AN OBSERVATIONAL MULTICENTER CLINICAL STUDY TO ASSESS THE LONG-TERM SAFETY AND EFFECTIVENESS OF THE OMNI® SURGICAL SYSTEM IN COMBINATION WITH CATARACT SURGERY IN EYES WITH OPEN ANGLE GLAUCOMA (GEMINI 2.0)

PROTOCOL ID #: 07408

CURRENT REVISION: Rev B

REVISION DATE: 03/18/2022

SPONSOR:

Sight Sciences, Inc.
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Agreement of Principal Investigator

I, _____ agree to conduct this trial in accordance with this clinical protocol and any amendments.

_____ _____
Signature Date

_____ _____
Center Name City, State, Country

ClinicalTrials.gov NCT #05044793

Revision History

[redacted]			

PROTOCOL SUMMARY OF CHANGES

Revision	Section	Description and Rationale for Change	Location of Change
A	N/A	Original	N/A
B	N/A	The protocol was revised to include a second cohort of subjects who did not receive hypotensive medication washout prior to treatment	Th oughout the Protocol
	Synopsis & Section 2	Study Objective: Revised this section to specify the subjects who will be enrolled and observed n the study	Pages 6 and 10
	Synopsis & Section 6.2	Effectiveness Endpoints: Revised the effectiveness endpoints to reflect how study endpoints will be reviewed for the second c hort	Pages 7 and 14
	Synopsis & Section 7.1	Inclusion Criteria: Elaborated on inclu ion criterion # 1 to reflect the second cohort	Pages 8 and 14
	Synopsis & Section 7.2	Removed exclusion crit ion # 4	Pages 9 and 15
	5	The Study Desig section was revised to clarify that only subjects who underwent hypotensive medicatio washout p or to OMNI surgery will receive a washout of hypotensive medications at the 24- a d 36-month visits, if using hypotensive m dication(s) at those visits.	Page 13
	8	Revised this section to show 2 study visit schedule : One for each cohort. Table 1 to reflect a Washout visit, and Table 2 without a washout visit.	Page 16
	8.3	Revised this section to clarify the number of subjects to be enrolled in each cohort, and which subjects will receive a hypotensive medication washout	Page 18
	8.7.1	Revised this section to specify which subjects will receive a hypotensive medication washout	Page 19
	17	Revised Appendix A, to specify what procedures should be completed for each cohort: Washout of hypotensive medications, BCVA, Visual field and IOP	Pages 38-46
	N/A	Insignificant editorial changes were made to provide further clarity as needed	Throughout the Protocol

TABLE OF CONTENTS

1 PROTOCOL SYNOPSIS

Protocol Title	An observational multicenter clinical study to assess the long-term safety and effectiveness of the OMNI® Surgical System in combination with cataract surgery in eyes with open angle glaucoma (Gemini 2.0)
Protocol ID Number	[redacted]
Study Device	OMNI® Surgical System
Study Objective	The purpose of this study is to evaluate the long-term safety and effectiveness of the OMNI® Surgical System in subjects who were treated with the OMNI Surgical System following Cataract Extraction, at least 700 days prior to enrollment.
Study Design	This is a multicenter, observational study with no planned surgical interventions. Both prospective and retrospective data on participating subjects will be collected in the study.
Primary Safety Endpoint	• Rate of occurrence of sight-threatening adverse events (AEs)
Secondary Safety Endpoints	• Rates of ocular AEs • Reduction in best corrected distance visual acuity (BCVA) from baseline • Secondary Ocular Surgical Interventions, including laser, for intraocular pressure (IOP) control

Effectiveness Endpoints	For eyes that underwent washout prior to OMNI surgery: • Reduction in mean unmedicated diurnal IOP (DIOP) from the preoperative unmedicated DIOP • Reduction in mean number of IOP-lowering medications from screening • Percent of eyes with a ≥20% reduction in unmedicated diurnal IOP from the preoperative unmedicated DIOP • Percent of eyes with unmedicated diurnal IOP between 6 and 18 mmHg inclusive For eyes that did not undergo washout prior to OMNI surgery: • Reduction in mean medicated IOP from pre-operative medicated IOP • Reduction in mean number of IOP-lowering medications from screening • Percent of eyes with a ≥20% reduction in mean medicated IOP from pre-operative medicated IOP • Percent of eyes with medicated IOP between 6 and 18 mmHg inclusive

Inclusion Criteria	**<u>Inclusion Criteria</u>** To be included in the study, individuals must meet each eligibility criterion presented as follows: 1. Treated with the OMNI Surgical System in combination with cataract extraction [redacted]. Two cohorts will be enrolled: a. Subjects who underwent a pre-operative washout of ocular hypotensive medications with post-washout DIOP of [redacted] OR b. Subjects without a preoperative washout of ocular hypotensive medications with pre-operative medicated IOP [redacted] mmHg and on [redacted] hypotensive medications Note: Mild to moderate open angle glaucoma as documented in subjects' medical record substantiated using funduscopic exam or OCT and at least one visual field test. The visual field test may be historical (within 6 months prior to OMNI surgery). 2. Is able to understand study requirements and willing to follow study instructions 3. Is willing to return for required study follow-up visits

Exclusion Criteria	The presence of any of the following characteristics will exclude individuals from study participation: • Systemic disease that, in the opinion of the Investigator, would put the subject's health at risk and/or prevent completion of required study visits • Ocular pathology which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate washout, place the subject at risk of significant vision loss during the study period (e.g., wet age macular degeneration (AMD), corneal edema, Fuch's dystrophy, active intraocular infection or inflammation within 30 days prior to Screening Visit, etc.), or interfere with compliance to elements of the study protocol (e.g., returning to Investigator's office for follow-up visits) • Women of childbearing potential if they are currently pregnant or intend to become pregnant during the study period; are breast-feeding; or are not in agreement to use adequate birth control methods to prevent pregnancy throughout the study
Number of Subjects Enrolled and Treated	Up to 130 subjects will be enrolled
Number of Sites	Up to 15 study sites in US
Schedule of Visits	24 Month, 36 Month

2 STUDY OBJECTIVE

The purpose of this study is to evaluate the long-term safety and effectiveness of the OMNI® Surgical System in subjects who were treated with the OMNI Surgical System in combination with Cataract Extraction, at least 700 days prior to enrollment.

3 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Glaucoma is a progressive disease leading to irreversible damage to retinal ganglion cells with the global burden expected to rise to 111.8 million people by the year 2040.[1] Primary open angle glaucoma (POAG) is the most prevalent form of glaucoma and elevated IOP is the only treatable risk factor.[2] Hypotensive eye drops are commonly used as the first line clinical management for POAG.[3] Ocular side effects, such as allergies, ocular surface disorders, blepharitis, pemphigoid, and abnormal pigmentation, and systemic side effects, such as bradycardia, headaches, depression, anxiety, confusion, dysarthria, hallucinations, lethargy, polyuria, weight loss, and metabolic acidosis, can occur during long term use of topical medications.[4] There is also a documented low rate of compliance with eye drops that increases the risk of disease progression and loss of vision.[5]

The Ocular Hypertension Treatment Study showed that reduction of IOP by an average of 22.5% through medical intervention decreased conversion from ocular hypertension to glaucoma over a 5-year period to approximately half that of untreated controls (4.4 vs. 9.5%).[4] Similarly, the Early Manifest Glaucoma Trial (EMGT) showed that treatment of newly diagnosed POAG with argon laser trabeculoplasty plus betaxolol reduced the risk of disease progression at 6 years to half of that for untreated controls (hazard ratio, 0.50; 95% confidence interval, 0.35–0.71).[6] Each mmHg of IOP reduction decreased the risk of progression by approximately 10%.[7]

[1] [redacted]

The Advanced Glaucoma Intervention Study (AGIS) showed that eyes with 100% of visits with IOP less than 18 mmHg over 6 years had mean changes from baseline in visual field defect score close to zero during follow-up.[7]

