SIGHT SCIENCES

A PROSPECTIVE, RANDOMIZED, MULTICENTER STUDY TO COMPARE THE SAFETY AND EFFECTIVENESS OF THE OMNI® SURGICAL SYSTEM AND THE ISTENT INJECT IN PSEUDOPHAKIC EYES WITH OPEN ANGLE GLAUCOMA-THE TRIDENT EUROPEAN TRIAL

[redacted] [redacted]

CURRENT REVISION:	F
REVISION DATE:	September 14, 2021
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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, Country

This protocol contains confidential information for use by the Investigators and their designated representatives participating in this clinical investigation. It must be held confidential and maintained in a secure location. Do not copy or distribute without written permission.

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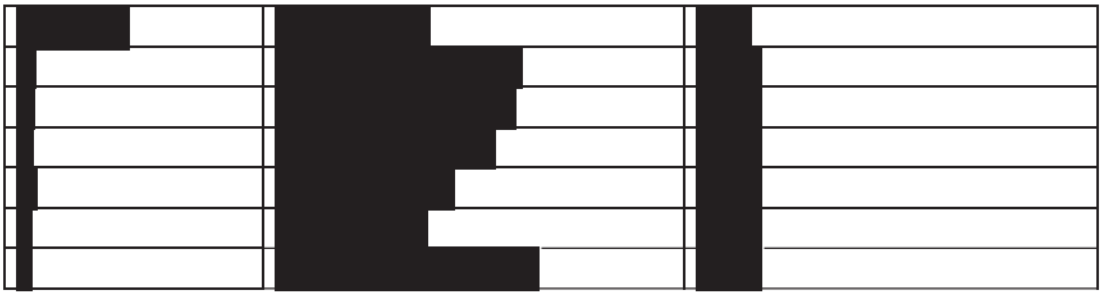

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1 PROTOCOL SYNOPSIS

Protocol Title	A Prospective, Randomized, Multicenter Study to Compare the Safety and Effectiveness of the OMNI® Surgical System and the iStent Inject in Pseudophakic Eyes with Open Angle Glaucoma- The TRIDENT European Trial
[redacted]	[redacted]
Study Device	OMNI Plus Surgical System (OMNI Surgical System)
Study Objectives	First, to compare safety and effectiveness outcomes for canaloplasty and trabeculotomy using the OMNI Surgical System to implantation of the iStent inject in lowering intraocular pressure (IOP) in pseudophakic eyes with open angle glaucoma (OAG), and second, to compare safety and effectiveness outcomes for canaloplasty alone (using the OMNI Surgical System) to implantation of the iStent Inject in lowering IOP in pseudophakic eyes with OAG.
Study Design	This is a prospective, randomized, multicenter, parallel group, comparative postmarket study in which a total of 459 subjects will be randomized in an equal allocation ratio (1:1:1) to either the OMNI (canaloplasty AND trabeculotomy), OMNI (canaloplasty only), or iStent inject and followed for 12 months after surgery.
Study Population	Pseudophakic adults with OAG.
Primary Effectiveness Endpoint	• Mean change in **unmedicated** DIOP from baseline at the 12-month postoperative examination The study hypotheses success will be evaluated using the primary effectiveness endpoint

Other Effectiveness Endpoints	• Proportion of eyes with a ≥ 20% decrease in **unmedicated** mean diurnal IOP (DIOP) from baseline at the 12-month postoperative examination • Proportion of eyes with **unmedicated** mean DIOP between 6 and 18 mmHg inclusive at the 12-month postoperative examination • Mean change in the number of ocular hypotensive medications at the 12-month postoperative visit compared to Screening • Percent change in **unmedicated** DIOP from baseline to 12 months • Change in Ocular Surface Disease Index (OSDI) and Glaucoma Quality of Life (GQL-15) scores from screening at 12 months. These are the exploratory endpoints and will not be used to evaluate the study success.
Safety Endpoints	• Rates of ocular adverse events (intraoperative, postoperative) • Reduction in best corrected distance visual acuity (BCDVA) from screening. • Secondary Ocular Surgical Interventions, including laser, for IOP control

Inclusion Criteria (Ocular criteria apply to the study eye only)	1. Male or female subjects, 18 years or older 2. Pseudophakic. History of uncomplicated cataract surgery and posterior chamber IOL implantation without compromise to the lens capsule, zonular dehiscence/rupture or vitreous prolapse, [redacted]. 3. Diagnosis of open angle glaucoma (OAG) including pigmentary and pseudoexfoliation substantiated using funduscopic exam (or OCT) and at least one reliable visual field test with the Humphrey automated perimeter using the SITA Standard 24-2 testing algorithm or an Octopus perimeter program G1 or G1X. Mean deviation score must be ≥-12.0 dB (Humphrey) or ≤ 12.0 dB (Octopus). The visual field test may be historical (within 6 months prior to Screening Visit). If needed, visual field testing may be repeated between the Screening Visit and the Baseline Visit. 4. At the Screening visit, on 1-5 ocular hypotensive medications (fixed combinations counted as number of components) with a **medicated** IOP of ≤ 33 mmHg. 5. At the Baseline visit, unmedicated diurnal IOP of ≥22 mmHg (≥24 mmHg for at least one timepoint and no less than 21 mmHg at any time point) and ≤36 mmHg and ≥3 mmHg higher than the medicated IOP at the Screening visit. 6. Scheduled for ab-interno minimally invasive canal-based glaucoma surgery. 7. Shaffer grade of ≥3 in all four quadrants 8. Able and willing to comply with the protocol, including all follow-up visits. 9. Understands and signs the informed consent.
Exclusion Criteria	1. Any of the following prior treatments for glaucoma: ○ Suprachoroidal stent [redacted]

(Ocular criteria apply to the study eye only unless otherwise stated)	○ Implanted with a MIGS or other glaucoma device [redacted] ○ Trabeculectomy or other bleb forming procedure [redacted] ○ Prior canaloplasty, goniotomy, or trabeculotomy including procedures [redacted] ○ Ciliary ablation procedures including Endocyclophotocoagulation (ECP), Cyclophotocoagulation (G probe), Micropulse laser, or high intensity focused ultrasound (HIFU) [redacted] 2. Any other form of glaucoma other than OAG 3. Use of topical ocular steroids that cannot be stopped [redacted] 4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications. 5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet 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). 6. History of penetrating keratoplasty or other corneal transplant; corneal abnormality that would prevent reliable IOP measurement (e.g. keratoconus, abnormally thick [≥600 µM] or thin [≤500 µM] cornea based on optical or ultrasound pachymetry of central corneal thickness [CCT])

