONE POINT ASSAY	The samples were found to be non-inhibitory.
GUINEA PIG MAXIMIZATION (SENSITIZATION)	The samples were found to be non-irritating.
INTRAOCULAR IRRITATION (BSS EXTRACT)	There were no significant differences between the test and control eyes
INTRAOCULAR IRRITATION (SC AND CSO EXTRACT)	There was no evidence of significant irritation in the test eye or control eye of any rabbit.
SYSTEMIC ANTIGENICITY	The test article extract was considered to be non-antigenic.
AMES MUTAGENICITY	The samples were found to be non-mutagenic.

Table 2

Additional Biological Tests Performed on the STAAR Surgical manufactured Aquaflow™ Collagen Glaucoma Drainage Device material:

TEST	RESULT
CYTOTOXICITY AGAR OVERLAY – DIRECT CONTACT	There was no evidence of cell lysis.
CYTOTOXICITY MEM ELUTION	There was no evidence of lysis or cytopathic effects.
INTRAOCULAR IRRITATION (BSS EXTRACT)	There were no significant differences between the test and control eyes.
INTRAMUSCULAR IMPLANTATION (7-DAY)	The test sample reaction was not significant as compared to the USP negative control implant material.
INTRAMUSCULAR IMPLANTATION (28-DAY)	The test sample reaction was not significant as compared to the USP negative control implant material
AMES MUTAGENICITY (SC EXTRACT)	The samples were found to be non-mutagenic.
AMES MUTAGENICITY (DMSO EXTRACT)	The samples were found to be non-mutagenic.

USP SYSTEMIC INJECTION TEST (SC)	None of the test article extract treated animals were observed with adverse clinical signs at any of the observation periods.
USP SYSTEMIC INJECTION TEST (CSO)	None of the test article extract treated animals were observed with adverse clinical signs at any of the observation periods.
USP INTRACUTANEOUS (SC AND CSO)	There was no evidence of significant irritation or toxicity.
USP RABBIT PYROGEN TEST	None of the animals exhibited a temperature rise greater than 0.2 °C and therefore the test response is below the USP 23 limit.

Pre-clinical Physical/Chemical Testing

The material used to fabricate the AquaFlow™ Collagen Glaucoma Drainage Device was analyzed to characterize the collagen material used for the device via Fourier Transmission Infrared Spectroscopy (FTIR) and Differential Scanning Colorimetry (DSC) testing of the material. Other characteristics of the device are:

Configuration:	Cylindrical shape; 2.5 mm long x 0.5 mm wide (when dry)
Material:	Lyophilized, cross-linked porcine collagen
Tensile Strength:	25×10^5 N/m^2
Specific Gravity (hydrated):	1.001 g/cm^2
Total Protein Concentration:	0.5 - 1.5 %

Pre-clinical Microbiological Testing

The following information summarizes the testing performed to verify the effectiveness of the gamma radiation sterilization cycle. Radiation sterilization leaves no toxic residues. Testing was performed to measure the bioburden (number of viable bacteria present prior to sterilization) of devices as one aspect in the evaluation and development of the sterilization process.

The recommended sterilization dose for the CGDD was established by first determining the minimum radiation dose required. The minimum radiation dose required was determined to ensure that the target dose of 25 kGy will be sufficient to achieve the 10^6 reduction required for labeling the product as sterile. This study was based on practices recommended by ANSI/AAMI/ISO 11137 - 1995 and EN552:1994. The method used for determining the minimum sterilization dose followed Method 1 in Annex B of ANSI/AAMI/ISO 11137 - 1995. Pre-sterilization bioburden levels were determined and used to select an appropriate sub-lethal verification dose for the CGDD. Recommendations for a routine minimum sterilization dose were based on evaluation of microbial survivors following exposure of products to the verification dose. Once the routine dose was established, testing was

performed to determine any adverse effects on both the packaging and CGDD at this level of exposure.

The validation was successfully completed indicating that the sterilization of the AquaFlow™ Collagen Glaucoma Drainage Device with the specified packaging/loading configuration and the target dose of 25 kGy is sufficient for the sterilization of the CGDD devices.

The results of Pyrogen testing using the USP LAL Pyrogen Test demonstrated that devices were pyrogen free.