Minimally (or micro) invasive glaucoma surgery (MIGS) provides an alternative to more invasive surgical methods (i.e. trabeculectomy or glaucoma drainage devices). MIGS procedures can generally be done along with cataract surgery or as standalone procedures. Several studies have demonstrated MIGS to provide long-term IOP lowering and the potential to reduce or eliminate the need for medications (and therefore reliance on patient adherence).[8,9]

MIGS techniques that re-establish the aqueous outflow through the physiological pathways are gaining acceptance among glaucoma surgeons. Canaloplasty (originally described as ab externo) is one such procedure that is intended to restore the natural aqueous outflow system through microcatheterization and viscodilation of Schlemm's canal with a well-documented safety and efficacy profile in reducing IOP.[10,11,12] Trabeculotomy is another such procedure that relieves the resistance to aqueous flow by cleaving the trabecular meshwork and the inner wall of Schlemm's canal, resulting in pressure reductions.[13,14]

Cataract is often seen as a comorbidity present in patients with glaucoma; together, they serve as leading causes of blindness worldwide.[15] Cataract accounts for 33% of visual disability worldwide and may have a causal relationship with increased IOP in OAG.[16] Cataract surgery is known to reduce IOP in glaucoma patients. A review of cataract surgery in glaucoma patients found that, in U.S. patients, cataract surgery (not involving washout of IOP-lowering medications) was associated with a reduction in IOP ranging between 0.6 to 2.5 mm Hg at one

[7] [redacted]

year.[redacted]

Combined glaucoma and cataract surgery often result in a greater decrease in IOP and use of glaucoma medications compared with cataract surgery alone. [20,21,22,23] When a patient with glaucoma also requires surgical intervention for cataract, the ophthalmologist often performs simultaneous cataract and glaucoma surgery.

Note: A summary of known and potential risks to humans, as identified in the literature or through preclinical testing and/or prior clinical evaluations for the study devices can be found in the Instructions for Use for the OMNI Surgical System.

This is a multicenter, observational clinical study with no planned surgical intervention. Both prospective and retrospective data on participating subjects will be collected in the study.

4 STUDY DEVICE

4.1 DEVICE DESCRIPTION

The OMNI® Surgical System ("OMNI") is indicated for canaloplasty (microcatheterization and transluminal viscodilation of Schlemm's canal) followed by trabeculotomy (cutting of trabecular meshwork) to reduce IOP in adult patients with POAG.

[17] [redacted]

[redacted]

4.2 TRAINING

All surgeons would have received training in accordance with Sight Sciences, Inc.'s requirement for using the OMNI Surgical System. OMNI surgery will not be conducted in this trial therefore study specific training on the device will not be required.

5 STUDY DESIGN

This is a multicenter, observational research study with no planned surgical interventions. Both prospective and retrospective data on participating subjects will be collected in the study.
Up to 130 subjects will be enrolled. Subjects will be followed from 24-months (700 – 1040 days) through 36-months (1,050 – 1,110 days) post-surgery. Pre-operative and surgery data will be collected retrospectively.
Prospective data will be collected for all study specific post-operative visits following enrollment into the study.

The study will employ a medication washout at the 24-, and 36-month endpoints for the subjects who received medication washout prior to the OMNI procedure and are using hypotensive medications at those visits.

5.1 STUDY SITES

This clinical study will be conducted at up to 15 sites in the United States.

6 STUDY ENDPOINTS

6.1 PRIMARY SAFETY ENDPOINT

Rate of occurrence of sight-threatening adverse events (AEs)

6.1.1 SECONDARY SAFETY ENDPOINTS

- Rate of ocular AEs
- Reduction in best corrected distance visual acuity (BCVA) from baseline
- Secondary Ocular Surgical Interventions, including laser, for IOP control

6.2 EFFECTIVENESS ENDPOINTS

For eyes that underwent washout prior to OMNI surgery:

- Reduction in mean unmedicated diurnal IOP (DIOP) from the preoperative unmedicated DIOP
- Reduction in mean number of IOP-lowering medications from screening
- Percent of eyes with a ≥20% reduction in unmedicated diurnal IOP from the preoperative unmedicated DIOP
- Percent of eyes with unmedicated diurnal IOP between 6 and 18 mmHg inclusive

For eyes that did not undergo washout prior to OMNI surgery:

- Reduction in mean medicated IOP from pre-operative medicated IOP
- Reduction in mean number of IOP-lowering medications from screening
- Percent of eyes with a ≥20% reduction in mean medicated IOP from pre-operative medicated IOP
- Percent of eyes with medicated IOP between 6 and 18 mmHg inclusive

7 [redacted]

7.1 [redacted]

[redacted]

b. [redacted]

7.2 EXCLUSION CRITERIA

[redacted]

3. [redacted]

8 STUDY PROCEDURES

8.1 STUDY SCHEDULE – PRE-OPERATIVE WASHOUT (SUBJECTS THAT UNDERWENT MEDICATION WASHOUT PRIOR TO OMNI)

Table 1: Study Visit Schedule

Note: The fellow eye should be followed per the PI's usual practice based on the ocular health of the fellow eye.

	RETROSPECTIVE DATA			OBSERVATIONAL PROSPECTIVE DATA			
PROCEDURE	PRE-WASHOUT (DAY -45 TO -6)	POST-WASHOUT (DAY -6 TO 0)	OMNI SURGERY (DAY 0)	24 M[1] (DAY 700-1,040)	24 M WASHOUT [2] (DAY 700-1,040)	36 M (DAY 1,050-1,110)	36 M WASHOUT[2] (DAY 1,050-1,110)
Informed Consent and demographics[1]				X		X	
Medical & Ocular History	X	X		X	X	X	X
Medication Log[3]	X	X		X	X	X	X
Monocular BCVA[4]	X	X		X	X	X	X
Visual Field (Humphrey 24-2 SITA)	X			X		X	
IOP (Goldmann)[5]	X	X		X	X	X	X
Slit Lamp Exam	X	X		X		X	
Gonioscopy	X			X		X	
Dilated Fundus Exam/C:D Ratio	X			X		X	
Surgery			X				
Adverse Events	X	X	X	X	X	X	X

1. [redacted]

8.2 STUDY SCHEDULE – No PRE-OPERATIVE WASHOUT

Table 2: Study Visit Schedule

Note: The fellow eye should be followed per the PI's usual practice based on the ocular health of the fellow eye.

	RETROSPECTIVE DATA		OBSERVATIONAL PROSPECTIVE DATA	
PROCEDURE	**PRE-SURGERY BASELINE** (DAY -45 TO -6)	**OMNI SURGERY** (DAY 0)	**24 M[1]** (DAY 700-1040)	**36 M** (DAY 1,050-1,110)
Informed Consent and demographics[1]			X	
Medical & Ocular History	X		X	X
Medication Log[2]	X		X	X
Monocular BCVA[3]	X		X	X
Visual Field [4]	X		X	X
IOP (Goldmann) [5]	X		X	X
Slit Lamp Exam	X		X	X
Gonioscopy	X		X	X
Dilated Fundus Exam/C:D Ratio	X		X	X
Surgery		X		
Adverse Events	X	X	X	X

1. [redacted]

8.3 Number of Subjects, Duration of Follow-up and Study Duration

Up to 130 subjects will be enrolled. Eligible subjects will be enrolled at the 24-month follow up timepoint as shown by Table 1 or 2 as applicable. At least 50 subjects will be enrolled in each cohort. For subjects in cohort A, diurnal IOP measurements will be measured at both visits for those subjects who underwent medication washout and where DIOP was measured pre-operatively (Cohort A). Cohort A subjects using ocular hypotensive medication(s) at 24 and 36 months will undergo a medication washout (Table 3) and return for diurnal IOP measurements at a second visit within the same window, as shown in Table 1. There will be no diurnal IOP measurements for subjects in cohort B. IOP measurements will be measured as shown in Table 2.

It is anticipated that site initiation, recruitment and follow-up of subjects, data collection and site close-out will require approximately 60 months.

8.4 Informed Consent and Point of Enrollment

The pre-operative and Surgery data will be collected retrospectively by performing a review of medical charts. Any patients identified as meeting the study eligibility criteria will then be consented for the study for the prospective observational data collection.

