AN OBSERVATIONAL MULTICENTER CLINICAL STUDY TO ASSESS THE SAFETY AND EFFECTIVENESS OF THE OMNI® SURGICAL SYSTEM IN PSEUDOPHAKIC EYES WITH PRIMARY OPEN ANGLE GLAUCOMA (ORION 2.0)

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SPONSOR:	Sight Sciences, Inc. 4040 Campbell Avenue Suite 100 Menlo Park CA 94025 877-266-1144

Agreement of Principal Investigator

I, _____ agree to conduct this trial in accordance with this clinical protocol and any amendmen s

_____ _____

Signature Date

_____ _____

Center Name City, State, Country

Revision History

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A	April 22, 2021	[redacted]
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1 PROTOCOL SYNOPSIS

Protocol Title	An Observational Multicenter Clinical Study to Assess the Safety and Effectiveness of the OMNI® Surgical System in Pseudophakic Eyes with Primary Open Angle Glaucoma
[redacted]	[redacted]
Investigational Device	OMNI® Surgical System
Study Objective	[redacted]
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.
Primary Safety Endpoint	1. Rate of occurrence of sight-threatening adverse events (AEs)
Secondary Safety Endpoints	1. Rate of ocular AEs 2. Reduction in best corrected distance visual acuity (BCVA) from baseline 3. Secondary Surgical Interventions, including laser, for IOP control
Effectiveness Endpoints	[redacted]

Inclusion Criteria	[redacted]
[redacted]	individuals [redacted]

Number of Subjects Enrolled and Treated	Up to 100 subjects. Up to 50 subjects who received OMNI intervention post medication washout and up to 50 subjects who received OMNI intervention without medication washout will be enrolled
Number of Sites	Up to 15 study sites in United States.
Schedule of Visits	<u>The following visits will be captured retrospectively:</u> - Subjects with preoperative medication washout: Pre-washout, Post-washout, Surgical - Subjects without a medication washout: Preoperative, Surgical <u>The following visits will be captured prospectively:</u> - Months 6*, 12*, 18 and 24. *Subjects with a preoperative washout will also undergo washout for the 12- and 24- month visits if they are on ocular hypotensive medication at these visits and return for an exam following appropriate washout period.* * The 6- and 12-month data can be retrospective or prospective depending on date of enrollment.
Interim analysis	100% subjects reaching 12 Month visit

2 STUDY OBJECTIVE

The purpose of this study is to evaluate the safety and effectiveness of the OMNI® Surgical System in subjects who have undergone canaloplasty and trabeculotomy using OMNI® Surgical System without any concomitant surgery in pseudophakic eyes with mild to moderate primary open angle glaucoma (POAG) at least 150 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] POAG is the most prevalent form of glaucoma and elevated IOP is the only treatable risk factor.[2] Hypotensive eye

[1] Tham YC, Li X, Wong TY, et al. Global prevalence of glaucoma and projections of glaucoma burden through 2040: a systematic review and meta-analysis. Ophthalmology. 2014;121:2081–2090.
[2] European Glaucoma Society. Terminology and guidelines for glaucoma 4th edition Savona, Italy: Editrice PubliComm, 2014.

drops are commonly used as the first line clinical management for POAG.[3] Ocular side effects such as allergies, ocular surface disorders, blepharitis, pemphigoid, abnormal pigmentation etc. and systemic side effects such as bradycardia, headaches, depression, anxiety, confusion, dysarthria, hallucinations, lethargy, polyuria, weight loss, metabolic acidosis, etc. 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 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] 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

[3] Kass MA, Heuer DK, Higginbotham EJ, Johnson CA, et al. The Ocular Hypertension Treatment Study: a randomized trial determines that topical ocular hypotensive medication delays or prevents the onset of primary open-angle glaucoma. Arch Ophthalmol. 2002; 120:701–713.

[4] Kenji Inoue. Managing adverse effects of glaucoma medications. Clin Ophthalmol. 2014; 8: 903–913. Published online 2014 May 12. doi: 10.2147/OPTH.S44708.

[5] Newman-Casey PA, Robin AL, Blachley T, Farris K, Heisler M, Resnicow K, Lee PP. The Most Common Barriers to Glaucoma Medication Adherence: A Cross-Sectional Survey. Ophthalmology. 2015 Jul; 122(7):1308-16.

[6] Leske MC, Heijl A, Hussein M, et al. Factors for glaucoma progression and the effect of treatment: The Early Manifest Glaucoma Trial. Arch Ophthalmol 2003;121:48–56.

[7] The Advanced Glaucoma Intervention Study (AGIS): the relationship between control of intraocular pressure and visual field deterioration. The AGIS Investigators. Am J Ophthalmol 2000;130:429–40.

[8] Francis BA, Singh K, Lin SC, et al. Novel glaucoma procedures: a report by the American Academy of Ophthalmology. Ophthalmology 2011;118:1466–1480.

[9] Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. Curr Opin Ophthalmol 2017;28:187–193.