	7. BCDVA of 6/60 (20/200) or worse in the fellow eye not due to cataract 8. Participation of the study eye in any other ocular interventional study ≤ 30 days prior to Baseline visit and throughout this study 9. 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	459 (153 per treatment group) to complete 411 (137 per group) at 12 months postoperative assuming a 10% drop-out rate
Number of Sites	A minimum of 24 and up to 26 sites in the European Union, United Kingdom, and/or Switzerland
Schedule of Visits	Screening, Baseline, Surgery (Day 0), Day 1, Week 1, 1 Month, 3 Month, 6 Month, 12 Month, 12 Month Washout
Treatments	• Ab-interno canaloplasty (360 degrees) and up to 360 degrees trabeculotomy using the OMNI Surgical System • Ab-interno canaloplasty (360 degrees) using the OMNI Surgical System • Ab-interno implantation of iStent inject (2 microstents)

2 STUDY OBJECTIVE

First, to compare safety and effectiveness outcomes for canaloplasty and trabeculotomy using the OMNI Surgical System to implantation of the iStent inject in lowering intraocular pressure (IOP) in pseudophakic eyes with open angle glaucoma (OAG), and second, to compare safety and effectiveness outcomes for canaloplasty alone (using the OMNI Surgical System) to implantation of the iStent Inject in lowering intraocular pressure (IOP) in pseudophakic eyes with open angle glaucoma (OAG).

Objective 1:

The first objective is to evaluate, if for pseudophakic eyes with OAG, OMNI (canaloplasty AND trabeculotomy), is superior in lowering IOP to iStent inject.

Mean change in **unmedicated** DIOP from baseline at the 12-month postoperative examination will be used as a primary effectiveness endpoint to evaluate superiority of OMNI (canaloplasty AND trabeculotomy) compared to iStent inject in lowering IOP in pseudophakic eyes with OAG.

Objective 2:

The second objective is to evaluate if canaloplasty alone is non-inferior in lowering IOP (with a non-inferiority margin of 1.5 mmHg for comparing mean unmedicated diurnal IOP reduction at 12 months postoperative) to the iStent inject.

Mean change in **unmedicated** DIOP from baseline at the 12-month postoperative examination will be used as a primary effectiveness endpoint to evaluate non-inferiority of OMNI canaloplasty compared to iStent inject in lowering IOP in pseudophakic eyes with OAG.

The hypothesis is that the combined canaloplasty + trabeculotomy will be superior to iStent Inject and canaloplasty alone will be non-inferior to iStent Inject in lowering the IOP. Unmedicated diurnal IOP will be used to measure the change in the IOP as the primary effectiveness endpoint. The statistical approach is described in detail in Section 10 of this protocol. Diurnal IOP takes into consideration the fluctuations in IOP throughout the day and medication washout allows for isolating the effect of study treatments (1. Canaloplasty + Trabeculotomy, 2. Canaloplasty alone and 3. Trabecular bypass shunt i.e. iStent inject).

3 BACKGROUND AND JUSTIFICATION FOR THE STUDY

Glaucoma is the leading cause of irreversible blindness worldwide and is a silent, progressive disease with global prevalence estimated at 76 million currently and 112 million by 2040.[1] The lack of symptoms (for OAG) and that significant loss of retinal ganglion cells can occur before glaucomatous visual field changes are detected underscore the need for consistent, effective treatment.[2,3] Elevated IOP is the primary risk factor (and the only treatable) for glaucoma, and treatment for glaucoma is directed at lowering IOP either medically or surgically.[4] 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%).[5] Similarly, the EMGT showed that treatment of newly diagnosed primary OAG 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%.[6] 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] Preservation of vision in patients with glaucoma is clearly dependent on control of intraocular pressure. With medical therapy generally the first line of treatment, successful control of intraocular pressure is largely dependent on patient adherence.[8–10] Unfortunately, nonadherence with medical glaucoma therapy is recognized to be a serious problem; Olthoff et al. concluded that nonadherence was commonplace.[11]

Minimally (or micro) invasive glaucoma surgery (MIGS) provides an alternative to more invasive surgical methods (i.e. trabeculectomy or glaucoma drainage devices) or to laser procedures. MIGS procedures can generally be done along with cataract surgery minimizing additional risk 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).[12,13]

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.[14-16] 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.[17,18]

The OMNI Surgical System (Sight Sciences Inc, Menlo Park, CA) is a manually operated device indicated for the delivery of small amounts of viscoelastic fluid and to cut trabecular meshwork tissue during trabeculotomy procedures. The OMNI allows doctors to perform viscoelastic delivery in conjunction with trabeculotomy through a single clear corneal incision. Alternatively, the OMNI may be used to perform canaloplasty only (without trabeculotomy). The OMNI Surgical System may be used in a combined procedure with phacoemulsification cataract surgery, or as a standalone procedure in pseudophakic patients.

The iStent inject (Glaukos Corp., San Clemente, CA) is intended to reduce intraocular pressure safely and effectively in patients diagnosed with primary open-angle glaucoma, pseudoexfoliative glaucoma or pigmentary glaucoma. The iStent inject can deliver two (2) stents on a single pass, through a single incision. The implant is designed to stent open a passage through the trabecular meshwork to allow for an increase in the facility of outflow and a subsequent reduction in intraocular pressure.
The device is safe and effective when implanted in combination with cataract surgery in those subjects who require intraocular pressure reduction and/or would benefit from glaucoma medication reduction. The device may also be implanted in patients who continue to have elevated intraocular pressure despite prior treatment with glaucoma

medications and conventional glaucoma surgery. The CE mark for this device was obtained in 2011.

This prospective, multicenter, randomized, comparative trial will evaluate and compare clinical outcomes for ab-interno canaloplasty and trabeculotomy performed using the OMNI Surgical System, for canaloplasty only using the OMNI Surgical System, and for the iStent inject, all used as standalone procedures (i.e., not in combination with cataract surgery) in patients with OAG.

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 or the iStent inject.

4 STUDY DEVICE

4.1 INDICATIONS FOR USE

The OMNI Plus Surgical System is CE marked and has the following indication for use:

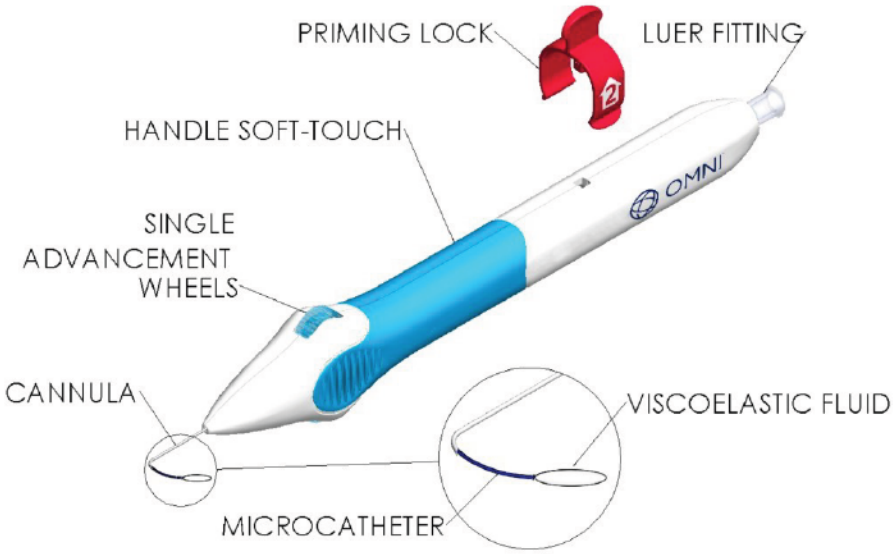
Catheterization and transluminal viscodilation of Schlemm's canal and the cutting of trabecular meshwork to reduce intraocular pressure in adult patients with open-angle glaucoma.