The IRB-approved informed consent document (ICD) will be presented and explained to each prospective subject by the Investigator or a delegated, trained clinical professional. Once the patient has had ample time to read the consent form, has been informed of all aspects of the study, and has had an opportunity to ask questions, the patient will be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the informed consent document. After signing the ICD and the HIPAA (Health Insurance Portability and Accountability Act) authorization, the subject can then proceed with the study visits. The subject has the right to withdraw from the study at any time without consequences, as indicated in the ICD.

The subject's signed and dated informed consent must be obtained before conducting any study-specific procedures that are not part of the standard of care.

The investigative site must retain the original, signed written ICD. A copy of the written ICD must be given to the subject.

8.5 Eligibility and Study Entry

Subjects will be recruited from the Investigators' patient records. Eligible subjects will consist of those patients meeting all inclusion criteria and none of the exclusion criteria.

8.6 DATA EXTRACTION

Data for the pre-operative) and surgery visits will be collected retrospectively onto case report forms (CRFs). The data collected will be in accordance with Tables 1 and 2 (8.1 & 8.2: Study Schedule).

Following signing of the ICD, a subject ID number will be assigned consisting of a two-digit study identification number, a two-digit site identification number followed by a two-digit subject number ([redacted] Subject ID numbers will be assigned sequentially.

Medical records will be reviewed for demographic and medical history information, pre-operative, medication use data, adverse events, and surgical information, including clock hours of canaloplasty and trabeculotomy. Intra-operative complications will be abstracted from the Operative Notes.

8.7 PROSPECTIVE VISITS

After obtaining an understanding of the purpose of this study and reviewing and signing the ICD, all subjects will begin the prospective study visits. These visits should be performed according to the schedule provided in Tables 1 and 2. All attempts should be made to conduct each visit within the time interval specified in Tables 1 and 2. Evaluations conducted outside the prescribed time period will be considered protocol deviations.

[redacted]

8.7.1 WASHOUT OF HYPOTENSIVE MEDICATIONS

Subjects who underwent washout prior to OMNI surgery (Cohort A) and who are taking hypotensive medications at the 24- and 36-month visits will be instructed to discontinue their ocular hypotensive medication regimen and to return for a post-washout visit after completing the appropriate washout period.

[redacted]

If the study subject fails to remember to not use ocular hypotensive medication for the study eye per the required washout period, they can restart washout and return for the

appropriate visit upon completion of washout and as long as it falls within the specified visit window. The minimum wash-out periods are specified in Table 3 below.

Table 3: Ocular Hypotensive Medication Washout Periods

Brand Name/Chemical Name	Minimum washout period
Carbonic Anhydrase Inhibitors	
Diamox® (Acetazolamide) – oral Rx	5 days
Neptazane® (Methazolamide) – oral Rx	5 days
Azopt® (Brinzolamide)	5 days
Trusopt® (Dorzolamide Hydrochloride)	5 days
Muscarinic Agonists	
Salagen, Pilocar (Pilocarpine)	5 days
Alpha Adrenergic Agonist	
Alphagan® (Brimonidine)	14 days
Iopidine® (Apraclonidine Hydrochloride)	14 days
Beta Blockers	
Betagan® (Levobunolol Hydrochloride)	28 days
Betoptic® (Betaxalol Hydrochloride)	28 days
OptiPranolol® (Metipranolol)	28 days
Timoptic/Betimol® (Timolol Maleate)	28 days
Prostaglandin Analogs	
Lumigan® (Bimatoprost)	28 days
Travatan® (Travoprost)	28 days
Xalatan® (Latanoprost)	28 days
Zioptan® (Tafluprost)	28 days
Vyzulta® (Latanoprostene Bunod)	28 days
Rho Kinase Inhibitor	
Rhopressa® (Netarsudil)	28 days
Combined Medications	
Combigan® (Brimonidine Tartrate/Timolol Maleate)	28 days
Cosopt® (Dorzolamide Hydrochloride/Timolol Maleate)	28 days
Simbrinza® (Brinzolamide/Brimonidine Tartrate)	28 days
Rocklatan® (Netarsudil/Latanoprost)	28 days
Krytantek (Brimonidine Tartrate/ Dorzolamide Hydrochloride/ Timolol Maleate)	28 days
Ganfort (Bitmaprost/ Timolol Maleate)	28 days
Other	Contact Sponsor

NOTE: A safety IOP check anytime during the wash-out period may be performed at the Investigator's discretion to ensure subject safety and should reported as unscheduled visits.

8.8 UNSCHEDULED VISITS

An unscheduled visit will be any visit to the clinical site, other than those specified in the protocol. The Investigator and/or qualified investigational staff will perform the procedures necessary to evaluate the study participant at these visits and will record the visit in the subject's CRF. No specific testing is required.

8.9 MANAGEMENT OF IOP

For subject safety, a change in medical therapy may be implemented or additional surgical measures may be performed at any time during the study at the Investigator's discretion in the event it is required. The primary concern of the Investigator and Sponsor at all times is the health and safety of the subjects. Usage of hypotensive medications specifically indicated for prevention of IOP spikes following Nd:YAG capsulotomy and administered for up to 72 hours after Nd:YAG capsulotomy will not be considered rescue therapy.

Medications which have been re-started by the Investigator may be discontinued if the Investigator's judgment is that the target intraocular pressure has been reached and the continued use of some or all of the therapy may not be required. Discontinuation of medications after re-introduction is recommended to be in the reverse order of re-introduction. The rationale for discontinuation should also be documented in the subject's medical record.

A record of all ocular hypotensive medications added, discontinued or changed will be documented on the appropriate CRF for each scheduled visit or on a CRF for an Unscheduled Visit, if necessary.

8.9.1 PARACENTESIS

If a pressure rise is observed, a paracentesis may be performed, as necessary. If a paracentesis is performed and there is no protocol-defined adverse event, the paracentesis will be documented in the subject's medical record, the applicable visit CRF, and the Ocular Procedures log. If, however, the paracentesis is performed in conjunction with an AE, then the AE is recorded as such, and the paracentesis is also recorded on the AE CRF as a treatment for the protocol-defined AE (as well as the other CRFs mentioned above).

8.9.2 Secondary IOP-Lowering Interventions to Control IOP

If the subject requires another glaucoma procedure to control their IOP, the subject should continue to be followed according to standard of care until the adverse event resolves or 1-month post-re-intervention, whichever is longer. Following this procedure, the subject should be withdrawn from the study.

Subjects who have had a secondary IOP-lowering intervention will be considered treatment failures for the purpose of the endpoint analyses.

8.10 Withdrawal and Discontinuation

All subjects have the right to withdraw at any point during the study without prejudice. The Investigator can discontinue any subject at any time at his/her discretion, or if continued participation in the study would result in harm to the subject. All efforts should be made by the Investigator to retain the subject in the study. If a subject withdraws prematurely from the study, a genuine effort must be made to determine the reason(s) the subject discontinued the study. The reason must be recorded in the subject's file and on the Study Exit Case Report Form. A subject may withdraw from the study on his/her own or can be withdrawn by the study investigator for reasons including but not limited to non-compliance, being unresponsive, or no longer qualifying under the protocol. A subject may be withdrawn by the Sponsor for reasons including but not limited to early closure or discontinuation of the study. For every subject that withdraws/is withdrawn from the study prior to completing the study, the study investigator should bring the subject back for a final study visit if possible unless the subject has had a recent visit and, in the Investigator's discretion, does not need a final visit. If a subject cannot be returned for a final study visit, the reason should be documented in the subject's study record.

8.11 Subjects Lost to Follow-up

Subjects who do not show up for a follow-up must be contacted to attempt to have them come for the follow-up. For those subjects who cannot be reached, every attempt to contact with the subject should be documented. If a subject misses two consecutive follow-up visits without any contact with the study staff, the subject will be considered lost-to-follow-up unless there is a further communication by the subject.

9 Adverse Events (AEs)

Adverse Events are defined below. Adverse events that occur in the eye during the trial must be documented in the subject's records. Date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device will be recorded

on the Adverse Event CRF. Conditions which exist at the time the subject is enrolled will be considered pre-existing conditions and will not be recorded as adverse events unless they increase in severity during the study. Sites should document any known existing medical and ophthalmic conditions at the time of eligibility determination.

