Spinal Singularity

Evaluation of the Safety and Clinical Performance of the Gen 2 Connected Catheter – Wireless Urinary Prosthesis for Management of chronic Urinary Retention

Short Title: FREEDOM Study

Protocol Number: CIP-0002 (formerly ES-NIH-01) - Revision 03

Date: September 2020

Investigation Device:
Gen 2 Connected Catheter System and Accessories

ClinicalTrials.gov ID:
NCT04059159

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Sponsored By:
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This study will be conducted in compliance with the clinical investigation protocol and applicable regulatory requirements.

CONFIDENTIAL INFORMATION

Evaluation of the Safety and Clinical Performance of the Gen 2 Connected Catheter – Wireless Urinary Prosthesis for Management of chronic Urinary Retention

FREEDOM Study

Protocol Signature Page

CIP-0002 (formerly ES-NIH-01), Revision 03

September, 2020

The Principal Investigator (PI) and Spinal Singularity, Inc. (Sponsor) hereby agree to conduct this clinical study in accordance with the study design and specific provisions of this clinical investigation protocol (CIP). Further the Principal Investigator and the Sponsor agree to conduct this clinical study in accordance with applicable US FDA CFRs, EN ISO 14155:2011, other applicable regulatory requirements and applicable legal requirements. The recording and reporting of Serious Adverse Events (SAEs) must be followed according to the SAE Handling Plan provided within this CIP.

With signatures below, the following persons below confirm their acceptance of the content of this CIP and agree to adhere to the requirements. The PI will provide copies of this CIP and all pertinent information to the study personnel under their supervision and their site or the central Independent Ethics Committee/Institutional Review Board (IEC/IRB). The PI will discuss this material with them and ensure they are fully informed regarding the conduct of the study according to this CIP, applicable regulatory requirements, and site or central IEC/IRB requirements.

With signatures below, I agree to and understand the material presented in this CIP and will not publicly disclose in any manner the design, results, or conclusions of this clinical investigation without prior written consent of Spinal Singularity, Inc.

_____

Clinical Site Name

_____ _____

Site Principal Investigator (Signature) Date

_____

Site Principal Investigator (Printed Name)

_____ _____

Sponsor (Signature) Date

_____

Sponsor (Printed Name)

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1 PROTOCOL SYNOPSIS

Study Title	Evaluation of the Safety and Clinical Performance of the Gen 2 Connected Catheter – Wireless Urinary Prosthesis for Management of chronic Urinary Retention
Short Title	FREEDOM Study
Study Sponsor	Spinal Singularity, Inc. (San Clemente, California, USA)
Protocol Number	CIP-0002 (formerly ES-NIH-01)
Study Objective	The objective of this study is to evaluate the safety and essential performance of the Gen 2 Connected Catheter in males with chronic Urinary Retention, both in a clinical setting and an extended period of home use. This is a non-significant risk (NSR) study.
Study Design	Multi-center, single-arm NSR study.
Estimated Study Duration	12 months
Investigational Device	Gen 2 Connected Catheter System and Accessories
Proposed Indications for Use	The Gen 2 Connected Catheter is a replaceable urinary prosthesis that is intended for use in male patients (subjects) 18 years of age or older who have impaired bladder emptying due to chronic Urinary Retention, and who are capable of operating the device in accordance with the provided instructions for use, or who have trained caregivers capable of doing the same. The device must be replaced every 7 days (or less).
Number of Subjects	The number of subjects to be enrolled in the study (ITT) as defined by EN ISO 14155; is 36 subjects. Of these, it is expected only 24 of the subjects will be found to meet the basic eligibility criteria to be tested for device tolerability screening. Assuming a 33% dropout after the device tolerability screening, the final number of evaluable subjects required is a minimum of 16 subjects.
Duration of Study and Follow-up	The study will be divided into 3 phases after the Eligibility Screening. Each subject will be in the study for a total of 7 weeks. 1. Device Tolerability Screening – up to one week of Gen 2 Connected Catheter use 2. Test – 4 weeks of Gen 2 Connected Catheter use 3. Follow-up – Phone screen for AE for 2 weeks During each phase, there will be weekly appointments to evaluate the subjects and device performance.

Study Population	Adult males with chronic Urinary Retention
Study Sites	Up to 4 sites in the USA
Inclusion Criteria	1. Males ≥ 18 diagnosed with chronic Urinary Retention 2. Must be clinically suitable and capable of safely managing bladder using an intermittent voiding or indwelling strategy a. Must have stable urinary management history as determined by the Investigator OR: b. Must have urodynamic profile suitable for the Gen 2 Connected Catheter (including bladder capacity ≥ 200mL without uninhibited bladder contractions) 3. Subject's lower urinary tract anatomy must fall within the ranges serviceable by the Gen 2 Connected Catheter device, as specified in the Investigational Device Instructions For Use.
Exclusion Criteria	1. Active symptomatic urinary tract infection, as defined in this clinical investigation protocol (*subjects may receive the device after UTI has been treated*) 2. Significant risk profile or recent history of urethral stricture (e.g. stricture within past 90 days) 3. Significant risk profile or recent history of clinically significant (uncontrolled) autonomic dysreflexia 4. Significant intermittent urinary incontinence (between catheterizations) 5. Uninhibited bladder contractions and/or Vesicoureteral reflux that is not reliably controlled with medication or alternate therapy (e.g. Botox injection) 6. Pre-existing urinary pathologies and/or morphological abnormalities of the lower urinary tract or bladder (assessed during in-depth medical screening, including cystoscopy and urine analysis) a. Urinary tract inflammation or neoplasm b. Urinary fistula c. Bladder diverticulum (outpouching) > 5cm in size d. Chronic pyelonephritis (secondary to upper urinary tract infection(s) within past 6 months) e. Impaired kidney function or renal failure f. Active gross hematuria g. Active urethritis

	h. Bladder stones 7. Dependence on an electro-magnetic medical implant (e.g. cardiac pacemaker or implanted drug pump) or external device 8. Any unsuitable comorbidities as determined by the Investigator or complications related to use of certain medications 9. Any physical or cognitive impairments that diminish the subject's ability to follow directions or otherwise safely use the Gen 2 Connected Catheter System 10. Catheter Assessment Tool screening yields unacceptable results
Primary Efficacy Endpoint	**Primary efficacy**: Post-void residual urine volume (PVR) with the use of the Connected Catheter A subject is considered a responder to the treatment if a minimum of 80% of their PVR values met the following criteria PVR is ≤ 50 mL OR PVR is ≤ baseline PVR with the standard of care catheter If a subject drops out before the conclusion of the study after passing the Device Tolerability Screening, their PVR data will still be included in the primary analysis.
Primary Safety Endpoint	Rate of device related SAE
Secondary End Points	1. Successful device insertion, anchoring, and removal 2. Successful sealing of the catheter valve 3. Quality of life improvement as measured by SCI-QOL Survey 4. UTI occurrence rate 5. Lower Urinary Tract injury rate
Study and Data Management	Spinal Singularity, Inc. 105 Avenida De La Estrella, Suite 3 San Clemente, CA 92672, USA Tel: +1 (949) 436-7974 Fax: + 1 (949) 607-3175
Study Safety Monitor	Dr. Jaime Landman, MD, Professor of Urology and Radiology Chairman, Department of Urology

	University of California, Irvine

2 LIST OF ABBREVIATIONS

Abbreviation	Definition
AE	Adverse Event
AD	Autonomic Dysreflexia
ASIA	American Spinal Injury Association
BPH	Benign Prostatic Hyperplasia
CAT	Catheter Assessment Tool
CAUTI	Catheter Associated Urinary Tract Infection
CIC	Clean Intermittent Catheterization
CFU	Colony Forming Units
CRA	Clinical Research Associate
eCRF	Electronic Case Report Form
EC	Ethics Committee
EDC	Electronic Data Capture
FDA	Food & Drug Administration
HAI	Healthcare Acquired Infection
IC	Informed Consent
ICF	Informed Consent Form
IR	Insertion / Removal
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
ITT	Intent to Treat Population
LUT	Lower Urinary Tract
NIDRR	National Institute of Disability and Rehabilitation Research
PVR	Post-Void Residual Volume
SAE	Serious Adverse Event
SADE	Serious Adverse Device Event
SCI	Spinal Cord Injury
SCI-QOL	Spinal Cord Injury Quality of Life
UADE	Unanticipated Adverse Device Effect
USADE	Unanticipated Serious Adverse Effect
UTI	Urinary Tract Infection

3 INTRODUCTION AND BACKGROUND

3.1 Chronic Urinary Retention

Urinary retention is a condition in which an individual is unable to fully empty their bladder from urine. While urinary retention is not a disease, it can be a symptom of many other health issues in both males and females. Urinary retention presents itself in both acute and chronic cases. Acute Urinary Retention is sudden and can be extremely painful.

