Peri-vasectomy safety and clinical validation study of the Plan A™ Delivery Lumen Access Device (DLAD)

Protocol CIP100C

Rev A
April 8, 2025

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SIGNATURE PAGE

By signing below, I confirm that I have read and will abide by this protocol, the signed investigator agreement and all applicable regulations.

Principal Investigator's Name (print)	
Principal Investigator's Signature	Date (DD/MMM/YYYY)

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REVISION HISTORY

Version	Effective Date	Justification for Revision
A	4/8/2025	Initial version.

INVESTIGATIONAL PLAN SUMMARY

Title	Peri-vasectomy safety and clinical validation study of the Plan A™ Delivery Lumen Access Device (DLAD)
Protocol No.	CIP100C
Version	Revision A, April 8, 2025
Sponsor	NEXT Life Sciences, Inc.
Device Name	Plan A™ Delivery Lumen Access Device (DLAD)
Study Design	Prospective, multi-center, single-arm, open label, clinical validation trial
Study Objectives	1. Evaluate the safety and performance of DLAD for: a. Entering the lumen of the vas deferens b. Passing a guidewire 5cm into the lumen of the vas deferens c. Insertion of the 2Fr sheath over the guidewire 1cm to 1.5cm into the vas deferens lumen d. Delivery of saline into the vas deferens e. Removal of the DLAD system 2. Obtain physician user feedback
Primary Safety Outcome Measure	Collection of all adverse events, analyzed by seriousness, severity, device relatedness, procedure relatedness and whether anticipated
Primary Product Performance Measures	1. Physician usability 2. Intraluminal access to the vas deferens evaluating each of following*:* - Visual confirmation that the guidewire or the sheath are not outside of the vas deferens - Tactile sensation that the guidewire and sheath were inserted with ease into the vas deferens lumen - Easy flow of saline into the vas deferens lumen - Visual confirmation that saline has not accumulated into the tissues outside of the vas deferens
Additional Analyses	Physician ergonomics
Sample Size	Up to 30 male subjects will be consented, screened and enrolled with a goal to have a minimum of 20 subjects with evaluable data. Study sites in the United States will enroll a maximum of 10 subjects who undergo the procedure within the overall sample size of 30.
Study Duration	An estimated total of up to 3 months for screening, enrollment and follow-up
Follow-up	2-week follow-up for adverse event assessment
Investigational Site Information	This study may be conducted at up to 5 centers. Study sites may be in the United States and/or outside the United States.

TRIAL CONTACTS

Please refer to the current trial contact list provided separately.

1. INTRODUCTION

NEXT Life Sciences is developing the Plan A™ Male Contraceptive System to address the global problem of unintended pregnancies that total 121 million each year according to the State of World Population report (UNFPA, 2022). Globally, an estimated 257 million women who want to avoid pregnancy are not using safe, modern methods of contraception.

The current options for contraception and family planning focus mostly on female fertility, burdening women with a majority of the responsibility for reproductive planning. Male birth control options have traditionally been limited to vasectomy, condoms, and withdrawal. Vasectomy is effective but reversal is expensive and unpredictable. Condoms reduce disease transmission, but their pregnancy protection failure rate in typical use is 13%. The withdrawal method typically has an even higher failure rate.

The development of a non-hormonal, long-lasting, and reversible male birth control option would offer a greater choice of birth control for both individuals and couples when planning their future. The mission of NEXT Life Sciences is to design and develop that new option through Plan A™.

The Plan A™ Male Contraceptive System utilizes a proprietary hydrogel, called Vasalgel®. The Plan A™ Occlusion System includes Vasalgel®, which is intended to occlude the vas deferens, and the Delivery Lumen Access Device (DLAD), which is intended to deliver the Vasalgel® into the vas deferens. Vasalgel® can be characterized as a soft solid implant and is intended to act as a flexible barrier to sperm. The Plan A™ Reversal System is designed to remove Vasalgel® from the vas deferens with the administration of sodium bicarbonate into the vas deferens using the Reversal Lumen Access Device (RLAD) to restore the flow of sperm.

The company is embarking on a series of clinical trials to evaluate the Plan A™ Male Contraceptive System. The clinical development plan includes six studies across two phases.

First Phase - Feasibility studies:

a. Peri-vasectomy safety and clinical validation of the Delivery Lumen Access Device (DLAD) to access the vas deferens

b. Local reaction safety of Vasalgel®

c. Safety and feasibility of the Plan A™ Occlusion System and procedure to occlude the vas deferens

d. Safety and feasibility of the Plan A™ Reversal System and procedure to reverse the occlusion achieved with the Plan A™ Occlusion System

Second Phase - Pivotal trials:

a. Safety and effectiveness evaluation of Plan A™ Male Contraceptive System

b. Safety and effectiveness evaluation of reversing Plan A™ Male Contraception

The study described herein is the first trial within the first phase of feasibility studies. This trial is intended to evaluate the safety and clinical validation of the Delivery Lumen Access Device (DLAD) to achieve intraluminal access to the vas deferens immediately prior to a scheduled vasectomy. Vasalgel® will not be evaluated in this study.

2. INVESTIGATOR BROCHURE

An Investigator Brochure will provide a detailed summary of the prior pre-clinical testing of the Plan A™ Delivery Lumen Access Device.

3. INVESTIGATIONAL DEVICE DESCRIPTION

3.1. DEVICE DESCRIPTION

The complete Plan A™ Male Contraceptive System is comprised of the following:

- Plan A™ Occlusion System:
  - Vasalgel®
  - Delivery Lumen Access Device (DLAD)

- Plan A™ Reversal System:
  - Reversal Lumen Access Device (RLAD)
  - Irrigation tubing to connect to 8.4% USP, sterile for injection sodium bicarbonate solution and aspiration tubing to connect to the aspiration device

The Plan A™ occlusion procedure will require the following commercially available products to be provided by the user: ring clamps, dissecting forceps, gauze, local anesthetic, hypodermic needle and syringe, and closing tape.

The Plan A™ reversal procedure will require the following commercially available products to be provided by the user: ring clamps, dissecting forceps, gauze, local anesthetic, hypodermic needle and syringe, and closing tape, 8.4% USP, sterile for injection sodium bicarbonate solution and aspiration device.

The Delivery Lumen Access Device (DLAD) being evaluated in this study is discussed in more detail below.