Information regarding adverse events that occurred intra and post-operatively up to enrollment into the study will also be collected.

9.1 DEFINITIONS OF AE, SAE, SADE, USADE

Adverse Event	Any untoward medical occurrence in a subject who has been treated with the device that does not necessarily have causal relationship with the treatment.
Adverse Device Effect	Any unfavorable and unintended sign (including an abnormal laboratory finding), symptom, or disease that is possibly related to the study device.
Serious Adverse Event (SAE)	Any untoward medical occurrence that: • Results in death • Is life-threatening • Requires in-patient hospitalization or prolongs existing hospitalization • Necessitates medical or surgical intervention to preclude permanent impairment of a body function or permanent damage to a body structure • Sight-threatening
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational plan; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (21 CFR 812.3(s)). Any sight-threatening event, whether listed in the protocol or not, is considered to be reportable as a UADE.

9.2 [redacted]

[redacted]

[redacted]

[24] [redacted]

Adverse events may occur intra-operatively or post-operatively.

9.3 Reporting Adverse Events and Unanticipated Adverse Device Effects

Identification, collection and reporting of adverse event information is the responsibility of the Principal Investigator. The Investigator records the date of the event, its severity, treatment (if any) and the assessed relationship of the event to the study device on the AE CRF.

Any ocular **serious adverse event** (SAE) should be reported to the study sponsor within one business day of learning of the event. Non-ocular SAEs should be reported to the study sponsor within two working days of learning of the event. Enter data in electronic data capture (EDC) system within two working days of learning of the event.

Any **unanticipated adverse device effects (UADE)** must be reported to the following two entities:

1. The study sponsor – Within one working day of the investigator first learning of the event enter data in EDC; and
2. The reviewing IRB – As soon as possible, but no later than 10 working days after the investigator first learns of the event, report per the IRB's instructions.

The sponsor will conduct an evaluation of unanticipated adverse device effects. If the sponsor determines that an unanticipated adverse device effect presents an unreasonable risk to subjects, parts of the investigation presenting risks will be terminated. Termination will occur no later than 5 working days after the sponsor

makes such a determination and no later than 15 working days after the sponsor first received notice of the effect.

10 STATISTICAL CONSIDERATIONS

10.1 SAMPLE SIZE CALCULATION

This is a descriptive study and is not designed to test pre-planned hypotheses. The sample size is based on an understanding of the approximate number of eligible patients available at the participating sites and not on formal sample size calculation. With an assumed standard deviation of 3.5 mmHg for intraocular pressure, a minimum change in IOP of 5.0 mmHg from a pre-operative baseline of mean = 21 mmHg, and alpha = 0.05, a sample size of minimum 50 subjects is required to get at least 90% power to detect statistical significance.

With a total sample size of up to 130, adverse events with a frequency of approximately 3% would be detected with 97.5% probability.

10.2 ANALYSIS POPULATIONS

The intent-to-treat (ITT) analysis population includes all subjects who are enrolled and treated, regardless of whether or not they have a protocol deviation. The per-protocol analysis population (PP) is a subset of ITT, which includes all subjects who have canaloplasty and trabeculotomy after uneventful cataract surgery, 36-month IOP (or hypotensive medications washed out IOP if the medications can be washed out) and medication data, and have no clinically significant protocol deviations. It should be noted that the ITT subjects with an uneventful study procedure but with secondary surgical interventions (SSIs) before the 36-month visit will be included in the PP population even if they do not have the 36-month IOP and medication data.

The safety data will be summarized based on the ITT population.

10.3 DEMOGRAPHICS AND BASELINE CHARACTERISTICS

Demographic variables gender, race, ethnicity, and age will be summarized for all enrolled subjects treated with OMNI Surgical System, along with medical history. Descriptive statistical summaries of pre-treatment parameters (min, max, median, mean, and standard deviation) will also be provided. The same analyses will be performed for the ITT and PP populations.

10.4 EFFECTIVENESS ENDPOINTS AND ANALYSIS METHODS

Descriptive statistics on continuous variables will include mean, standard deviation, median, minimum, and maximum. Confidence intervals for change from baseline will be included for selected endpoints. Categorical variables will be summarized using frequency counts and percentages. Exact confidence intervals for point estimates may be provided. Statistical testing will be one-sided with a significance level of 0.025 or two-sided significance level of 0.05 unless specify otherwise. Data listings of individual subject data may be provided.

Subjects with washout and those without washout will be analyzed separately.

10.5 SAFETY ANALYSIS

All safety analyses will be performed on the ITT population based on all available data descriptively.

10.5.1 ADVERSE EVENTS

AEs will be classified as pretreatment, intraoperative or postoperative. The number and the percent of eyes reporting at least 1 adverse event of a given type will be summarized. Additionally, the number of reports of each type of AEs will be provided.

For each AE, the number and the percent of eyes reported with the event will be summarized by the severity level. For eyes with multiple reports of the same type of AE, the maximum severity will be used. Similarly, the AE relationship to the procedure will be summarized. For eyes with multiple reports of the same type of AE, the closest relationship to the procedure will be used.

10.5.2 BEST CORRECTED VISUAL ACUITY

The number and percent of eyes reporting with BCVA of 20/20 or better, 20/25 or better, 20/32 or better, 20/40 or better, worse than 20/40 to 20/80, worse than 20/80 to 20/200, and worse than 20/200 at each visit will be summarized. The number and percent of eyes reporting BCVA of increase $\geq$ 10 letters, increase 10 letters, increase $\geq$ 5 letters to < 10 letters, within 5 letters change, decrease $\geq$ 5 letters to < 10 letters, decrease 10 letters, and decrease $\geq$ 10 letters at each postoperative visit will be calculated.

10.5.3 Other Safety Outcomes

The number and percent of eyes reported with each kind of slit lamp findings, gonioscopy findings, and dilated fundus examination findings at each visit will be provided.

The descriptive statistics for the continuous variables will be derived for the visual field mean deviation (MD) and pattern standard deviation (PSD).

10.6 Interim Analysis

An interim analysis providing descriptive statistics for the outcomes may be completed following completion of the 24-Month follow-up visit by 100% of the enrolled subjects. Endpoints listed below will be analyzed at an interim analysis. No device effectiveness will be claimed based on the interim analysis outcomes.

Subjects with washout and those without washout will be analyzed separately.

Effectiveness outcomes up to 24 months will be summarized descriptively, as follows:

1. Percent of eyes with a ≥20% reduction from pre-operative baseline in IOP with no increase in IOP-lowering medications compared to the pre-operative visit;
2. Percent of eyes with IOP between 6 and 18 mmHg with no increase in IOP-lowering medications compared to pre-operative visit;
3. Percent of eyes with IOP between 6 and 21 mmHg with no increase in IOP-lowering medications compared to pre-operative visit;
4. Mean reduction in DIOP from the pre-operative DIOP (Cohort A), or Mean reduction in medicated IOP from the pre-operative medicated IOP (Cohort B); and
5. Reduction in mean number of IOP-lowering medications from the pre-operative visit.

The primary safety endpoint is the rate of occurrence of sight-threatening AEs.

The secondary safety endpoints are the rates of ocular adverse events, the reduction in BCVA from baseline, and secondary ocular surgical interventions, including laser, for IOP control.

10.7 Deviation from the Statistical Plan

Any deviations from the statistical plan will be noted in the final report.