Chronic Urinary Retention develops over time and is the persistent inability to completely empty the bladder resulting in elevated post-void residual (PVR) volumes. Chronic Urinary Retention generally occurs over a long period and is typically not painful. The causes of chronic Urinary Retention can be categorized as obstructive, infectious/inflammatory, neurologic, pharmacologic, or other. Table 3-1 gives examples of these categories.

Table 3-1: Examples of Causes of Chronic Urinary Retention

Category	Examples
Obstructive[1]	Benign prostatic hyperplasia (BPH) Meatal stenosis Paraphimosis Penile constricting bands Phimosis Prostate cancer Urethral stricture
Infectious or Inflammatory[1]	Guilliain-Barre syndrome Balanitis Prostatic abscess Prostatitis Herpes simplex virus
Neurological[1]	Spinal cord injury Intervertebral disk disease Spinal stenos Spinal bifida occulta Stroke Multiple sclerosis

Category	Examples
	Diabetes mellitus
Pharmacological[1-3]	Anticholinergics Tricyclic antidepressants Anti-psychotics Antispasmodics Antihistamines, NSAIDs Muscle relaxants Opioid analgesics Amphetamines
Other	Trauma Post-operative complications Psychogenic conditions

Common methods to manage Chronic Urinary Retention from a physiological standpoint include medication and catheterization. In some cases, surgical intervention may be required, but are invasive and are only used as a last resort. Medications such as alpha-blockers have been effective in both males and females, but have many possible side effects such as:

- Dizziness
- Fainting
- Headaches
- Lightheadedness
- Low blood pressure
- Rash or itchiness of the skin
- Nausea
- Swollen legs or ankles.
- Tiredness, weakness or feeling lethargic.
- Sleep disturbance.
- Tremor.
- In some cases, erectile dysfunction in males

Because of these side effects, catheterization is often used as an alternative to manage chronic Urinary Retention . Both intermittent catheterization and the use of indwelling catheter are valid treatment options, although indwelling catheters are typically only used when long-term care is needed. With both methods of catheterization there is risk of urethral injury and UTI with the rate of occurrence for UTI being higher with the use of indwelling catheters. Indwelling urinary catheters also require the subject to have a drainage bag with them to collect the urine which can negatively affect the subject's quality of life. Traditional indwelling catheters are typically fixated within the bladder with an inflatable balloon. If the balloon bursts it cause bladder injury and the catheter will migrate or fall out of the patient completely. Additionally, the catheter often extends outside of the body which interferes with sexual activity.

The Gen 2 Connected Catheter aims to bring an improved experience for patient's requiring catheterization. The Gen 2 Connected Catheter does not need to be replaced as often as catheters used for intermittent catheterization but does not remain in place as long as typical indwelling urinary catheters. It also provides increased convenience over indwelling urinary catheters as the device does not protrude outside of the body, allowing for sexual activity, and does not require the subjects to carry a drainage bag. It also does not have a balloon as it uses two anchoring features located in the urethra and the bladder. The Gen 2 Controller allows the subjects to control voiding. Additionally, the increased frequency of replacement versus indwelling catheters may decrease the occurrence of UTI in the subjects versus traditional indwelling catheters that may be left in the body for up to 29 days.

4 INVESTIGATIONAL DEVICE DESCRIPTION

To address the many drawbacks of current standard-of care urinary catheters, Spinal Singularity, Inc. has developed the Gen 2 Connected Catheter System and Accessories. The Gen 2 Connected Catheter System consists of the Gen 2 Connected Catheter (hereafter referred to as the Connected Catheter), the Gen 2 Insertion / Removal Tool (hereafter referred to as the IR Tool) and the Gen 2 Controller (hereafter referred to as the Controller). The Gen 2 Catheter Assessment Tool (hereafter referred to as the CAT) is an optional accessory for clinicians to support initial and continued determination of whether the Connected Catheter may be an option for a suitable potential patient. The Connected Catheter (Figure 4-1) is a fully internal, indwelling urinary prosthesis designed for improved bladder management in males with urinary retention disorders requiring catheterization. The Connected Catheter is a sterile, disposable, extended-use device that resides fully internally to the male lower urinary tract (urethra + bladder neck) for an intended use life of up to 7 days per Connected Catheter.

In contrast to indwelling Foley and clean intermittent catheters, the Connected Catheter enables both natural bladder filling and convenient, voluntary voiding by the user, without the need for external drainage apparatus or frequent self-catheterization. Instead, the user initiates voiding by placing a wireless hand-held Controller near the magnetic valve in the base of the penis. When activated, the Controller will open the valve and actively pump urine from the bladder, then seal once voiding is complete. The Connected Catheter is retained in place by using varying diameters to provide anchoring at different locations in the urethra. The Connected Catheter is designed to be easily inserted and removed either by a clinician, caregiver, or the user himself, using a sterile, single-use, IR Tool.

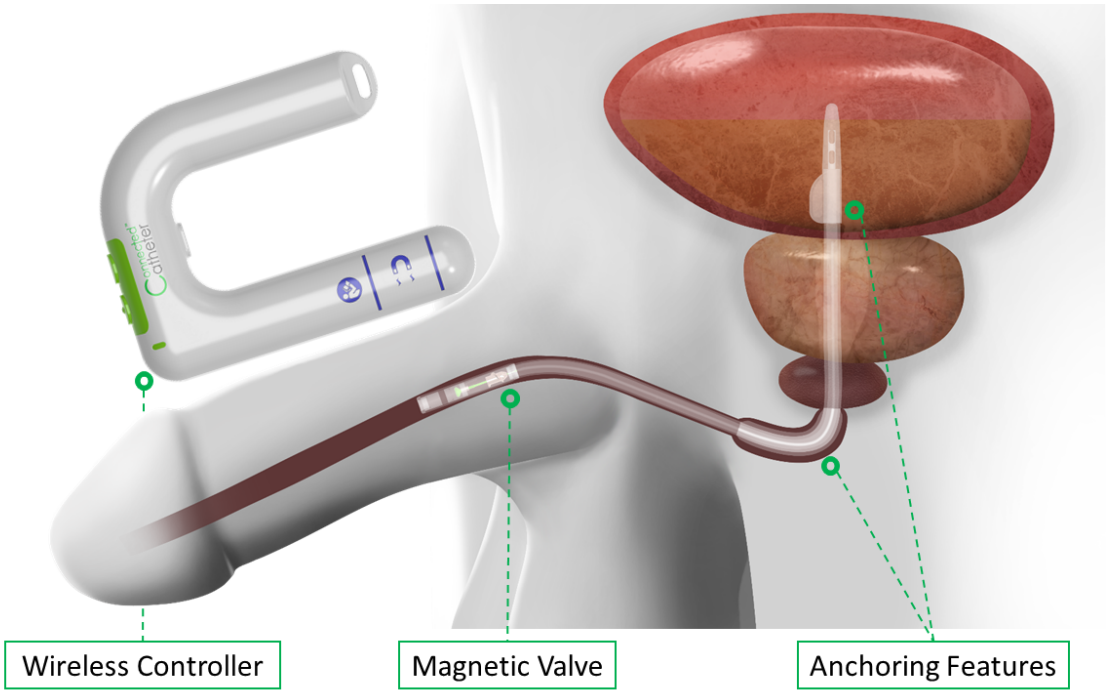

Figure 4-1: Overview of System

The Gen 2 Connected Catheter System and Accessories are manufactured by Spinal Singularity, Inc. Each device (Connected Catheter, IR Tool, Controller and CAT) are manufactured and labeled in accordance with Spinal Singularity Inc.'s Quality Management System procedures. These procedures are in compliance with applicable FDA regulations and in conformance with ISO standards for Device Traceability and Identification. In doing so, Spinal Singularity, Inc. and Research Staff will maintain full traceability of every investigational device throughout the duration of the study using lot numbers and serial numbers. Accountability of all investigational devices will be maintained by the clinical research staff and Spinal Singularity, Inc. will also track serial numbers of each investigational device utilized in the study.

All portions of the Gen 2 Connected Catheter System and Accessories will contact the subject's body in some fashion for a period of time. To maintain subject's safety, thorough testing of each device has been conducted to ensure appropriate levels of electrical safety, biocompatibility and

sterility. Although the requirements for each device are different, test results have shown that the product meets applicable FDA regulations and ISO standards.

4.1 Principles of Operation

The basic principle of the Connected Catheter is to allow the subject to void their bladder using a wireless Controller and a magnetic valve. A summary of the treatment is provided below only as an overview. The IFU should always be followed and if different from this section, the IFU should be followed.

1. Using the IR tool and lubrication, the Connected Catheter is inserted in the urethra. The valve (end of the Catheter) should be positioned near the scrotum before the IR tool is removed.
2. To urinate, locate the valve by feeling with a hand. Position the Controller near the valve – the end of the valve should align with the blue line on the Controller.
3. Press and hold the button on the Controller for 3 seconds to open the valve and urinate. The Controller should be kept in line with the valve as much as possible.
4. When the bladder has been emptied, re-align the Controller with the valve and press the button on the Controller and move the Controller towards the tip of the penis. This will close the valve.
5. Empty the receptacle if necessary.