Package integrity and physical stability data support a shelf-life expiration date of 18 months.

X. SUMMARY OF CLINICAL STUDIES

Objectives and Study Design

The primary objective of this clinical investigation was to document the safety and effectiveness of the STAAR AquaFlow™ device, as compared to literature controls, in human eyes for the reduction of intraocular pressure (IOP) in male or female patients with open-angle glaucoma who are candidates for primary filtration surgery.

The AquaFlow™ Collagen Glaucoma Drainage Device clinical study was designed as a prospective multi-center clinical investigation conducted at 9 sites throughout the U.S. Patients meeting the study eligibility criteria were enrolled in a non-randomized fashion with study results to be compared to trabeculectomy literature controls.

The following enrollment criteria were used during this study:

1) Adults of any race, between 35 and 85 years of age at the time of surgery
2) One of following types of open-angle glaucoma in the study eye:
   - Primary open-angle glaucoma in a phakic eye,
   - Open-angle glaucoma in a phakic eye 4 weeks or more after a laser iridotomy, provided the eye is not inflamed, steroids have not been used for a week and less than $1/12^{th}$ of the trabecular meshwork circumference is blocked by peripheral anterior synechiae, or
   - Pigmentary and/or pseudoexfoliative glaucoma
3) Study eye on *maximal tolerated medical therapy*
4) IOP >/= 18 mmHg in study eye while on *maximal tolerated medical therapy.* This IOP criteria had to be verified twice over a 30 day period before enrollment.
5) Best corrected vision of 20/80 or better in study eye
6) Patient able to cooperate with study procedures and able to perform tests reliably
7) Patient willing to sign informed consent
8) Patient able and willing to complete postoperative follow-up requirements

Patients were not enrolled in the study if they met any of the following conditions:

1) Discernable congenital anomaly of the anterior chamber angle.
2) Eyes with secondary glaucoma.
3) Concurrent active disease in the study eye that may affect intraocular pressure or its measurement.
4) Patient was on kidney dialysis.
5) History of laser or incisional surgery in the eye considered for study, except laser iridotomy; laser retinal treatment anterior to the vortex vein ampullae; or local retinal cryotherapy, involving less than two quadrants, for retinal holes anterior to the vortex vein ampullae.
6) Eyes that have undergone gonioplasty in more than 180° of the anterior chamber angle circumference.
7) Eyes with proliferative or severe non-proliferative retinopathy.
8) Eyes with (dilated) pupil diameter of less than 2 mm.
9) Eyes with field loss attributed to a non-glaucoma condition.
10) Eyes with failed deep sclerectomy procedures (i.e., penetration of the globe occurred indicated by excessive drainage or sclerectomy was not sufficiently deep as indicated by little or no percolation of aqueous).

Intraocular pressure at the 6 and 12 months postoperative visits was the primary measure of efficacy for this clinical study. The overall incidence of postoperative adverse events for the entire postoperative period (ALL) as well as the occurrence of each adverse event at or after the 1 week follow-up exam (≥ 1 week) are provided in section VIII above.

A total of 194 cases were enrolled in this clinical investigation of the STAAR AquaFlow™ Collagen Glaucoma Drainage Device as of May 25, 2000, the date for inclusion in the "Cohort" for this application. The PMA Cohort is comprised of all eyes with available 12 month follow-up at the date of the database cut-off. A total of 194 eyes of 130 patients were available for inclusion in the PMA cohort. Only one patient was excluded from the PMA cohort due to a previous LASIK (laser-assisted in situ keratomileusis) procedure in the study eye (a protocol violation). The IOP in this eye was controlled throughout the postoperative period without the use of glaucoma medications.

Subject compliance with postoperative follow-up visits (the % Accountability) exceeded 97% of eyes seen at both the 6 and 12 month postoperative visits. Accountability was 92% or higher (92% to 99%) at all postoperative visits.