11 MONITORING PROCEDURES

Sight Sciences, Inc. ("Sight") or contract research organization (CRO) personnel will monitor the study in a manner consistent with FDA regulations, good clinical practices (GCPs), and the clinical research standards adopted by Sight. Study monitoring will be executed using on-site and remote monitoring visits as needed and as determined by the study team. The frequency and necessity of visits will be determined by the study team. Study monitoring will involve the following elements:

- Site Qualification: Sight or CRO personnel will meet with investigators and clinical study staff prior to the initiation of the study in order to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study, and to familiarize the investigator with the study protocol. If Sight or the CRO have recently been involved with an investigator for another study, a site qualification visit may not be necessary.
- Site Initiation: Sight and/or CRO personnel will meet with the investigator(s) and clinical study staff when the site is ready to begin enrolling subjects in order to train them in how to properly select subjects, perform the study procedure, and record study data. The site initiation visit may be conducted remotely and may include a grouping of multiple sites. This visit will include, but not be limited to a review of the following:
    - Detailed review of the protocol;
    - Informed consent procedures;
    - Instructions for the surgical procedure; and
    - Records and reports.
- Interim Monitoring: Sight or CRO personnel will conduct routine visits during the course of the study to review charts, perform source document verification, ensure proper adherence to the study protocol, and to review regulatory documents. Interim monitoring visits and telephone consultation will occur as necessary during the course of the study to ensure the proper progress and documentation of the study findings.
- Study Close Out Visit: At the conclusion of the trial there will be a study closure visit during which several actions, including but not limited to the following, will be performed:
    - A final inspection of the study binder;
    - Accountability and return of all devices and non-consumable ancillary study supplies to the sponsor;
    - Discussion of record retention requirements with the investigator; and
    - Close-out notification to the IRB.

12 DATA AND QUALITY MANAGEMENT

12.1 DATABASE MANAGEMENT

The study database will be designed using an electronic data capture (EDC) system that is compliant with 21 CFR Part 11 and relevant guidance documents. The EDC will be developed and maintained by an independent, qualified data management firm.

The database will incorporate time-stamped audit trails, protection of human subjects, restricted access, and data security at the component level. Each database module, including each individual electronic case report form (eCRF), will be validated by conducting a series of standard tests that demonstrate usability and correctness of the database system. The database will be maintained on an ongoing basis and will be routinely backed up.

12.2 SUBJECT IDENTIFICATION

The subjects will be identified by a six-digit subject number composed of a double-digit study identification number, a two-digit center identification number followed by a two-digit sequential subject number. A subject identification number will be assigned after informed consent is obtained. This will ensure that identifiable subject information has been removed and kept confidential.

12.3 SUBJECT ACCOUNTABILITY

All subjects enrolled in this clinical investigation shall be monitored for the duration of the investigation. The clinical investigation shall be considered completed when all subjects that have been enrolled in the investigation have reached the final reporting period, excluding subjects who were withdrawn.

12.4 CONFIDENTIALITY

All medical records associated with the clinical investigation will be made available for review by Sight personnel, its CRO, and governmental/regulatory agencies involved. The results of the study may be published in the future for scientific and marketing purposes, but the identity of each subject will not be revealed. All records will be stored in a secure area at the investigator's facility, the CRO, the data management firm, and Sight.

12.5 Source Data and Case Report Forms

Source data will be entered into a validated electronic system at each site by trained personnel in accordance with 21 CFR Part 11 requirements. Electronic entries will be verified against corresponding source data at the sites and queried/corrected if needed to the extent possible. Medical site records serve as source data. In addition, data that are collected exclusively for the purpose of this study and not normally recorded in the subjects' medical records can be collected directly on any study CRFs or tools provided by the sponsor, and these will serve as the source data.

Source data and study CRFs are to be maintained at the site in the subject records or in the medical records. All data entries must be made in accordance with ALCOA (**A**ttributable, **L**egible, **C**ontemporaneous, **O**riginal, **A**ccurate) standards and GDP (Good Documentation Practices).

Study data acquired from sites will be collected on eCRFs for submission to sponsor. Sites will enter data entered on source documents into the electronic case report forms for Sponsor review and analysis.

12.6 Retention Period

Clinical sites are to retain any and all clinical trial material (documentation, photographs, etc.) for a period of two years from the date a marketing application is approved or two years after the investigation has been discontinued, or as directed by their institutional document retention requirements, whichever is the longest. After that time, the items must be returned to Sight for archiving.

13 Protocol Modifications and Deviations

Protocol modifications may occur during the study. Each will be approved by the sponsor before implementation. Each will undergo Institutional Review Board (IRB) review and approval, as necessary.

Any deviations from this protocol intended to protect the life or physical well-being of a subject in an emergency are to be reported to Sight and the IRB as soon as possible, and no later than 5 working days after the emergency occurred.

All protocol deviations will be documented using the Protocol Deviation CRF or Source Tool.

14 ETHICAL CONSIDERATIONS

14.1 DECLARATION OF HELSINKI

This study shall be conducted in accordance with the Declaration of Helsinki (Appendix D).

14.2 INSTITUTIONAL REVIEW BOARDS (IRB)

The study shall not begin at a site until approval has been obtained from the reviewing IRB. It is the Investigators' responsibility to obtain and maintain written approval of the study protocol and Informed Consent documents from the appropriate IRB. It is also the Investigators' responsibility to notify and obtain approval from (if needed) that body about any amendments to these documents and to follow the IRBs rules regarding the reporting of AEs and Protocol Deviations related to the investigational device and/or this study. Copies of all written approvals (identifying the study, the submitted and approved documents and the date reviewed) and the approved versions of the documents must be provided to Sight or its CRO.

The Investigators must file all correspondence with the IRB and forward copies of such correspondence to Sight.

14.3 INFORMED CONSENT DOCUMENT (ICD)

An Informed Consent template that covers all protocol procedures and follows GCP guidelines will be prepared by Sight Sciences and made available to each Investigator. The Investigator may adapt these templates to the requirements of the local IRB and of the institution where the study is conducted, but any revisions made to the ICD must be submitted to the sponsor for review prior to submission to the IRB. A copy of each IRB-approved ICD version is to be made available to Sight and its CRO. The approved, IRB-stamped ICD is to be kept in its full length in the study Regulatory Binder. Original, signed ICDs are to be maintained in study records and must be made available for monitoring review.

14.4 PUBLIC LISTING OF STUDY

The study will be listed on the NIH website www.clinicaltrials.gov.

15 STUDY ADMINISTRATION

15.1 EARLY TERMINATION OR SUSPENSION OF THE STUDY OR AN INVESTIGATIONAL SITE

Sight may terminate the study, in which case the investigators and associated IRBs will be notified in writing. Possible reasons for study termination include but are not limited to:

- The discovery of an unexpected, significant, or unacceptable risk to the study subjects;
- Withdrawal of FDA clearance of the OMNI device;
- Insufficient enrollment in the study; and
- Determination by the Sponsor that enough data has been collected for the study, and no further data are needed.

Sight reserves the right to stop the study at a particular site any time after the initiation visit if there have been no subject enrollments or if there have been significant protocol deviations/violations at the site.

Likewise, a principal investigator may terminate the study at his/her institution. This decision must be followed by written notification to Sight within five working days, stating the reasons for termination.

If the study is terminated, every effort should be made to obtain final follow-up from all subjects.

In the event that there are significant human use issues with the device, the Investigator will be consulted to make a determination of whether the study should be terminated or not.

15.2 INVESTIGATOR RESPONSIBILITIES

15.2.1 GENERAL RESPONSIBILITIES OF INVESTIGATORS

An Investigator is responsible for ensuring that an investigation is conducted according to the signed agreement, the investigational plan and applicable FDA regulations, for protecting the rights, safety, and welfare of subjects under the Investigator's care, and for the control of devices under investigation. An Investigator also is responsible for ensuring that informed consent is obtained in accordance with 21 CFR Part 50.

15.2.2 SPECIFIC RESPONSIBILITIES OF INVESTIGATORS

1. Awaiting approval - An Investigator may determine whether potential subjects would be interested in participating in an investigation but shall not request the written informed consent of any subject to participate, and shall not allow any subject to participate before obtaining IRB approval.
2. Subject Qualification -The Investigator is responsible for ensuring that all subjects entering the study conform to the subject selection criteria.
3. Compliance - An Investigator shall conduct an investigation in accordance with the signed agreement with the Sponsor, the investigational plan, all applicable FDA regulations, and any conditions of approval imposed by an IRB.