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]

The OMNI® Surgical System is indicated for canaloplasty (microcatheterization and transluminal viscodilation of Schlemm's canal) followed by trabeculotomy (cutting of trabecular meshwork) to reduce intraocular pressure in adult patients with primary open-angle glaucoma.

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 is indicated for canaloplasty (microcatheterization and transluminal viscodilation of Schlemm's canal) followed by trabeculotomy (cutting of trabecular meshwork) to reduce intraocular pressure in adult patients with primary open-angle glaucoma.

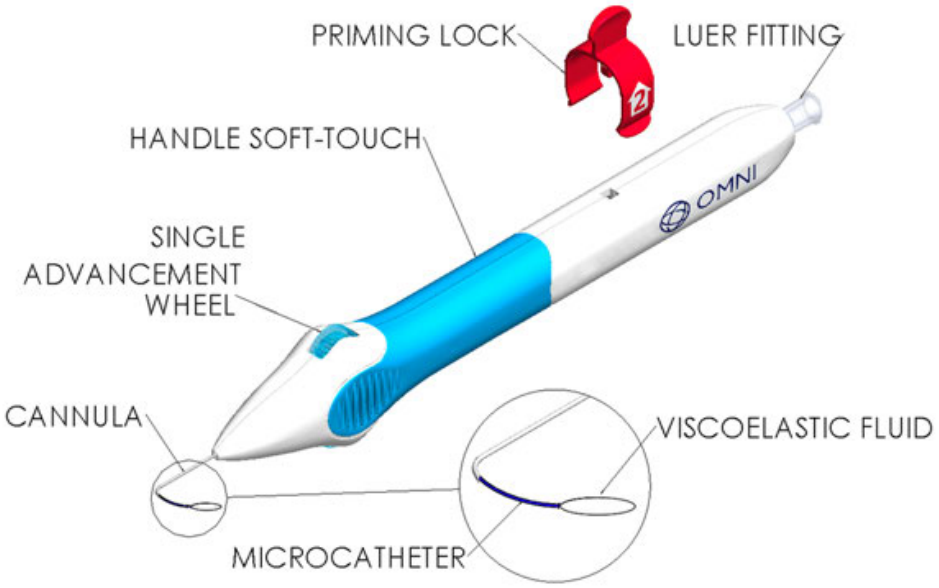
The OMNI is designed to function with commonly used viscoelastic fluids made commercially available by companies such as Johnson & Johnson Vision, Bausch & Lomb, and Alcon. The OMNI dispenses fluid on the principle of exchanging volumes much like a syringe. The handheld instrument includes a cannula, microcatheter, internal reservoir and plunger tube, and finger wheels. The finger wheel on the handle of the device allows the OMNI device to be used in either eye (OD or OS) and in either hand of the surgeon (left or right), by turning the device 180 degrees along its vertical axis and is used to advance and retract the microcatheter. In addition, when the device is being used to deliver viscoelastic, retraction of the microcatheter causes the plunger tube to advance into the viscoelastic fluid reservoir thereby dispensing viscoelastic fluid.

[10] Francis BA, Singh K, Lin SC, et al. op cit.
[11] Vinod K, Gedde SJ. Clinical investigation of new glaucoma procedures. Curr Opin Ophthalmol 2017;28:187–193.
[12] Lewis RA, von Wolff K, Tetz M, et al. Canaloplasty: circumferential viscodilation and tensioning of Schlemm canal using a flexible microcatheter for the treatment of open-angle glaucoma in adults. Two-year interim clinical study results. J Cataract Refract Surg 2009;35:814-824.
[13] Sarkisian SR, Mathews B, Ding K, et al. 360°ab-interno trabeculotomy in refractory primary open-angle glaucoma. Clin Ophthalmol 2019;13:161-168.
[14] Grover DS, Smith O, Fellman RL, et al. Gonioscopy-assisted transluminal trabeculotomy: an ab interno circumferential trabeculotomy: 24 months follow-up. J Glaucoma 2018;27:393-401.

The microcatheter can be advanced/retracted up to 20 mm per cycle. The microcatheter can be fully advanced/retracted up to 5 times (i.e. 5 full cycles of 20 mm each). Dispensation of viscoelastic can only occur during the first two 20-mm cycles.

The OMNI can deliver approximately 5.5 microliters of viscoelastic in each 20 mm cycle (total volume = 11 microliters).

Figure 1: OMNI Surgical System



4.2 TRAINING

All surgeons would have received training in accordance with Sight Sciences' 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.

[redacted]

The study will employ a medication washout at the 12- and 24-month endpoints only for the subjects that received the OMNI procedure post-medication washout.