Patient Population and Demographic Data

The PMA cohort is comprised of 194 eyes from 130 subjects. Seventy-six of the 130 subjects treated (58.5%) were female. The majority of the subjects were Caucasian (79.2%), with 12.3% of the study cohort Black, 6.2% Hispanic, 1.5% Filipino and 0.8% Native American. The mean age +/- standard deviation at the time of surgery (first surgery in subjects having both eyes treated) was 66.6 +/- 11.6 years with a range of 25 to 85 years. Approximately half

of the subjects (49.2%) were over 70 years of age at the time of surgery; 73.0% over 60 years of age.

One hundred eighty eight of the 194 eyes in the study (96.9%) were diagnosed prior to implantation of the AquaFlow™ with open angle glaucoma. The remainder of the study cohort had diagnoses of pigmentary glaucoma (1.5%), pseudoexfoliation (1.0%) and 1 eye with both open angle glaucoma and pseudoexfoliation (0.5%). The majority of study eyes had pre-existing cataract; 154 of the 194 eyes (79.4%). Seven eyes (3.6%) had a previous diagnosis of macular degeneration.

Forty-three eyes (22.2%) had undergone argon laser trabeculoplasty prior to enrollment in the study. Four eyes (2.1%) previously underwent iridectomy/iridotomy. No eyes in the study cohort had undergone previous filtering surgery prior to enrollment.

Statistical modeling showed that age was a significant predictor of postoperative IOP level, with increasing age associated with lower postoperative IOP. The magnitude of the yearly effect of age on postoperative IOP value was small, with IOP predicted to be 0.5 to 0.7 mmHg lower postoperatively for every decade of increased age. Age above 60 was significantly associated with increased probability of an overall successful outcome, as defined by achieving IOP of 21 or lower. Race also appeared to have an effect on overall success, with Blacks achieving an overall successful result less often than other study participants. However, statistical modeling indicated that Black race was not a significant predictor of postoperative IOP level. Because the study was carried out largely on Caucasian subjects, there was insufficient information to further evaluate the effect of race on clinical outcome. Gender appeared to have an effect on the binary outcome of complete success (IOP at or below 21 with NO medications) but there were also gender differences in medications, which may have impacted on this particular evaluation. Gender was not a significant predictor of postoperative IOP or of overall success. These results were taken into account in the review of this study and statements were added to the labeling to reflect these results.

Data Analysis and Results

Safety Outcomes

The adverse event rates associated with the AquaFlow™ device are compared to reported rates from peer reviewed trabeculectomy literature in Section VIII. No significant differences are observed.

Change in best spectacle corrected visual acuity (BSCVA) was also evaluated as a safety outcome. At 12 months after surgery, 85.4% of eyes were seeing 20/40 or better compared to 79.2% preoperatively; at the 6-month visit, 20/40 or better BSCVA was 82.2%.
At the 6 and 12 month postoperative visits, the proportion of study eyes that experienced an improvement, or were within one line of their preoperative best spectacle corrected visual acuity, were 81.4% and 84.4%, respectively.

Fourteen cases at 6 months, 15 cases at 12 months, and 2 cases at 24 months, had a loss of >2 lines of BSCVA. Some patients lost BSCVA at more than one visit so this really constituted only 24 eyes or 12.4% of the total cohort.

The reasons for loss of BSCVA are listed below.

Cataract Progression	16/194 (8.2%)
Worsening Macular Degeneration	3/194 (1.5%)
Branch Vein Occlusion	1/194 (0.5%)
Central Retinal Artery Occlusion	1/194 (0.5%)
End Stage Glaucoma (Tx Failure)	1/194 (0.5%)
Posterior Capsular Haze	1/194 (0.5%)
Unknown	1/194 (0.5%)
Total	24/194 (12.4%)

Safety Summary

In summary, the overall incidence of complications, both surgical and postoperative in the AquaFlow™ U.S. clinical study is low. The surgical complication rate was 1.0% (2 study eyes) with no long-term repercussions. Both surgical complications were procedurally related and did not occur as a result of implantation of the AquaFlow.

The overwhelming majority of complications in the AquaFlow™ U.S. clinical study occurred before the one week postoperative visit and were transient in nature. These events occur in conjunction with the normal healing process during the first few days after surgery and resolve spontaneously without any needed intervention. Excluding cataract progression, only 2 complications were reported at 6 months or later; 1 case of transient hyphema and the iris prolapse that was the result of trauma.