Delivery Lumen Access Device (DLAD)

The Delivery Lumen Access Device (DLAD) is intended to deliver Vasalgel® into the vas deferens to block the flow of sperm. In this study, the DLAD will be used to deliver saline into the vas deferens. The single-use, sterile DLAD is comprised of a 2Fr Sheath Assembly, a 0.014" Guidewire Assembly, and a Handle Assembly. These components are shown below in Figures 1 and 2. Two DLAD devices, one for each vas deferens, are required for the procedure.

Figure 1. DLAD Sheath Assembly with Preloaded Guidewire Assembly

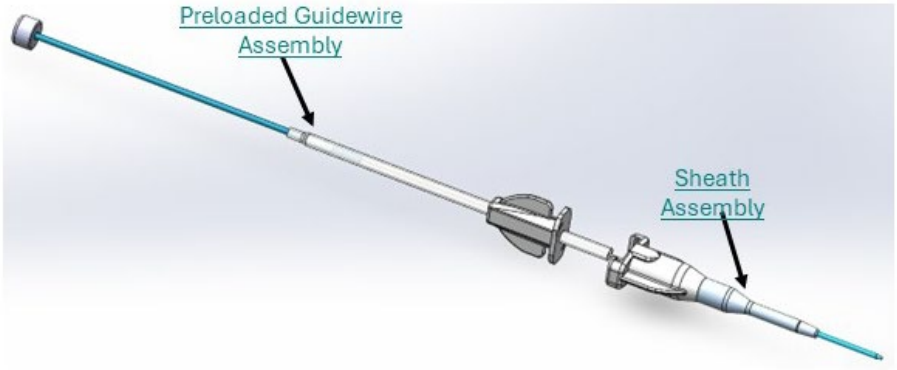
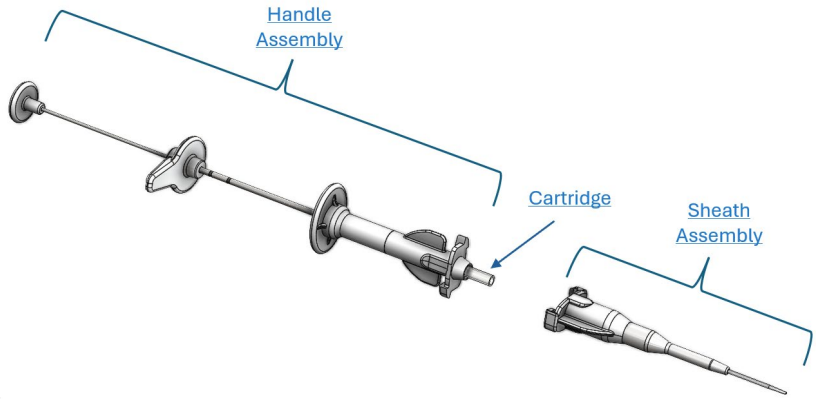


Figure 2. DLAD Sheath Assembly Cartridge and Handle Assembly



Vasalgel® will not be delivered or evaluated in this study.

3.2. DEVICE MODEL NUMBER

The current device model number is provided in Table 1.

Table 1. Device Model Number

Note: Model numbers may change during the course of the study according to the company's Quality System process.

Description	Code / Model Number
Plan A™ Delivery Lumen Access Device	DLAD 1000
Accessory Items (provided by the institution)	
Use of DLAD for this study will require the following commercially available products to be provided by the user: ring clamps, dissecting forceps, gauze, local anesthetic, hypodermic needle and syringe, closing tape, and sterile saline.	

3.3. INDICATIONS FOR USE

DLAD is a component of the Plan A^{TM} Male Contraceptive System that is being developed to support the following future commercial Indications for Use:

> The Plan A^{TM} Male Contraceptive System is intended for men age 18 or over who desire a long-acting, reversible contraceptive method by occlusion of the vas deferens.

The DLAD is intended to deliver Vasalgel® into the vas deferens to block the flow of sperm. In this study, the device will be used to deliver 5.1 ml of sterile saline into the vas deferens immediately prior to a scheduled vasectomy. Vasalgel® will not be delivered or evaluated in the clinical study.

3.4. TRAINING AND EXPERIENCE

Investigators must have sufficient experience in performing no scalpel vasectomy procedures within males seeking permanent sterilization and experience in performing vas deferens luminal access procedures such as a vasogram or mucosal cautery during vasectomy.

Prior to using the investigational DLAD, Investigators must:

- Undergo device use training conducted by NEXT personnel or designee;
- Ensure adjunct personnel are also familiar with the training materials prior to use of the DLAD.

4. STUDY PROTOCOL

4.1. OBJECTIVES AND HYPOTHESIS

4.1.1 OBJECTIVES

- Evaluate the performance of DLAD for:

- Entering the lumen of the vas deferens
- Passing a guidewire 5cm into the lumen of the vas deferens
- Insertion of the 2Fr sheath over the guidewire 1cm to 1.5cm into the vas deferens lumen
- Delivery of 5.1 ml of sterile saline into the vas deferens
- Removal of the DLAD system

o Obtain physician user feedback

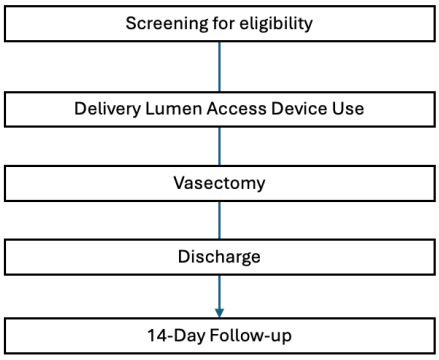
4.1.2 HYPOTHESIS

There is no formal hypothesis testing as this is a feasibility study.

4.2. STUDY DESIGN

This study is a prospective, multicenter, single-arm, open label, clinical validation trial. A graphic of the study design is presented below in Figure 3.

Figure 3. Study Design



4.3. MEASURES TAKEN TO MINIMIZE OR AVOID BIAS

Bias will be minimized in this study by utilizing objective eligibility criteria.

4.4. STUDY SAMPLE SIZE

Up to 30 male subjects may be consented, screened and enrolled with a goal to have a minimum of 20 evaluable subjects. A study site in Australia will enroll a maximum of 10 subjects who undergo the procedure within the overall sample size of 30.

4.5. STUDY DURATION

Study duration is an estimated total of up to three (3) months for screening, enrollment and follow-up.

4.6. PRIMARY SAFETY OUTCOME MEASURE

The primary safety outcome measure will be collection of all adverse events analyzed by seriousness, severity, device relatedness, procedure relatedness and whether anticipated.