5 PROPOSED INTENDED USE

The Gen 2 Connected Catheter is a replaceable urinary prosthesis that is intended for use in male patients (subjects) 18 years of age or older who have impaired bladder emptying due to chronic Urinary Retention, and who are capable of operating the device in accordance with the provided instructions for use, or who have trained caregivers capable of doing the same. The device must be replaced every 7 days (or less).

The Gen 2 Connected Catheter System is intended for use by prescription only.

6 STUDY RATIONALE

The FREEDOM study is designed to show that the Connected Catheter is able to effectively drain the bladder and the patient to control voiding function. Measurement of post void residual (PVR) volume will be a key performance parameter in this study. The study is designed to show that the subject's PVR volume with the Connected Catheter is similar to using standard catheter (CIC or indwelling Foley-type catheters) without compromising the safety of the subjects. We expect an improvement in the subject's quality of life with the Connected Catheter once he is used to having the Connected Catheter inside the anterior urethra.

The Connected Catheter does not need to be replaced as often as catheters used for intermittent catheterization, but does not remain in place as long as typical indwelling urinary catheters. It also

provides increased convenience over indwelling urinary catheters as the device does not protrude outside of the body, allowing for sexual activity, and does not require the subjects to carry a drainage bag. It uses two anchoring features, one located in the bulbar urethra and one in the bladder. The Controller allows the subjects to control their voiding while using normal restroom facilities. Additionally, the increased frequency of replacement versus indwelling catheters may decrease the occurrence of UTI in the subjects versus traditional indwelling catheters that may be left in the body for up to 29 days.

7 RISK-BENEFIT ANALYSIS

7.1 Risk Analysis

Complications and risks that exist for other indwelling urinary catheters may also exist for the Connected Catheter. Section 11.9 contains an extensive list of possible adverse events. The major risks and symptoms are described below.

Table 7-1: Major Risks for the Connected Catheter

Risk	Description
Urinary Tract Infection (UTI)	UTI is defined in this protocol as bacteriuria $\geq 10^5$ CFU per mL, plus at least one NIDRR consensus-defined symptom. If infection is suspected, appropriate diagnostic and therapeutic measures should be taken.
Asymptomatic Bacteriuria	The presence of bacteria in the properly collected urine of a patient that has no signs or symptoms of a urinary tract infection.
Bladder Spasms	When the bladder muscle squeezes suddenly without warning, causing an urgent need to release urine. The spasm can force urine from the bladder, causing leakage.
Dysuria	Pain experienced while urinating. Dysuria can be caused by UTI, inflammation of the LUT, sexually transmitted diseases, and more. The operation of the device should not cause pain while voiding. If this occurs, a clinician should evaluate the subject to determine the likely cause and follow the standard of care. If necessary, the device may be removed.
Genitourinary pain	Initial discomfort may occur when first using the device. Pain should be properly evaluated by a clinician and the cause(s) identified. Genitourinary pain can have many causes unrelated to the device itself ranging from enlarged prostate to fibromyalgia to infection. The proper standard of care should be followed once the cause(s) are identified.

Risk	Description
Hematuria	Blood in the urine may be caused by LUT injury, UTI, kidney or bladder stones, enlarged prostate, the device itself (from insertion, removal, migration, improper sizing), and more. During initial use of the device minor hematuria may be observed. If it continues or worsens, then follow the standard of care to diagnose and alleviate the symptom.
Stricture	Hardening of the tissue. May be caused by frequent catheter use and/or false passage.
Urethral Trauma	False passage may be associated with improper and/or frequent catheter use.
Urinary Incontinence	Leaking may occur through or around the catheter if the bladder spasms, or the catheter valve is not closed properly.
Urinary retention	If patient is unable to empty the bladder, then Urinary Retention may occur.
Discomfort	Discomfort is often associated with frequent catheterization.

These complications may occur at any time during (or shortly following) Connected Catheter insertion, usage, or removal, and may require additional medical treatment. All the above medical complications can be easily treated by the standard of care. Each of the above risks is comparable or lower with the Connected Catheter compared to intermittent catheterization in terms of likelihood and severity. In addition to the above risks, there may be other risks that are unforeseen at this time.

7.2 Risk Mitigation

Spinal Singularity, Inc. is committed to minimizing the risks to human research subjects in all of its clinical studies, and has taken measures to minimize risk, including the following:

The Gen 2 Connected Catheter System and Accessories have been designed and developed according to Spinal Singularity Inc.'s Product Development Process (PDP), which is utilized in conjunction with a rigorous standard operating procedure (SOP) for Risk Management (including risk mitigation). This Risk Management SOP is based on the industry best-practice standards detailed by EN ISO 14971:2012 ("Application of Risk Management to Medical Devices"). Spinal Singularity, Inc. also maintains detailed procedures (SOPs and DOPs) for Risk Evaluation, Design Controls, and Control of Quality Records.

Pre-clinical performance testing of the Gen 2 Connected Catheter System: the essential functions of the Gen 2 Connected Catheter System (insertion, voiding, sealing, and removal) has been thoroughly tested in a series of design verification and validation tests. Connected Catheter product will not be released by Spinal Singularity, Inc. for investigational clinical use until the Gen 2

Connected Catheter System has passed a defined set of performance and acceptance criteria required for clinical product.

The subject eligibility criteria for participation in this study have been carefully defined to ensure their medical suitability and minimize the risk of complications.

This clinical investigation protocol specifies that the initial insertion and Clinic Assessment of the Gen 2 Connected Catheter System will be performed in a clinical setting, with subjects under direct supervision, where the Connected Catheter device can be immediately removed and any necessary medical care can be administered in the case of any acute medical complications (device-related or otherwise).

This protocol involves close subject monitoring and evaluation at consecutive stages of Connected Catheter performance assessment, with subjects allowed to progress to the Test Phase of the study only if they exhibit good Connected Catheter tolerability and demonstrate the ability to effectively use the Gen 2 Connected Catheter System as trained.

As part of their training to use the Gen 2 Connected Catheter System, subjects will be trained to remove the Connected Catheter using the IR Tool and will be provided with an IR Tool to keep available at all times throughout the Test Phase, in the event that the Connected Catheter must be removed at any time.

During the Test Phase of the Study, subjects will maintain the phone number of the clinic should any adverse events arise. Staff will provide any necessary medical or device-related guidance.

All Study Investigators will be thoroughly trained in this clinical investigation protocol, including the Gen 2 Connected Catheter System and Accessories Clinician Instructions for Use (IFU) and procedural elements of the study.

7.3 Potential Benefits

The potential benefits to future patients suffering from chronic Urinary Retention are listed below. For study subjects, similar benefit may be experienced albeit temporary only during the study until the device is commercially available. However, the potential longer-term benefit to the patients suffering with chronic Urinary Retention outweigh the risks of participation in this study.

The benefits when using the Connected Catheter may include, but are not limited to, the following:

1. Improvement in the comfort and/or convenience of urinary management while using the Gen 2 Connected Catheter System.
2. Improvement in quality of life related to urinary function and overall social confidence.
3. Reduction in the risk of urinary tract infection, genitourinary injury, and other medical complications associated with the use of standard urinary catheters.
4. A collection bag is not required while using the Connected Catheter.

8 CLINICAL STUDY DESIGN

The FREEDOM Study is a prospective, open, single-arm, non-significant risk (NSR) study to be performed in the United States with consecutive enrollment to evaluate the safety and efficacy of the Connected Catheter System in treating subjects with chronic Urinary Retention. All patients

that sign an informed consent form are considered to be part of the intended-to-treat (ITT) population.

The study will be broken up into 4 phases – Eligibility screening, Device Tolerability screening, Connected Catheter use, and Follow-Up. Figure 8-1 shows an overview of the study with the estimated sample size enrolled and treated.

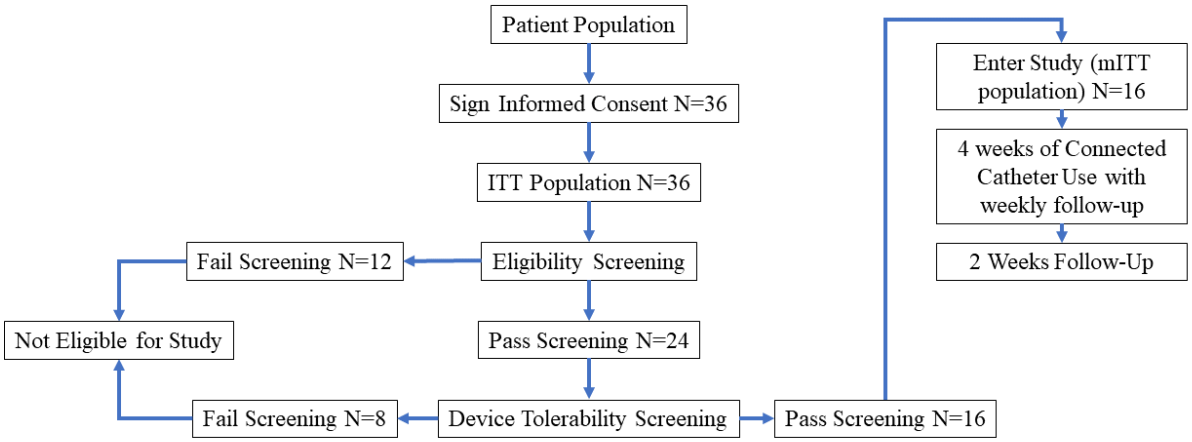

Figure 8-1: Study and Subject Flowchart

8.1 Study Objective

The objective of this study is to evaluate the safety and essential performance of the Connected Catheter in males with chronic Urinary Retention, both in an acute clinical setting and an extended period of home use.