4.2 DEVICE DESCRIPTION

The OMNI Plus Surgical System "OMNI") is a single-handed, manually operated device designed to provide metered delivery of viscoelastic gel into Schlemm's canal and to cut trabecular meshwork tissue using a microcatheter. The device integrates an access cannula, a microcatheter, an internal fluid reservoir, and a simple catheter advancement and retraction wheel mechanism all into a single disposable handheld device.

Using only a single clear corneal incision to access the trabeculocanalicular aqueous outflow system, the OMNI Glaucoma Treatment System facilitates the transluminal viscodilation of all 360 degrees of Schlemm's canal and the cutting of up to all 360 degrees of trabecular meshwork from an ab interno approach. The system can be used with commercially available viscoelastics, such as Healon® PRO or Healon GV® PRO from Johnson & Johnson Vision, Amvisc® from Bausch & Lomb, or PROVISC® from Alcon. Viscoelastic fluid is not provided with the device.

[redacted]



5 STUDY DESIGN

This is a prospective, randomized, multicenter, parallel group, comparative study in which a total of 459 subjects will be randomized in an equal allocation ratio (1:1:1) to either the OMNI (canaloplasty AND trabeculotomy), OMNI (canaloplasty only), or iStent inject and followed for 12 months after surgery.

The study will employ a medication washout pre-randomization and at the 12-month endpoint which eliminates the potential confounding influence of ocular hypotensive medications in the assessment of device effectiveness.

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

Approximately 459 subjects will be randomized (1:1:1) to treatment, approximately 153 in each group. This assumes a 10% drop-out rate over the 12-month follow-up period and ensures that 137 subjects per group will complete the 12 month study. No site will randomize more than 25% of the total number of subjects.

It is estimated that up to 40% of subjects will not meet IOP eligibility criteria following medication washout, or other inclusion/exclusion criteria failure preventing

randomization therefore up to 762 subjects may be enrolled in order to meet the targeted randomization of 459 subjects.

Study subject participation will be for approximately 12 months, 5 days (at a minimum) to 14 months, depending on the length of the required medication washout prior to baseline and if a terminal washout is needed (required for subjects presenting at the Month 12 visit and on ocular hypotensive medication).

It is anticipated that site initiation, subject recruitment and follow-up, and site close-out will require approximately 24 months.

5.2 Methods Used to Minimize Bias

This study is randomized using block (a block of 6) randomization and neither the Investigator, the investigative site staff, or Sponsor clinical personnel will have knowledge of or access to the randomization scheme. Randomization to treatment group will be performed using a 1:1:1 ratio and will be stratified by site. Treatment allocation bias will thus be avoided. Once randomized into the study, the Investigator, the investigative site staff, Sponsor clinical personnel and the subject will be unmasked to the treatment assignment for each subject.

The study is multicenter with sites in at least 5 countries. The potential bias inherent in single-center trials is thus eliminated. Moreover, no site can randomize more than 25% of the study subjects. The location of sites in multiple countries incorporates greater diversity in the patient population as well as subtle geographic differences in treatment norms/standard of care allowing greater generalizability of the study results.

Mean diurnal IOP is the basis for the primary endpoint. DIOP averages three separate IOP measurements taken at different times of day. This mitigates the risk of a single measurement being unusually high or low and subsequent regression to the mean. IOP measurements will be taken using Goldmann applanation tonometry with routine and documented calibration required. IOP will be measured by 2 different study personnel (an operator and a recorder) closely following the procedure used in AGIS.[19] This technique prevents unintentional bias on the part of the Investigator or technician measuring and recording the IOP.

Reintroduction and discontinuation of ocular hypotensive medications will follow a protocol defined procedure to ensure standardization across sites and remove the potential for bias in treatment regimen.

5.3 STUDY DEVICE

The study device is the OMNI Plus Surgical System. Subjects randomized to one of the two OMNI treatment groups will undergo either ab-interno transluminal viscoelastic delivery for both hemispheres (360 degree treatment must be attempted) and trabeculotomy for one hemisphere (360 degree treatment must be attempted) (OMNI group), or to canaloplasty only (360 degree treatment must be attempted).

The Comparator group is:

- iStent inject (original or "W")

5.4 STUDY SITES

Study sites and surgeons will be selected based on experience and necessary resources to conduct clinical research and surgeon experience with the iStent inject and other MIGS.
This study will be conducted at up to 24 sites in the European Union, the United Kingdom, and/or Switzerland.

6 STUDY ENDPOINTS

6.1 EFFECTIVENESS ENDPOINTS

The **Primary effectiveness endpoint** is:

Mean change in **unmedicated** DIOP from baseline at the 12-month postoperative examination

Other effectiveness endpoints are:

- Proportion of eyes with unmedicated mean DIOP between 6 and 18 mmHg inclusive at the 12-month postoperative examination
- Proportion of eyes with a ≥ 20% decrease in unmedicated mean diurnal IOP (DIOP) at the 12-month postoperative examination
- Mean change in the number of ocular hypotensive medications at the 12-month postoperative visit compared to Screening
- Percent change in unmedicated DIOP from baseline to 12 months
  Change in Ocular Surface Disease Index (OSDI) and Glaucoma Quality of Life (GQL-15) scores from screening at 12 months.

6.2 SAFETY ENDPOINTS

- Rates of ocular adverse events (AE) (intraoperative, postoperative)
- Reduction in best corrected distance visual acuity (BCDVA) from screening
- Secondary Ocular Surgical Interventions, including laser, for IOP control

7 STUDY SELECTION CRITERIA

7.1 INCLUSION CRITERIA

For inclusion in this study, subjects must meet all the following criteria (only one eye of each subject is eligible, and all ocular criteria apply to the study eye only unless otherwise indicated):

1. Male or female subjects, 18 years or older

2. Pseudophakic. History of uncomplicated cataract surgery and posterior chamber IOL implantation without compromise to the lens capsule, zonular dehiscence/rupture or vitreous prolapse, [redacted].

3. Diagnosis of open angle glaucoma (POAG) including pigmentary and pseudoexfoliation substantiated using funduscopic exam (or OCT) and at least one reliable visual field test with the Humphrey automated perimeter using the SITA Standard 24-2 testing algorithm or an Octopus perimeter program G1 or G1X. Mean deviation score must be ≥-12.0 dB (Humphrey) or ≤ 12.0 dB (Octopus). The visual field test may be historical (within 6 months prior to Screening Visit). If needed, visual field testing may be repeated between the Screening Visit and the Baseline Visit.