4.7. PRIMARY PRODUCT PERFORMANCE MEASURES

The primary product performance measures are:

- Physician usability
- Intraluminal access to the vas deferens evaluating each of the following*:*
  - Visual confirmation that the guidewire or the sheath are not outside of the vas deferens
  - Tactile sensation that the guidewire and sheath were inserted with ease into the vas deferens lumen
  - Easy flow of saline into the vas deferens lumen
  - Visual confirmation that saline has not accumulated into the tissues outside of the vas deferens

4.8. ADDITIONAL DATA ANALYSES

Planned additional analyses include the following:

- Physician ergonomics

4.9. STUDY POPULATION

The study population will include male subjects who have already planned to undergo a vasectomy. Subjects must provide written informed consent and meet the study entry criteria noted below.

4.10. INCLUSION/EXCLUSION CRITERIA

4.10.1 INCLUSION CRITERIA

A subject must meet **all** the following criteria to participate in this study:

1. Male subject who has already planned to undergo a vasectomy
2. Male subject who has voluntarily signed and dated the Institutional Review Board (IRB)/Ethics Committee (EC) approved informed consent form (ICF) for this study prior to initiation of any screening or study specific procedures
3. 18 to 65 years of age at the time of consent
4. Good health for undergoing a vasectomy as confirmed by medical history and physical examination
5. In the opinion of the Investigator, subject is suitable to undergo a vasectomy as a form of long-term contraception

4.10.2 EXCLUSION CRITERIA

A subject will be excluded from participating in the study if **any** of the following conditions apply:

1. On exam, has any of the following: one or both vasa not present, abnormal scrotum, large varicocele, hydrocele, filariasis or elephantiasis of scrotum, or intrascrotal mass that would make the subject not suitable for the study
2. Prior testicular surgery, testicular injury or prior vasectomy with vasovasostomy (vasectomy reversal)

3. Has local genital infections such as balanitis, scrotal skin infection, epididymitis, or orchitis, or tender (inflamed) tip of the penis, but may be enrolled after resolution of an acute infection
4. History of prostatitis or benign prostatic hypertrophy requiring treatment
5. Has known current coagulopathy or other bleeding disorders
6. Known allergy to DLAD materials, including nickel, stainless steel and silicone
7. Has cystic fibrosis
8. Has history of inguinal hernia repair
9. Subject belongs to a vulnerable population. Vulnerable subject populations are defined as individuals who are incarcerated, handicapped, have cognitive challenges, mental disability, persons in nursing homes, children, impoverished persons, homeless persons, economically or educationally disadvantaged persons, nomads, refugees and those permanently incapable of giving informed consent. Vulnerable populations also may include members of a group with a hierarchical structure such as university students, subordinate hospital and laboratory personnel, employees of the sponsor, members of the armed forces and persons kept in detention.
10. Currently participating in another study involving an investigational device or drug within the last 30 days prior to the first screening
11. Any site staff member with delegated study responsibilities or a family member of a site staff member with delegated study responsibilities
12. In the opinion of the Investigator, there are issues or concerns that may compromise the safety of the subject or confound the reliability of compliance and information acquired in this study
13. Has any condition that, in the opinion of the Investigator, would interfere with evaluation of DLAD product performance or interpretation of patient safety or study results

4.11. SUBJECT PRE-SCREENING

4.11.1 RECRUITMENT

Various forms of advertising may be deployed to recruit potential candidates for the study. Men responding to the advertising may be directed to a study website, to an investigational site, be sent an informational email, or accept to be contacted by a research nurse to learn more about the study and continue with an initial screening process. Men may also be informed about the study by their medical doctor at the time of a pre-vasectomy consultation.

4.11.2 INITIAL SCREEN

Potential study candidates will answer select inclusion/exclusion questions. The study website or investigational site will inform the candidate if he is not eligible to continue with the screening process.

Recruitment and initial screening will be managed directly by site coordinators at centers where there is no advertising or a study website.

4.12. SUBJECT SCREENING

The Investigator or designee will perform an initial evaluation of the patient by reviewing the inclusion and exclusion criteria to determine study eligibility. Study-specific evaluations may only be performed following informed consent. A sample informed consent form is provided under a separate cover.

4.13. INFORMED CONSENT

Prior to the initiation of any study-specific procedures, the Investigator or his/her authorized designee will conduct the informed consent process with each subject as outlined in section 10.4.

4.14. ENROLLMENT

A subject is considered enrolled after providing written informed consent and passing all required screening tests.

4.15. TREATMENT

A subject will be considered treated if the DLAD is inserted into at least one vas deferens, regardless of whether the procedure can be completed.

4.16. SUBJECT WITHDRAWAL

A study subject may be discontinued for the following reasons:

- Subject Withdrawal: Withdrawal in a clinical trial is voluntary and the subject may choose to discontinue at any time and for any reason without penalty or loss of benefits.
- Investigator Termination: The Investigator may terminate the subject without regard to his consent if the Investigator believes it is medically necessary. In the event of termination by the Investigator, reason for termination will be documented.
- Sponsor Termination: The Sponsor may terminate the site or study, and therefore subject participation based on section 4.17 of this clinical investigational plan.

4.17. STUDY/SITE SUSPENSION OR EARLY TERMINATION

The study can be discontinued at the discretion of the study Sponsor for reasons including, but not limited to, the following:

- Occurrence of adverse events unknown to date in respect to their nature, severity, or duration, or the unexpected incidence of known adverse events;
- Insufficient recruitment of subjects;
- Unanticipated adverse device effect (UADE) presenting an unreasonable risk to subjects;

- Persistent non-compliance with the protocol;
- Persistent non-compliance with IRB/EC or regulatory requirements; or
- Business reasons.

If the study is discontinued or suspended prematurely, the Sponsor will promptly inform the clinical Investigator/investigational center of the termination or suspension and the reason(s) for the termination or suspension. The IRB/EC will also be informed promptly and provided with the reason(s) for the termination or suspension by the Sponsor or by the clinical Investigator/investigation center.

5. STUDY PROCEDURES

5.1. STUDY SCHEDULE OF ASSESSMENTS

The study schedule of assessments is provided in Table 2.