8.2 Screening Phase

The Screening Phase is divided into two phases – Standard Eligibility and Device Tolerability phases. During Standard Eligibility screening, subjects will be evaluated according to the inclusion and exclusion criteria listed in this clinical investigation protocol including assessment of their urinary status using their standard of care management system. Additionally, the subjects will be assessed as outlined in Section 9.2.

Subjects that pass the eligibility screening will enter a 7-day trial period (Device Tolerability Screening) in which they will use the Connected Catheter. They will be taught how to insert and remove the Connected Catheter as well as how to operate the device. Any subject that is unable to demonstrate proficiency in the operation of the device will not continue to the Test Phase of the study. During this time, subjects that use the Connected Catheter will be assessed for any pain or discomfort while using the device. Subjects that are unable or unwilling to complete the days of device use will not continue to the Test Phase of the study.

8.3 Test Phase

During this period, the subjects will use the Connected Catheter to manage their chronic Urinary Retention. The subjects will remove the device themselves under supervision of a trained clinician. A new Connected Catheter will be inserted by the subjects under the supervision of a

trained clinician. There will be weekly follow-ups during this period to complete assessments as outlined in Table 9-2.

8.4 Follow-Up Phase

This phase is 2 weeks long, and the subjects will return to using their previous method to manage their chronic Urinary Retention. There will be weekly phone calls during this period to screen for any signs or symptoms of Adverse Events as outlined in Table 9-2.

8.5 Primary Endpoints

8.5.1 Primary Efficacy

During each follow-up, and during the initial device insertion and evaluation, the Post-Void Residual (PVR) urine volume will be measured via ultrasound.

A subject will be considered a responder to the device if at least 80% of the subject's available PVR values are:

a. Less than 50 mL OR
b. Equal or less than baseline PVR with the standard urinary management system

If a subject drops out before the conclusion of the study after passing the Device Tolerability Screening, their PVR data will still be included in the primary analysis.

8.5.2 Primary Safety

Any adverse events and serious adverse events related to the use of the investigational device will be analyzed with descriptive statistics and nominal 95% confidence interval. There will be no formal statistical hypothesis test for primary safety.

8.6 Secondary Endpoints

The following secondary endpoints will provide additional characterization of the Connected Catheter in the treatment of chronic Urinary Retention and to support potential labeling claims.

1. Successful device insertion, anchoring, and removal
2. Successful sealing of the Connected Catheter valve
3. Quality of life improvement as measured by SCI-QOL Survey and other surveys
4. UTI occurrence rate
5. Lower Urinary Tract injury rate

These endpoints will be analyzed with descriptive statistics and nominal 95% confidence interval.

8.7 Subject Selection

Only subjects who meet all inclusion criteria and no exclusion criteria, agree to comply with the follow-up visit schedule and provide informed consent will be eligible to be treated and participate in the study. If a subject moves away during the study, every effort should be made to maintain

the follow-up schedule including having an appropriate physician follow the subject.

8.7.1 Inclusion Criteria

1. Males ≥ 18 years old diagnosed with chronic Urinary Retention
2. Must be clinically suitable and capable of safely managing bladder using an intermittent voiding or indwelling strategy
3. Must have stable urinary management history as determined by the Investigator

   OR:
4. Must have urodynamic profile suitable for the Connected Catheter (including bladder capacity ≥ 200mL without uninhibited bladder contractions)
5. Subject's lower urinary tract anatomy must fall within the ranges serviceable by the Connected Catheter device, as specified in the Investigational Device Instructions For Use.

8.7.2 Exclusion Criteria

1. Active symptomatic urinary tract infection, as defined in this protocol (*subjects may receive the device after UTI has been treated*)
2. Significant risk profile or recent history of urethral stricture (e.g. stricture within past 90 days)
3. Significant risk profile or recent history of clinically significant (uncontrolled) autonomic dysreflexia
4. Significant intermittent urinary incontinence (between catheterizations)
5. Uninhibited bladder contractions and/or Vesicoureteral reflux that is not reliably controlled with medication or alternate therapy (e.g. Botox injection)
6. Pre-existing urinary pathologies and/or morphological abnormalities of the lower urinary tract or bladder (assessed during in-depth medical screening, including cystoscopy and urine analysis)
7. Urinary tract inflammation or neoplasm
8. Urinary fistula
9. Bladder diverticulum (outpouching) > 5cm in size
10. Chronic pyelonephritis (secondary to upper urinary tract infection(s) within past 6 months)
11. Impaired kidney function or renal failure
12. Active gross hematuria
13. Active urethritis
14. Bladder stones
15. Dependence on an electronic medical implant (e.g. cardiac pacemaker or implanted drug pump) or external device

16. Any unsuitable comorbidities as determined by the Investigator or complications related to use of certain medications
17. Any physical or cognitive impairments that diminish the subject's ability to follow directions or otherwise safely use the Connected Catheter System
18. Catheter Assessment Tool screening yields unacceptable results

8.8 Number of Sites and Sample Size

Up to 4 sites in the United States are planned for this study.

The number of subjects to be enrolled in the study (ITT) as defined by EN ISO 14155; is 36 subjects. Of these, it is expected only 24 of the subjects will be found to meet the basic eligibility criteria to be tested for device tolerability screening.

Assuming a 33% dropout after the device tolerability screening, the final number of evaluable subjects required is a minimum of 16 subjects (See 10.1).

8.9 Study Duration

Each subject will enter the study for 6 weeks after passing the Device Tolerability Screening. The study duration to complete enrollment, monitor and collect the data is anticipated to be 12 months.

8.10 Site and Physician Selection

Sites will be selected based on the availability of the subject pool to be included in the study and the sites' ability to perform the research in compliance with FDA regulations and guidelines and applicable international standards and regulations.

The sites and physicians are required to comply with FDA regulations and guidelines and applicable international standards and regulations (the definition of subject enrollment is per this clinical investigation protocol). In addition, the sites must be able to comply requirements specified by the central institutional review boards (IRB) or ethics committees (EC) and / or the sites respective IRB or EC.

Physicians selected must have experience in performing cystoscopies and treating Urinary Retention and other urological conditions for adult males. Selected physicians will be trained in the use of the Gen 2 Connected Catheter System and Accessories prior to enrolling subjects. The principal investigator will ensure that only trained sub-investigators who satisfy the physician selection criteria can perform any part of the study interventional procedure.

Healthcare professionals or site staff that assist or perform the follow-up evaluations do not need to be trained on the use of the Gen 2 Connected Catheter System and Accessories, but must be delegated and trained to perform the follow-up visit procedures.

9 STUDY PROCEDURE

Throughout the study, any urinary or other health issues potentially related to use, and requiring medical attention, will be treated according to Standard of Care. Table 9-2 outlines the evaluations completed during each visit. The site may pre-screen potential subjects by reviewing medical records to identify potential study subjects. Once identified, these subjects are approached to discuss the study, asked to participate and sign the IRB approved informed consent form. The site

may not initiate any study-specific (non-standard of care) procedures without first obtaining informed consent.

9.1 Informed Consent Procedure

Written Informed Consent must be obtained for each prospective subject before any study- specific tests or screening procedures are performed on that subject. The informed consent process must be performed by the Principal Investigator (PI) or their authorized designee. They will be responsible for ensuring subjects understand all relevant aspects of the study.

9.2 Eligibility Screening

Eligibility screening of prospective subjects will be conducted by a Site Investigator and/or a designated Research Coordinator. Subjects who wish to enroll will undergo the following assessments at Screening Appointment. The subject will sign an Informed Consent Form administered by a designated Principal Investigator or authorized designee.

Subject eligibility will be assessed on the basis of Screening Appointment data, according to the eligibility criteria listed above.