4. At the Screening visit, on 1-5 ocular hypotensive medications (fixed combinations counted as number of components) with a medicated IOP of ≤ 33 mmHg.

5. At the Baseline visit, unmedicated DIOP of ≥22 mmHg (≥24 mmHg for at least one timepoint and no less than 21 mmHg at any time point) and ≤36 mmHg and ≥3 mmHg higher than the medicated IOP at the Screening visit.

6. Scheduled for ab-interno minimally invasive canal-based glaucoma surgery.

7. Shaffer grade of ≥3 in all four quadrants

8. Able and willing to comply with the protocol, including all follow-up visits.

9. Understands and signs the informed consent.

7.2 EXCLUSION CRITERIA

A subject who meets any of the criteria listed below (in the study eye, unless otherwise indicated) will be excluded from the study:

1. Any of the following prior treatments for glaucoma:
   - Suprachoroidal stent [redacted]
   - Laser trabeculoplasty ≤ 8 weeks prior to Baseline visit
   - Implanted with a MIGS or other glaucoma device [redacted]
   - Trabeculectomy or other bleb forming procedure [redacted]
   - Prior canaloplasty, goniotomy, or trabeculotomy [redacted]
   - Ciliary ablation procedures including Endocyclophotocoagulation (ECP), Cyclophotocoagulation (G probe), or Micropulse laser, or high intensity focused ultrasound (HIFU) ≤ 6 months prior to Baseline visit
2. Any other form of glaucoma other than OAG
3. Use of topical ocular steroids that cannot be stopped a[redacted]
4. In the Investigator's judgement, predisposed to significant risk because of washout of ocular hypotensive medications.
5. Concurrent ocular pathology or systemic medical condition which, in the Investigator's judgment, would either place the subject at increased risk of complications, contraindicate surgery, place the subject at risk of significant vision loss during the study period (e.g., wet 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).
6. History of penetrating keratoplasty or other corneal transplant; corneal abnormality that would prevent reliable IOP measurement (e.g. keratoconus, abnormally thick [≥600 µM] or thin [≤500 µM] cornea based on optical or ultrasound pachymetry of central corneal thickness [CCT])

7. BCDVA of 6/60 (20/200) or worse in the fellow eye not due to cataract

8. Participation of the study eye in any other ocular interventional study ≤ 30 days prior to Baseline visit and throughout this study

9. 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)

8 STUDY PROCEDURES

8.1 PROCEDURES PER STUDY VISIT

Procedures required by the protocol to be conducted at each study visit are listed in the Table 1, Study Visit Schedule and detailed in Appendix A, Section 19.1 CLINICAL TRIAL PROCEDURES.
A brief summary of the procedures performed by visit is provided here.

- At Screening, the subject will complete the informed consent process and sign an informed consent document. Standard procedures will be performed to determine subject eligibility. If needed, a second visual field exam may be conducted before surgery to confirm study eligibility. Wash-out of ocular hypotensive medications will commence.
- At Baseline, eligibility will be confirmed including meeting the unmedicated DIOP criteria. Eligible subjects will be randomized to treatment and scheduled for surgery. Ineligible subjects will be exited.
- At Surgery, subjects will either receive canaloplasty and trabeculotomy in the study eye with the OMNI Surgical System, canaloplasty with the OMNI Surgical System or be implanted with the iStent inject.
- At postoperative follow-up (Week 1, Months 1, 3, 6, and 12), safety and effectiveness assessments will be performed.

8.2 SELECTION OF THE STUDY EYE

Only one qualified eye per subject may be treated under the study protocol. If both eyes qualify for the study during screening, the eye with the higher DIOP at the Baseline visit will be designated as the study eye. If the DIOP of both eyes is the same, then the Investigator will determine the study eye.

[redacted]

8.4 STUDY VISITS

8.4.1 SCREENING VISIT

Informed Consent and Point of Enrollment

Informed consent will be obtained in writing from all subjects and the process documented prior to the performance of any procedure specific to the study using the Ethics Committee approved informed consent form. The Investigator or a trained authorized designee will conduct the informed consent process. Subjects will be given ample time to read and understand the informed consent form and to consider participation in the study. Subjects will be given a copy of the signed and dated informed consent form.

After obtaining an understanding of the purpose of this study, then providing written informed consent, all potential subjects will undergo an initial screening examination in order to determine their eligibility for the study. Exams and tests listed in the Screening column of Table 1 should be performed. Refer to Appendix A for instructions for performing the exams.

The Investigator must retain the original, signed written informed consent document.

Eligibility and Study Entry

Below is a list of study procedures to be undertaken at Screening Visit which must take place from 45 days to 6 days before surgery. Data collected at screening are considered baseline data. Conduct ocular assessments in both eyes.

1. [redacted]

[redacted]

Following confirmation of eligibility per study inclusion and exclusion criteria, subjects will be scheduled for the Baseline visit allowing sufficient time for complete washout of ocular hypotensive medication (refer to Table 2). Ineligible subjects must be exited from the study. The reason for ineligibility must be documented for each enrolled subject.

[redacted]

Subjects who are currently taking IOP-lowering medications will undergo the washout procedure described below and in Table 2 before the Baseline visit.

Subject exam data collected prior to enrollment as part of routine patient care may serve as Screening data as long as it was collected within 15 days prior to the visit with the following exceptions:

- IOP and IOP-lowering medications. These data must be collected at the Screening visit.

- Visual fields: A historical visual field may be used IF conducted per the protocol method (Humphrey automated perimeter using the SITA Standard 24-2 testing algorithm or an Octopus perimeter program G1 or G1X.) AND is within 6 months of the Screening visit.

Washout of Hypotensive Medications

Subjects who meet all screening eligibility criteria will be instructed to discontinue their ocular hypotensive medication regimen, and to return for a Baseline visit after completing the appropriate washout period. [redacted]

All subjects on ocular hypotensive medication(s) at Screening and Month 12 will be instructed to undergo a washout prior to the Baseline or Month 12 postoperative visit, respectively. If the study subject fails to remember to not use ocular hypotensive medication for the study eye per the required washout period, they can be reinstructed and restart the washout. If deemed necessary by the PI, a subject can be given hypotensive medications after the baseline visit until the day of surgery. An oral hypotensive medication can be used between baseline to surgery. The minimum wash-out periods are specified in Table 2 below.

NOTE: A safety IOP check mid-way through the wash-out period may be performed at the Investigator's discretion where warranted to ensure subject safety.

Table 2: 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

8.4.2 BASELINE VISIT (9:00 AM ± 1 HR, NOON ± 1 HR, 4:00 PM ± 1 HR)

Below is a list of study procedures to be undertaken at the Baseline Visit which must take place no more than 14 days prior to surgery and only after satisfying the medication washout (Section 8.4.1. "Washout of Hypotensive Medications" and Table 2). Conduct ocular assessments in both eyes.