Table 2. Study Schedule of Assessments

Assessments	**Screening** Within 30 days prior to procedure	**DLAD Use Procedure**	**14-Day** +/-3 days	*Unscheduled Visit*
Visit Type	Clinic or phone	Clinic	Phone*	Clinic
Study Informed Consent	X**	X		
Demographics	X			
Medical History	X			
Physical Exam	X***			
Delivery Lumen Access Device (DLAD) Use****		X		
Physician Usability and Ergonomics Questionnaire		X		
Adverse Event Evaluation		X	X	*X*
Concomitant Medication Review	X	X	X	*X*
Vasectomy		X		

** 14- day visit may be conducted in clinic if deemed necessary by the Investigator.*
*** If screening is done by phone, the patient will be sent the consent form by e-mail and he will sign it on the day of the intervention.*
**** If screening is done by phone, the physical exam will be done on the day of the intervention.*
***** A total of 5.1ml of saline will be delivered into the vas deferens (100ul followed by 5ml).*

5.2. BASELINE EVALUATIONS

5.2.1 EVALUATIONS

The following baseline evaluations must be completed within 30 days prior to DLAD use to verify eligibility per the inclusion and exclusion criteria.

- Medical history
- Physical exam
- Concomitant Medication
- Demographics

5.3. DELIVERY LUMEN ACCESS DEVICE (DLAD) USE

Within 30 days after all screening is completed, subjects will undergo DLAD use immediately prior to their planned vasectomy.

5.3.1 PREPARATION

Subjects will be prepared for DLAD use per standard of care guidelines for conducting a vasectomy.

5.3.2 ACTIVE INFECTION EVALUATION

At the time of DLAD use, subjects exhibiting signs of active, local infection will be excluded from the study or delayed from the procedure. Readmittance to the study will only occur when all signs of infection are clear in the judgment of the Investigator.

5.3.3 SUBJECT ANESTHESIA AND SETTING OF CARE

The method and amount of anesthesia will be left to the discretion of the Investigator. The procedure may be performed in an office setting, ambulatory surgery center or in an operating room. All procedure settings must be fully equipped to respond in case of an emergency.

5.3.4 DLAD PROCEDURE

Please refer to the DLAD Directions For Use (DFU) for details on how to conduct the DLAD procedure.

5.3.5 VASECTOMY

Directly following DLAD use, vasectomy will be performed according to standard of care.

5.3.6 POST-PROCEDURE

Subjects will undergo post-procedure monitoring and recovery per standard of care for a vasectomy procedure.

An assessment will be made for any procedure-related or device-related adverse events prior to discharge.

5.3.7 PHYSICIAN USABILITY AND ERGONOMICS

The Investigator who used the DLAD will complete a usability and ergonomics questionnaire to provide feedback about device use.

5.4 INVESTIGATIONAL PRODUCT DISPOSITION

Disposition of all investigational product must be documented using the Device Accountability logs provided. See section 10.11 for additional guidance regarding device accountability.

5.5 FOLLOW-UP ASSESSMENTS

5.5.1 14-DAY FOLLOW-UP (+/-3 days)

Subjects will be contacted by phone 14 days (+/- 3 days) following DLAD use to evaluate the following:

- Adverse events
- Change in medications

The visit may be conducted in clinic if deemed necessary by the Investigator.

5.5.2 UNSCHEDULED VISIT

At the Investigator's discretion, a subject may be asked to return to the clinic for an unscheduled visit to assess an adverse event. This information will be recorded on the adverse event Case Report Form. Any associated changes to concomitant medications will also be recorded.

5.6 TERMINATION

The Subject Disposition case report form will be completed following the 14-day follow-up visit, or whenever study participation has been terminated. Subjects will be instructed to return to their managing physician for routine care.

If a subject does not complete the required follow-up, but has not officially withdrawn consent, then all reasonable efforts should be made by the site personnel to locate and communicate with the subject. A minimum of three (3) attempts to contact the participant, preferably using different modes of communication (phone, email, letter) must be recorded before documenting the subject as lost to follow-up.

5.7 PROTOCOL DEVIATIONS

Except in the event of a medical emergency or where it is necessary to protect the safety, rights or welfare of the study subject, any changes to the protocol will require written approval of NEXT Life Sciences or designee and IRB/EC and government health authority, if applicable. Deviations from the Clinical Investigational Plan to protect the health and safety of the subject will be reported to the IRB/EC and government health authority as required by applicable regulations.

All deviations from the protocol should be recorded on the electronic case report forms (eCRFs). A deviation may be identified by the Investigator, NEXT Life Sciences, or the monitoring staff. Investigators will be asked to provide an explanation for the deviation. NEXT Life Sciences, or designee, will be responsible for analyzing deviations and will implement corrective actions as necessary.

6 ADVERSE EVENTS

6.1 DEFINITIONS

Adverse Events (AE), per ISO 14155:
Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including abnormal laboratory findings) in subjects, whether or not related to the medical device. For users or other persons, this definition is restricted to events related to investigational medical devices.

Adverse Device Effect (ADE), per ISO 14155:
Adverse event related to the use of an investigational medical device. This definition includes any event resulting from insufficient or inadequate deployment, implantation, installation or operation or any malfunction of the investigational device.

Serious Adverse Events (including subject death) (SAE), per ISO 14155:

The investigator must decide whether an event meets the definition of a 'serious' adverse event (SAE), which is an event that:

a) led to a death,
b) led to a serious deterioration in the health of the subject that either resulted in:
    1) a life-threatening illness or injury, or
    2) a permanent impairment of a body structure or a body function, or
    3) in-patient or prolonged hospitalization, or
    4) medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function.
c) led to fetal distress, fetal death or a congenital abnormality or birth defect.

NOTE 1: This includes device deficiencies that might have led to a serious adverse event if: a) suitable action had not been taken; or b) intervention had not been made; or c) if circumstances had been less fortunate. These are handled under the SAE reporting system.

NOTE 2: A planned hospitalization for pre-existing condition, or a procedure required by the Clinical Investigational Plan, without a serious deterioration in health, is not considered to be a serious adverse event.

Serious Adverse Device Effect (SADE), per ISO 14155:

Any adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event or that might have led to any of these consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less fortunate.

Unanticipated Adverse Device Effect (UADE) per 21 CFR 812.150:

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.

Severity Grading

The Investigator will use the following Common Terminology Criteria for Adverse Events (CTCAE) definitions to grade the severity of each adverse event:

Table 3. Adverse Event Severity

Severity Grade	Description
Grade 1 Mild	Asymptomatic or mild symptoms; clinical or diagnostic observations only; intervention not indicated.
Grade 2 Moderate	Minimal, local or noninvasive intervention indicated; limiting age-appropriate instrumental ADL*.