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

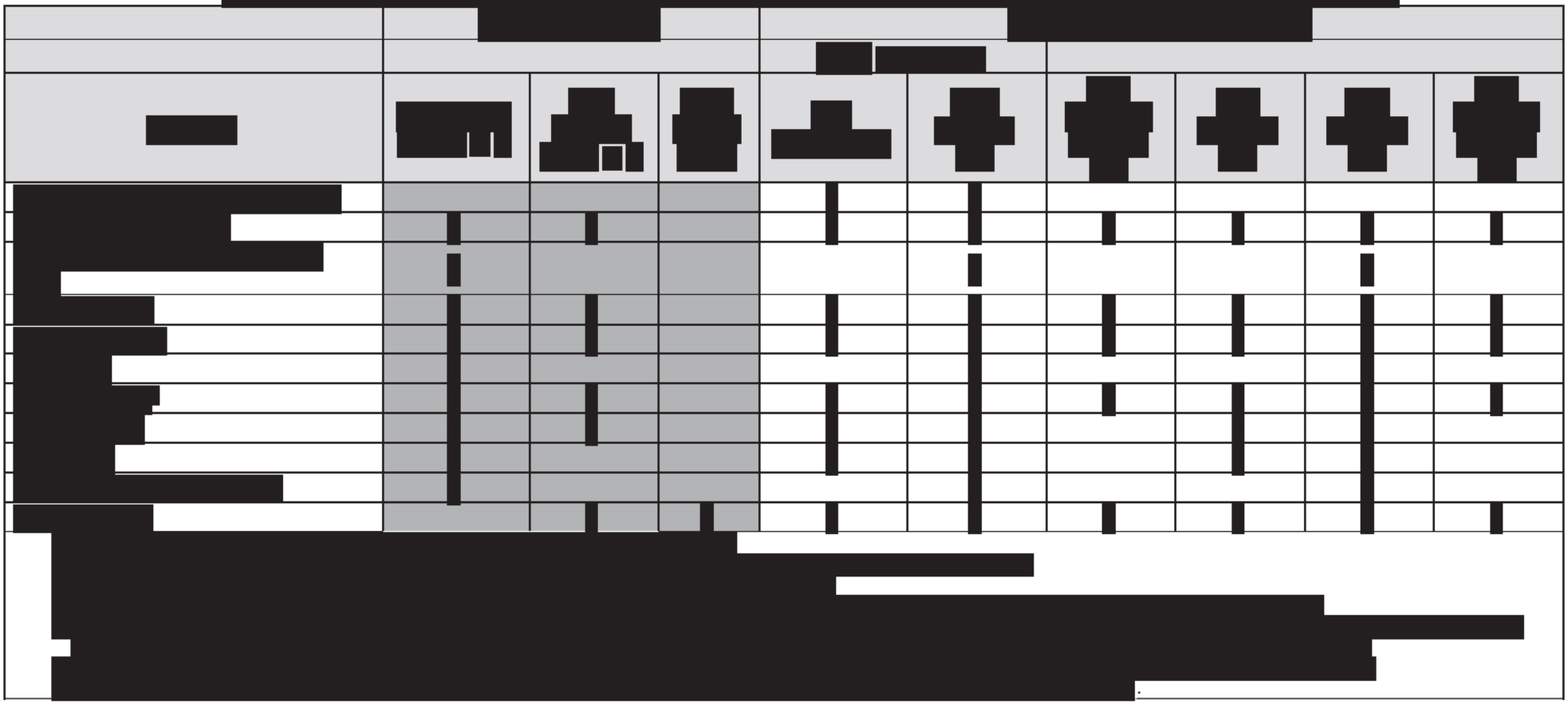
[redacted]

