A PROSPECTIVE MULTI-CENTER STUDY OF ANTERIOR LENS CAPSULOTOMY USING THE MYNOSYS ZEPTO™ SYSTEM

IDE PROTOCOL: MYN-002

STUDY SPONSOR:
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Revision A
Revision Date: July 06, 2016

I have read and agree to follow the study procedures as outlined in this protocol.

_____
Print Name of Investigator

_____ _____
Investigator's Signature Date

This protocol contains confidential proprietary information with respect to the Zepto™ System and clinical trials of this product. I agree to hold this information in confidence and not to disclose it to any third parties for a period of (3) years from the date of this agreement, or until said information shall become a matter of public knowledge or until a formal written agreement for that purpose has been entered into by the parties

_____ _____
Investigator's Signature Date

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II. INTRODUCTION AND RATIONALE

The Mynosys Zepto™ System ("Zepto™") is a surgical instrument for intervention in the eye based on the use of short energy pulses to create the rapid phase transition of water molecules in or near tissues to create a tissue cutting force. The same fundamental mechanism of action is found in other approved devices for anterior lens capsulotomy such as the FugoBlade and the femtosecond laser.

Lens cataract surgery with phacoemulsification is the standard of care for the treatment of symptomatic lens cataract. A critical step in cataract surgery is anterior lens capsulotomy in which a circular opening is created in the capsule that surrounds the diseased lens. This opening allows the lens material to be removed safely from the eye via phacoemulsification, and an intraocular lens (IOL) to be implanted within the capsular bag.

Zepto™ provides a means to create capsulotomy openings that are consistent in shape and size.

This clinical study is being undertaken to demonstrate the effectiveness and safety of Zepto™ as a surgical instrument for performing anterior lens capsulotomies in subjects undergoing cataract surgery with phacoemulsification.

III. PRE-CLINICAL TESTING

All of the following pre-clinical test results have been peer-reviewed and published [1].

1) Ocular Condition After Zepto™ Capsulotomy

A GLP study was conducted in twenty rabbits in which one eye received a Zepto™ capsulotomy and the other eye, a continuous curvilinear capsulorhexis (CCC), both followed by lens phacoemulsification and IOL implantation. No differences were noted in ocular condition and recovery between either groups at 1 day, 3 days, 1 week and 4 weeks after surgery. No difference in inflammation was observed between the two groups from gross or microscopic pathology examination.

2) Anterior Chamber Temperature Changes

Temperature changes were recorded using thermocouples in the anterior chamber during Zepto™ capsulotomies in living rabbit eyes. Temperature changes of 1-2°C were measured for 2-4 seconds directly adjacent to the Zepto™ suction cup and at the corneal endothelium closest to the Zepto™ suction cup. Both the magnitude and duration of these temperature changes were significantly below the thresholds required for cellular damage [2].

3) Corneal Endothelial Cell Condition

The corneal endothelium was examined as part of the GLP study and no differences were found in corneal endothelial cell damage between eyes that received a Zepto™ capsulotomy versus a CCC.

IV. REPORT OF PRIOR INVESTIGATIONS

The Mynosys Zepto™ System has been used in human clinical studies in San Salvador, El Salvador with approval by the government of El Salvador.

In the first study, 10 subjects with symptomatic age-related lens cataract received Zepto™ capsulotomies during cataract surgery with phacoemulsification and implantation of a foldable one-piece acrylic IOL. All 10 Zepto™ capsulotomies resulted in complete 360° capsule openings with free-floating capsule buttons. All 10 subjects received intracapsular IOL fixation. All subjects reported good vision at one-week and at 30-days post procedure.

A second study of 10 subjects was undertaken to investigate a slightly smaller suction cup and ring combination, with all other aspects of the Zepto™ capsulotomy system remaining the same. Zepto™ capsulotomies in the first 4 subjects resulted in some tissue bridges causing the capsule button to remain attached to the capsule. These capsulotomies were completed manually using forceps. All 4 subjects underwent successful phacoemulsification with intracapsular IOL fixation. The cause of these incomplete capsulotomies with remaining tissue bridges was traced to a small suction leak in the handpiece that reduced the delivery of suction to the suction cup and affected Zepto™'s performance. The study was stopped and the remaining 6 subjects underwent manual CCC, phacoemulsification, and IOL implantation. The sponsor identified an incorrect setting on the Zepto™ handpiece leak tester at the contract manufacturer that resulted in the leaks not being identified during production. This problem has now been resolved.

A third study was conducted in 10 subjects to investigate using the introduction of BSS following Zepto™ capsulotomy as a means to separate the capsule button off the roof of the suction cup, and at the same time float off the suction cup from the capsule. In addition, the last 5 subjects received a slightly longer duration of suction to create apposition of the nitinol ring against the capsule. In these 5 cases, suction was maintained until the surgeon verified visually that small bubbles in the OVD ceased movement, indicating full suction. All 10 subjects that received Zepto™ capsulotomies had complete capsulotomies with a capsule button separated

from the suction cup and remaining in the anterior chamber. All underwent successful phacoemulsification with intracapsular IOL fixation. Eight out of the 10 subjects returned for follow up at 4 weeks. There were no adverse clinical findings and no capsule related problems. All 10 Zepto™ capsulotomies were successful, and visual confirmation of full suction provided assurance of capsulotomy completion.

A fourth study of 10 subjects was undertaken to re-confirm the effectiveness of the BSS float-off mechanism to separate the capsule button from the suction cup and to float-off the suction cup from the capsule. In all cases, the surgeon was also instructed to wait for visual confirmation of cessation in OVD movement prior to initiating Zepto™ capsulotomy. All 10 Zepto™ capsulotomies resulted in complete round capsule openings with no residual tissue bridges. All 10 capsule buttons were free floating and easily identified and retrieved by the surgeon. All 10 subjects underwent successful phacoemulsification with intracapsular IOL fixation.

V. STUDY OBJECTIVE

This study will evaluate outcome in subjects who have elected to have Zepto™ capsulotomies during cataract surgery with phacoemulsification.

VI. PARAMETERS

A. Primary Effectiveness Endpoint - Complete Capsulotomy (At least 95% of cases)

Clinical Discussion - In clinical practice, a successful capsulotomy results in a rounded, anterior capsular opening through which the cataract can be extracted. The capsulotomy preserves a bag-like configuration of the remaining lens capsule, which enables secure intracapsular fixation of the IOL.

A successful complete Zepto™ capsulotomy is defined in this protocol to be one that results in a complete 360° capsulotomy without any residual tissue bridges visible to the surgeon. If there are such tissue bridges, the surgeon completes the capsulotomy manually.

Effectiveness Rate – An effectiveness rate of 95% complete capsulotomies provides reasonable assurance that the Zepto™ system is effective.

Data Recording - The presence of a complete capsulotomy without tissue bridges will be recorded by the surgeon as a Yes or No following each Zepto™ capsulotomy.

B. Primary Safety Endpoint - Posterior Capsular Rupture & Vitreous Loss (4% or less)

Clinical Discussion - Posterior capsular rupture & vitreous loss is generally considered one of the most significant complications of cataract surgery that occurs with some frequency. One well recognized cause is posterior extension of an anterior capsular radial tear. It is noteworthy however, that the majority of anterior capsular tears do not

adversely impact visual outcome.[3] Posterior capsular rupture and vitreous loss subject the patient to additional risks of postoperative complications commonly resulting in suboptimal best corrected visual acuity, and usually precludes intracapsular IOL fixation. Due to its potential adverse impact on best corrected visual acuity, posterior capsular rupture and vitreous loss related to Zepto™ capsulotomy is chosen as the primary safety endpoint.