Severity Grade	Description
Grade 3 Severe	Medically significant but not immediately life-threatening; hospitalization or prolongation of hospitalization indicated; disabling; limiting self-care ADL**.
Grade 4 Life Threatening Consequences	Urgent intervention indicated.
Grade 5 Death	Death related to AE

Activities of Daily Living (ADL)

**Instrumental ADL refer to preparing meals, shopping for groceries or clothes, using the telephone, managing money, etc.*

***Self-care ADL refer to bathing, dressing and undressing, feeding self, using the toilet, taking medications, and not bedridden.*

Adverse Event Relationship:

The relationship of the adverse event to the Investigational device will be assessed according to the following definitions.

Table 4. Adverse Event Device Relationship

Relationship	Description
Not Related	• Not associated with device application • Due to an underlying or concurrent illness
Unlikely	• Little or no temporal relationship to the study device **and/or** • A more likely etiology exists
Probable	• Temporal sequence is relevant **or** • Event abates upon device application completion/removal **or** • Event cannot be reasonably explained by the patient's condition
Definitely Related	• Has a reasonable temporal relationship to device application **and** • Could not readily have been produced by the patient's clinical state or have been due to environmental or other interventions **and** • Follows a known pattern of response to intervention

The relationship of the adverse event to the procedure will be assessed according to the following definitions.

Table 5. Adverse Event Procedure Relationship

Relationship	Description
Not Related	• Not associated with procedure • Due to an underlying or concurrent illness
Unlikely	• Little or no temporal relationship to procedure **and/or** • A more likely etiology exists
Probable	• Temporal sequence is relevant **or** • Event abates upon procedure completion **or** • Event cannot be reasonably explained by the patient's condition
Definitely Related	• Has a reasonable temporal relationship to procedure **and** • Could not readily have been produced by the patient's clinical state or have been due to environmental or other interventions **and** • Follows a known pattern of response to intervention

6.2 ADVERSE EVENT REPORTING

Adverse event reporting will be performed in accordance with the applicable regulations and the requirements of the reviewing IRB/EC.

All adverse events following the subject's consent for study participation will be recorded in the subject's medical records and eCRFs whether or not the AE is considered related to the investigational device. All adverse events should be followed until they are adequately resolved or not expected to change. Adverse events will be recorded on the eCRF by the Investigator or his/her designee. However, it is the responsibility of the Investigator to ensure that all information is correct and appropriately documented.

A list of adverse events that may result from the procedure can be found in the Risk and Benefit section of this protocol (section 7).

The Investigator will submit to the Sponsor a report of any Serious Adverse Event (SAE), Serious Adverse Device Effect (SADE), Adverse Device Effect (ADE), or Unanticipated Adverse Device (UADE) occurring during an investigation according to the following schedule:

Table 6. Adverse Event Reporting Schedule

Type of Report	Submission Schedule
Adverse Device Effect (ADE)	Report within 7 calendar days
Patient Death	Report within 2 calendar days
Unanticipated Adverse Device Effect (UADE)	Report within 2 calendar days
Serious Adverse Event (SAE) / Serious Adverse Device Effect (SADE)	Report within 2 calendar days

The Investigator will report adverse events to the reviewing IRB/EC (as applicable) according to the applicable reporting requirements.

The Sponsor is responsible for informing the relevant regulatory authorities and other investigators, according to applicable regulations, of any device or procedure-related SAE and/or UADE that has occurred.

6.3 MEDICAL MONITOR REVIEW OF ADVERSE EVENTS

Adverse events will be reviewed regularly by the Sponsor's Medical Monitor and Clinical Advisors as required.

6.4 DEVICE DEFICIENCIES

A device deficiency is defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, usability, safety or performance.

Note 1: Device deficiencies include malfunctions, use errors, and inadequacy in the information supplied by the manufacturer, including labelling.

Note 2: This definition includes device deficiencies related to the investigational medical device.

Should a device failure occur, it is essential that the device is returned to the study Sponsor for assessment of the device and the nature of the failure.

6.5 DEVICE MALFUNCTION

A device malfunction is defined as failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or Clinical Investigation Plan or Investigator Brochure.

6.6 USE ERROR

Use error is defined as user action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user.

Note 1: Use error includes the inability of the user to complete a task.

Note 2: Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment.

Note 3: Users might be aware or unaware that a use error has occurred.

Note 4: An unexpected physiological response of the patient is not by itself considered a use error.

Note 5: A malfunction of a medical device that causes an unexpected result is not considered a use error.

7 RISK AND BENEFITS

7.1 POTENTIAL RISKS

The risks of undergoing a vasectomy will be discussed with the subject by the Investigator and are separate from the intent of this study. The potential risks to subjects participating in the clinical investigation are similar to those for a vasectomy and include the following:

- Bleeding or a blood clot (hematoma) inside the scrotum
- Blood in the semen
- Bruising of the scrotum
- Infection

- Mild pain or discomfort
- Swelling
- Allergic reaction
- Inflammation caused by leaking sperm (granuloma)
- An abnormal cyst (spermatocele) that develops in the small, coiled tube located on the upper testicle that collects and transports sperm (epididymis)
- A fluid-filled sac (hydrocele) surrounding a testicle that causes swelling in the scrotum

The DLAD could also result in the following:

- Injury to the vas deferens
- Nerve damage
- Device fracture or dislodgment in the subject

Infusion of saline into the lumen of the vas deferens in the direction of the bladder neck and urethra may result in the sensation of the urge to urinate. Leakage of a small volume of saline out of the lumen of the vas deferens is expected to occur when vasectomy is performed following the DLAD procedure. The leakage of saline is not expected to pose any additional risks to subjects as saline is widely used in medical procedures. In the event of incorrect sheath placement, there is a risk that the 5.1 ml of saline may be delivered to non-target tissues/spaces, including the wall of the vas deferens, fascia, or other scrotal tissues. This may result in temporary swelling, localized edema, and pain, though the saline is likely to drain out once the vas is cut for the vasectomy. The risk of misplacement is very low due to risk mitigation steps including the device warning not to advance the DLAD guidewire against resistance. When injecting the 5cc of saline, the physician is advised to inject saline slowly and stop if resistance is felt while depressing the 5cc syringe plunger.

There may also be risks that are unanticipated at this time.