The overall incidence of postoperative complications in the AquaFlow™ U.S. clinical study is lower or comparable to the complication rates reported in peer reviewed trabeculectomy literature controls. This holds true for series where no antimetabolite therapy was administered as well as those where antimetabolites were used. In conclusion, DSCI with the AquaFlow™ represents a safe surgical treatment alternative for primary open angle glaucoma.

Effectiveness Outcomes

Changes in IOP, glaucoma medication usage, and "success/failures" (defined below) were evaluated to determine the effectiveness of the AquaFlow™ device.

IOP

The mean postoperative intraocular pressure (IOP) measurements showed a consistent decrease from the preoperative baseline of 24.2 mmHg with postoperative values as follows: at 1 month (16.7mmHg), 3 months (16.07mmHg), 6 months (16.34mmHg) and at 12 months

(16.51mmHg).

At 12 months after surgery, 92.0% of eyes had an IOP of </= 21 mmHg compared to 36.1% preoperatively; while 65.9% of eyes were </= 17 mmHg at the 12 month exam vs. 0.0% before surgery. The proportion of eyes with an IOP of </= 21 mmHg at 6 months after surgery was 92.3%; an IOP of </= 17 mmHg was reported in 63.2% of eyes at 6 months postoperative. Zero eyes (0.0%) had an IOP </= 5 mmHg at the 6 or 12 month exams.

The mean change in IOP at 6 and 12 months was -7.37 mmHg, and -7.2 mmHg, respectively. Given that the 95% confidence intervals are quite distant from zero change, these results are highly statistically significant.

At 12 months, 60.9% of eyes experienced a decrease of greater than 5 mmHg and 21.7% had a decrease of greater than 10 mmHg . At the 6-month visit, a decrease of greater than 5 mmHg was observed in 65.9% of eyes while 26.4% had a decrease of greater than 10 mmHg.

Glaucoma Medication

Preoperatively, the mean number of glaucoma medications used at the time of enrollment in the PMA cohort was 2.31 medications. Those eyes not on glaucoma medication at the time of study enrollment were unable to tolerate medication or were non-compliant with medical therapy. The mean number of required glaucoma medications dropped from 2.31 at the time of study enrollment to 0.269 at 6 months and 0.362 medications at 12 months after surgery.

The proportion of study eyes requiring no glaucoma medication at the 12-month visit, increased significantly from the proportion of eyes not on medication preoperatively (79.0% at 12 months vs. 8.2% at baseline). It should be kept in mind that eyes not on glaucoma medication preoperatively did require medication for IOP control but were not taking any due to medication intolerance and/or non-compliance with medical therapy. The proportion of study eyes being prescribed 1 or fewer glaucoma medications at 12 months was 91.3% compared to 26.3% prior to surgery. At the six-month postoperative visit, 79.7% of study eyes required no glaucoma medications; and 95.6% were using 1 or fewer medications.

The mean decrease in the number of glaucoma medications used at 6 and 12 months was –1.99 medications and –1.93 medications, respectively. Given that the 95% confidence interval is quite distant from zero change, the decrease in glaucoma medication is highly statistically significant.

The proportion of study eyes that experienced a decrease of >/= 1 glaucoma medications prescribed at their 12-month postoperative exam was 82.6% . At the 12 month visit, 35.5% reported a decrease of >/= 2, 10.1% a decrease of >/= 3 and 1.4% a decrease of >/= 4 glaucoma medications. Six months after surgery, 87.4% reported a decrease of >/= 1 glaucoma medication with a decrease of >/= 2 in 36.8%, a decrease of >/= 3 in 8.8% and a decrease of >/= 4 glaucoma medications in 1.6% of study eyes.

At the 12 month postoperative timeframe, 82.6% of all study eyes experienced a decrease in the number of prescribed glaucoma medications. The proportion of study eyes with no change in glaucoma medication compared to their preoperative status was 15.2% and an increase in glaucoma medications was reported in only 2.2% of eyes.

At 6 months after surgery 87.4% of the PMA cohort achieved a reduction in their glaucoma medications and 12.6% had no change in the number of glaucoma medications. Zero eyes (0.0%) experienced an increase in glaucoma medications at the 6 month timeframe compared to their preoperative exam.