Table 9-1: Subject Screening Criteria

Evaluation	Accepted interval prior to Eligibility Screening Appointment (unless specified otherwise)	Condition
Informed consent	Within 30 days prior	Prior to any study-specific procedures
General Medical Evaluation a. baseline vitals b. physical examination c. Lower Urinary Tract (LUT) function and measurements	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
Medical History a. Date and etiology of Urinary Retention diagnosis b. Review of past medical history (neurological, urological and systemic)	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment

Evaluation	Accepted interval prior to Eligibility Screening Appointment (unless specified otherwise)	Condition
c. Urinary management history: method(s) of bladder management and dates of major changes d. History of urinary complications (UTIs, false passage, stricture, etc.) e. Level and severity of spinal cord injury (if applicable; including ASIA Score, if known by subject)		
Lower Urinary Tract Evaluation – visual evaluation of lower urinary tract, and baseline anatomical measurements.	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
Catheter Assessment Tool (CAT) Evaluation	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
Baseline Urinalysis and Urine Culture	Within 30 days prior	If the patient has a UTI (bacteriuria $\geq 10^5$ CFU per mL, plus at least one NIDRR consensus-defined symptom), they must undergo treatment before the initial insertion.
Voiding Characterization a. Pre-Void Bladder Volume – measured by ultrasound b. Voided urine volume c. Post-Void Residual Volume – measured by ultrasound	Within 30 days prior	Bladder must contain at least 200 mL of urine before conducting the test.

Evaluation	Accepted interval prior to Eligibility Screening Appointment (unless specified otherwise)	Condition
Bladder Management SCI-QOL Survey (short form)	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
Current Catheter Experience Survey	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
USQNB-IC Survey	Within 30 days prior	Evaluation is complete and adequately documented in report for assessment
Medications	Within 30 days prior	All medications taken are properly documented.

All subjects screened for this study will be captured on the site's Screening and Enrollment Log, which will record at a minimum, the prospective subject's ID #, subject's initials, date of screening and the reason(s) for study exclusion (if applicable). The Screening and Enrollment Log will use numeric subject identifier numbers.

9.2.1 Insertion and Initial Voiding Assessment

The Insertion Procedure is to begin with the insertion of the Connected Catheter using the IR Tool, according to device training procedures and Instructions for Use (IFU). The initial insertion will be performed by a trained clinician. Once the Connected Catheter has been placed, a urine sample will be collected and sent out for urinalysis and urine culture. Note that the subject must have at least 200 mL of urine in the bladder, as measured by ultrasound, prior to voiding and sample collection. After the bladder is emptied, a member of the research team (physician, nurse, etc.) will measure PVR volume using an ultrasound bladder scanner and record this reading.

9.2.2 User (Subject) Training

A trained, designated member from the Sponsor or a trained member of Study Site's research team will instruct the subject on how to use the Connected Catheter - insertion, bladder voiding, and removal - using a training model. A short, initial training will take place before insertion of the Connected Catheter and will continue intermittently throughout the Insertion Appointment, in between the positioning and sizing assessment, as well as between voiding cycles, until the subject demonstrates proficiency in Connected Catheter insertion, voiding, and removal procedures to the research staff. If the subject is unable to demonstrate proficiency in the Connected Catheter voiding

or removal procedure, then he may be allowed to complete the Clinic Assessment, but not allowed to proceed to the Test Phase. Each subject will be requested to refrain from sexual activity until the first follow-up appointment (up to 7 days). After the first Connected Catheter use is completed, the subjects will be informed that normal sexual activity may occur with caution. Device performance and impact on sexual will be evaluated in the Connected Catheter Safety and Performance Survey administered during each appointment where the device is replaced.

9.2.3 Device Positioning and Sizing Assessment

The subject will undergo a positioning and sizing assessment to evaluate if any migration of the Connected Catheter has occurred in the lower urinary tract by performing a set of mobility maneuvers intended to simulate the subject's activities of daily living. These maneuvers will be tailored to the subject's physical ability level (e.g. ambulatory vs. non-ambulatory) and will include common motions such as walking (or wheeling), sit-to-stand transitions, ascending and descending stairs as applicable to each subject. Any observed instances of Connected Catheter migration will be recorded. If an observed instance of migration is suspected to be due to incorrect sizing, the Connected Catheter may be removed, and a different size inserted (per IFU).

9.2.4 Bladder Filling Period

In between voiding cycles, the subject is to remain in the vicinity of the study site until voiding urgency is felt or the scheduled timed void(s) has occurred. During this bladder filling period, the subject should consume adequate fluids (>300 mLs) to promote bladder filling. The bladder must contain at least 200 mL of urine, as measured by ultrasound, before performing the voiding assessment. Subjects must consume fluid until the required minimum volume of urine in the bladder is achieved.

9.2.5 Voiding Assessment(s)

Prior to bladder voiding, the research staff will task the patient to locate the Connected Catheter end and assess if any migration has occurred. Next, the subject is to perform bladder voiding using the Controller, and the PVR Volume is then measured and recorded. The subject will remain in the vicinity of Study clinic premises for additional bladder filling and voiding cycles, to be conducted in the same manner without repeating the positioning and sizing assessment. A total of 3 voiding cycles will be performed during the initial insertion visit and twice during each Test Phase visit.

9.2.6 Expectation Management for New Users – Anti-Cholinergic and other medications

Subjects transitioning from other methods of bladder management should expect a short period of time in which their body adapts to the Connected Catheter. This may include various symptoms including discomfort and pain. The Clinical Research staff should educate and inform the subject about this possibility and help to manage their expectations as they become accustomed to the device.

Subjects with higher levels of sensation may have a more difficult time adapting to the Connected Catheter. For all subjects, the clinician should review subject's history for any anti-cholinergic or other medications (e.g. Myrbetriq) that the subject has been treated with previously and consider starting an appropriate course of medication 1-2 weeks prior to the initial insertion and continue at least 1-2 weeks after the Connected Catheter has been inserted. This medication may help to alleviate any discomfort as the subject transitions to the Connected Catheter. Additionally, it may

help indwelling catheter users to increase bladder capacity as they begin using the Connected Catheter.

There are no other medical devices or medications that will be utilized during this study.

9.2.7 Clinic Assessment Completion and Subject Discharge

Prior to discharge, the subject will complete the Connected Catheter User Experience Survey. If the Connected Catheter fulfills the objective performance criteria for all areas of essential performance (insertion, voiding and anchoring) then the subject will leave with their current Connected Catheter inserted, be scheduled for the next office appointment (at Day 7 ± 1), and will be discharged from the Study Site for the Device Tolerability Screening Phase.

9.3 Device Tolerability Screening

During the Device Tolerability Screening, subjects will use the Connected Catheter to manage their chronic Urinary Retention . The duration of Tolerability Screening will be up to 7 days after the patient has had the first device inserted. The purpose of this screening is to ensure that the subjects can both tolerate the device and learn how to operate it properly. Any subject that experiences significant discomfort or cannot demonstrate proficiency in the operation of the device (or does not have a caretaker) will not proceed to the test phase of the study. Patients that are able to successfully use the device for up to 7 days and wish to continue the study will progress to the test phase. The data collection during the Device Tolerability Screening is identical to the data during the Test Phase. The subjects will be trained to manage his bladder using the Connected Catheter via the Controller on an intermittent voiding strategy. Instructions for Use (IFU) will be provided to the subject regarding how to properly use the Connected Catheter. The same assessments used in the Test Phase will be done at the end of the Device Tolerability Screening phase.

9.4 Test Phase

The Test phase will require three (3) Exchange Appointments and a final Removal Appointment. Each appointment will assess PVR, voided volume, quality-of-life (QOL), and urinary tract injury, adverse events, medication, and other study assessment. Additionally, the subjects will be asked to fill out a User Experience Survey and Safety and Performance Survey and the device will be evaluated for fit, migration, placement, and removal.

At each exchange visit, the clinic research staff will follow these procedures:

1. Patient Arrival – Vital Signs and other measurements
2. Bladder Volume – Measurement using Ultrasound to ensure at least 200 mL of urine
3. Patient empties bladder – PVR volume measurement using Ultrasound
4. Patient removes Connected Catheter
5. Patient waits for bladder to fill – additional surveys completed
6. Patient inserts new Connected Catheter and bladder emptied – PVR volume measured
7. Patient Departure

For the final device removal visit the clinic research staff will follow these procedures:

1. Patient Arrival – Vital Signs and other measurements
2. Bladder Volume – Measurement using Ultrasound to ensure at least 200 mL of urine
3. Patient empties bladder – PVR volume measurement using Ultrasound
4. Patient removes Connected Catheter
5. Patient completes all surveys
6. Patient departure

Once the patient completes the final device removal visit the patient will enter the follow-up phase.

9.5 Follow-Up Phase

During the Follow-Up Period, subjects will use their previous method of bladder management for 2 weeks following their Final Device Removal Appointment. During this period, the patient will receive a phone call each week to screen for the occurrence and/or persistence of lower urinary tract symptoms and other issues that may be related to Connected Catheter usage, using the Follow-Up Phone Call Survey. If any issues are identified that may require clinician intervention, then the research staff will schedule the patient for a clinic appointment with the appropriate provider. At this appointment, the clinician will screen for any complications and attempt to document any symptoms that may be indicative of a complication related to Connected Catheter use.