15.2.3 INVESTIGATOR RECORDS

A participating Investigator shall maintain the following accurate, complete, and current records relating to the Investigator's participation in an investigation for the period specified in Section 12.6:

1. All correspondence with another Investigator, an IRB, the Sponsor, a clinical research associate (CRA) or monitor, or FDA, including required reports.
2. Records of each subject's case history and exposure to the device. Case histories include the subject's study clinic record, certified copies of medical record as applicable, and supporting documents including, signed and dated consent forms. Such records shall include:
    a) Documents evidencing informed consent.
    b) All relevant observations, including records concerning adverse device effects (whether anticipated or unanticipated), information and data on the condition of each subject upon entering, and during the course of, the investigation, including information about relevant previous medical history and the results of all diagnostic tests.
3. The protocol, with documents showing the dates and reasons for each deviation from the protocol.
4. Any other records that FDA requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

15.2.4 INVESTIGATOR REPORTS

An Investigator shall prepare and submit the following complete, accurate, and timely reports:

1. Unanticipated Adverse Device Effects - An Investigator shall submit to the Sponsor and to the reviewing IRB a report of any unanticipated adverse device effect occurring during an investigation as soon as possible, but in no event later than 10 working days after the Investigator first learns of the effect.
2. Withdrawal of IRB Approval - An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing IRB of the Investigator's part of an investigation.
3. Progress - An Investigator shall submit progress reports on the investigation to the Sponsor, the monitor, and the reviewing IRB at regular intervals, but in no event less often than yearly.
4. Deviations from the Investigational Plan - An Investigator shall document and report to the Sponsor any deviation from the investigational plan.
5. Informed Consent - If an Investigator enrolls a subject without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing IRB within 5 working days after the use occurs.
6. Final Report - An Investigator shall, within 3 months after termination or completion of the investigation or the Investigator's part of the investigation, submit a final report to the Sponsor and the reviewing IRB.
7. Other - An Investigator shall, upon request by a reviewing IRB or FDA, provide accurate, complete, and current information about any aspect of the investigation.

15.3 INVESTIGATOR AGREEMENT

The principal investigators in each center shall agree to the clinical protocol and any amendments and indicate their approval and agreement by signing and dating the cover page of the study protocol and the Investigator Responsibility Agreement.

16 [redacted]

[redacted]

[redacted]

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17 APPENDIX A – METHODS FOR EXAMS, TESTS AND QUESTIONNAIRES

17.1 LIST OF STUDY PROCEDURES

1. Informed Consent
2. Demographics, Medical & Ocular History
3. Medication Log
4. BCVA
5. Visual Field (Humphrey 24-2 SITA- Standard)
6. IOP (Goldmann Tonometry)
7. Unmedicated Diurnal IOP
8. Gonioscopy
9. Slit Lamp Exam
10. Dilated Fundus Exam/C:D Ratio
11. Eligibility Assessment
12. AE Assessment

17.2 BEST CORRECTED VISUAL ACUITY

Best corrected visual acuity (BCVA) will be collected using the same method that was used at the pre-surgery baseline visit. For the prospective scheduled study visits, a manifest refraction should be conducted if the initial BCVA acquired is ≥ 2 lines worse compared to the pre-surgery baseline. If the BCVA continues to be ≥ 2 lines worse compared to baseline even after manifest refraction, pinhole visual acuity should be completed.

In order to provide a standardized and well-controlled assessment of visual acuity, visual acuity assessments for all subjects should be performed under consistent conditions (e.g., the same lighting conditions, viewing distance, etc.) at each visit.

17.3 MEASUREMENT OF INTRAOCULAR PRESSURE

The Goldmann tonometer will be used for measuring intraocular pressure for all visits including the retrospective visits. IOP should be measured as shown in Table 1.

For the retrospective visits the type of tonometer should be the Goldman tonometer

however, the method (e.g. operator/reader) for measuring IOP will be based on the Investigator's discretion

For the prospective visits, a reader-operator technique for measuring and recording the IOP should be followed to minimize observer bias; the individual operating the tonometer (operator) should not view the dial during the measurement. A separate individual (reader/recorder) should view the dial and note the measurement. Take two measurements of IOP. If the measurements differ by more than 2 mmHg, take a third measurement. If two measurements are taken, record the mean on the case report form. If three measurements are taken, record the median on the case report form.

At all scheduled study visits, every attempt should be made to have these measurements taken at the same time interval to minimize the effect of daily fluctuations in pressure.

[redacted]

5. [redacted]

Errors in measurement can arise from a number of factors, including the following:

1. Inadequate fluorescein staining of the tear film causes an underestimation of intraocular pressure.
2. Elevating the eyes more than 15° above the horizontal causes an overestimation of intraocular pressure. Widening the lid fissure excessively causes an overestimation of intraocular pressure.
3. Repeated tonometry reduces intraocular pressure, causing an underestimation of the true level. This effect is greatest between the first and second readings, but the trend continues through a number of repetitions.
4. A scarred, irregular cornea distorts the fluorescein rings and makes it difficult to estimate intraocular pressure.
5. The thickness of the cornea affects intraocular pressure readings. If the cornea is thick because of edema, intraocular pressure is underestimated. If the cornea is thick because of additional tissue, intraocular pressure is overestimated. The Goldmann tonometer is accurate after epikeratophakia.
6. If the examiner presses on the globe or if the subject squeezes his eyelids, intraocular pressure is overestimated.
7. If corneal astigmatism is greater than 3 diopters, intraocular pressure is underestimated for with the rule astigmatism and overestimated for against

the rule astigmatism. The intraocular pressure reading is inaccurate 1 mm Hg for every 3 diopters of astigmatism.

Calibration Verification and Documentation
The calibration of the tonometer will be checked at least once every three months with the weight system at 0, 2, and 6 grams as supplied by the manufacturer. When the verification steps provide readings within ± 2 mmHg of the target value for each weight, the tonometer is considered adequately calibrated. However, if the variation exceeds this amount, a different adequately calibrated instrument should be used for IOP measurements.

The investigator must maintain documentation of the calibration checks of each tonometer used at the beginning and throughout the study period, and make these records available to study monitors for review. Documentation must describe the unit (by model and serial number or other permanent identifier), the date of each calibration, the name or initials of the person performing the calibration check, and an indication as to whether or not the unit meets the calibration requirement at each check. If a unit does not meet calibration parameters, this should be documented, and the unit should not be used for study measurements until it has been brought back into calibration specifications. Following any repair or recalibration, another verification should be conducted, and the results documented to show that the unit is back within calibration parameters, prior to using in the study. Where applicable, sites should keep significant documentation in regard to calibration/recalibration or repair of a tonometer that is being used in the study.

Diurnal IOP
Diurnal IOP (IOP) will be completed as shown in Table 1 for the Cohort A subjects (those who had a pre-operative, post-washout DIOP at baseline). In order to determine the mean diurnal intraocular pressure measurements at 24 months and 36-months, [redacted]. The three IOP measurements should then be averaged to determine the mean diurnal IOP.

17.4 VISUAL FIELD EXAMINATION

Visual field tests obtained prior to enrollment into the study may be of the investigator's discretion (SITA Standard with 24-2 algorithm is preferred but not required). For consistency, the type of visual field test or standard used pre-operatively should be used for the post-operative visits.

Visual field tests are to be performed with a non-dilated pupil unless, in the opinion of the investigator, the pupil is so miotic that dilation is required (e.g., < 3mm). If dilation

was performed at the pre-surgery visit, it should be performed at all subsequent visual field examinations. However, dilation should not be performed before the IOP measurement on the appropriate visits.

The appropriate trial lens as defined by the perimeter should be used.

17.5 DILATED FUNDUS EXAMINATION

A mydriatic should be used to dilate the pupil so that an examination of the fundus can be conducted with an indirect ophthalmoscope and slit lamp biomicroscopy (with contact lens, Hruby lens or 60-, 66-, 78-, or 90 diopter lens). The appearance of the optic disc, macula, vessels and periphery should be evaluated and reported on the applicable study visit form. A measurement of the cup to disc ratio should be made and reported.

17.6 SLIT LAMP EXAMINATION

The clinician will examine the conjunctiva, cornea, anterior chamber, lens and anterior vitreous of the eye with the aid of a slit lamp, which is a table-mounted binocular microscope. Fluorescein dye will be instilled into the ocular cul-de-sac to facilitate this examination. In addition to the following, any evidence of pigment dispersion visible in slit lamp examination should be evaluated and noted.