[redacted]

[redacted]

Subjects meeting all criteria at the Baseline Visit will be scheduled for surgery and be randomized to a treatment arm. Randomization to treatment group will be performed using a 1:1:1 ratio and will be stratified by site. Computer-generated randomization will be administered through the electronic data capture (EDC) system with separate block randomization (block of 6) sequences for each clinical site.

8.4.3 SURGICAL VISIT

The Surgical visit must occur no more than 45 days after the Screening visit and no more than 14 days after the Baseline visit.

Study investigators will be experienced with iStent inject implantation and will have received training on the OMNI Surgical System prior to site activation. Surgery will take place after the subject successfully completes all screening and baseline assessments and is confirmed eligible to participate in the study per inclusion / exclusion requirements.

Surgeons should follow their standard peri-operative medication regimen.

[redacted]

[redacted]

The following information will be captured at this visit:

- Surgical complications
- Number of iStent inject stents implanted (1, or 2), implantation attempts, number of injectors used, any difficulties with implantation
- Intraoperative AEs
- Perioperative medications (topical hypotensive medications administered)

8.4.4 DAY 1

1. Document changes in ocular hypotensive medications.
2. Measure IOP with Goldmann tonometer is recommended between 8:00 am and 10:00 am. Refer toAppendix A, Section 19.1.3.
3. Conduct slit lamp examination. Refer to Appendix A, Section 19.1.4 for gradingscales.
4. Record any ocular AE.
5. Schedule the subject to return for the Week 1 Visit between the recommended time frame of 8:00 am and 10:00 am.

8.4.5 WEEK 1 (DAYS 5 TO 9), MONTH 1 (DAYS 21 TO 35), MONTH 3, (DAYS 70 TO 98), MONTH 6 (DAYS 150 TO 210)

[redacted]

[redacted]

8.4.6 MONTH 12 (DAYS 330 TO 420)

The Month 12 visit is the final visit for any subjects that are not currently on any ocular hypotensive medications. For patients on medications, all assessments except the DIOP will be completed (listed below for 9 am), however, depending on the medications used, will return in from 5 to 30 days following medication washout for the DIOP assessment.

[redacted]

[redacted]

[redacted]

[redacted]

8.4.7 MONTH 12 WASHOUT VISIT (DAYS 330 TO 420)

The Month 12 Washout visit is only intended for subjects presenting at the Month 12 visit on ocular hypotensive medication. This visit is conducted on the completion of medication washout for the purpose of obtaining an unmedicated IOP.

[redacted]

[redacted]

[redacted]

[redacted]

8.5 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.

8.6 POSTOPERATIVE OCULAR HYPOTENSIVE MEDICATIONS

In general, the primary consideration for the reintroduction of hypotensive medication is the preservation of the retinal nerve fiber layer, optic nerve and visual field. Ocular

hypotensive medication "rescue therapy" will be introduced 1 month postoperatively or later to any subject if his/her IOP increases to > 21 mmHg at two consecutive visits **within** a two-week period. Administration of glaucoma medication in subjects with IOP < 21 mmHg will be considered on a case-by-case basis by the study Investigator and the Medical Monitor.

Re-introduction of hypotensive medications will be standardized as follows:

- The same medication class(es) as used preoperatively will be re-introduced
- Only one medication class may be reintroduced at any single visit.

Dependent on preoperative IOP medication use, the reintroduction/addition of IOP medications postoperatively should follow the order below:

1. Prostaglandin Analogues
2. Alpha Agonists
3. Beta Blockers
4. Carbonic Anhydrase Inhibitors (CAIs).

No more than one ocular hypotensive agent should be added at a single visit or within a 2-week period, without prior approval of the Medical Monitor.

[redacted]

8.7 SECONDARY SURGICAL INTERVENTIONS TO CONTROL IOP

If the subject requires another glaucoma procedure (surgical or laser) to control their IOP, the subject should continue to be followed according to standard of care until the AE that required the surgical treatment resolves or 1-month post-re-intervention, whichever is longer. Following this, the subject should be withdrawn from the study.

Subjects who have a secondary IOP-lowering intervention will be considered treatment failures for the purpose of the effectiveness evaluation. For the primary effectiveness endpoint of the study, the corresponding baseline unmedicated DIOP will be used to impute the 12-month unmedicated DIOP. These subjects will be included in the Safety Endpoint analyses through their withdrawal from the study.

8.8 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, and must do so 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 CRF.

8.9 SUBJECTS LOST TO FOLLOW-UP

Subjects who do not show up for a scheduled follow-up visit must be contacted to attempt to have them come for the visit. Every attempt at contacting the subject must 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.

9 ADVERSE EVENTS (AE)

Adverse Events are defined below. AE that occurred in the study eye during the trial, whether they are considered to be device related or not, must be documented in the subject medical records and will be collected on the CRF. 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 Form (AEF). Conditions which existed prior to subject enrollment do not need to be recorded as AE unless they increase in severity or frequency during the study.

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 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

[redacted]

9.3 REPORTING ADVERSE EVENTS

Identification, collection and reporting of AE information is the responsibility of the 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-related **serious adverse event** (SAE) should be reported to study sponsor's clinical team within one business day of learning of the event. Non-ocular related SAEs should be reported to the study sponsor's clinical team within two working days of learning of the event. Email the AE CRF to OMNIsafety@sightsciences.com.

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 ofthe event, e-mail the AE CRF to OMNIsafety@sightsciences.com; and

2. The responsible Ethics Committee – As soon as possible, but no later than 10 working days after the investigator first learns of the event, report per the EC'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 OF THE STUDY

The sample size calculation is based on the primary effectiveness endpoint, mean change in unmedicated DIOP from baseline at the 12-month postoperative examination. The study goal is to determine, in reducing the IOP in the pseudophakic eyes with OAG, either OMNI (canaloplasty AND trabeculotomy) is superior to the iStent inject, or OMNI

(canaloplasty alone) is not inferior to the iStent inject in lowering the IOP with a non-inferiority margin of 1.5 mmHg. Due to the multiplicity, the significance level is adjusted to a two-sided significance level of 0.025 for each of the two hypotheses. The statistical hypotheses for the primary effectiveness endpoint are as follows:

[redacted]

10.2 Analysis Populations

10.2.1 Safety Population

The safety analysis population will contain all subjects for whom either the OMNI (canaloplasty alone), OMNI (canaloplasty AND trabeculotomy), or iStent inject is attempted. The attempt is defined as the OMNI instrument or iStent inject touching the study eyes even if the procedure is not completed. Subjects will be grouped according to their actual treatments.

10.2.2 As Treated

The Intent to Treat (ITT) analysis population will include all subjects randomized and grouped according to their randomization assignment (as randomized) regardless if they actually undergo the assigned procedure. The As Treated (AT) population consists of the subjects that actually undergo the assigned procedure and will be grouped according to their actual treatments. For this study, the AT population will be used for the primary analyses of the primary and other effectiveness endpoints. The effectiveness analyses may be performed for the ITT population if needed.