Posterior Capsule Rupture & Vitreous Loss Rate – The incidence of posterior capsular rupture and vitreous loss has been documented in 13 peer-reviewed publications over the period between 1999-2011. With one exception, all of these studies have shown rates ranging from 1.1 to 4.4 percent depending on surgeon group [4-16]. A posterior capsular rupture and vitreous loss rate within the range of this published data in subjects receiving Zepto™ capsulotomies will provide reasonable assurance that the Zepto™ capsulotomy system acceptably meets the safety endpoint in the proposed study.

Data Recording – The occurrence of a posterior capsular rupture and vitreous loss will be recorded by the surgeon as a Yes or No following the completion of surgery.

C. Other Parameters To Be Captured

1) Anterior Capsule Tear – The occurrence of an anterior capsule tear will be recorded by the surgeon as a Yes or No after the completion of Zepto™ capsulotomy.

2) Corneal Touch - The occurrence of corneal touch by the Zepto™ capsulotomy tip during its use will be recorded by the surgeon as a Yes or No after the completion of Zepto™ capsulotomy.

3) Capsulotomy Diameter – The diameter of the Zepto™ capsulotomy will be measured during surgery by the surgeon using an intraocular rhexis ruler.

VII. STUDY DESIGN

This study is a prospective, non-randomized, multi-site clinical study with up to 8 clinical sites enrolling a total of 100 eyes of subjects aged 22 and older, who will have Zepto™ capsulotomy followed by conventional phacoemulsification and IOL implantation.

Subjects will be screened for eligibility and informed consent will be obtained from those who meet screening criteria and are interested in participation in the study. Eligible subjects will be examined preoperatively to obtain a medical history and to establish a baseline for ocular condition. Baseline measurements will be collected as outlined in Section IX.

VIII. SUBJECT POPULATION

Subjects with symptomatic age-related lens cataract desiring lens extraction and IOL implantation.

A. INCLUSION CRITERIA

1. Subjects must be age 22 or older,
2. Subjects consenting to undergoing phacoemulsification and IOL implant surgery for the treatment of symptomatic age related lens cataract, and then electing to undergo Zepto™ capsulotomy,
3. Subjects must be willing and able to return for scheduled treatment and follow-up examinations for 1 month.

B. EXCLUSION CRITERIA

1. Disease or pathology in the treatment eye that will compromise visual performance or refractive outcome (e.g. previous refractive surgery),
2. Zonular abnormality,
3. Posterior polar cataract,
4. Fellow eye with acuity less than 20/200,
5. Any prior ocular surgery of the study eye,
6. Advanced glaucoma (greater than 0.8 cup: disk) or intraocular pressure ≥ 30 mmHg in the study eye,
7. Pupillary dilation during the pre-operative exam of less than 7 mm in diameter,
8. Proliferative diabetic retinopathy,
9. Disorders of the ocular muscles, such as nystagmus or strabismus,
10. Chronic uveitis,
11. Abnormal corneal endothelium,
12. Subjects on medications with, in the opinion of the surgeon, significant ocular side effects,
13. Pregnant or nursing (lactating) women,
14. Implanted ocular device or drug in the study eye,
15. Any other condition, which in the judgment of the investigator would prevent the subject from completing the study (e.g. documented diagnosis or treatment for symptoms associated with dementia, mental illness),
16. Current participation in another drug or device clinical study, or participation in such a clinical study within the six months.

IX. STUDY MATERIALS AND METHODS

A. SUBJECT ENTRY

The investigator will identify potential subjects for this study based on routine ocular examination of the investigator's patients. No study specific procedures will be conducted prior to obtaining informed consent from the subject. The investigator or qualified site personnel will explain the study purpose, procedures, and subject responsibilities to the potential participant. The subject's willingness and ability to meet the follow-up requirements will be determined. The investigator or his/her designee will answer all pertinent questions asked by the subject. When it has been established that the subject is likely to be eligible for participation, written informed consent will be obtained. The subject will sign and date the informed consent form in the presence of a witness. The investigator will also sign and date the consent form. One copy of the informed consent form will be retained with the subject records and a copy will be provided to the subject. The consent process will be documented in a brief medical note in the subject's source file.

After the subject has signed the consent form, the subject will be assigned a subject ID number for the study. Once a subject has been consented, he/she will only be identified with his/her personal ID number and name initials. All other identification data will be held confidential.

Once the subject has been consented, the subject may undergo study specific procedures, including surgery with the Zepto™ capsulotomy surgery. Baseline examination will be performed no more than 2 weeks prior to Zepto™ capsulotomy surgery. After the baseline examination, if the subject meets the inclusion and exclusion criteria, the subject will be scheduled for cataract surgery with Zepto™ capsulotomy.

For subjects with bilateral cataracts and who meet all inclusion and exclusion criteria in both eyes, only one eye will be selected for Zepto™ capsulotomy. This study eye will be chosen randomly by drawing left eye / right eye ballots.

Only subjects discontinued prior to Zepto™ capsulotomy may be replaced in the study. Those subjects who are enrolled to replace withdrawn subjects will receive new ID numbers.

B. CLINICAL PARAMETERS

The following list of clinical parameters is typically collected as part of routine pre-operative testing. If they are not collected as part of the routine pre-operative examination, they will be collected as study specific procedures prior to cataract surgery.

1. Manifest refraction
2. Uncorrected distance visual acuity (UCVA)
3. Best spectacle corrected distance visual acuity (BSCVA)
4. Dilated pupil size
5. Slit lamp and fundus examination

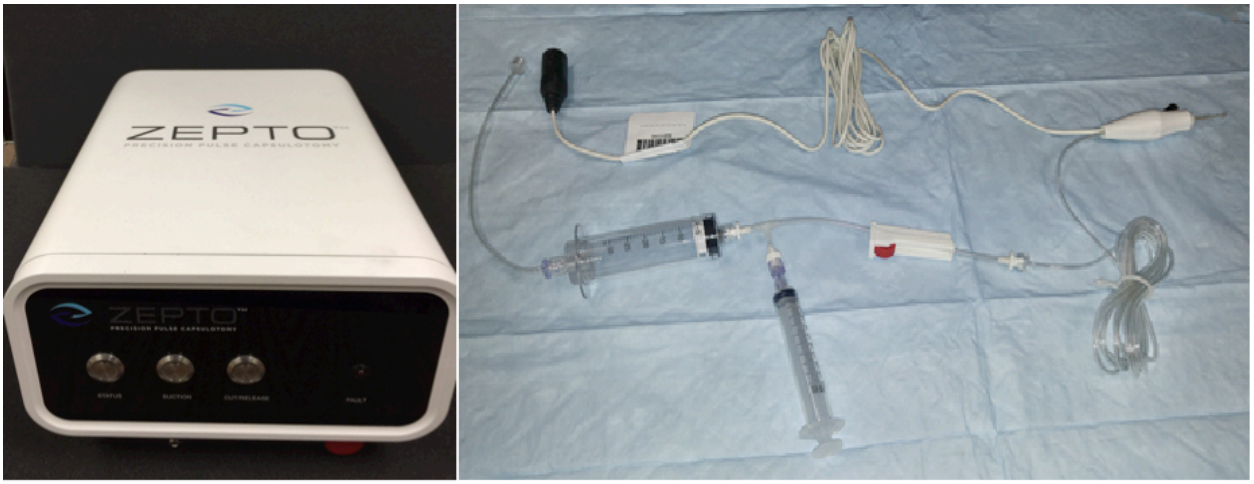
C. EXAMINATION SCHEDULE

Subjects enrolled in the study will be required to commit to the following examination schedule and take part in the clinical evaluations as outlined in Appendix 2.