Iris

Findings of Atrophy/Erosion; Peaking; and Rubeosis should be noted. Each will be evaluated using a scale of None (0), Mild (+1), Moderate (+2) and Severe (+3).

Cornea - Edema

None (0)	Transparent and clear or less than mild
Mild (+1)	Dull glassy appearance
Moderate (+2)	Dull glassy appearance of epithelium with large number of vacuoles
Severe (+3)	Epithelial bullae and/or stromal edema, localized or diffuse, with or without stromal striae

Cornea - Staining/Erosion

None (0)	No fluorescein staining of epithelium, OR less than mild
Mild (+1)	Slight fluorescein staining confined to a small focus
Moderate (+2)	Regionally dense fluorescein staining (1 mm or greater in diameter) with underlying structure moderately visible
Severe (+3)	Marked fluorescein staining or epithelial loss

Anterior Chamber

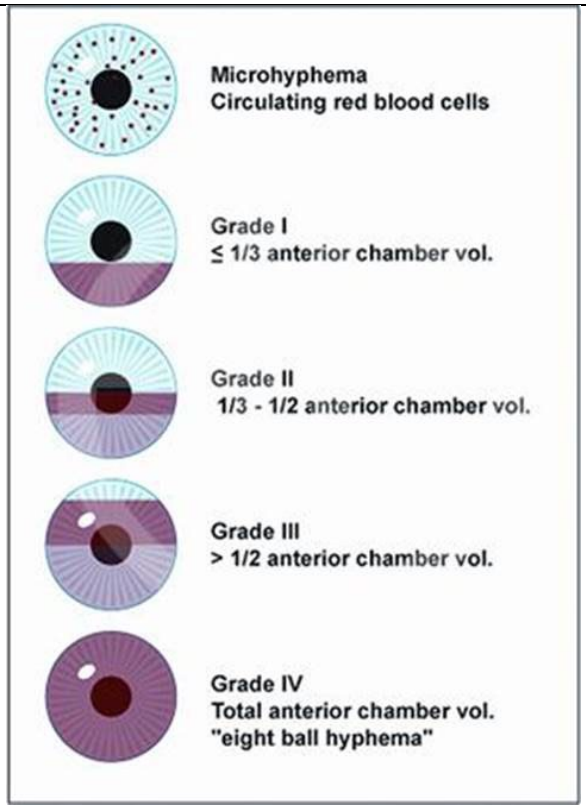
The following system is recommended for grading of aqueous cells and flare using a slit beam 1.0 mm wide and 1.0 mm long.

Cells
0 = < 1 cell seen
0.5+ = 1-5 cells seen
1+ = 6-15 cells seen
2+ = 16-25 cells seen
3+ = 26-50 cells seen
4+ = > 50 cells seen

Flare
0 = None
1+ = Faint
2+ = Moderate (iris and lens details clear)
3+ = Marked (iris and lens details hazy)
4+ = Intense (fibrin or plastic aqueous)

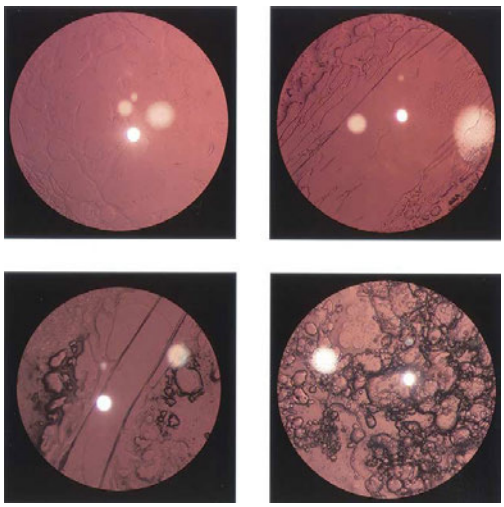
The presence of hypopyon is recorded separately. The presence of "microhyphema" or "layered hyphema" in the anterior chamber should also be recorded. Layered hyphema will be graded using the following scale (If Grade 1, also record size in mm on the CRF).[26]

[26] http://www.aao.org/image/hyphema-grading-system-2



Posterior Capsule Opacification

As a routine part of the slit lamp examination, posterior capsule opacification (PCO) will be evaluated using the following scale:



NONE

Minimal (Top left image)

Mild (Top right image)

Moderate (bottom left image)

Severe (bottom right image)

Other Slit Lamp Findings (complete for each finding)

- Trace
- Mild
- Moderate
- Severe

17.7 GONIOSCOPY

During eligibility determination, prospective subject charts will be reviewed to confirm eligible gonioscopy data is present and will be repeated at post-operative follow up visits as shown in Table 1. Gonioscopy information will be used to verify that the subject has an open angle and to identify any anterior synechiae as well as determine if there is any pigment dispersion. A Zeiss, Sussman or similar lens should be used and gonioscopy conducted in a dark room with a narrow, short slit beam that does not pass through the pupil and without a fixation light being used. The Shaffer method will be used as follows: grade 4, wide open (35°-45°): grade 3, moderately open (25°-34°); grade 2, moderately narrow (20°); grade 1, very narrow (10°); grade 0, closed (0°). The grade number will be reported for each quadrant of the eye in the appropriate location on the form.

17.8 OCULAR HYPOTENSIVE MEDICATIONS

Each ocular hypotensive medication will be recorded on the study record. Combination medications will be counted by their individual components. For example, if a subject is taking Cosopt this is to be counted as two medications even though this is only in 1 bottle.

18 APPENDIX B - DECLARATION OF HELSINKI

I. PREAMBLE

1. The World Medical Association (WMA) has developed the Declaration of Helsinki as a statement of ethical principles for medical research involving human subjects, including research on identifiable human material and data.

   The Declaration is intended to be read as a whole and each of its constituent paragraphs should be applied with consideration of all other relevant paragraphs.

2. Consistent with the mandate of the WMA, the Declaration is addressed primarily to physicians. The WMA encourages others who are involved in medical research involving human subjects to adopt these principles.

II. GENERAL PRINCIPLES

1. The Declaration of Geneva of the WMA binds the physician with the words, "The health of my patient will be my first consideration," and the International Code of Medical Ethics declares that, "A physician shall act in the patient's best interest when providing medical care."

2. It is the duty of the physician to promote and safeguard the health, well-being and rights of patients, including those who are involved in medical research. The physician's knowledge and conscience are dedicated to the fulfilment of this duty.

3. Medical progress is based on research that ultimately must include studies involving human subjects.

4. The primary purpose of medical research involving human subjects is to understand the causes, development and effects of diseases and improve preventive, diagnostic and therapeutic interventions (methods, procedures and treatments). Even the best proven interventions must be evaluated continually through research for their safety, effectiveness, efficiency, accessibility and quality.

5. Medical research is subject to ethical standards that promote and ensure respect for all human subjects and protect their health and rights.

6. While the primary purpose of medical research is to generate new knowledge, this goal can never take precedence over the rights and interests of individual research subjects.

7. It is the duty of physicians who are involved in medical research to protect the life, health, dignity, integrity, right to self-determination, privacy, and confidentiality of personal information of research subjects. The responsibility for the protection of research subjects must always rest with the physician or other health care professionals and never with the research subjects, even though they have given consent.

8. Physicians must consider the ethical, legal and regulatory norms and standards for research involving human subjects in their own countries as well as

applicable international norms and standards. No national or international ethical, legal or regulatory requirement should reduce or eliminate any of the protections for research subjects set forth in this Declaration.

9. Medical research should be conducted in a manner that minimizes possible harm to the environment.

10. Medical research involving human subjects must be conducted only by individuals with the appropriate ethics and scientific education, training and qualifications. Research on patients or healthy volunteers requires the supervision of a competent and appropriately qualified physician or other health care professional.

11. Groups that are underrepresented in medical research should be provided appropriate access to participation in research.

12. Physicians who combine medical research with medical care should involve their patients in research only to the extent that this is justified by its potential preventive, diagnostic or therapeutic value and if the physician has good reason to believe that participation in the research study will not adversely affect the health of the patients who serve as research subjects.