10.3 Demographics and Baseline Characteristics

Subject demographics (age, race/ethnicity and gender) will be summarized by study group for the ITT, AT, and Safety populations using descriptive statistics. Age will be summarized as a continuous variable and categorized into the four groups based on the observed quartiles.
The baseline medicated IOP and washout (unmedicated) IOP will be summarized by study groups for the ITT and AT populations. They will be treated as continuous variables. The number of glaucoma medications in use at enrollment will be prepared for each of the study groups using descriptive statistics for categorical variables.

Medical and Ocular history will be summarized for each study group by number and percentage of subjects in the ITT and AT population.
For the Safety Population, ITT, and AT populations, subject accountability will be prepared based on Table G.1 of ANSI Z80.27-2014.

[redacted]

10.4.1 [redacted]

[redacted]

[redacted]

10.4.2 SENSITIVITY ANALYSIS

A tipping-point analysis will be performed for the primary effectiveness endpoint. Let n and m be the number of OMNI and iStent inject subjects that do not have the 12-month washed out DIOP due to any reasons other than the first four criteria listed in Section 10.4.1. [redacted]

[redacted]

10.4.3 COVARIATE ANALYSIS

The following variables will be examined for their prognostic value to the primary effectiveness endpoint using the AT population with the imputation used for the primary analyses:

- Age group (based on observed quartiles)
- Gender (male and female)
- Race/ethnicity
- Baseline unmedicated DIOP group (based on observed quartiles)
- Number of ocular hypotensive medications at screening
- Study Site

For the primary effectiveness endpoint, two-way ANOVA with study group (three groups), one of the factors listed above, and the interaction between the study group and the factor will be used to check the possible covariate effects. A p-value of 0.15 will be used for evaluating the possible covariate effects. It should be noted that the subgroups of these covariates will be re-examined and may be re-categorized or eliminated due to small sample size (if there are < 10 subjects within each subgroup).

The scatter plots of the 12-month unmedicated DIOP versus the baseline unmedicated DIOP along with a 45° line will be provided. The scatter plot of the percent change in unmedicated DIOP from baseline to 12 months versus the baseline unmedicated DIOP will also be provided. The Box plots of the change and percent change in unmedicated DIOP from baseline to 12 months will be prepared for each category of the covariates (except for the study site).

10.4.4 OTHER EFFECTIVENESS ENDPOINTS

The statistical analyses for the other effectiveness endpoints will be based on the available data of the AT population. The percent change in unmedicated DIOP from baseline at 12 months will be calculated for each study eye as

$$\% \text{ change} = (\text{12-month unmedicated DIOP} - \text{Baseline unmedicated DIOP}) \div (\text{Baseline unmedicated DIOP}) \times 100\%.$$

The number and percent of subjects achieving $\geq$ 20% reduction in unmedicated DIOP from baseline at 12 months (i.e., 12-month responder) will be calculated. The exact 95% confidence interval of the 12-month responder rate will be calculated by the binomial distribution for each study group separately. The difference in the 12-month responder between OMNI (canaloplasty AND trabeculotomy) and iStent inject groups and the corresponding 95% confidence interval per normal distribution will be calculated. The same statistics will be provided for the difference in the 12-month responder between OMNI (canaloplasty alone) and iStent inject groups. The same statistical methods will be used to summarize the subjects with an unmedicated DIOP between 6 and 18 mmHg

inclusive at 12 months.

The descriptive statistics for the continuous variables will be used to summarize the change in number of ocular hypotensive medications used from screening to 12 months. The ANOVA with study treatment group (three groups) as the factor will be used to compare the mean difference in the change in number ocular hypotensive medications used from screening to 12 months. The mean difference between OMNI (canaloplasty AND trabeculotomy) and iStent inject groups and that between OMNI (canaloplasty alone) and iStent inject groups will be evaluated using Dunnett's test. The same methods will be used to analyze the percent change in unmedicated DIOP from baseline to 12 months.

The analyses described in this section are exploratory in nature.

[redacted]

10.4.5 [redacted]

[redacted]

- -10% < Change < 0% (i.e. 0% < decrease < 10%)

[redacted]

10.5 Safety Analysis

All safety analyses will be performed on the safety analysis population based on all available data by the three study groups separately.

10.5.1 Adverse Event

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

Each AE will be summarized by incidence, percentage and the corresponding 95% confidence interval.

10.5.2 Best Corrected Distance Visual Acuity (BCDVA)

BCDVA data collected at the subject Baseline, and the Week 1, 1, 3, 6, and 12 month postoperative visits. The number and percent of eyes reporting with BCDVA 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. Also, shift tables from baseline will be presented with counts, percentages, and 95% confidence intervals.

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 6 follow-up visit by 80% of the randomized subjects. Endpoints listed below will be analyzed at an interim analysis. No device effectiveness will be claimed based on the interim analysis outcomes.

Effectiveness outcomes up to 6 months will be summarized descriptively:

1. Percent of eyes with a ≥20% reduction in IOP with no increase in IOP-lowering medications compared to screening visit
2. Percent of eyes with IOP between 6 and 18 mmHg with no increase in IOP-lowering medications compared to screening visit
3. Percent of eyes with IOP between 6 and 21 mmHg with no increase in IOP-lowering medications compared to screening visit
4. Reduction in mean IOP from screening visit; and
5. Reduction in mean number of IOP-lowering medications from screening visit

Safety endpoints:

1. Rates of ocular adverse events (intraoperative, postoperative)
2. Reduction in BCDVA from screening (note: reduction in BCDVA due to worseningof PCO will not be treated as a safety event
3. 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 or contract research organization (CRO) personnel will monitor the study in a manner consistent with FDA and relevant competent authority (CA) regulations, good clinical practices and the clinical research standards adopted by Sight Sciences. Study monitoring will be executed using on-site visits, via remote means, or a combination of both, and will involve the following elements:

- Site Qualification: Sight Sciences or CRO personnel will meet with Investigators and clinical study staff either on site or via phone 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. 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 either remotely or in-person, visit the clinical site as specified in the Monitoring plan during the course of the study to review charts, and to perform source document verification, to 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 Closure: 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 EC

12 DATA AND QUALITY MANAGEMENT

12.1 DATABASE MANAGEMENT

The study database will be designed using an electric 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 EDC 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 ID number composed of a two-digit study identification number, a two-digit center identification number followed by a two digit sequential subject number. The subject ID number will be assigned on subject provision of written informed consent. In this way, information contained in the study records will be de-identified and kept as confidential as possible.

12.3 SUBJECT ACCOUNTABILITY

All subjects enrolled and treated 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), contract CRAs and governmental/regulatory agencies involved. The results of the study may be published in the future for scientific and marketing purposes, but the identity (name) of each subject will not be revealed. All records will be stored in a secure area at the Investigator's facility, the CRO (if applicable), the data management firm (if applicable) and at Sight Sciences, Inc. per each organization's own SOPs and applicable data privacy laws.