7 STUDY SELECTION CRITERIA

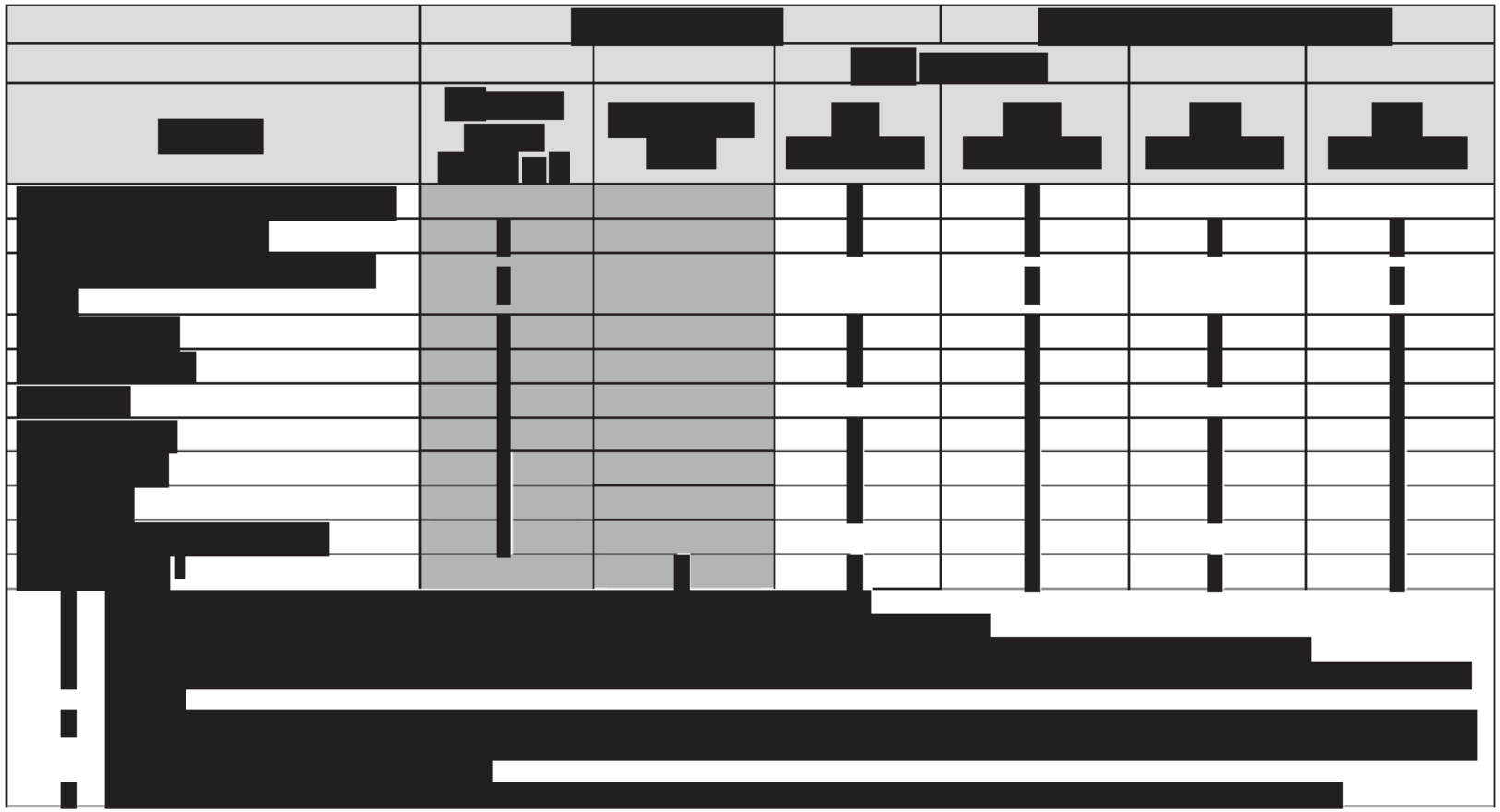
[redacted]

8 STUDY PROCEDURES

8.1 [redacted]



8.2 [redacted]



8.3 NUMBER OF SUBJECTS, DURATION OF FOLLOW-UP AND STUDY DURATION

Up to 100 subjects meeting eligibility criteria with a minimum of 150 days of follow-up post-surgery using the OMNI Surgical System will be enrolled in this study.

Enrollment is stratified. Up to 50 subjects will be enrolled for whom there was a pre-surgical washout of ocular hypotensive medications; up to 50 subjects will be enrolled for whom there was no pre-surgery washout.

It is anticipated that site initiation, data collection and site close-out will require approximately 30 months.

8.4 INFORMED CONSENT AND POINT OF ENROLLMENT

The pre-operative and surgery data (and in some cases, depending on enrollment date, Month 6 and Month 12) will be collected retrospectively by performing the 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 will be presented and explained to each prospective subject by the Investigator or a delegated, trained clinical professional. Once the subject 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 subject will be given a choice to voluntarily confirm his or her participation in the study as documented by completion of the Informed Consent. After signing the Informed Consent 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 Informed Consent Document.

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 Informed Consent Document. A copy of the written Informed Consent Document 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, and for whom the date of surgery using the OMNI Surgical System is at least 150 days prior to enrollment in the study.

- All potential subjects should be screened for enrollment, and all eligible cases will be included up to the enrollment limit for each site.
- For the subjects who received OMNI intervention after medication washout, the eye that received OMNI surgery post medication washout should be enrolled.
- For the subjects who received OMNI intervention without medication washout if both eyes qualify, the eye with higher pre-operative medicated IOP should be enrolled. If both eyes have same pre-operative medicated IOP, right eye should be enrolled.

8.6 DATA EXTRACTION

Data for the pre-surgery and surgery visits will be collected retrospectively onto CRFs. The data collected will be in accordance with Table 1 (8.1: Study Schedule).

Following signing of consent form, 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 (e.g., 16-02-01). Subject ID numbers will be assigned sequentially.

Medical records will be reviewed for demographic and medical history information, pre-operative, medication use data, and adverse events. 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, then reviewing and signing the Informed Consent Document, 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.

NOTE: A safety IOP check anytime between the predefined visits may be performed at the Investigator's discretion whenever warranted to ensure subject safety and should be documented as unscheduled visit.

8.7.1 WASHOUT OF HYPOTENSIVE MEDICATIONS

Subjects that had undergone a preoperative medication washout and who are on ocular hypotensive medication at the 12- and 24-month pos-operative 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.

Glaucoma medication discontinuation can be staged so that the pressure increase duration is minimized to the greatest possible extent during the washout period. For example, if a patient is on a prostaglandin (PGA) and a Carbonic Anhydrase Inhibitor (CAI), the PGA could be discontinued 4 weeks prior to the Baseline measurement but the CAI allowed to continue until 5 days before Baseline.