Preoperative Evaluation	(Day -14 to Day -1)
Operative Evaluation	(Day 0)
Day 1	(1 to 2 days postoperative)
Week 1	(5 to 12 days postoperative)
Month 1	(3 to 6 weeks postoperative)

D. DESCRIPTION OF DEVICE

The Mynosys Zepto™ System consists of a disposable surgical handpiece (104mm x 22mm (4.14" x 0.866") that is operated by the surgeon to perform the capsulotomy and which is connected to a small table-top control console (10"w x 14"d x 7"h) located within the surgical suite (see Figure 1). In use, the surgeon holds the device in a horizontal grip. The functional portion used for capsulotomy is the capsulotomy tip located at the front end of the handpiece and consists of a circular, soft silicone suction cup 1.18 mm in height and 6.10 mm in diameter. This silicone suction cup houses a nitinol ring that delivers the energy pulses to create the capsulotomy. The capsulotomy handpiece is connected to the console containing suction controls, electronic timing circuits, safety diagnostics, and an audio interface.



A Zepto™ capsulotomy is performed by applying suction to the suction cup causing the nitinol ring to be apposed to the lens capsule. A series of 12 electrical pulses lasting a total of 4 milliseconds is delivered to the nitinol ring causing rapid phase transition of water molecules trapped between the bottom edge of the nitinol ring and the capsule. The rapid volume expansion results in the capsule cutting action. Suction is then vented to atmosphere. The operating assistant will, upon command from the physician, introduce a small amount of Balanced Salt Solution (BSS) into the suction cup to allow for a gentle release of the suction cup from the capsule, and to allow the free-floating capsule button to stay behind in the anterior chamber for manual removal with forceps. Upon completion of the capsulotomy, the disposable Zepto™ Handpiece tip is removed from the eye.

E. ZEPTO™ CAPSULOTOMY PROCEDURE

The Zepto™ capsulotomy will be performed on Day 0 of the study according to the following instructions:

1. Patient Preparation
   1.1. Obtain preoperative dilation per standard protocol.
   1.2. Obtain anaesthesia per standard protocol.
   1.3. Clean the subject's eyelids and ocular adnexa with disinfecting solution.
   1.4. Apply sterile drapes.

2. Zepto™ System Setup
   2.1. Ensure that the red 'Emergency Off' button is in the 'Out' position.
   2.2. Plug the female end of the Zepto™ Power Cord into the rear of the Zepto™ Power Console, and then plug the male end of the power cord into a properly grounded electrical outlet.
   2.3. Make sure the area around the electrical outlet is clear and easily accessible, in case there is a need to unplug the Zepto™ Power Console from the outlet.
   2.4. Make sure that the electrical outlet that you use is not controlled by a light switch, and do not use an extension cord that has a switch. The Zepto™ Power Console must remain powered on at all times to work properly.
   2.5. Turn on power for the Zepto™ Power Console using the small switch located on the rear power entry module where the power cord plugs in. The Zepto™ Power Console will perform a self-check. A successful Zepto™ Power Console self-check will result in a flashing green Status light.
   2.6. Open the package, and pass the Fluid Isolator to the operating attendant.
   2.7. Aseptically remove the Mynosys disposable Zepto™ Handpiece from the outer pouch and aseptically transfer the inner pouch to the scrub nurse.
   2.8. Remove the Fluid Isolator from the pouch.
   2.9. After retrieving the Zepto™ Handpiece from the inner pouch in a sterile manner, connect the disposable Zepto™ Handpiece suction line to the Fluid Isolator.
   2.10. Connect the 10cc syringe to the Fluid Isolator.
   2.11. Connect the Fluid Isolator to the Luer-Lok connector at the front of the Zepto™ Power Console.
   2.12. Connect the electrical cable to the 5 pin receptacle at the front panel of the Zepto™ Power Console.
   2.13. After the Zepto™ Handpiece self-check is successfully completed, the flashing green light will convert to a constant ON green light, indicating the system is ready.
   2.14. Pull the protective tip cover off the end of the disposable Zepto™ Handpiece, being careful not to damage the Zepto™ tip.

3. Surgical Procedure
   3.1. Create a clear corneal incision of 2.2mm or greater.
   3.2. Use an Ophthalmic Viscosurgical Device to stabilize the anterior chamber.
   3.3. Submerge Zepto™ capsulotomy tip into sterile Balanced Salt Solution (BSS).
   3.4. Pull the syringe plunger to the end of travel.
   3.5. Slide the finger slider distally on the disposable Zepto™ Handpiece to elongate the Zepto™ capsulotomy tip for insertion into the corneal incision (Do not pull back on the finger slider until the Zepto™ capsulotomy tip has been inserted completely into the anterior chamber).
   3.6. Stabilize the eye with a Thornton fixation ring, and insert the Zepto™ capsulotomy tip through the corneal incision.
   3.7. Once the Zepto™ capsulotomy tip is fully within the anterior chamber, slide the finger slider proximally to return the capsulotomy tip to a circular state.
   3.8. Position the Zepto™ capsulotomy tip on the capsular bag, centering the device using the desired centration method.
   3.9. Instruct assistant to press the "Suction" button on the console to initiate suction cup and nitinol ring apposition onto the lens capsule.
   3.10. Visually confirm the flow of OVD has stopped by monitoring the movement of bubbles in the OVD. When the OVD ceases to flow, full suction has been achieved.
   3.11. Instruct assistant to press the "Cut/Release" button on the console to perform the capsulotomy (once capsulotomy energy is delivered, the suction is automatically vented to atmosphere).
   3.12. Instruct assistant to introduce small amount of pre-loaded BSS into the suction cup to gently release the suction cup from the capsule (this is done by the assistant moving a roller clamp on the suction tubing).
   3.13. Stabilizing the eye with the Thornton fixation ring, remove the Zepto™ Handpiece capsulotomy tip from the anterior chamber by manually withdrawing it through the corneal incision. The Zepto™ capsulotomy tip automatically folds and conforms to the incision as it is withdrawn from the eye.
   3.14. The excised capsule "button" (circular piece of capsule tissue that has been cut) from the capsulotomy will be free-floating within the anterior chamber and can be retrieved by forceps.
   3.15. In the event of an incomplete capsulotomy with remaining tissue bridges, use the manual Continuous Curvilinear Capsulorhexis technique to complete the capsulotomy.

F. POSTOPERATIVE CARE

The subject will be instructed by the operating physician on normal post-op cataract surgery instructions.

G. DATA REPORTING

A Case Report Form (CRF) binder will be used for each subject enrolled in the study. The appropriate CRF, provided under separate cover in a binder specific to this study, will be completed and signed by the investigator after each examination. All CRFs will be completed in a legible manner in ink. Any corrections will be made by drawing a single line through the incorrect entry, entering the correct information, and initialing and dating the change.