7.2 MINIMIZATION OF ANTICIPATED RISKS

Potential risks that may be associated with use of the DLAD have been minimized in this study by the following:

a. Establishing eligibility criteria that exclude patients who are at higher risk for experiencing an anticipated adverse event;

b. Conducting preclinical testing prior to the start of this trial;

c. Conducting a risk analysis and incorporating mitigations to eliminate and/or reduce risks to as low as reasonably practical (ALARP) in accordance with ISO 14971-Medical Devices – Application of risk analysis to medical devices.

d. Providing detailed device labeling to help ensure proper device usage;

e. Selecting investigators with proper level of training and experience;

f. Ensuring physicians and staff receive adequate training;

g. Closely monitoring subjects during the procedure;

h. Ensuring adequate monitoring is performed to identify any safety issues associated with the study procedure and subjects;

i. Regularly reviewing reported adverse events throughout the study and taking appropriate medical measures to resolve the adverse events.

Further, to minimize the risk of anticipated adverse events, clinical study participation of an individual subject will be stopped if any of the following events are observed that could be an early signal of a possible safety event:

- Inability to complete the intraluminal access confirmation;
- Inability to deploy the DLAD;
- Any condition that may impair the planned vasectomy of the study subject.

7.3 POTENTIAL RISKS TO SUBJECT CONFIDENTIALITY

In all clinical studies, confidentiality of protected health information may be breached due to study-related activities beyond those of routine clinical care. This risk will be minimized by not collecting personally identifying information on Case Report Forms (CRFs) or other study related documentation and tests to be provided to the study Sponsor, as well as by obscuring subject protected health information (PHI). PHI will be replaced by a unique study number as per section 10.5 of this clinical investigational plan.

7.4 POTENTIAL BENEFITS

There is no direct benefit to study subjects. The Subject's participation in this research may add knowledge to the field of male contraception.

8 STATISTICAL METHODOLOGY AND ANALYSIS

All data collected for all enrolled subjects, referred to in ICH E9 (Statistical Principles for Clinical Trials) as the "full analysis set," will be included in primary analyses of study outcomes.

Continuous variables will be summarized with standard statistics including the mean, standard deviation, median and range or interquartile range. Categorical variables will be summarized using frequency tables and cross-tabulations.

For events that can occur more than once in a single subject, such as adverse events (AEs), the percentage will be based on the number of subjects experiencing the event; both subject and event counts will be reported. Listings of all adverse events will be provided along with summary tables.

Data will be collected, tabulated and reported on all outcomes specified in this document as well as on baseline subject demographics, medical history, and other relevant characteristics.

As the objective of this investigation is to evaluate DLAD product performance to inform elements of subsequent studies, sample size is not driven by formal evaluations of power against predefined success criteria and no formal statistical hypothesis testing will be used to evaluate such criteria.

Statistical analyses will be performed in SAS version 9.4 or higher (SAS Institute, Cary, NC, USA) or R version 4.2 or higher (R Foundation for Statistical Computing, Vienna, Austria) or another validated statistical analysis package.

9 DATA MONITORING AND QUALITY CONTROL

All information and data concerning subjects or their participation in this study will be considered confidential. Only authorized personnel will have access to this confidential information. All data used in the analysis and reporting of this evaluation will be without identifiable reference to the subject.

9.1 CASE REPORT FORMS (CRF)

Electronic case report forms (eCRFs) specifically created for this study will be used to collect all subject data during the trial. The Investigator or her/his designee is responsible for providing all data for the trial into the study eCRFs. All appropriate sections of the eCRFs must be completed. This data should be entered within 5 business days of assessment.

The Investigator must review and sign the eCRFs. The Investigator is responsible for the accuracy and completeness of all data on the eCRFs.

Sponsor personnel or designee will review completed eCRFs at the investigational site at regular intervals throughout the trial. Information on the eCRFs will be compared to information originally recorded on source documents related to the trial (*i.e.,* professional notes, laboratory reports, etc.). Information on the eCRF must match the same information on the source documents or an electronic data query will be issued.

The Sponsor will use the study data for statistical and tracking purposes and will treat the information as confidential.

9.2 DATA COLLECTION

All required data for this trial will be collected on eCRFs.

Qualified trial staff at the investigational site will perform primary data collection drawn from source document (*e.g.,* medical/hospital chart) review. The Sponsor monitors and/or designees will perform clinical trial monitoring of 100% of the subjects that pass screening

evaluations and undergo the DLAD procedure. This monitoring will include review of eCRF data with verification to the source documentation.

All eCRFs will be reviewed for completeness, validity, and consistency. Queries will be generated and resolved with the sites and all protocol deviations will be recorded on the eCRF.

9.3 MONITORING OF CLINICAL SITES AND INVESTIGATORS

If the Sponsor determines that an Investigator is not in compliance with any requirements outlined in this investigational plan or the investigator agreement, the Sponsor shall promptly secure compliance or discontinue shipment of the investigational device.

In addition, assessments including overall compliance with the investigational plan, accurate eCRFs, and compliance with Good Clinical Practices (GCP), IRB/ECs and applicable regulatory requirements will be monitored on an ongoing basis by the Sponsor and/or its designees.

Periodic monitoring visits will be made at the investigational site throughout the clinical trial to ensure that the Investigator obligations are fulfilled, and all applicable regulations and guidelines are being followed. These visits will ensure that the facilities are still acceptable, the investigational plan is being followed, the IRB/EC and applicable authorities have been notified of approved investigational plan changes as required, complete records are being maintained, appropriate and timely reports have been made to the Sponsor and/or its designees and the IRB/EC, device and device inventory are controlled and the Investigator is carrying out all agreed upon activities. The Sponsor will reserve the right to remove either the Investigator or the investigational site from the trial for noncompliance with the investigational plan or regulations.

10 STUDY MANAGEMENT AND RESPONSIBILITIES

10.1 SPONSOR RESPONSIBILITIES

The Sponsor has the overall responsibility for the conduct of the study according to Good Clinical Practice Guidelines and all applicable regulatory requirements. For this study, the Sponsor will have certain direct responsibilities and may delegate other responsibilities to appropriate consultants and contract research organizations (CROs). Together, the Sponsor, consultants and CROs will ensure that the study is conducted according to applicable regulations. All personnel participating in the conduct of this clinical trial will be qualified by education and/or experience to perform their tasks.