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 2 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 Agonists	
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
Fixed Combination Medications	
Combigan® (Brimonidine Tartrate/Timolol Maleate)	28 days
Cosopt® (Dorzolamide Hydrochloride/ Timolol Maleate)	28 days
DuoTrav® (Travoprost/Timolol)	28 days
Ganfort® (Bimatoprost/Timolol)	28 days

Rocklatan® (Netarsudil/Latanoprost)	28 days
Simbrinza® (Brinzolamide/Brimonidine Tartrate)	28 days
Xalacom® (Latanoprost/Timolol)	28 days
Krytantek (Brimonidine Tartrate/ Dorzolamide Hydrochloride/ 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, at which the subject has a complaint regarding the study eye and/or treatment to the study eye is required or changed. 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 medical records and on the 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 after enrollment into the study, 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, the subject should be withdrawn from the study.

If such secondary surgical intervention had happened more than 1 month before enrollment into the study, the subject should be enrolled, examined as per 6-month or 12-month visit schedule depending on the date of enrollment and exited 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, can be withdrawn by the study investigator for reason's including but not limited to non-compliance, being unresponsive or no longer qualifies under the protocol, or 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 Case Report Form. 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.

Adverse events that occurred intra, and post-operatively up to enrollment into the study will also be collected.

9.1 DEFINITIONS OF AE, SAE, ADE, SADE, UADE, USADE[15]

Adverse Event (AE)	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	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

[15] All of these definitions are in conformance with the requirements 21 C.F.R. Part 803.

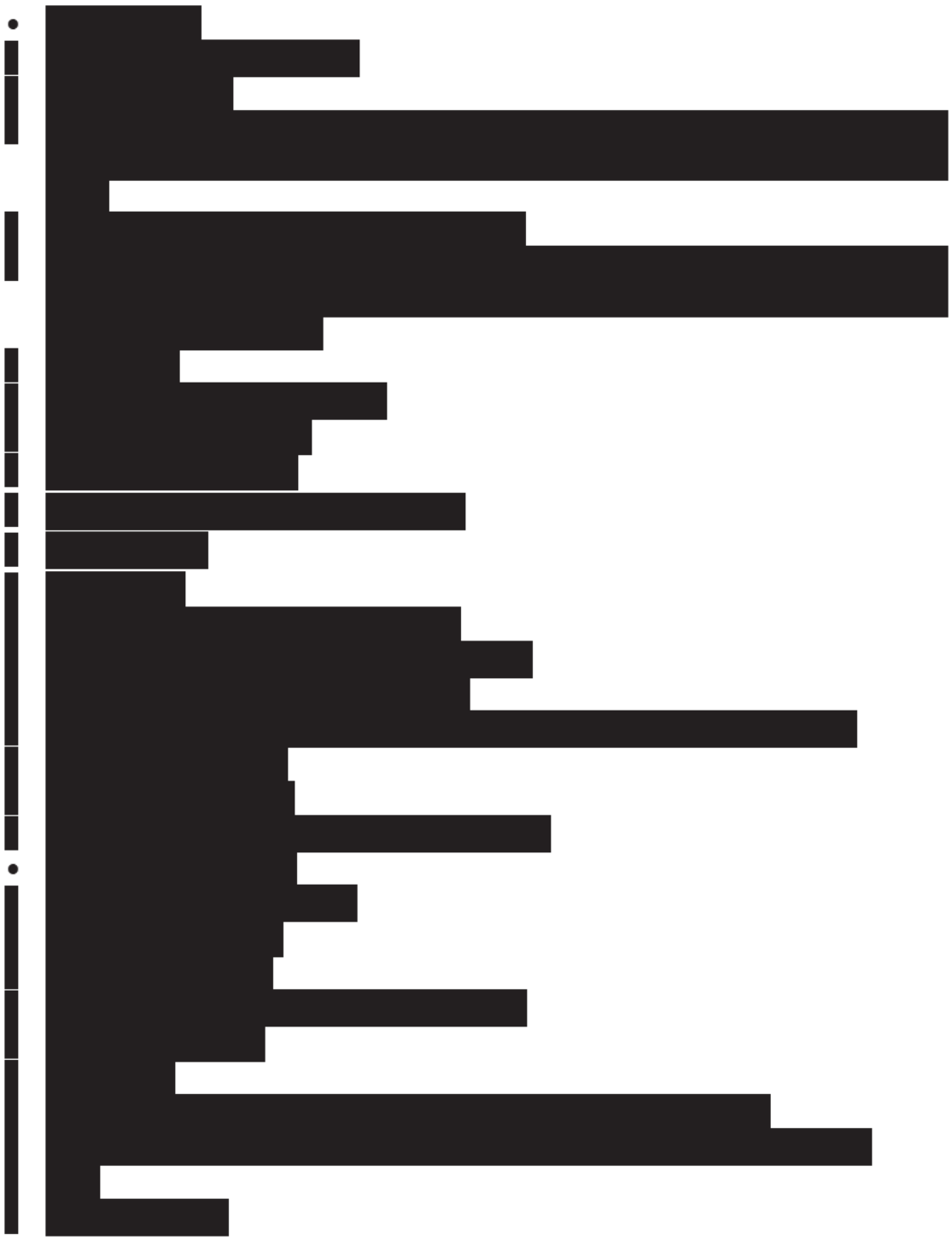
Unanticipated Adverse Device Effect	Any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the clinical investigational 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 USADE.