H. STUDY COMPLETION PROCEDURES

Subject Completion: Subjects are considered to have completed the study if they have completed all follow-up examinations through month 1.

Subject Termination: Subjects may be terminated from the study at the discretion of the Principle Investigator only for reasons related to the study regimen that would jeopardize the subjects' health and/or welfare if they were to continue in the study. However, every effort will be made to follow terminated subjects for safety reasons using the appropriate case report forms until the planned end of the study period.

Subjects Discontinuation/ Lost to Follow-up: Subjects may be discontinued from the study for non-study-related reasons only when no other option is possible. Reasons for discontinuation include, but are not necessarily limited to:

1) Voluntary withdrawal from the study by the subject;
2) Subject has moved from the area and is determined to be lost to follow-up;
3) Subject is unwilling or unable to cooperate with study requirements (follow-up visits, etc.).

The reason for discontinuation will be recorded on the appropriate CRF. Only subjects discontinued prior to Zepto^{TM} capsulotomy may be replaced in the study. Prior to discontinuing a subject, every effort should be made to contact the subject to either encourage the subject to maintain compliance with the protocol or to obtain as much follow-up data as possible regarding the subject's current visual status.

X. COMPLICATION AND ADVERSE EVENT REPORTING

Safety reporting, as part of clinical research, can be different from what normally happens in clinical practice. A clinical investigator has a dual role, as a physician and as an investigator. These responsibilities are not in conflict but can lead to confusion while collecting, evaluating and reporting adverse events. As an investigator participating in research, it is important to understand the definition of an adverse event from a regulatory perspective. As listed below, the regulatory definition of an adverse event does not always equal the clinical definition and such events will need to be collected and documented, and in some cases reported in an expedited fashion.

Regulations associated with clinical investigations generally define adverse events as undesirable occurrences or untoward medical occurrences. Most adverse events seen during a clinical investigation are not serious, as defined by the regulations. These non-serious adverse events are

collected and documented, but they do not need to be reported in an expedited fashion to the Sponsor, regulatory bodies, or the EC/IRB.

A clinical investigator is obligated, as soon as they become aware of the event, to report to the Sponsor any adverse event determined to be serious as defined by the regulations or protocol. This is done for two reasons: first, to ensure the safety of all participants in the clinical investigation, and second, to meet reporting requirements of regulatory agencies.

When a serious or non-serious adverse event occurs, the first concern will be the safety and welfare of the subject; treatment should be provided as appropriate for the event. During the study, the investigator should appropriately treat and follow-up each event until it resolves, stabilizes, or it is determined that further improvement is not expected.

A. Definitions

An **Adverse Device Effect (ADE)** is any untoward or unintended response to a medical device. This definition may include any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device or other device malfunctions. This definition includes any event that is a result of a user error.

An **Adverse Event (AE)** is any untoward medical occurrence in a subject.

A **Device Failure/Device Malfunction** is any occurrence where the medical device fails to operate in the intended manner or at all. Such a malfunction or failure may have no impact on subject treatment, may result in a subject related adverse event, or may prolong the total procedure time.

Serious Adverse Device Effect (SADE) is any adverse device effect that results in any of the consequences characteristic of a serious adverse event or that may lead to any of these consequences if suitable action is not taken, or intervention is not made, or if circumstances are less opportune.

Serious Adverse Events (SAEs) are adverse events that:

- Lead to death,
- Lead to serious deterioration in the health of the subject that:
  - Results in a life-threatening illness or injury,
  - Results in a permanent impairment of a body structure or function (i.e., blindness),
  - Requires in-patient hospitalization or prolongation of existing hospitalization,
  - Results in medical or surgical intervention to prevent permanent impairment to a body structure or a body function, or
  - Results in a potentially sight-threatening condition
- Lead to fetal distress, fetal death, a congenital abnormality, or birth defect.

Unanticipated Adverse Device Event (UADE) is any serious adverse effect on health or safety or 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 investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

Unanticipated Adverse Event (UAE) is any adverse event, the nature, severity, or frequency of

which is not consistent with either:

1. The known or foreseeable risk of adverse events associated with the procedures involved in the research that are described in (a) the protocol related documents, such as the IRB-approved research protocol, any applicable investigator brochure, and the current IRB-approved informed consent document, and (b) other relevant sources of information, such as product labeling and package inserts; or

2. The expected natural progression of any underlying disease, disorder, or condition of the subject(s) experiencing the adverse event and the subject's predisposing risk factor profile for the adverse event.

B. Identification and Collection

Identification and collection of an adverse event begins after informed consent has been obtained and documented. Standard sources for identifying adverse events include:

- Direct observation by the investigator
- Asking the study participant a non-specific question (i.e., "Have you had any problems since the last visit?")
- Unsolicited volunteering of information by the study participant (i.e., "Doctor, I have had numerous headaches since I started using this lens.")
- Subject symptoms/complaints reported via subject questionnaire
- Laboratory or test results that meet protocol requirements for classification as an adverse event (e.g., IOP over 30 mmHg)

The Investigator will review each event, assess its relationship to the Zepto^{TM} system and the severity of the event (see definitions provided below), will determine if the event is serious and if it is unanticipated. In addition, the Investigator will document subsequent treatment/intervention and resolution status for all Adverse Events.

All adverse events and adverse device effects observed or elicited by the investigator, reported by the subject, or resulting from a test result, etc., occurring during the clinical investigation must be documented in the source documentation. All ocular adverse events are transcribed to the Adverse Event CRF. During the study, the investigator should treat the study subject as appropriate to ensure his/her safety and welfare.

<u>Cataract Surgery Adverse Events</u>

Specific to this protocol, pre-existing conditions (including cataract/planned cataract surgery on the non-study eye) will not be considered adverse event/serious adverse events, but will be collected at the preoperative visit. A worsening of a pre-existing condition during the study should be documented as an adverse event and evaluated accordingly.

Although the following may be considered normal or expected events after cataract surgery, for purposes of this protocol, the following items must be documented as adverse events and evaluated accordingly:

- Anterior capsule tear

- Posterior capsule rupture with or without vitreous loss
- Choroidal effusion hemorrhage
- Corneal edema, corneal decompensation
- Corneal abrasion
- Post-operative uveitis
- Endophthalmitis
- Posterior capsule opacification
- Macular edema
- Retinal tear or retinal detachment
- Elevated intraocular pressure
- Decentered IOL
- Wound leak
- Posterior vitreous detachment
- Medication allergy or intolerance
- Ptosis
- Capsulotomy decentration
- Zonular instability
- Corneal burn
- Corneal endothelial tear
- Anterior capsule fibrosis/anterior capsule contraction syndrome

C. Evaluation

When evaluating adverse events, the investigator must determine if the event is serious, assess the severity of symptoms, the relationship of the event to the study device and study procedure, and whether or not the event was unanticipated using the following guidelines:

1. Severity

- Mild: Subject awareness of a sign or symptom that is easily tolerated, requires no treatment, and does not interfere with subject's daily activities
- Moderate: Subject awareness of a sign or symptom which may be a low level of concern to the subject and may interfere with daily activities, but can be relieved by simple therapeutic care
- Severe: A sign or symptom that interrupts the subject's daily activity and requires systemic therapy or other treatment.