Specifically, the Sponsor has the overall responsibility of the study and will ensure the following activities are conducted:

a) Select qualified monitors, investigators and contract research personnel

b) Provide the Investigational Plan and any subsequent amendments to the study site

c) Provide appropriate information and device training to Investigators and study site staff

d) Ensure that all deviations from the Investigational Plan are reviewed with the appropriate Investigator(s) and reported in the eCRF and the final report; also ensure that any necessary preventative or corrective action is taken

e) Ensure that all adverse events and all adverse device effects are reported and reviewed with the Investigator(s), and where appropriate, that all serious adverse events and all serious adverse device effects and unanticipated adverse device effects are reported to the relevant authorities and IRB/EC

f) Promptly inform the Investigators and, where applicable, any regulatory authorities and IRB/EC, if the study is prematurely terminated or suspended and the reason for the termination or suspension

g) Ensure proper device usage, uniform data collection and protocol compliance

h) Provide protocol initiation training to include review of the investigational device instructions for use, the protocol, eCRF instructions, and guidelines for obtaining informed consent

i) Provide the study device and all necessary components to the study center, in quantities to support study activities

j) Coordinate ongoing communication with CRO(s), consultants and the study center to resolve any problems concerning the protocol or data collection. Every effort will be made to ensure compliance with the protocol

k) Retain ownership of all clinical data generated in this study, and control the use of the data for purposes of regulatory submissions

l) Protect subject confidentiality

m) Collect, store and keep secure the following documents:

- A current, signed and dated Curriculum Vitae of each Investigator
- A copy of the current licensure of the Investigator
- A signed and dated copy of the Investigator Agreement
- A signed financial disclosure statement
- The IRB/EC opinion and / or approval, in writing, and relevant correspondence
- Correspondence with authorities (as required)
- Appropriate insurance certificates (as necessary)
- IRB/EC and regulatory authority approved informed consent form
- Records of any adverse events and adverse device effects
- Annual, Interim and Final report(s), as applicable

10.2 INVESTIGATOR RESPONSIBILITIES

The Investigator is responsible for ensuring that the clinical study is conducted according to the Investigator Agreement, Investigational Plan, all conditions of national regulatory requirements, the IRB/EC, and in accordance with the highest standards of medical and good clinical practice (GCP), and the Declaration of Helsinki.

The Investigator(s) shall be responsible for the day-to-day conduct of the investigation as well as for the safety and well-being of the human subjects involved in the clinical investigation. The Investigator(s) shall:

a) Have the resources to conduct the investigation properly

b) Obtain from the Sponsor the information which the Investigator(s) judges essential about the device and be familiar with this information

c) Be well acquainted with the protocol before signing it

d) Support the monitor, auditor, if applicable, in their activities to verify compliance with the protocol, to perform source data verification and to correct the eCRFs where inconsistencies or missing values are identified

e) Discuss with the Sponsor management any question or proposed modification of the protocol

f) Make sure that the protocol is followed by all responsible for the conduct of the study at his/her institution. Any deviation shall be documented and reported to the study Sponsor.

g) Make the necessary arrangements to ensure the proper conduct and completion of the investigation

h) Make the necessary arrangements for emergency treatment, as needed, to protect the health and welfare of the subject

i) Ensure that appropriate IRB/EC approvals are obtained prior to the start of the investigation

j) Provide the communication from the IRB/EC to the study sponsor

k) Inform the IRB/EC about any serious adverse device effects in accordance with the IRB/EC requirements.

l) Inform the Sponsor about any adverse events and adverse device effects in a timely manner and in accordance with the timelines laid out in this protocol

m) Endeavor to ensure an adequate recruitment of subjects

n) Ensure that the subject has adequate time and information to give informed consent

o) Ensure that informed consent is obtained and documented prior to any study specific evaluations or procedures being performed

p) Ensure that clinical records are clearly marked to indicate that the subject is enrolled in this study

q) Provide subjects with well-defined procedures for any emergency and safeguard the subject's interest

r) Ensure that information which becomes available as a result of the clinical investigation which may be of importance to the health of a subject and the continuation of the investigation shall be made known to: 1) the Sponsor; 2) the subject; and 3) the subject's personal clinician (with the subject's approval), if pertinent to the safety or well-being of the subject

s) Inform the subject and/or the subject's physician (with the subject's approval) about any premature termination or suspension of the investigation with a rationale for study termination

t) Have primary responsibility for the accuracy, legibility and security of all investigational data, documents and subject records both during and after the investigation

u) Sign each subject's eCRFs

v) Be responsible for the supervision and assignment of duties at his/her study center

w) Ensure that all investigational devices are accounted for (number of devices used, discarded and returned to the Sponsor)

x) Disclose to the Sponsor sufficient accurate financial information to allow the Investigator to submit complete and accurate certification or disclosure statements, and update the information during the course of the investigation and for one year following the completion of the study

y) Ensure that the Investigator discloses to the Sponsor if the Investigator has ever been associated with terminated research and the reason for such termination is provided

z) Ensure that the Investigator discloses to the Sponsor if the Investigator has ever been barred from conducting or participating in clinical research

10.3 ETHICAL CONSIDERATIONS

The rights, safety and well-being of clinical investigational subjects shall be protected consistent with the ethical principles specified in the Declaration of Helsinki and local and national regulations. This shall be understood, observed and applied at every step in this clinical investigation.

It is expected that all parties will share the responsibility for ethical conduct in accordance with their respective roles in the investigation. The Sponsor and the Investigator(s) shall avoid improper influence or inducement of the subject, monitor, the clinical Investigator(s) or other parties participating in or contributing to the clinical investigation.

10.4 INFORMED CONSENT

All patients must provide written informed consent in accordance with applicable law and approved by the site's IRB/EC and regulatory authority. Each investigational site must provide the Sponsor or designee with a copy of the investigational site's IRB/EC approval letter and the IRB/EC approved informed consent form as well as the corresponding approvals from the regulatory authority. The Sponsor or designee must review and approve the IRB/EC approved informed consent form prior to any subject enrollment. Each subject must sign their own IRB/EC approved and Sponsor approved informed consent form.

The person obtaining the informed consent shall:

- Avoid any coercion of, or undue influence of, subjects to participate
- Not waive or appear to waive subject's legal rights
- Provide complete, detailed description of study events, procedures, follow up and costs/reimbursements using language that is non-technical and understandable to the subject
- Ensure that the patient understands risks and responsibilities
- Provide ample time for the subject to consider participation, answer any questions and ensure that satisfactory answers are provided
- Include dated signatures of the subject and of the clinical investigator (as applicable)
- Shall ensure that applicable requirements are met for witness signatures
- Ensure that the patient understands the voluntary nature of participation
- Ensure protection of the subject's confidentiality
- Provide a copy of the Consent Form signed by the subject and the person presenting the information for the subject to take home

The process that leads to informed consent will be documented.