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. The selective electronic entries based on pre-defined targeted SDV monitoring plan will be 100% 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 the study worksheets provided by the sponsor and these study worksheets will serve as the source data.

Source data and study worksheets 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 Good Documentation Practices (GDP).

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 longer of the date the device is certified by a notified body in the EU 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, Sight Sciences must be contacted for instructions on record transfer and/ or disposition, at its discretion.

13 PROTOCOL MODIFICATIONS AND DEVIATIONS

Protocol modifications may occur during the study. Each will be approved in writing by the sponsor before implementation. Each will undergo Ethics Committee 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 Ethics Committee 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 form.

14 DEVICE FAILURES AND MALFUNCTIONS

All device failures or malfunctions should be recorded on the OMNI Customer Experience Form and reported to Sight Sciences.

15 ETHICAL CONSIDERATIONS

15.1 DECLARATION OF HELSINKI

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

15.2 RESEARCH ETHICS COMMITTEES (REC)

The protocol must be submitted for consideration, comment, guidance and approval to the concerned REC 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.
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 agents.

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

15.3 INFORMED CONSENT

Biomedical research involving interventions must not be allowed to proceed unless the potential research subject has given consent. For consent to be valid it must be informed and freely given. It includes but is not limited to: the purpose of the study, the intervention being tested, alternative treatments, that participation is voluntary, what will happen if consent is or is not granted, required study visits and other requirements for participants, that consent can be withdrawn at any time and for any reason, risks and side effects of the interventions, possible benefits from participation, confidentiality of study data, and what will happen if new information becomes available during the study. The original signed record of the consent should be kept by the Investigator as part of the study records.

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 REC and of the Institution where the study is conducted, but any revisions must be submitted to the sponsor for review prior to submission to the REC. A copy of each REC-approved informed consent document is to be made available to Sight Sciences and its CRO. The approved and, REC approved informed consent document is to be kept in its full length in the study Regulatory Binder. Original, signed informed consent for each subject must be maintained in study records and must be made available for monitoring review.

15.4 PUBLIC LISTING OF STUDY

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

16 STUDY ADMINISTRATION

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

Sight Sciences may terminate the study, in which case the Investigators and associated ECs 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 from the market for either safety or non-safety reasons.
- 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 any 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.

16.2 INVESTIGATOR RESPONSIBILITIES

16.2.1 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 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 applicable regulations.

16.2.2 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 REC 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 Competent Authority regulations, and any conditions of approval imposed by an REC.

16.2.3 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 REC, the Sponsor, the CRO, a monitor (i.e., CRA or clinical research associate), or the Competent Authority, including required reports.
2. Records of each subject's case history and exposure to the device. Case histories include the study CRF's/worksheets and supporting data including, for example, signed and dated consent forms and medical records. 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 the Competent Authority requires to be maintained by regulation or by specific requirement for a category of investigations or a particular investigation.

16.2.4 INVESTIGATOR REPORTS

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

1. Withdrawal of REC Approval - An Investigator shall report to the Sponsor, within 5 working days, a withdrawal of approval by the reviewing REC of the Investigator's part of an investigation.
2. Progress - An Investigator shall submit progress reports on the investigation to the Sponsor, the monitor, and the reviewing REC at regular intervals, but in no event less often than yearly.
3. Deviations from the Investigational Plan - An Investigator shall document and report to the Sponsor any deviation from the investigational plan.
4. Informed Consent - If an Investigator enrolls a subject without obtaining informed consent, the Investigator shall report such use to the Sponsor and the reviewing REC within 5 working days after the use occurs.
5. 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 REC.
6. Other - An Investigator shall, upon request by a reviewing REC or Competent Authority, provide accurate, complete, and current information about any aspect of the investigation.

16.3 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.

17 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 (or an independent contractor of 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.

19 APPENDICES

19.1 APPENDIX A - CLINICAL TRIAL PROCEDURES

19.1.1 BEST CORRECTED DISTANCE VISUAL ACUITY (BCDVA)

Use a standard Snellen eye chart at a distance of 6 or 4 meters. Ensure good natural light or illumination on the chart. It is important to ensure that the subject has the best possible chance of seeing and reading the test chart.

Explain the procedure to the subject. Tell subjects that it is not a test that they have to pass, but a test to help us know how their eyes are working. Tell them not to guess.

Ensure that any equipment that the subject touches is clean and is cleaned between subjects.

[redacted]

[redacted]

Manifest Refraction

Refraction will be performed by the Investigator or staff using standard clinical practice. Refractions will be performed prior to Goldmann tonometry and administration of anesthetic and dilating medication.

19.1.2 PRO INSTRUMENTS

19.1.2.1 GENERAL INSTRUCTIONS FOR QUESTIONNAIRES

The subject should complete all required questionnaires at the beginning of specified visits (screening, 6 months and 12 months) before conducting other clinical testing.

Provide a paper copy of the questionnaires and a blue or black ink pen to the subject. Review the instructions for each questionnaire with the subject and answer any questions they have about how to complete them. Then allow the subject to

complete the questionnaires on their own (i.e., self-administered) without any assistance.

Study staff should review the questionnaires before the subject leaves the office to check for missing or multiple answers on a given question. If these are found, please point this out to the subject and allow them to revise their response(s) to the specific question(s). Please confirm initials and date of the subject on the last page of the questionnaire. Do not allow the subject to take the questionnaires home.

[redacted]

[redacted]

[redacted]

19.1.3 GOLDMANN APPLANATION TONOMETRY

Tonometer Information

The tonometer should be checked for calibration accuracy according to the manufacturer's instructions. Verification of the calibration should be done at least quarterly and should be documented in a calibration log, a copy of which will be filed in the Investigator's study documentation. When checking calibration accuracy using

weighted bars at the 0, 20, and 60, the allowance range for the Goldmann tonometer is ± 2 mmHg. A tonometer where accuracy is outside ± 2 mmHg must be sent to the manufacturer for re-calibration and must not be used for IOP measurements in study subjects.