2. Relationship to Study Device or Study Procedures (Causality)

- Probably: Any untoward medical occurrence reported in a subject, user, or other person, which might have a direct relationship to the study device/study protocol, including any malfunction, failure, deterioration in the characteristics or deployment and/or performance of the device, as well as any inadequacy in the labeling or the instructions for use, and an alternative cause is unlikely or significantly less likely compared to the potential

relationship to the study device/study protocol.

- Possibly: Any untoward medical occurrence reported in a subject, user or other person, which might have a direct or indirect relationship to the study device/study protocol, including any malfunction, failure, deterioration in the characteristics or deployment and/or performance of the device, as well as any inadequacy in the labeling or the instructions for use and an alternative cause is equally or less likely compared to the potential relationship to the study device/study protocol.
- Unlikely: Any untoward medical occurrence reported in a subject, user or other person, which might have a little relationship to the study device/study protocol, including any malfunction, failure, deterioration in the characteristics or deployment and/or performance of the device, as well as any inadequacy in the labeling or the instructions for use and a likely alternative cause exists.
- Unrelated: Any untoward medical occurrence reported in a subject, user or other person, which has no direct or indirect relationship to the study device/study protocol, and a more likely alternative cause (underlying or concurrent illness, effect of another procedure/device/drug) is identified or strongly suspected.

D. Reporting

1. On-Site Serious Adverse Event (SAE) Reporting

The site should report any event to the Sponsor in an expedited manner if it meets the criteria for an SAE, or Serious Adverse Device Effect. Expedited reporting is calling, e-mailing, or faxing the Sponsor within 24 hours of becoming aware of the event. When calling or e-mailing the Sponsor to report an SAE or Serious Adverse Device Effect, the site should forward any supporting documents along with the SAE Report Form to the Sponsor within 24 hours of the initial call or e-mail and follow-up with CRF submission within 3 working days of identification. When faxing the notification and supporting documentation, the SAE Report should be included. Refer to the Personnel and Facilities section for Sponsor contact information for reporting of SAEs and Serious Adverse Device Effects. Sites must also report these events to the reviewing EC/IRB per their established reporting procedures.

2. Off-Site Serious Adverse Event (SAE) Reports

When participating in multi-center clinical trials, investigators may receive “off-site” reports (e.g., SAE Report). These are Sponsor reports of SAEs which occurred at other sites for the same trial, or in different trials using the same test article, that met the criteria for reporting to a regulatory agency. These will be reported to the applicable regulatory agency by the Sponsor. These should also be reported to the reviewing EC/IRB per their established reporting procedures.

3. Unanticipated Adverse Events (UAEs)/Unanticipated Adverse Device Events (UADEs) Reports

Unanticipated adverse events or unanticipated adverse device events must be reported either orally or in writing to the sponsor and the EC/IRB within 24 hours when it is known that the

event occurred.

4. Device Failure/Device Malfunction Reports

Where a device failure or device malfunction results in a serious or unanticipated adverse event/unanticipated adverse device event, the reporting requirements are those shown in (1) and (3) above. For cases where no serious adverse event or UAE/UADE occurs, the failure or malfunction should be reported to the Sponsor within 48 hours of the event being identified.

E. Adverse Event Reporting Matrix

The investigator will submit to the Sponsor representative a report of any SAE, SADE, ADE, UAE or UADE occurring during an investigation according to the following schedule. In addition, device failure or malfunction which did not result in a UAE/UADE will also be reported according to the following schedule.

Type of Report	**Submission Schedule**
Serious Adverse Event (SAE)/ Serious Adverse Device Effect (SADE)	verbal report within 24 hours followed by a written report within 3 working days
Adverse Device Effect (ADE)	verbal or written report within 10 working days
Unanticipated Adverse Event (UAE) or Unanticipated Adverse Device Event (UADE)	verbal report within 24 hours followed by a written report within 5 working days
Patient Death	verbal report within 24 hours followed by a written report within 5 working days
Device Failure or Malfunction not resulting in UAE or UADE	within 48 hours

F. Adverse Events (AEs) and Serious Adverse Events (SAEs) at Subject Exit

If a subject is still being treated for an event at their last study visit, the ongoing event needs to be evaluated to determine appropriate follow-up for study purposes. Further follow-up may be needed as indicated below.

1. Unrelated AEs and SAEs

Ongoing AEs and SAEs classified as “Not Related” to study device and study procedures will be treated and followed until resolution or as dictated by standard of care. Documentation in the CRF of this follow-up is not required although subject care should continue as appropriate.

2. Related AEs and SAEs

Ongoing AEs classified as “Related” to the study device and study procedures will be treated and followed until resolution or as dictated by standard of care. Documentation in the CRF of this follow-up is not required although subject care should continue as appropriate.

Ongoing SAEs classified as "Related" to the study device and study procedures will be followed until their medical endpoints are determined or until no further change in the conditions are expected.

XI. SAMPLE SIZE

A. Primary Effectiveness Endpoint - Complete Capsulotomy (At least 95% of cases)

The proposed sample size of 100 eyes, assuming a 95% success rate, will provide an exact 95% confidence interval of 88.72% to 98.36% around our point estimate.

B. Primary Safety Endpoint - Posterior Capsular Rupture & Vitreous Loss (4% or less)

The proposed sample size of 100 eyes, assuming a posterior capsular tear and vitreous loss rate of 4%, will provide an exact 95% Confidence Interval of 1.10% to 9.93% around our point estimate.

XII. DATA ANALYSIS

Continuous data will be summarized with descriptive statistics (N, mean, standard deviation, minimum, median, and maximum). Categorical variables will be summarized with N and percentage. Binary endpoints, including both primary safety and primary effectiveness, will be summarized with proportion success and associated exact (Clopper-Pearson) 95% confidence interval. All data summarized in tables will be presented in supportive line listings.

The diameter of all Zepto^{TM} capsulotomies will be summarized as a continuous endpoint. The proportion of Zepto^{TM} capsulotomies with anterior capsule tears or corneal touch will be reported along with its 95% exact confidence interval. The number and proportion of subjects experiencing specific adverse events will be tabulated by number and percentage of subjects experiencing those adverse events.

Hypothesis testing will not be performed. Point estimates and associated confidence intervals will be the basis of evaluation the effectiveness and safety of the device. All analyses will be performed using SAS software version 9.4

XIII. STUDY MONITORING

Mynosys clinical study trained personnel and / or personnel from a Contract Research Organization will monitor all clinical studies in a manner consistent with any applicable health authority regulations and the clinical research standards adopted by the Mynosys clinical

department. Mynosys clinical study trained personnel and / or personnel from a Contract Research Organization will:

1. Meet with investigator(s) prior to the initiation of the study to review the adequacy of the subject population, facilities, and equipment with respect to the needs of the study; to familiarize the investigator with the study protocol; and to reinforce GCP guidelines for clinical study conduct.

2. Conduct interim monitoring visits and telephone consultation as necessary during the course of the study to ensure the proper progress and documentation of the study findings.