Adverse events may be anticipated or unanticipated. All events will be assessed for seriousness, and relationship to the study device. Anticipated adverse events that are related to the study devices are ADEs (Adverse Device Effects) and when serious SADEs (Serious Adverse Device Effects). Unanticipated adverse events which are related to the study device are UADEs (Unanticipated Adverse Device Effects) and when serious SUADEs (Serious Unanticipated Adverse Device Effects).

9.2 [redacted]

[redacted]

[16] [redacted]



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 Adverse Event Case Report Form (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 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.

[redacted]

[redacted]

[redacted].

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, 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 EVENT

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 (BCVA)

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 Month 12 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.

[redacted]

Safety endpoints:

[redacted]

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 or contract research organization (CRO) personnel will monitor the study in a manner consistent with FDA regulations, good clinical practices and the clinical research standards adopted by Sight Sciences. 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 Sciences 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 Sciences or the CRO have recently been involved with an investigator for another study, a site qualification visit may not be necessary.
- Site Initiation: Sight Sciences 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
  - Records and reports
- Interim Monitoring: Sight Sciences 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
  - 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 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 three-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 Sciences personnel, its contract research organization (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 at Sight Sciences, Inc.

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 Electronic Case Report Forms (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 Sciences 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 Sciences, Inc. as well as 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 Adverse Events 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 Sciences or its CRO.

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

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 Sciences 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 Sciences 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 implanted with the device
- Withdrawal of FDA clearance of the OMNI device.
- Insufficient enrollment in the study
- The Sponsor determines that enough data has been collected for the study, and no further data are needed.

Sight Sciences 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 Sciences 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 subejct'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 PUBLICATION POLICY

Sight Sciences recognizes the value of disseminating research results. It is understood that the Study is part of the Multi-Center Clinical Trial and publication of results is expected. This publications policy applies to journal articles, conference abstracts, and conference presentations (posters and slides) covering Sight Sciences-sponsored clinical studies. This policy is in addition to any arrangement contained in the Clinical Trial Agreement between Sight Sciences and the investigator.

Multi-Site Data

Clinical site investigators are encouraged to propose publications and abstracts that include clinical or research data from multiple clinical sites; such projects will be coordinated by Sight Sciences. Authorship of papers and abstracts resulting from these projects will be determined collaboratively according to the following guidelines:

- The first author on such publications will be the person who primarily wrote the paper and took the lead on the research. In the case of clinical trial papers

where all authors contributed equally, authorship order may be based on site enrollment or other criteria at Sight Sciences' discretion.

- Other authors include those who significantly contributed to the specific work.
- At least one person from each clinical site whose study subjects appear in the work will be acknowledged in the manuscript/presentation in some way, either as an author group member, a non-author contributor, or listed in the acknowledgements, depending on the particular policies of the journal or conference.

Single Site Data

After publication of the multi-center study results in a peer-reviewed journal, or if Sponsor has not submitted a manuscript for publication in a peer-reviewed journal within twelve (12) months after the study has been completed, whichever occurs first, Investigators may publish the results of the Study generated by the Investigator, subject to the obligations of the Clinical Trial Agreement between Sight Sciences and the Investigator, and the prior approval of Sponsor in writing.

Publications Review Policy

Investigators must submit all presentations, posters, abstracts and manuscripts pertaining to this study to Sight Sciences for review in advance of their submission. Sight Sciences conducts this review to protect its proprietary rights to information, inventions, or products developed under the Study. Please use the following guideline to determine the absolute minimum advance time for submitting an item to Sight Sciences for review:

- Presentations/Posters: 5 business days in advance of presentation
- Abstracts: 5 business days in advance of submission
- Manuscripts: 30 calendar days in advance of submission for publication

In accordance with the Clinical Trial Agreement, these items must receive written approval from Sight Sciences in order for them to be submitted or presented. If an item is not received in the timeframe listed above, approval may not be granted due to insufficient time for considered review. In addition, since most of our Clinical Trial Agreements require that Sight Sciences has 60 days to review publications, Sight Sciences reserves the rights granted in those Agreements if circumstances require a longer review.