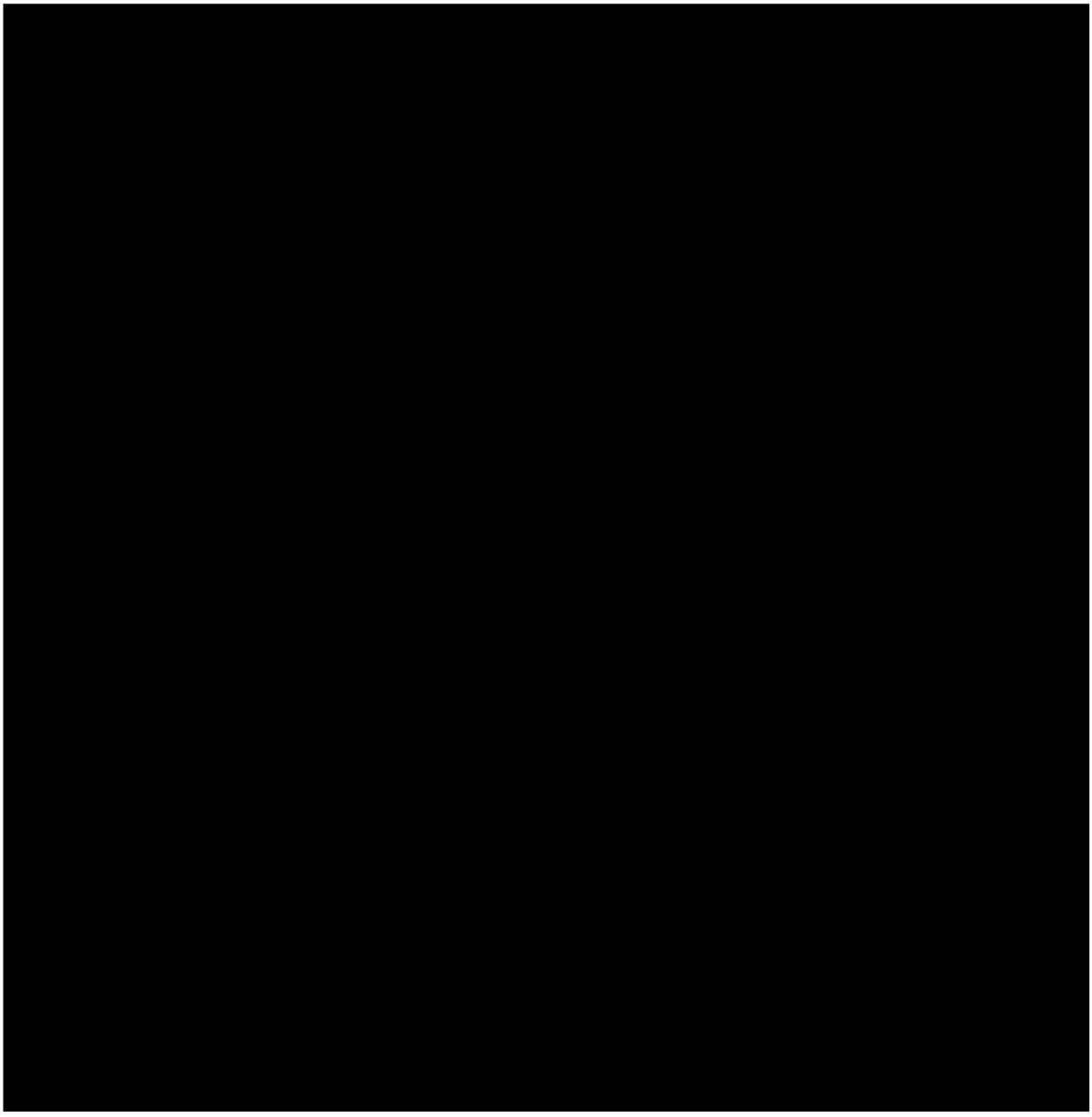
[redacted]

19.1.4 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. 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.

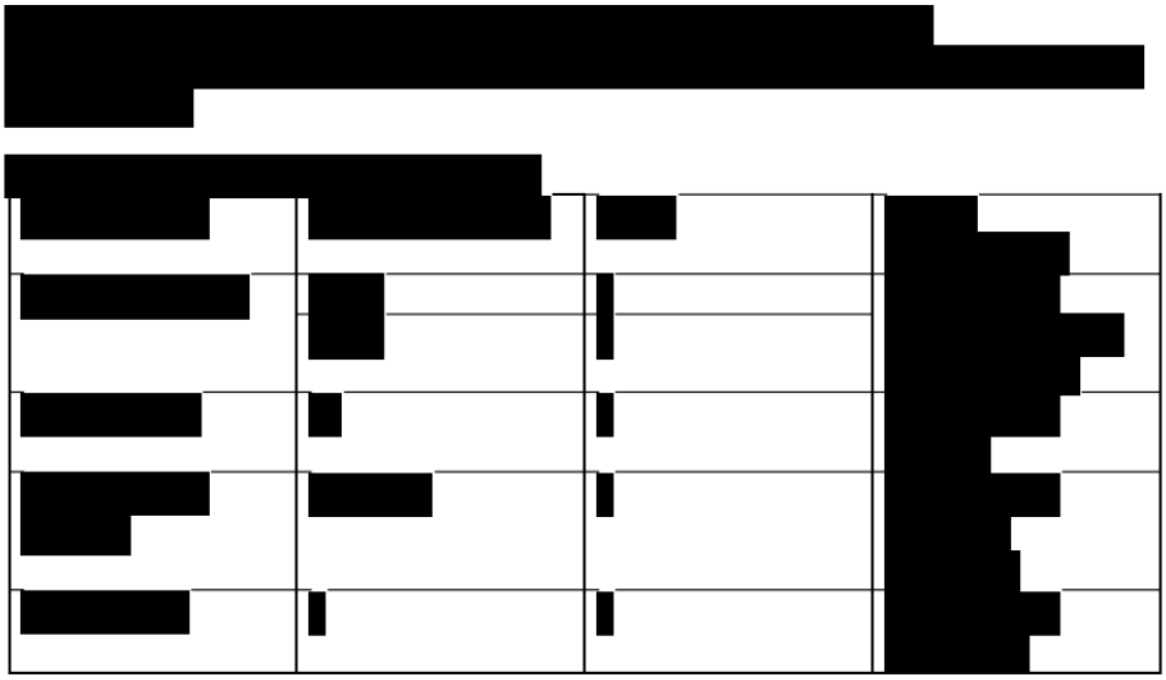
[redacted]

[redacted]



19.1.5 GONIOSCOPY

Gonioscopy should be performed prior to instillation of dilating or miotic drops, with high magnification, and with as little light as possible to potentiate visualization of the angle in its natural configuration. The angular width of the angle recess will be graded 0 (closed) to 4 (wide open). Refer to Table 3, below.



19.1.6 DILATED FUNDUS EXAM

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 Baseline form. A measurement of the cup to disc ratio should be made and reported.

19.1.7 PACHYMETRY

The pachymetry procedure should be conducted per sites standard operating procedures. This procedure requires topical anesthetic and should be completed after the IOP measurements, to prevent any effect on IOP measurements. Corneal pachymetry is a non-invasive ultrasonic technique for measuring centra corneal thickness (CCT). The CCT must be measured by optical or ultrasound pachymetry and the standard of care procedures should be followed. Three measurements must be recorded in source documents and the average of them must be noted down in the CRF.

19.2 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. 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 responsibilityfor 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.

7. 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.

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

9. 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.

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

11. 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.

12. 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 thestudy 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 participateat 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 ormental 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 forinvolving subjects with a condition that renders them unable to give informedconsent 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.