10.5 SUBJECT CONFIDENTIALITY

At all times throughout this study, all parties shall strictly observe the confidentiality of each subject's health information. All data shall be secured against unauthorized access. Each subject participating in this study will be assigned a unique identifier. All eCRFs will be tracked, evaluated, and stored using only this unique identifier.

The Investigator will maintain a confidential study subject list identifying all enrolled subjects. This list will contain the assigned study subject's unique identifier and name. The Investigator bears responsibility for keeping this list confidential. This list will not be provided to the study Sponsor and is only to be used at the study center.

Monitors and auditors will have access to the study subject list and other personally identifying information of study subjects to ensure that data reported in the eCRFs

corresponds to the person who signed the consent form, and the information contained in the original source documents. Such personal identifying information may include, but not limited to, the subject's name, address, date of birth, gender, race and medical record number.

Any source documents copied for monitoring purposes by the Sponsor or designee will be identified by using the assigned subject's unique identifier and obscuring personal identifying data to protect subject confidentiality.

10.6 SELECTION AND TRAINING OF CLINICAL SITES AND INVESTIGATORS

The primary requirements of selecting an Investigator for this study are: experience and adequate training, facilities and equipment, adequate patient volume, appropriate personnel and site research staff to support the conduct of the trial, and commitment to safety and adherence to the investigational plan.

Throughout the conduct of the trial, the Sponsor and/or its designees will closely monitor each site for the following:

- Compliance with the investigational plan
- Meeting enrollment commitments
- Accurate and timely submission of eCRFs and additional data
- Compliance with ICH Good Clinical Practice (GCP) guidelines
- Compliance with IRB/EC and applicable regulatory requirements

10.7 SITE QUALIFICATION

The Sponsor or its designee, prior to acceptance of the site into this study, will conduct a site qualification visit or phone contact. The site qualification visit/contact will be scheduled to include time with the Principal Investigator, co-investigators, study coordinator, and other study personnel as available. Areas of discussion include a review of personnel training, expertise, and prior government -regulated study experience, this study's specific requirements for procedures and equipment, and a review of staffing and equipment availability and appropriateness.

10.8 PRE-STUDY TRAINING

On-site pre-study training of involved trial personnel is the responsibility of the Sponsor or its designee. To ensure investigational plan and regulatory compliance and accurate data collection, site training will include a detailed review of this Clinical Investigational Plan, eCRF completion, monitoring logistics and regulatory requirements.

Prior to study implementation, the Study Monitor will ensure that study personnel:

- Have appropriate training, facilities, time, and willingness to comply fully with the study requirements.

- Submit this Investigational Plan to the IRB/EC for appropriate review and obtain written approval for the conduct of the study prior to the initiation of any subject enrollment into this study.
- Maintain all study correspondence, this Investigational Plan, training documentation, and all related and required records on file at their facility.
- Assume full responsibility for the study investigation at their individual medical practices, clinics, and medical facilities. The Study Monitor will create a written report of the pre-study site visit. Resolution of any concerns and/or completion of any appropriate study activities identified during the pre-study visit will be documented by the Study Monitor, discussed with the Sponsor and submitted to the Investigator.
- Complete any training required by the IRB/EC regarding protection of human subjects.

10.9 RECORD RETENTION

All trial records and reports will remain on file for a minimum of two (2) years (or longer if applicable law or hospital administration requires) after the latter of the following two dates: completion date of trial closure or the date that records are no longer required for purposes of supporting a marketing authorization for regulatory agencies. Trial records should only be discarded upon written notification by the Sponsor. All records and reports are subject to inspection at any time.

10.10 MAINTAINING RECORDS

The Sponsor and/or its designees will maintain copies of correspondence, data, shipment of devices, adverse device effects and other records related to the clinical trial. The Sponsor will maintain records related to the signed Investigator agreements.

10.11 DEVICE ACCOUNTABILITY

The Sponsor, or designee, shall ship investigational devices only to qualified Investigators. The Investigator shall maintain adequate records of the receipt and disposition of all investigational devices. The Investigator shall return any unused devices, opened or unopened, to the Sponsor or its designees when the trial has completed. If there is a device deficiency, malfunction or device-related adverse event that requires investigation, used devices must be returned to the Sponsor.

10.12 TRIAL CLOSEOUT

Upon completion of the clinical trial (when all subjects enrolled have completed the last required visit and the eCRFs and queries have been completed), the Sponsor and/or its designees will notify all investigational sites of closeout. All eCRFs, unused trial devices, and any unused trial materials and equipment will be collected and returned to the Sponsor and/or its designees.

10.13 AUDITS AND INSPECTIONS

The Investigator will permit access to original medical records and provide all requested information if the Sponsor and/or its designees or national/international regulatory authorities initiate any audits or inspections. In the case that it is a non-Sponsor initiated audit, the Investigator must contact the Sponsor as soon as possible after notification of intent to audit.

10.14 PUBLICATION POLICY AND FINAL REPORT

Prior to enrollment of the first subject, this study will be listed on ClinicalTrials.gov in accordance with the requirements of the International Committee of Medical Journal Editors (ICMJE).

All information concerning this study that has not been previously published is considered the confidential property solely of NEXT Life Sciences Inc. This information includes, but is not limited to, the protocol, workbooks, technical methodology, and resulting data. This information shall not be disclosed to others without prior written consent from NEXT Life Sciences, Inc. and shall not be used except in the performance of this study.

To allow for the use of the information derived from this study and to ensure compliance with current Federal Regulations (USA) and all applicable local regulations abroad, the Investigator is obliged to provide NEXT Life Sciences, Inc. with complete test results and all data developed from this study.

A final report will be completed even if the study is prematurely terminated. At the conclusion of the study, a multi-center abstract reporting the results will be prepared and may be presented at a medical association meeting(s). A multi-center publication may also be prepared for publication in a reputable scientific journal. The publication of results from any single center experience within the trial is not allowed until the aggregate study results have been published, unless there is written consent from the study Sponsor.

NEXT Life Sciences, Inc. will have final approval authority on the proposed content of the multi-center study manuscripts submitted for publication.