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18 APPENDIX A – METHODS FOR EXAMS, TESTS AND QUESTIONNAIRES

18.1 LIST OF STUDY PROCEDURES

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

18.2 PRO INSTRUMENTS

18.2.1 THE OSDI© QUESTIONNAIRE

The OSDI Questionnaire consists of 12 questions regarding ocular symptoms, environmental triggers, and vision-related functioning in patients with dry eye disease (Schiffman et al, 2000). The patient will be asked to rate each symptom using a 5-point scale (0 to 4), where 0 indicates none of the time; 1, some of the time; 2, half of the time; 3, most of the time; and 4, all of the time. Seven questions related to visual functioning allow a response of "N/A" (not applicable); no more than 3 of these 7 questions may be answered as N/A for the questionnaire to be evaluable. The total OSDI score is calculated as: ([sum of scores for all questions answered] X 100)/([total number of questions answered] X 4).

The OSDI questionnaire will only be administered to subjects who also had an OSDI administered at the pre-surgery visit.

18.3 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.

18.4 MEASUREMENT OF INTRAOCULAR PRESSURE

The Goldmann tonometer should be used each time IOP is measured.

For the retrospective visits the type of tonometer should be Goldman tonometer however the method 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.

Guidelines for performing Goldmann tonometry during prospective study visits are as follows:

1. The subject is told the purpose of the test and is reassured that the measurement is not painful. The subject is instructed to relax, maintain his or her position, and hold his or her eyes open widely.
2. One drop of a topical anesthetic, such as 0.5% proparacaine or 0.4% benoxinate, is placed in each eye, and the tip of a moistened fluorescein strip is touched to the tear layer on the inner surface of each lower lid. Alternatively, one drop of a combined anesthetic-fluorescein strip is touched to the tear layer on the inner surface of each lower lid. The tonometer and prism are set in correct position on the slit lamp.
3. The tension knob is set at 1 g. If the knob is set at 0, the prism head may vibrate when it touches the eye and damage the corneal epithelium. The 1 g position is used before each measurement. As a rule, it is more accurate to measure intraocular pressure by increasing rather than decreasing the force of applanation.
4. The 0 graduation mark of the prism is set at the white line on the prism holder. If the subject has more than 3 diopters of corneal astigmatism, the area of contact between the cornea and the prism is elliptic rather than

circular. In this situation the prism should be rotated to 45 degrees from the long axis of the ellipse-that is, the prism graduation corresponding to the least curved meridian of the cornea should be set at the red mark on the prism holder. An alternative approach is to average the intraocular pressure readings obtained with the axis of the prism horizontal and then vertical.

5. The cobalt filter is used with the slit beam opened maximally. The angle between the illumination and the microscope should be approximately 60º. The room illumination is reduced.
6. The subject is seated in a comfortable position on an adjustable stool or examining chair facing the slit lamp. The heights of the slit lamp, chair and chin rest are adjusted until the subject is comfortable and in the correct position for the measurement. The subject's chin is supported by the chin rest and the forehead by the forehead bar. The forehead bar should be well above the subject's eyebrows so the frontalis muscle can be used to open the eyes widely. The subject's collar and tie should be loosened if necessary. The subject should breathe normally during the test to avoid Valsalva's maneuver.
7. The palpebral fissure is a little wider if the subject looks up. However, the gaze should be no more than 15° above the horizontal to prevent an elevation of intraocular pressure that is especially marked in the presence of restrictive neuromuscular disease. A fixation light may be placed in front of the fellow eye. The subject should blink his eyes once or twice to spread the fluorescein-stained tear film over the cornea and then should keep his eyes open widely. In some subjects it is necessary for the examiner to hold the eyelids open with the thumb and forefinger of one hand. Care must be taken not to place any pressure on the globe because this raises intraocular pressure.
8. The operator sits opposite the subject in position to look through the microscope. The clinician moves the assembly toward the subject. When the black circle near the tip of the prism moves slightly, it indicates contact between the prism and the globe.
9. Alternatively, the assembly is advanced toward the subject until the limbal zone has bluish hue. The biprism should not touch the lids or lashes because this stimulates blinking and squeezing. Touching the lids also thickens the fluorescein rings, which may cause an overestimation of intraocular pressure.
10. The clinician observes the applanation through the biprism at low power. A monocular view is obtained of the central applanated zone and the surrounding fluorescein stained tear film. Using the control stick, the observer raises and lowers and centers of the assembly until two equal semicircles are seen in the center of the field of view. If the two semicircles are not equal in size, intraocular pressure is overestimated. The clinician turns the tension knob in both directions to ensure that the instrument is in good position. If the semicircles cannot be made "too small," the instrument

is too far forward. If the semicircles cannot be made "too large," the instrument is too far from the eye.