3. Visit the clinical site when all subjects have completed the final visit of the study to collect the CRFs.

XIV. APPENDICES

Appendix 1: Proposed Informed Consent Form

RESEARCH SUBJECT INFORMATION AND CONSENT FORM

TITLE:	**A PROSPECTIVE MULTI-CENTER STUDY OF ANTERIOR LENS CAPSULOTOMY USING THE MYNOSYS ZEPTO™ SYSTEM**	
.		
PROTOCOL NO.:	Sponsor WIRB® Protocol #	**MYN-002**
SPONSOR:	Name Address City, State, Zip Code Country	Mynosys Cellular Devices, Inc. 46710 Fremont Blvd Fremont CA 94538-6538 United States
INVESTIGATOR:	Name Address City, State, Zip Code Country	
STUDY-RELATED PHONE NUMBER(S):	Name Phone Number(s) (24-hour number required for studies that are more than minimal risk)	Dan Marinsik (510) 857-6296

A person who takes part in a research study is called a research or study subject. In this consent form "you" always refers to the research subject. If you are a legally authorized representative, please remember that "you" means the research (study) subject.

SUMMARY

You are being asked to be in a research study. The purpose of this consent form is to help you decide if you want to be in the research study.

You should not join this research study until all of your questions are answered.

Things to know before deciding to take part in a research study:

- The main goal of a research study is to learn things to help patients in the future.
- The main goal of regular medical care is to help each patient.
- The decision to join or not join the research study will not cause you to lose any medical benefits. If you decide not to take part in this study, your doctor will perform the cataract surgery using standard techniques.
- Parts of this study involve experimental (investigational) capsulotomy procedures that are being tested for a new device. An investigational device is one that has not been approved by the U.S. Food & Drug Administration (FDA).
- After reading the consent form and having a discussion with the research staff, you should know which parts of the study are experimental and which are standard medical care.
- Your medical records may become part of the research record. If that happens, your medical records may be looked at and/or copied by the sponsor of this study and government agencies or other groups associated with the study.
- Your medical insurance WILL be billed for any standard medical care you receive during the research study. You will be responsible for the costs of your standard medical care. You will not be charged for the study portion of your care. Your insurance company will not be billed for the research portion of your care. If your insurance company is billed then it may have access to the research records. Insurance companies may not pay for treatment that is part of a research study.

PURPOSE OF THE STUDY

The purpose of this study is to determine whether the Mynosys Zepto™ System is safe and effective in performing anterior capsulotomies during cataract surgery.

PROCEDURES

You will have eye surgery to have cataracts removed and as part of the surgery, a capsulotomy will be performed using the Mynosys Zepto™ System. A capsulotomy is a surgical procedure in which a circular incision is made into the capsule of the crystalline lens of the eye. This procedure will take less than 1 minute. After that, the device will be removed from your eye. After completion of the capsulotomy, the physician performs the rest of the cataract surgery procedure following his standard routine for this surgery.

After the surgery, you will be prescribed with antibiotic eye drops to prevent infection and anti-inflammatory eye drops to help reduce any internal inflammation. You'll need to apply the eye drops several times daily for about the first week during your recovery from cataract surgery. This medication is not part of the study, but is standard treatment for cataract surgery.

All qualified subjects in the study will have a capsulotomy created by the Mynosys Zepto™ system. If both your eyes require cataract surgery, only one eye will have a capsulotomy with the Zepto™ system. The other eye will receive a capsulotomy using your physician's standard technique. The eye receiving the Zepto™ capsulotomy will be chosen randomly.

RISKS AND DISCOMFORTS

- **What are the possible risks or discomforts?**
- ***Risks of Eye Examination and Dilation:***
- As part of the eye exam, drops will be put in your eyes to dilate the pupils. This is a standard procedure during cataract surgery and not specific to the study. The drops may blur your vision and make you sensitive to light for several hours. There is a small risk of an allergic reaction to the drops. There is also a small risk that the drops could cause the eye pressure to raise. If this happens, it will be treated, but there is a very small risk of losing vision from the pressure rise. Due to the blurring effect of your vision and possible light sensitivity, you will be advised not to drive until the drops have worn off and, if necessary, to have someone come with you who can drive after the exam.

- ***Other Risks from Cataract Surgery:***
- You should be aware that there may be additional risks or side effects that are currently unknown and unforeseeable, such as capsular tears, corneal edema, corneal abrasion, infection or bleeding inside of the eye, and blurred vision.

Women who are pregnant may not take part in this study. Women that have not been confirmed to be post-menopausal or surgically sterilized will be given a Serum β-HCG test prior to your cataract surgery to confirm that you are not pregnant.

Other Risks
Your condition may not get better or may get worse during this study.

BENEFITS

It is possible that the Mynosys Zepto™ System could improve your outcome after cataract surgery. However, this is an initial study so there is no clinical evidence to support this at this time.

COSTS

You will be charged for standard medical care. You will not be charged extra for the study portion of your care. Tests and procedures that are done only for the study will not be billed to you or your insurance company.

PAYMENT FOR PARTICIPATION

You will receive limited payment for travel expenses for being in this study. You will be reimbursed $25 for each study visit after the initial screening visit. Reimbursement is to defray travel costs.

Transportation assistance will be provided (if needed for subsequent visits) in the form of up to $50 taxi fare reimbursement, or arrangement for other transportation. Please ask the study staff if you need transportation assistance.

ALTERNATIVE TREATMENT
If you choose not to participate in this study, your doctor will discuss alternative surgical techniques to perform the capsulotomy required for your cataract surgery.

You do not have to take part in this study to receive treatment for your condition. One of the surgical alternatives available to people with cataracts requiring a capsulotomy is a technique called a Continuous Curvilinear Capsulorhexis (CCC). The treatment may also be done using a femtosecond laser. You may also choose to receive no treatment at all.

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:

- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:

- Working for or with the sponsor, or
- Owned by the sponsor.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Confidentiality
Information from this study will be given to the sponsor. "Sponsor" includes any persons or companies that are contracted by the sponsor to have access to the research information during and after the study.

The information will also be given to the U.S. Food and Drug Administration (FDA). It may be given to governmental agencies in other countries where the Zepto™ System may be considered for approval. Medical records which identify you and the consent form signed by you will be looked at and/or copied for research or regulatory purposes by:

- the sponsor,
- Promedica, an agent for the sponsor,
- Kevin Waltz, O.D., M.D., the medical monitor for this study,

And may be looked at and/or copied for research or regulatory purposes by:

- the FDA,
- Department of Health and Human Services (DHHS) agencies,
- California State Food and Drug Branch
- governmental agencies in other countries, and
- Western Institutional Review Board® (WIRB®).

Absolute confidentiality cannot be guaranteed because of the need to give information to these parties. The results of this research study may be presented at meetings or in publications. Your identity will not be disclosed in those presentations.

COMPENSATION FOR INJURY
If you are injured or get sick as a result of study procedures, call the study doctor immediately. The study doctor will provide emergency medical treatment.

VOLUNTARY PARTICIPATION AND WITHDRAWAL
Your participation in this study is voluntary. You may decide not to participate or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are entitled.

Your participation in this study may be stopped at any time by the study doctor or the sponsor without your consent for any reason, including:

- if it is in your best interest
- if you do not consent to continue in the study after being told of changes in the research that may affect you

If you leave the study before the planned final visit, you may be asked by the study doctor to have some tests or procedures done so that you leave the study safely.

QUESTIONS
If you have questions about your rights as a research subject or if you have questions, concerns or complaints about the research, you may contact:

Western Institutional Review Board® (WIRB®)
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 1-800-562-4789 or 360-252-2500
E-mail: Help@wirb.com

WIRB is a group of people who independently review research.

WIRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WIRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

Do not sign this consent form unless you have had a chance to ask questions and have gotten satisfactory answers.