9.6 Unscheduled Follow-up Visits

If subjects are seen for unscheduled/interim visits because of an AE, appropriate Case Report Form(s), including the AE CRF, will be completed, if applicable. At the investigator's discretion, some of the evaluations and tests may be repeated if indicated. Sponsor requests that if any additional tests or procedures listed within this clinical investigation protocol are performed during an unscheduled visit the investigator provide the results on the Unscheduled Visit CRF.

Table 9-2: Schedule of Visits

	Eligibility Screening	**Device Tolerability Screening**	**Test Phase**	**Follow-Up**	**Unscheduled**
Compliance window		**7 ± 1 days**	**7 ± 1 days**	**7 ± 1 days**	
Basic Vital Measurements	√	√	√		√
Physical Examination	√				
Urinary Tract Visual Examination	√				

	Eligibility Screening	Device Tolerability Screening	Test Phase	Follow-Up	Unscheduled
(cystoscopic, if necessary)					
Catheter Assessment Tool (CAT) Evaluation	√				
Medical History	√				
UTI Assessment including Urinalysis	√	√	√		
PVR Measurement	√	√	√		
Voiding Volume Measurement	√	√	√		√
SCI-QOL Bladder Management Survey	√	√	√		
Current Catheter Experience Survey	√				
Medication(s) used	√	√	√		√
Connected Catheter User Experience Survey		√	√		
Connected Catheter Safety and Performance Survey		√	√		
USQNB-IC Survey	√	√	√		
Connected Catheter Weekly Assessment Includes: • Device Insertion Assessment • Device Sizing		√	√		

	Eligibility Screening	Device Tolerability Screening	Test Phase	Follow-Up	Unscheduled
and Positioning • Catheter Sealing • PVR Measurement • Voided Volume • Catheter Migration • Urethral Injury Assessment • Device Removal Assessment • QOL Survey					
Follow-Up Phone Screening for Potential AE				√	
Adverse event(s) review		√	√	√	√
There are weekly appointments during the Test Phase and weekly phone calls during the Follow-Up Phase					

9.7 Subject Loss to Follow-Up or Withdrawal

9.7.1 Subject Discontinuation/Withdrawal Criteria

9.7.1.1 Voluntary Withdrawal

Participation in this clinical investigation is entirely voluntary. Further, once the subject has been enrolled in the study, he may withdraw his consent to participate in the study at any time, without further obligation or penalty. If a subject officially withdraws from the study, the investigator must ensure that the reason for the withdrawal is documented.

If the subject had an AE, the subject should be followed until the resolution of the AE, if possible. Data from these subjects will be included in the analysis up to the point of each subject's withdrawal.

9.7.1.2 Involuntary Withdrawal

Likewise, there may be a reason identified by the Investigator that deems the subject no longer suitable for the study, in which case the subject may be withdrawn by an Investigator. In either case, the Investigator should contact the Sponsor to discuss the circumstances for discontinuation/withdrawal. Reasons for discontinuation or withdrawal may include, but are not limited to the following:

1. Subject is uncooperative with compliance of required study tests, medical management and/or Study procedures
2. Investigator determines that subject has developed a condition for which continued participation in the study is potentially harmful to the subject
3. Subject withdraws his consent
4. Subject is lost to follow-up
5. Subject has a significant protocol violation
6. Subject is found to have been incorrectly enrolled in the study
7. Sponsor terminates the study

9.7.1.3 Data Withdrawal Due to Exclusion Criteria

A subject's data may be excluded from the analysis if the subject is later found not to meet one or more major exclusion criteria. However, these subjects will continue to be followed per the requirements of their particular arm unless instructed otherwise by the IRB/EC.

9.7.1.4 Subjects Lost to Follow Up

All reasonable efforts (at least 3 contact attempts via phone/email, or registered letters) will be made to obtain complete data for all subjects, before they are considered lost to follow-up. Missing observations may occur due to subjects who are lost to follow-up or demonstrate noncompliance with the required assessments.

9.7.1.5 Data Collection & Follow-Up for Discontinued/Withdrawn Subjects

All subjects enrolled in the study are considered eligible for follow-up and will be required to adhere to the assessment schedule found in Table 9-2. Subjects may withdraw from the clinical study or discontinue their participation at any time without any further obligation, penalty, or prejudice. If a subject withdraws from the study, the reason for withdrawal will be documented. If the withdrawal is a result of an adverse event, an Adverse Event Form must also be completed. Subjects who withdraw consent after treatment will not be required to undergo follow-up but will still be considered part of the subject cohort. In addition to withdrawing from the study voluntarily, subjects may also be withdrawn from the study by the investigative team, as necessary to ensure each subject's safety and welfare. Regardless of who initiates a given withdrawal, every attempt will be made to conduct an exit/final appointment prior to each subject withdrawal from the study. The reason for early discontinuation will be documented in the source documents and electronic case report forms (eCRFs). Data collected up to the time of study withdrawal will be included in the data analysis.

9.8 End of Study

Subjects receiving the device may exit the study at the end of the study (i.e., the study is discontinued by the Sponsor) or when the subject has completed the final follow-up visit, whichever comes first, unless the subject opted to find an alternative treatment.

An End of Study CRF will be completed at the time the study is completed, discontinued, or lost to follow-up for each subject.

10 STATISTICAL CONSIDERATIONS

10.1 Primary Endpoint Hypothesis

The primary endpoint analysis consists of a one-sided test of the null hypothesis that no more than 60% of users are responders to the device against the alternative that more than 60% of users are responders, as given below:

$$Ho: \quad R \leq 60\ \%$$

$$Ha: \quad R > 60\ \%$$

Where,

R = % of users who are responders

In this study, R is estimated as the percent of subjects who are responders, and a subject will be considered a responder to the device if at least 80% of that subject's individual available PVR values are:

a. Less than 50 mL OR
b. Equal or less than baseline PVR with the subject's standard urinary management system

10.2 Sample Size Justification

Based upon historical data and experience with the device, the estimate of R is expected to exceed 90% in this study. Limited descriptive statistical methods will be utilized to analyze data collected from this protocol. Although there will be limited power achieved with the number of patients completing this study, this data will provide a foundation for further clinical research with additional statistical rigor.

10.3 Statistical Analysis

Data from all the sites will be pooled together assuming poolability analysis show that the data are poolable.

The primary efficacy endpoint will be hypothesis tested based on the mITT population. An analysis of all subjects that dropped out during or after the device tolerability screening will be provided.

The primary efficacy outcome will be assessed using an exact binomial test at the 0.05 significance level, in a one-sided test of the null hypothesis that the user responder rate is 0.60 or less, against the alternative hypothesis that the user responder rate is greater than 0.60.

For the primary safety endpoint, device related SAE will be analyzed with descriptive statistics and nominal 95% confidence intervals. Serious adverse events from all subjects that were treated with the investigational device will be included. Based on the sample size calculations, the source of the SAE will be from all 60 subjects that tested the device. There will be no formal statistical hypothesis testing.

Similarly, the secondary endpoints will be analyzed with descriptive statistics and nominal 95% confidence intervals.

Tipping point analyses will be conducted to investigate issues such as the possible impact of missing data.

11 DEFINITION OF ADVERSE EVENTS

11.1 Adverse Event (AE)

An Adverse Event is defined as any untoward medical occurrence, unintended disease or injury or any untoward clinical signs (including an abnormal laboratory finding) in subjects, users or other persons, whether or not related to the investigational medical device.

Adverse Event Identification: A condition that is one of the following:

1. A unique symptom or event that is a change from the subject's baseline status
2. A series of symptoms or events that can be categorized as a single entity based on definitions found herein
3. A specific diagnosis responsible for a clinical change
4. A worsening or exacerbation of a pre-existing condition

11.2 Serious Adverse Event (SAE)

An adverse event is considered to be a serious adverse event (SAE) when the subject outcome is any of the following:

1. Death
2. Life-threatening
3. In-patient hospitalization or prolongation of an existing hospitalization
4. Persistent or significant disability/incapacity
5. Substantial disruption of a person's ability to conduct normal life functions, i.e. the adverse event resulted in a significant, persistent or permanent change, impairment, damage or disruption in the subject's body function/structure including chronic diseases, physical activities and/or quality of life
6. Congenital anomaly or birth defect
7. Required medical or surgical intervention to prevent permanent impairment of a body function or damage to a body structure
8. If the AE does not fit the other outcomes, but the event may jeopardize the health of the subject or require medical or surgical intervention (treatment) to prevent one of the

outcomes listed above

An SAE may or may not be related to the study procedure.

Note: A planned hospitalization for a pre-existing condition, or a procedure required by the protocol without serious deterioration in health, is not considered a serious adverse event.

11.3 Unanticipated Adverse Device Effect (UADE)

Any serious adverse effect on health and 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, related documentation or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subject.

11.4 Serious Adverse Device Effect (SADE)

An adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event.

11.5 Unanticipated Serious Adverse Device Effect (USADE)

A serious adverse device effect which by its nature, incidence, severity or outcome, has not been identified in the current version of the risk analysis report.