At 12 months after implantation of the AquaFlow, in those eyes with no change or an increase in IOP compared to preoperative levels, 71.4% nonetheless obtained a decrease in their glaucoma medications. Furthermore 77.8% of those eyes with a 1-4 mmHg decrease in IOP obtained a decrease in glaucoma medications and 90.3% of eyes with a 5-9 mmHg decrease in IOP at 12 months also had a reduction in their prescribed glaucoma medications. A similar trend was seen at 6 months after surgery.

In summary, although the reduction in IOP is seen as the primary variable for assessing the effectiveness of any glaucoma treatment, a decrease in glaucoma medications also plays a critical role in assessing the clinical outcome of a glaucoma procedure.

In the AquaFlow™ U.S. clinical study, a decrease in the number of glaucoma medications was achieved in the overwhelming majority of the PMA cohort despite the amount of reduction in IOP. Even that small subset of eyes (n = 4) that obtained no change or an increase in their IOP level, had a decrease in their glaucoma medications. It should be noted that zero eyes (0.0%) with less than a 5 mmHg decrease in IOP at 6 or 12 months postoperative (no change to increase in IOP and 1-4 mmHg decrease) experienced an increase in glaucoma medication. Prescribing postoperative glaucoma medication was at the discretion of each investigator. If any of the small subset of eyes with less than a 5 mmHg decrease in IOP (no change to increase in IOP and 1-4 mmHg decrease) had received an increase in their glaucoma medications it would be anticipated that some amount of corresponding decrease in IOP levels would have been achieved. This possibly could have resulted in a greater overall success rate (IOP control with or without glaucoma medications).

Success/Failure

These definitions were used to evaluate effectiveness:

Complete success - The most commonly used definitions for "Complete" Success (trabeculectomy literature controls):

- IOP less than or equal to 21 mmHg with no glaucoma medications
- IOP less than or equal to 20 mmHg with no glaucoma medications

Results – IOP less than or equal to 21 mmHg with no glaucoma medications

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature (With and Without) Antimetabolites
72.3%	(88%)	(49-90%)

Results – IOP less than or equal to 20 mmHg with no glaucoma medications

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature (With and Without) Antimetabolites
71.7%	(58-91%)	(48-97%)

Overall success - The most commonly used definitions for "Overall" Success were (trabeculectomy literature controls):

- IOP less than or equal to 21 mmHg with or without glaucoma medications
- IOP less than or equal to 20 mmHg, with or without glaucoma medications.
- IOP less than or equal to 20 mmHg with a 20% or more decrease in IOP if patient is on more than one glaucoma medication.

Results – IOP less than or equal to 21 mmHg with or without glaucoma medications

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
90.1%	(94%)	(73-100%)	(74-91%)

Results – IOP less than or equal to 21 mmHg with or without glaucoma medications

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
88.6%	(80-97%)	(68-73%)	(92-94%)

Results- 20% decrease in IOP or no more than 1 glaucoma medication

PMA Cohort	Trabeculectomy Literature (With and Without) Antimetabolites
87.9%	(46-92%)

Failure - The most commonly used definitions for "Trabeculectomy Failure" in the peer reviewed literature were:

- IOP greater than 21 mmHg or repeat filtering surgery.
- IOP greater than 20 mmHg or repeat filtering surgery.

Another more stringent definition was:

- IOP greater than 20 mmHg or less than 20% decrease in IOP if on more than one glaucoma medication or repeat filtering surgery.

Results – IOP > 21 mmHg "with/without" glaucoma medications

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
9.9%	(6% > 21 mmHg) (3-20% > 20 mmHg)	(27-0%)	(26-9%)

Additional Filtering Surgeries

Additional filtering surgery was performed in 3 study eyes in the PMA Cohort (1.5%). This PMA Cohort rate is lower than the majority of reports from the trabeculectomy literature (with/without antimetabolite therapy). The incidence of additional filtering surgery reported in the DSCI with AquaFlow™ literature is comparable to that reported in the trabeculectomy literature controls.