13. Appropriate compensation and treatment for subjects who are harmed as a result of participating in research must be ensured.

III. RISKS, BURDENS AND BENEFITS

- In medical practice and in medical research, most interventions involve risks and burdens.

  Medical research involving human subjects may only be conducted if the importance of the objective outweighs the risks and burdens to the research subjects.

- All medical research involving human subjects must be preceded by careful assessment of predictable risks and burdens to the individuals and groups involved in the research in comparison with foreseeable benefits to them and to other individuals or groups affected by the condition under investigation.

  Measures to minimize the risks must be implemented. The risks must be continuously monitored, assessed and documented by the researcher.

- Physicians may not be involved in a research study involving human subjects unless they are confident that the risks have been adequately assessed and can be satisfactorily managed.

  When the risks are found to outweigh the potential benefits or when there is conclusive proof of definitive outcomes, physicians must assess whether to continue, modify or immediately stop the study.

IV. VULNERABLE GROUPS AND INDIVIDUALS

- Some groups and individuals are particularly vulnerable and may ha e an increased likelihood of being wronged or of incurring additional harm.

  All vulnerable groups and individuals should receive specifi ally considered protection.

- Medical research with a vulnerable group is only ju tified if the research is responsive to the health needs or priorities of this group and the research cannot be carried out in a non-vulnerable gr up. In addition, this group should stand to benefit from the knowledge, practices or interventions that result from the research.

V. SCIENTIFIC REQUIREMENTS AND RESEARCH PROTOCOLS

- Medical resea ch invol ng human subjects must conform to generally accepted scientif c pri ciples, be based on a thorough knowledge of the scientific literature, other relevant sources of information, and adequate laboratory and, as appropriate, animal experimentation. The welfare of animal used f r research must be respected.

- The design and performance of each research study involving human subjects must be clearly described and justified in a research protocol.

  The protocol should contain a statement of the ethical considerations involved and should indicate how the principles in this Declaration have been addressed. The protocol should include information regarding funding, sponsors, institutional affiliations, potential conflicts of interest, incentives for subjects and information regarding provisions for treating and/or compensating subjects who are harmed as a consequence of participation in the research study.

In clinical trials, the protocol must also describe appropriate arrangements for post-trial provisions.

VI. RESEARCH ETHICS COMMITTEES

- The research protocol must be submitted for consideration, comment, guidance and approval to the concerned research ethics committee before the study begins. This committee must be transparent in its functioning, must be independent of the researcher, the sponsor and any other undue influence and must be duly qualified. It must take into consideration the laws and regulations of the country or countries in which the research is to be performed as well as applicable international norms and standards but these must not be allowed to reduce or eliminate any of the protections for research ubjec set forth in this Declaration.

  The committee must have the right to monitor ongoing studies. The researcher must provide monitoring information to the committee, especially information about any serious adverse events. No amendment to the protocol may be made without consideration and approval by the committee. After the end of the study, the researchers must submi a final report to the committee containing a summary of the study's findings and conclusions.

VII. PRIVACY AND CONFIDENTIALITY

- Every precaution must be taken to protect the privacy of research subjects and the confidentiality of heir personal information.

VIII. INFORMED CONSENT

- Part cipation by individuals capable of giving informed consent as subjects in medical research must be voluntary. Although it may be appropriate to consult family members or community leaders, no individual capable of giving informed consent may be enrolled in a research study unless he or she freely agrees.

- In medical research involving human subjects capable of giving informed consent, each potential subject must be adequately informed of the aims, methods, sources of funding, any possible conflicts of interest, institutional affiliations of the researcher, the anticipated benefits and potential risks of the study and the discomfort it may entail, post-study provisions and any other relevant aspects of the study. The potential subject must be informed of the right to refuse to participate in the study or to withdraw consent to participate

at any time without reprisal. Special attention should be given to the specific information needs of individual potential subjects as well as to the methods used to deliver the information.

After ensuring that the potential subject has understood the information, the physician or another appropriately qualified individual must then seek the potential subject's freely-given informed consent, preferably in writing. If the consent cannot be expressed in writing, the non-written consent must be formally documented and witnessed.

All medical research subjects should be given the option of being informed about the general outcome and results of the study.

- When seeking informed consent for participation in a research study the physician must be particularly cautious if the potential subject is in a dependent relationship with the physician or may consent under duress. In such situations the informed consent must be sought by an appropriately qualified individual who is completely independent of this relationship.

- For a potential research subject who is incapable of giving informed consent, the physician must seek informed consent from the legally authorized representative. These individuals must not be included in a research study that has no likelihood of benefit for them unless it is intended to promote the health of the group represented by the potential subject, the research cannot instead be performed with persons capable of providing informed consent, and the research ent ils o ly minimal risk and minimal burden.

- When a potential research subject who is deemed incapable of giving informed consent is able to give assent to decisions about participation in research, the physician must seek that assent in addition to the consent of the legally authorized representative. The potential subject's dissent should be respected.

- Research involving subjects who are physically or mentally incapable of giving consent, for example, unconscious patients, may be done only if the physical or mental condition that prevents giving informed consent is a necessary characteristic of the research group. In such circumstances the physician must seek informed consent from the legally authorized representative. If no such representative is available and if the research cannot be delayed, the study may proceed without informed consent provided that the specific reasons for involving subjects with a condition that renders them unable to give informed consent have been stated in the research protocol and the study has been approved by a research ethics committee. Consent to remain in the research

must be obtained as soon as possible from the subject or a legally authorized representative.

- The physician must fully inform the patient which aspects of their care are related to the research. The refusal of a patient to participate in a study or the patient's decision to withdraw from the study must never adversely affect the patient-physician relationship.

- For medical research using identifiable human material or data, such as research on material or data contained in biobanks or similar repositories, physicians must seek informed consent for its collection, storage and/or reuse. There may be exceptional situations where consent would be impossible or impracticable to obtain for such research. In such situations the research may be done only after consideration and approval of a research ethics committee.

IX. USE OF PLACEBO

- The benefits, risks, burdens and effectivene s of a new intervention must be tested against those of the best proven intervention(s), except in the following circumstances:

  Where no proven intervention exists, the use of placebo, or no intervention, is acceptable; or

  Where for compell ng and scientifically sound methodological reasons the use of any intervention le s effective than the best proven one, the use of placebo, or no intervention is necessary to determine the efficacy or safety of an intervention

  and he patients who receive any intervention less effective than the best proven one, placebo, or no intervention will not be subject to additional risks of serious or irreversible harm as a result of not receiving the best proven intervention.

  Extreme care must be taken to avoid abuse of this option.

X. POST-TRIAL PROVISIONS

- In advance of a clinical trial, sponsors, researchers and host country governments should make provisions for post-trial access for all participants who still need an intervention identified as beneficial in the trial. This

information must also be disclosed to participants during the informed consent process.

XI. RESEARCH REGISTRATION AND PUBLICATION AND DISSEMINATION OF RESULTS

- Every research study involving human subjects must be registered in a publicly accessible database before recruitment of the first subject.

- Researchers, authors, sponsors, editors and publishers all have ethical obligations with regard to the publication and dissemination of the results of research. Researchers have a duty to make publicly available the results of their research on human subjects and are accountable for the completeness and accuracy of their reports. All parties should adhere to accepted guidelines for ethical reporting. Negative and inconclusive as well as positive results must be published or otherwise made publicly available. Sources of funding, institutional affiliations and conflicts of interest must be declared in the publication. Reports of research not in accordance with the principles of this Declaration should not be accepted for publication.

XII. UNPROVEN INTERVENTIONS IN CLINICAL PRACTICE

In the treatment of an individual patient, where proven interventions do not exist, or other known interventions have been ineffective, the physician, after seeking expert advice, with informed consent from the patient or a legally authorized representative, may use an unproven intervention if in the physician's judgment it offers hope of saving life, re-establishing health or alleviating suffering. This intervention should subsequently be made the object of research, designed to evaluate its safety and efficacy. In all cases, new information must be recorded and, where appropriate, made publicly available.