If you agree to be in this study, you will receive a signed and dated copy of this consent form for your records.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

CONSENT

I have read this consent form (or it has been read to me). All my questions about the study and my part in it have been answered. I freely consent to be in this research study.

I authorize the release of my medical and research records for the purpose of this study.
By signing this consent form, I have not given up any of my legal rights.

_____
Subject Name (printed)

_____ _____
Signature of Subject Date

_____ _____
Printed Name of Person Conducting the Informed Consent Discussion Position

_____ _____
Signature of Person Conducting the Informed Consent Discussion Date

ASSENT SIGNATURES, For Subjects with a Legally Authorized Representative:

Assent:
For subjects who have a legally authorized representative, I confirm that:

- I have explained the study to the extent compatible with the subject's understanding, and the subject has agreed to be in the study.
  OR
- The subject is not able to assent due to lack of mental capacity.

_____ _____
Signature of Person Conducting Assent Discussion Date

ASSENT SECTION:

Statement of person conducting assent discussion:

- I have explained all aspects of the research to the subject to the best of his or her ability to understand.
- I have answered all the questions of the subject relating to this research.
- The subject agrees to be in the research.
- I believe the subject's decision to enroll is voluntary.
- The study doctor and study staff agrees to respect the subject's physical or emotional dissent at any time during this research when that dissent pertains to anything being done solely for the purpose of this research.

Ver. 07/06/2016

Appendix 2: Schedule of Visits and Clinical Parameters

	Screening	Day 0	Day 1	Week 1	Month 1
Informed Consent	X				
Ophthalmic History	X				
Inclusion/Exclusion	X				
Dilated Pupil Size	X				
Intraocular Pressure	X				
Manifest Refraction	X				
Uncorrected distance visual acuity (UCVA)	X				
Best spectacle corrected distance visual acuity (BSCVA)	X				
Slit Lamp	X				
Fundus Examination	X				
Zepto™ Capsulotomy		X			
Completeness of Capsulotomy		X			
Observation of Corneal Touch		X			
Observation of Posterior Capsule Rupture		X			
Observation of Anterior Capsule Tear		X			
Capsulotomy Diameter		X			
Adverse Events		X	X	X	X

Appendix 3: Methods of Clinical Evaluation

A. Dilated Pupil Size

Pupil size will be measured preoperatively by the slit lamp beam. The slit lamp beam will be adjusted vertically using the micrometer scale. The vertical size of the pupil will be recorded, understanding that the measured pupil size by this technique will be approximately 1.15x of the actual pupil size.

B. Measurement of Intraocular Pressure

Intraocular pressure should be measured using Goldmann or Pascal applanation tonometry or other validated methods.

C. Completeness of Capsulotomy

By surgeon observation during surgery

D. Observed Corneal Touch

By surgeon observation during surgery

E. Observed Posterior Rupture

By surgeon observation during surgery

F. Observed Anterior Tear

By surgeon observation during surgery

G. Capsulotomy Size

The diameter of the Zepto™ capsulotomy will be measured by the surgeon using a rhexis ruler (MST Seibel Capsulorhexis Forceps with Rhexis Ruler™ and ViewPort, dull tips (Cat. DFH-0029). The rhexis ruler is inserted into the anterior chamber after Zepto™ capsulotomy. The rhexis ruler is placed gently on top of the capsulotomy opening and the capsulotomy diameter is read off the markings on the rhexis ruler. The capsulotomy diameter is recorded and the rhexis ruler is removed from the anterior chamber.

Appendix 4: Sponsor's Commitments

Mynosys Cellular Devices is committed to:

1. Complying with the Declaration of Helsinki and all applicable health authority regulations governing the conduct of clinical trials.

2. Protecting the rights, health, safety, and welfare of study subjects.

3. Informing the clinical Investigators of any new information about the study which may affect the health, safety or welfare of the subjects, or may influence their decision to continue participation in the study.

4. Providing the clinical Investigators with the study protocol, and a full set of Case Report Forms (CRFs) to document the study report writing resources necessary to complete reporting of the study results.

5. Providing the statistical analysis and study report writing resources necessary to complete reporting of the study results.

6. Ensuring equity of consideration among all Investigators in multi-center studies in all matters of publications, meeting presentations, etc.

Appendix 5: Investigator's Qualifications and Responsibilities

Each investigator must be a licensed physician who has completed a residency or preceptorship in ophthalmology. The investigators have the following responsibilities

1. **Subject Selection:** The investigator is responsible for assuring that all subjects entering the study conform to the subject selection criteria.

2. **Informed Consent:** The Investigator is responsible for fully reviewing the nature of the study, the possible risks, and alternative treatments with prospective subjects prior to their enrollment in the study. The investigator is responsible for obtaining written Informed Consent in compliance with 21 CFR 50 for each subject, prior to enrollment in the trial. A copy of the signed Informed Consent Form will be maintained in the subject's medical record and a copy will be given to the subject.

3. **Subject Evaluations and Data Reporting:** The Investigator is responsible for performing the subject evaluations as described in the study protocol. All information generated by the subject evaluation will be recorded on the Subject Case Report Forms (CRFs) provided by the Sponsor. The CRFs will be filled out in black ink or will be typewritten. Any corrections will be made by lining out the incorrect information, entering the correct information, and initialing and dating the change. Correction fluid will not be used. The Investigator will sign and date each individual form upon its completion and will return the originals, not copies, to the Sponsor. Copies of all CRFs will be retained in the Investigator's office in order to be available for monitoring by Mynosys personnel.

Immediately upon completion of each subject examination the completed, signed, and dated CRF shall be submitted to the Sponsor for review and statistical analysis. Investigators will not deviate from the study protocol without prior approval of Mynosys unless protection of the health, safety or welfare of study subjects requires prompt action.

4. **Institutional Review Board (IRB) Approval:** The Investigator must obtain approval for his participation in this protocol from the IRB for the institution at which the procedure will be performed, prior to entering any subjects in the study. The Informed Consent document to be used will also be submitted by the Investigator to the IRB for approval prior to initiation of the study.

5. **Conduct of the Study:** The Investigator will conduct the study in accordance with Good Clinical Practice as set forth by the FDA.

6. **Record Retention:** The Investigator shall maintain all subject records for whichever of the following periods is shortest:

a. A period of five years after the date on which the FDA approves the marketing of the device for the purpose that was the subject of the study.

b. A period of five years after the date on which the results of the study are submitted to the FDA in support of the marketing of the device for the purpose that was the subject of the study.

Appendix 6: Investigator Agreement

Clinical Study Agreement

This Clinical Study Agreement ("Agreement") is by and between Mynosys Cellular Devices Inc., a Delaware corporation, located at 46710 Fremont Blvd Fremont CA 94538 ("SPONSOR") and (Insert Physician's Name), located at (Insert Physician's Address) ("ORGANIZATION").

SPONSOR is performing a clinical investigation under the Study Protocol "A PROSPECTIVE MULTI-CENTER STUDY OF ANTERIOR LENS CAPSULOTOMY USING THE MYNOSYS ZEPTO™ SYSTEM" ("Protocol"), attached hereto as Exhibit A.

1. Study Services

ORGANIZATION will provide the following operative study services under the "Protocol:"

- Routine procedure-related disposables and consumables required for a successful outcome.