11.6 Device Technical Observation

An observation of a medical device with respect to its identity, quality, durability, reliability, safety or performance. Device deficiencies that did not lead to an AE but could have led to a medical occurrence will be reported, under the following circumstances:

1. if either suitable action had not been taken,
2. if intervention had not been made, or
3. if circumstances had been less fortunate.

11.7 Adverse Event Classification and Reporting Requirements

Adverse events will be assigned an attribution according to the Investigator's believed primary cause. Events will be categorized by relationship to the Investigational Device, Insertion Procedure, concomitant medications, pre-existing condition, intercurrent condition, intercurrent intervention, or other.

Adverse events should be classified according to their underlying cause, if known (e.g., fever resulting from infection should be reported as "infection"). Symptoms related to a diagnosis should not be reported as separate AEs. In the above example, fever is a symptom caused by infection and should be reported as infection only.

Concomitant AEs that are unrelated (in the clinician's judgment) should be reported as separate events.

AE determination is based on three levels of evidence:

Level 1 – final diagnosis

Level 2 – signs

Level 3 – symptoms

Every effort should be made to collect Level 1 evidence of any AE. If an AE has all three levels of evidence, the AE should be reported only once at the highest level of severity, which is the final diagnosis (Level 1). A single AE should not be reported as multiple AEs based on separate symptoms and signs.

In cases where a diagnosis is not possible, AE determination should be based on the next highest level of evidence (i.e., Level 2: signs), followed by symptoms (Level 3), if symptoms are all that are available to the investigator.

A corrective action (e.g. catheterization) itself is not an AE but the reason of the catheterization may be an AE. The AE determination always should be based on the reason that a corrective action was taken. Note: there may be multiple signs or symptoms representing only one AE.

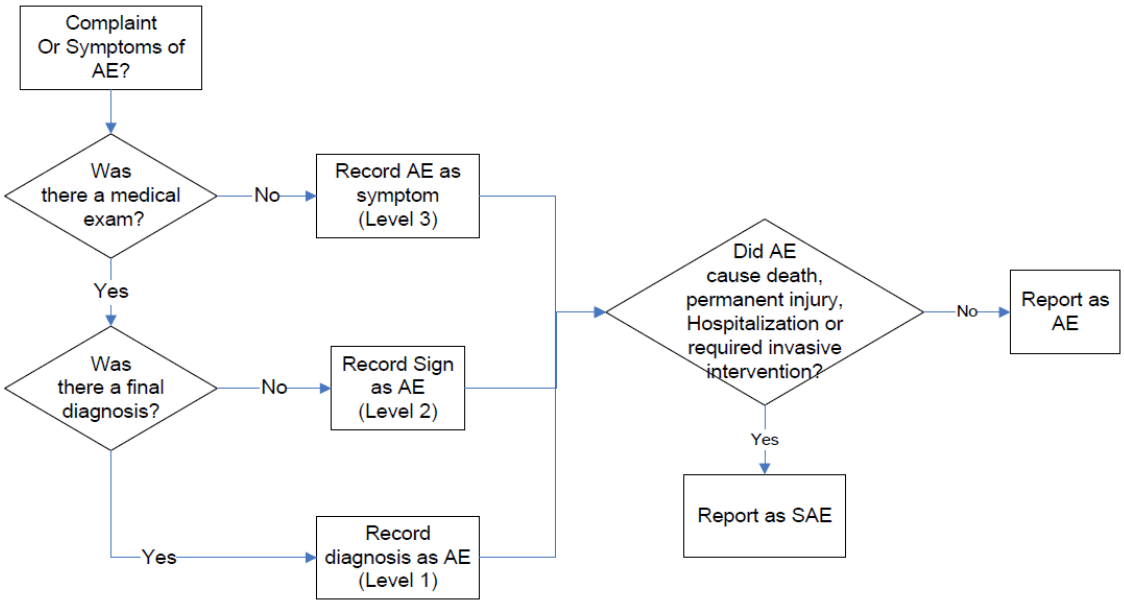

Figure 11-1: AE Determination and Outcome Flowchart

The AEs in the study may be further coded by Medical Dictionary for Regulatory Activities (MedDRA) and graded according to Common Terminology Criteria for Adverse Events (CTCAE) for the purpose of regulatory reporting or publication.

11.8 Reporting of all Adverse Events

The signs, symptoms and sequelae of an underlying AE should not be reported as separate AEs.

All AEs must be documented on an eCRF. All AEs also must be described by (a) duration (start and resolution dates); (b) adjudicated for severity; (c) relationship to the study device; (d) action taken to resolve the event; (e) outcome of the event; and (f) whether or not such event is considered to have been serious. Additional information, such as procedural notes, treatment notes, or a signed clinical summary, may be required as supporting documentation for the reported AE.

11.8.1 Device and Procedure-Related Adverse Event

A description of how an AE relates to the study procedure will be reported on the Adverse Event eCRF and starts from the first use of the device and be determined by the Investigator using the following definitions:

- ***Definite*:** The AE follows a reasonable temporal sequence from the time of the first insertion procedure, which includes AEs that occur during the index procedure or during the follow-up period.
- ***Probable***: The AE follows a reasonable temporal sequence from the time of the first insertion procedure, and the possibility can be excluded that factors other than the index procedure, such as underlying disease, concomitant drugs, or concurrent treatment caused the AE.
- ***Possible***: The AE follows a reasonable temporal sequence from the time of the first insertion procedure and the possibility of insertion procedure involvement cannot be excluded. However, other factors such as underlying disease, concomitant medications, or concurrent treatment are presumable.
- ***Unlikely***: The AE has an improbable temporal sequence from the time of the first insertion procedure, or such AE can be reasonably explained by other factors, including underlying disease, concomitant medication, or concurrent treatment.
- ***Not related***: The AE has no temporal sequence from the time of the first insertion procedure, or it can be explained by other factors, including underlying disease, concomitant medication, or concurrent treatment.

11.8.2 Concomitant Medication-Related Adverse Event

An adverse event is considered to be concomitant medication related when, in the judgment of the Investigator, it is reasonable to believe that the event is associated with concomitant medications used in conjunction with the Investigational Device and is not otherwise specific to the Investigational Device (e.g. bleeding associated with anticoagulation medication).

11.8.3 Pre-Existing Condition-Related Adverse Event

An adverse event is considered to be related to a pre-existing condition when, in the judgment of the Investigator, it is reasonable to believe that the event is associated with the subject's pre-existing condition and is not specific to the Investigational Device or Insertion Procedure. Pre-existing conditions that are aggravated or become more severe during or after the Insertion Procedure should be evaluated on a case-by-case basis to determine if the event may be more appropriately classified as device or Insertion Procedure-related.

11.9 Anticipated Adverse Events

The following is a list of potential anticipated adverse events that may occur while using the Connected Catheter.

1. Asymptomatic Bacteriuria
2. Autonomic Dysreflexia (for individuals with spinal cord injury)

3. Bladder or Urethral Perforation (False Passage)
4. Bladder or Urethral Spasms
5. Change in frequency or urgency to urinate
6. Discharge or Cloudy Urine
7. Discomfort
8. Dysuria (Painful Urination)
9. General Fever
10. Genitourinary pain
11. Hematuria (Blood in Urine)
12. Injury to the Lower Urinary Tract (LUT) and/or Genitals
13. Interference with Sexual Activity
14. Part or All of the Connected Catheter Becoming Temporarily Stuck in the LUT
15. Scarring of LUT
16. Systemic Infection
17. Urinary Incontinence
18. Urinary Retention
19. Urethral Stricture
20. Urinary Tract Infection
21. Urinary Tract Inflammation or Irritation

12 TRAINING

The Sponsor will be responsible for training of appropriate clinical site study personnel. To ensure proper procedural technique, uniform data collection and protocol compliance, the Sponsor will present a formal training session to personnel at each study site. At this training session, the study protocol, techniques for the identification of eligible subjects, instructions on data collection, schedule follow-ups, and regulatory requirements will be reviewed.

The training of clinical site personnel will be the responsibility of Spinal Singularity (Sponsor). This procedure may only be performed by qualified Investigators who are familiar with the Connected Catheter procedures and techniques. A formal training program consisting of instructive and interactive sessions will be performed with participating Investigators and study personnel identified at each site prior to subject treatment. Spinal Singularity-affiliated personnel will be available to assist with the technical aspects of the device/procedure training, as well as protocol-related training. During the Site Initiation Visit (SIV) or other site visit, training related to specific procedures for using the EDC system such as entering and editing eCRF data, and reviewing and resolving queries will be provided to investigative sites. This training will be documented on a training record. It is ultimately the responsibility of the Investigator to ensure that all clinical site personnel participating in this study are properly trained.

13 DATA MANAGEMENT

13.1 Subject Identification

Subjects that successfully pass the screening tests and wish to participate in the study will be assigned a unique identification code (ID) that is numeric.