11. The fluorescein rings should be approximately 0.25 to 0.3 mm in thickness, that is, one tenth the diameter of the flattened area. If the rings are too narrow, the subject should blink two or three times to replenish the fluorescein; additional fluorescein may be added if necessary. If the fluorescein rings are too wide, the subject should dry his eyes lightly with a tissue, and the front surface of the prism should be dried with lint-free material. An excessively wide fluorescein ring is less of a problem than a very narrow ring but can cause the intraocular pressure to be overestimated.
12. The fluorescein rings normally undergo a rhythmic movement in response to the cardiac cycle. The tension knob is rotated until the inner borders of the fluorescein rings touch each other at the midpoint of their pulsations. The intraocular pressure is the mean of these 2 readings.
13. Intraocular pressure is measured in the study eye twice. If the 2 readings differ by 2 mmHg or less the average is the IOP. If the 2 readings differ by > 2 mm Hg, a third reading is taken.
14. The reading obtained in grams is multiplied by 10 to give the intraocular pressure in millimeters of mercury. This value is recorded along with the date, time of day, list of ocular medications, and time of last instillation of ocular medication if IOP is measured on different days, an attempt should be made to standardize the time.

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 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 calibration 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 written documentation in a log (hardcopy or electronic format acceptable) of the calibration 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, and an indication as to whether or not the unit passed the calibration. If not calibrated successfully, a note should be entered in the log about contacting the authorized manufacturer's representative for repair and what repairs were required. Following any repair, another calibration should be documented prior to clinical use.

Diurnal IOP
Diurnal IOP (IOP) will be completed as shown in Table 1 or 2 as applicable. In order to determine the mean diurnal intraocular pressure measurements at 12 months and 24-months, IOP measurements should be taken at 9:00AM ±1.5 hours, 12:00PM ± 1 hour, and 4:00PM ± 2 hours. The three IOP measurements should then be averaged to determine the mean diurnal IOP.

18.5 VISUAL FIELD EXAMINATION

Visual field tests obtained prior to enrollment into the study may be of the investigator's discretion (SITA Standard or G-pattern 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.

18.6 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.

18.7 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.

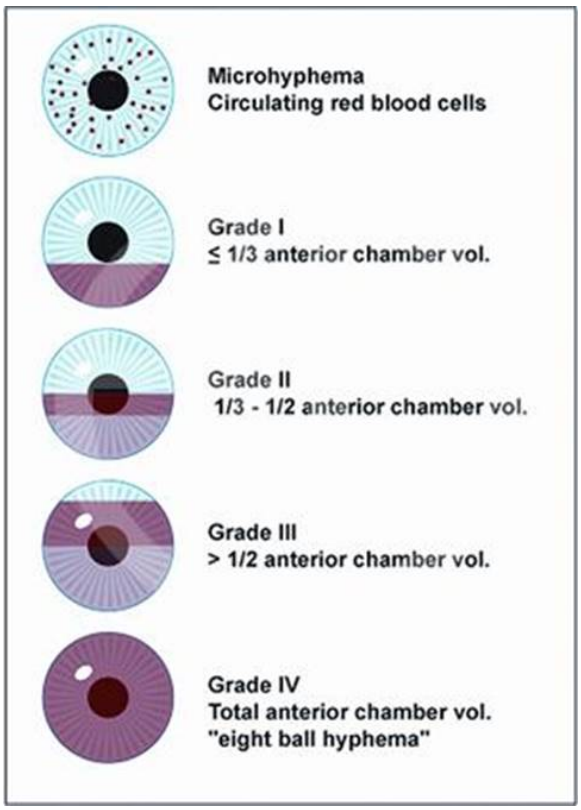
Cells

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)

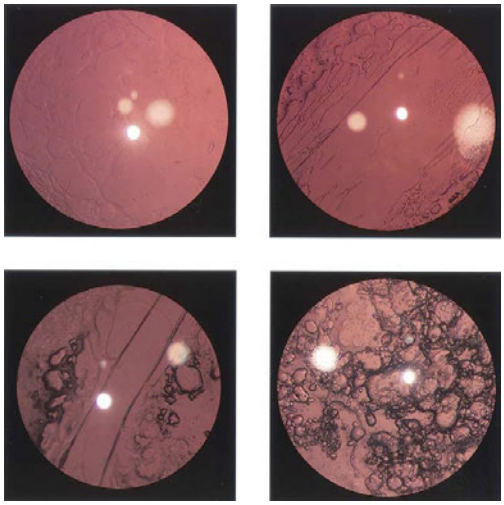
The presence of hypopyon is recorded separately. The presence of "microhyphema" or "layered hyphema" in the anterior chamber should also be recorded. Layered hyphema will be graded using the following scale (If Grade 1, also record size in mm on the CRF).[18]



[18] 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

18.8 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. Gonioscopy. 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.

18.9 OCULAR HYPOTENSIVE MEDICATIONS

Each ocular hypotensive medication will be recorded on the study record. If subjects are taking combination medications such as Cosopt this is to be counted as two medications even though this is only in 1 bottle.

19 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 have an increased likelihood of being wronged or of incurring additional harm.

  All vulnerable groups and individuals should receive specifically considered protection.

- Medical research with a vulnerable group is only justified 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 group. 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 research involving human subjects must conform to generally accepted scientific principles, 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 animals used for 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 subjects 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 submit 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 their personal information.

VIII. INFORMED CONSENT

- Participation 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 entails only 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 effectiveness 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 compelling and scientifically sound methodological reasons the use of any intervention less 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 the 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.