PMA Cohort	DSCI (AquaFlow™) Literature	Trabeculectomy Literature No Antimetabolites	Trabeculectomy Literature With Antimetabolites
All 1.5%	(0-2%)	(0-28%)	(0-27%)

Goniopuncture (incidence and rationale)

Thirty-three goniopuncture procedures were performed on 28 eyes (14.5%); a second goniopuncture was performed on 5 eyes. Twenty-nine of these 33 procedures were performed at or before the 6 month visit timeframe. Placement of the AquaFlow™ facilitates the performance of a successful Nd:YAG laser goniopuncture to salvage a failing bleb if indicated. Nd:YAG treatment has been less successful in reinitiating aqueous flow through the surgical site in non-penetrating deep sclerectomy procedures without the AquaFlow™. The ability to reestablish filtration is a unique feature associated with the implantation of the AquaFlow. Presumably, the presence of the collagen implant in the first 6 to 9 months postoperatively provides a subscleral space that can be perforated internally by the Nd:YAG treatment. While the performance of a goniopuncture theoretically converts this non-penetrating procedure to a penetrating one, it allows for control of the sclerostomy opening again minimizing the likelihood of hypotony and/or flat chamber. Thus, this 2-step approach (DSCI followed by goniopuncture, if necessary) allows for a significant number of cases to remain non-penetrating in nature and the remainder to have a more controlled sclerostomy.

Prior to the deep sclerectomy procedure the mean IOP was 26.6 mmHg +/- 8.8; with IOP measurements as high as 56 mmHg. Immediately before goniopuncture, the mean IOP was

slightly lower at 24.9 mmHg +/- 6.9; with IOP measurements as high as 38 mmHg. After goniopuncture, the mean IOP was reduced and remained very stable between the 1 week and 12 month follow-up visits: 1 week-18.3 mmHg, 1 month-17.8 mmHg, 3-6 months-18.8 mmHg and 12 months-17.6 mmHg. At all postoperative visits after the goniopuncture, the maximum reported IOP measurement was below the maximum IOP measured immediately before goniopuncture.

Effectiveness Summary

The results from the AquaFlow™ clinical study demonstrate the efficacy of the DSCI with AquaFlow™ procedure. The DSCI with AquaFlow™ procedure effectively achieved a reduction in both IOP and the number of glaucoma medications. The AquaFlow™ U.S. clinical study success outcomes demonstrate the effectiveness of this technique in the treatment of primary open angle glaucoma. Success rates are better or comparable to reports from the peer reviewed trabeculectomy literature. In conclusion, the STAAR AquaFlow™ Collagen Glaucoma Drainage Device is effective for the indications for use outlined in this application.

XI. CONCLUSIONS DRAWN FROM THE STUDIES

The preclinical testing indicates that:

1. the AquaFlow™ material should be well-tolerated in the eye; and

2. the manufacturing processes should result in a product that consistently meets performance specifications.

The clinical trials indicate that:

1. the overall incidence of postoperative complications in the AquaFlow™ U.S. clinical study is lower or comparable to the complication rates reported in peer reviewed trabeculectomy literature controls; and

2. the non-penetrating Deep Sclerectomy with Collagen Implant (DSCI) with AquaFlow™ procedure effectively achieved a reduction in IOP greater than or comparable to reports from the peer reviewed trabeculectomy literature and also resulted in a reduction in the number of glaucoma medications.

XII. PANEL RECOMMENDATION

At an advisory meeting held on November 8, 2000, the Ophthalmic Devices Panel recommended that Staar Surgical Company's PMA for the AquaFlow™ be approved

subject to submission to and approval by the Center for Devices and Radiological Health (CDRH) of modifications to the physician labeling.

XIII. CDRH DECISION

In an amendment dated January 22, 2001, Staar Surgical Company submitted revised labeling. This information was reviewed by CDRH and found to comply with the Panel's recommendations. FDA issued an approval order on JUL 12 2001.

The applicant's manufacturing facility was inspected on March 12 – 14, 2001 and was found to be in compliance with the device Good Manufacturing Practice regulations.

XIV. APPROVAL SPECIFICATIONS

Directions for use: See the labeling.

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

Postapproval Requirements and Restrictions: See approval order.

XV. REFERENCES

General Program Memorandum #G91-1: Device Labeling Guidance