2. Privacy Laws

SPONSOR agrees that it's use and disclosure of patient health and medical information is subject to compliance with applicable state and federal privacy laws. SPONSOR, therefore, agrees to take all reasonable steps to protect the confidentiality of any patient health and medical information that it has access to and comply with applicable state and federal privacy laws, including the Health Insurance Portability and Accountability Act of 1996, Public Law 104-191 (HIPAA). The obligations set forth in this Section shall survive the termination of this Agreement.

3. Indemnification

SPONSOR agrees to indemnify, defend and hold harmless ORGANIZATION, its trustees, officers, agents and employees against any claims, suits or judgments made or instituted against ORGANIZATION to the extent that they are caused by the defect or malfunction of the investigational device or product used in STUDY, except to the extent that such claim or judgment is based upon negligence or willful malfeasance by ORGANIZATION. ORGANIZATION agrees to notify SPONSOR as soon as it becomes aware of any such claim or action and to cooperate with and authorize SPONSOR to carry out the sole management and defense of any such claim or action. SPONSOR agrees, at its own expense, to provide attorneys to defend against any actions brought or filed against ORGANIZATION, its trustees, officers, agents, employees with respect to the indemnity contained herein, whether or not such claims or actions are rightfully brought or filed.

ORGANIZATION agrees to indemnify, defend and hold harmless SPONSOR, its trustees, officers, agents and employees against any claims, suits or judgments made or instituted against SPONSOR arising out of or connected with any activities of ORGANIZATION that result from the negligence or willful malfeasance of ORGANIZATION or any of its authorized agents,

except to the extent that such claims, suits or judgments are based upon negligence or willful malfeasance by SPONSOR.

4. Insurance

SPONSOR shall maintain the following minimum levels of insurance or self-insurance: $1 million per occurrence and $3 million aggregate (i) Worker's Compensation and Employers Liability insurance, (ii) Commercial General Liability insurance, and (iii) Errors and Omissions insurance.

ORGANIZATION shall maintain the following minimum levels of insurance or self-insurance:$1 million per occurrence and $3 million aggregate (i) Worker's Compensation and Employers Liability insurance, (ii) Commercial General Liability insurance, and (iii) Errors and Omissions insurance.

5. Independent Contractors

The relationship between ORGANIZATION and SPONSOR is that of independent contractors. The ORGANIZATION is not in a relationship of joint venture, partnership or employer-employee with SPONSOR. None of the provisions of the Agreement shall be construed to create nor are they intended to create a relationship of partnership, agency, joint venture or employment between ORGANIZATION and SPONSOR.

6. Jurisdiction

This Agreement shall be interpreted and governed by the laws of the State of California.

7. Term and Termination

This Agreement shall be effective upon the execution of this Agreement by both parties, and will end upon completion of the study in accordance with approved protocol. Either party may terminate this Agreement upon thirty (30) days written notice.

8. Notices

Any notice given pursuant to this Agreement will be written and sent to:

(Insert Physician's Name, Practice and address)

The individuals signing this Agreement are authorized to do so and all necessary approvals and authorizations have been made prior to the signing of this Agreement.

Mynosys Cellular Devices, Inc.

_____
Signature

_____
Name

_____
(Date)

Physician's Practice

_____
Signature

_____
Name

_____
(Date)

Appendix 7: Declaration of Helsinki

BASIC PRINCIPLES

1. Biomedical research involving human subjects must conform to generally accepted scientific principles and should be based on adequately performed laboratory and animal experimentation and on a thorough knowledge of the scientific literature.
2. The design and performance of each experimental procedure involving human subjects should be clearly formulated in an experimental protocol, which should be transmitted to a specially appointed independent committee for consideration, comment and guidance.
3. Biomedical research involving human subjects should be conducted only by scientifically qualified persons and under the supervision of a clinically competent medical person. The responsibility for the human subject must always rest with a medically qualified person and never rest on the subject of the research, even though the subject has given his or her consent.
4. Biomedical research involving human subjects cannot legitimately be carried out unless the importance of the objective is in proportion to the inherent risk to the subject.
5. Every biomedical research project involving human subjects should be preceded by careful assessment of predictable risks in comparison with foreseeable benefits to the subject or to others. Concern for the interests of the subject must always prevail over the interests of science and society.
6. The right of the research subject to safeguard his or her integrity must always be respected. Every precaution should be taken to respect the privacy of the subject and to minimize the impact of the study on the subject's physical and mental integrity and on the personality of the subject.
7. Doctors should abstain from engaging in research projects involving human subjects unless they are satisfied that the hazards involved are believed to be predictable. Doctors should cease any investigation if the hazards are found to outweigh the potential benefits.
8. In publications of the results of his or her research, the doctor is obliged to preserve the accuracy of the results. Reports of experimentation not in accordance with the principles laid down in this Declaration should not be accepted for publication.
9. In any research on human beings, each potential subject must be adequately informed of the aims, methods, anticipated benefits and potential hazards of the study and the discomfort it may entail. He or she should be informed that he or she is at liberty to abstain from participation in the study and that he or she is free to withdraw his or her consent to participation at any time. The doctor should then obtain the subject's freely given informed consent, preferably in writing.
10. When obtaining informed consent for a research project the doctor should be particularly cautious if the subject is in a dependent relationship to him or her or may consent under duress. In that case the informed consent should be obtained by a doctor who is not engaged in the investigation and who is completely independent of this official relationship.
11. In case of legal incompetence, informed consent should be obtained from the legal guardian in accordance with national legislation. Where physical or mental incapacity makes it impossible to obtain informed consent, or when the subject is a minor, permission from the responsible relative replaces that of the subject in accordance with national legislation.

12. The research protocol should always contain a statement of the ethical considerations involved and should indicate that the principles enunciated in the present Declaration are complied with.

II. MEDICAL RESEARCH COMBINED WITH PROFESSIONAL CARE (CLINICAL RESEARCH)

1. In the treatment of the sick person, the doctor must be free to use a new diagnostic and therapeutic measure, if in his or her judgment it offers hope of saving life, reestablishing health, or alleviating suffering.
2. The potential benefits, hazards and discomfort of a new method should be weighed against the advantages of the best current diagnostic and therapeutic methods.
3. In any medical study, every subject – including those of a control group, if any – should be assured of the best-proven diagnostic and therapeutic methods.
4. The refusal of the subject to participate in a study must never interfere with the doctor-subject relationship.
5. If the doctor considers it essential not to obtain informed consent, the specific reasons for this proposal should be stated in the experimental protocol for transmission to the independent committee (I.1).
6. The doctor can combine medical research with professional care, the objective being the acquisition of new medical knowledge, only to the extent that medical research is justified by its potential diagnostic or therapeutic value for the patient.

III. NON-THERAPEUTIC BIOMEDICAL RESEARCH INVOLVING HUMAN SUBJECTS (NON-CLINICAL BIOMEDICAL RESEARCH)

1. In the purely scientific application of medical research carried out on a human being, it is the duty of the physician to remain the protector of the life and health of that person on whom biomedical research is being carried out.
2. The subjects should be volunteers – either healthy persons or patients for whom the experimental design is not related to the patient's illnesses.
3. The investigator or the investigating team should discontinue the research if in his/her or their judgment it may, if continued, be harmful to the individual.
4. In research on man, the interest of science and society should never take precedence over considerations related to the well-being of the subject.

Appendix 8: References

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