In addition to the ID, each subject's initials will be used as an identifier included on documentation submitted to the Sponsor, as applicable.

13.2 Central Database

Applicable study documentation will be collected and compiled in a central database or in hard copy files, as applicable. Appropriate quality control measures will be established to ensure accurate and complete transfer of information from the study documentation to the central database or other document location(s).

The Investigator or designee must record the information required by this clinical investigation protocol in source documentation that must be made available to Sponsor representative or designee for review. An authorized site representative will enter all applicable data into a 21 CFR 11 compliant Electronic Data Capture (EDC) system via Electronic Case Report Forms (eCRFs).

13.3 Data Monitoring and Quality Control

Spinal Singularity, Inc. will designate a qualified Monitor (Clinical Research Associate [CRA]) to verify that study data is supported by adequate source documentation, which is complete, accurate and verifiable. Instances of inconsistent, missing or illogical data will be communicated to the Investigator or designee and queried for resolution.

Completed eCRFs will be verified by the qualified CRA at the investigational sites at regular intervals throughout the study. The Investigator will allow the monitor and/or representative of the Sponsor, and any regulatory body to review and inspect the study files, subject eCRFs, subject medical records and other study related documents as required.

Spinal Singularity, Inc. will monitor and manage the data for this investigational study.

The main clinical contact at Spinal Singularity, Inc. will be:

Shannon Metzger
Shannon@spinalsingularity.com
+1 (602) 391-9310

The alternate clinical contact at Spinal Singularity, Inc. will be:

Derek Herrera
Derek@spinalsingularity.com
+1 (470) 222-5323

All general Study inquiries may also be sent to ES01@spinalsingularity.com

Data will be reviewed periodically by an independent research monitor and a Data and Safety Monitoring Board (DSMB). These monitors will ensure overall safety of the study by analyzing any potential trends or issues that result during the study. The research monitors will assist the Sponsor in ensuring safe execution of this clinical investigation protocol and, if any issues arise, help determine any time when it may be necessary to temporarily halt the study.

The Independent Safety Monitor for the Study will be:

Dr. Jaime Landman, MD,
Professor of Urology and Radiology Chairman,
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14 STUDY RESPONSIBILITIES AND MANAGEMENT

The proposed study will be performed in accordance with all requirements set forth in the U.S. regulations, 21 Code of Federal Regulations (CFR) Parts 812.2(b), 50, 54, and 56, the World Medical Association Declaration of Helsinki, EN ISO 14155:2011 (as applicable) and any other applicable local laws, regulations, or guidelines.

14.1 Investigator Responsibilities

Each investigator is responsible for ensuring the investigation is conducted according to all signed agreements, this clinical investigation protocol, EC/IRB requirements, and applicable laws and regulations. Also, Investigators may not begin enrollment until Sponsor or its designee receives and approves (when necessary) the following documents:

- Signed Investigator Agreement
- Financial disclosure forms for all participating investigators
- EC/IRB roster (or IRB registration number from the Office of Human Research Protection)
- EC/IRB protocol and ICF approvals
- Investigators' current curricula vitae (CV)
- Signed Site Delegation of Authority (DOA) Log

It is acceptable for Investigators to delegate one or more of the above functions to an associate or Co or Sub-Investigator, or a trained Study Coordinator; however, the Investigator remains responsible for the proper conduct of the clinical investigation, including obtaining and documenting proper study informed consent, collecting all required data, submitting accurate and complete eCRFs, etc.

At each study site, appropriate procedures must be followed to maintain subject confidentiality according to appropriate local regulations (e.g., Health Insurance Portability and Accountability Act (HIPAA) in the U.S.). Each site may have its own internal procedures or requirements for use and release of subject medical information in research studies. Each Investigator is responsible for obtaining appropriate approvals, consents, or releases of medical information as dictated by their relevant subject privacy laws.

The study is not transferable to other sites attended by the Investigator unless prior approval is obtained from the appropriate EC/IRB and the Sponsor.

14.2 Subject Enrollment Process

All study candidates, after pre-screening, must appropriately consent to participate in the study, as administrated by qualified study site personnel using an IRB and Sponsor-approved informed consent form (ICF) prior to beginning any aspect of the study procedure or tests that are not standard of care for the site. Investigational sites will be required to document the consent process within each enrolled subject's medical record. Administering the questionnaires can be done prior to signing the ICF.

Only subjects who meet the inclusion/exclusion criteria, who signed the study enrollment informed consent will be considered enrolled in the study.

Timely communication by each site is critical to avoid over enrolling when the enrollment is close to the end of each phase.

14.3 Ethics Committee (EC) / Institutional Review Board (IRB)

Investigators must submit this clinical investigation protocol to their respective Ethics Committee (EC) and or Institutional Review Board (IRB) and obtain the EC's/IRB's written approval before being allowed to conduct and participate in the study. Each Investigator is responsible for fulfilling any conditions of approval imposed by their respective EC/IRB, such as regular reporting, study timing, etc. Investigators will provide the Sponsor or its designee with copies of such approvals and reports.

14.4 Informed Consent Form (ICF)

The Sponsor will provide a template informed consent form (ICF) to each study site for EC/IRB submission. The template may be modified to suit the requirements of the individual study site but the Sponsor must pre-approve all changes to the ICF prior to initial submission to the EC/IRB.

Each Investigator or assigned designee must administer this approved ICF to each prospective study subject and obtain the subject's signature or a legally-approved designee's signature along with the date of consent prior to enrollment in the study. The ICF must be obtained in accordance with the applicable guidelines on 21 CFR 50, 54 and 56, the Declaration of Helsinki, EN ISO 14155 or local regulations and laws, whichever represents the greater protection of the individual. Subjects must be informed about their right to withdraw from the study at any time and for any reason without sanction, penalty, or loss of benefits to which the subject is otherwise entitled and also be informed that withdrawal from the study will not jeopardize their future medical care. A copy of their signed ICF must be given to each subject enrolled in the study. The institutional standard subject consent form does not replace the Connected Catheter study ICF.

14.5 Case Report Forms (CRFs)

The Sponsor will provide standardized case report forms (CRFs) for each individual subject. The CRFs will be electronic via a 21 CRF Part 11 compliant EDC, and will be used to record study data, and are an integral part of the study and subsequent reports.

The electronic CRFs for individual subjects will be provided by the Sponsor via a web portal. After the data have been monitored and submitted, corrections will be initiated via a data query to

be completed by study site personnel. This data query will be done electronically via the web portal. Electronic CRFs must be approved and signed by the Investigator in the appropriate spaces provided using his/her electronic signature.

Electronic Case Report Forms (eCRFs) will be used to collect all subject data during the course of the study. eCRFs must be fully completed for each subject and electronically signed by the Investigator when complete. The eCRFs should be a complete and accurate record of subject's data collected during the study according to EN ISO 14155:2011 standard. Regulations and Good Clinical Practice (GCP) guidelines require that Investigators maintain information in the study subject's medical records that corroborate data collected on the eCRFs. To comply with these regulatory requirements, the following information should be maintained:

1. Medical history/physical condition of the subject before involvement in the study sufficient to verify protocol entry criteria.
2. Dated and signed notes on the day of entry into the study including the study Investigator, study name, subject number assigned and a statement that consent was obtained.
3. Dated and signed notes from every subject appointment with reference to the CRFs for further information, if appropriate (for specific results of procedures and exams).
4. Information related to adverse events.
5. Subject's condition upon completion of or withdrawal from the study.
6. Discharge summaries/procedure reports.

14.6 Records

Each Investigator must maintain the following accurate, complete, and current records relating to the conduct of the study investigation. The final responsibility for maintaining such records remains with the Investigator. These records include, but not limited to:

- All signed agreements;
- IRB/EC approval letter(s);
- Signed ICF;
- Records of AEs, including supporting documents;
- Records of protocol deviations, including supporting documents
- Records showing receipt, use and disposition of all investigational devices, including:
    - Date, quantity, model and lot or serial numbers of devices received,
    - Name of person(s) who received, used or disposed of each device,
    - The number of devices returned to the Sponsor and the reason(s) for return;
- All correspondence related to the study;
- Records of each subject's case history, including study-required CRFs, signed ICF, all relevant observations of AEs, the condition of each subject upon entering and during the course of the investigation, relevant medical history, the results of all diagnostic testing, etc.;

- Study personnel visit log;
- Signature authorization and delegation log; and,
- Any other records that applicable regulation requires to be maintained.

14.7 Reports

Table 14-1 lists those reports that are the investigator's responsibility to deliver to the Sponsor. Each study investigator must follow the EC/IRB reporting requirements for their respective site. If applicable regulations or EC/IRB requirements mandate stricter reporting requirements than those listed, the stricter requirements must be followed.

Table 14-1: Reports Required from Investigators to Sponsor

Type of Report	Prepared by PI for	Notification Time Frame
UADE	Sponsor, EC/IRB	Within 10 working days of knowledge
Death	Sponsor, EC/IRB	Written reports (e.g., via e-mail) within 48 hours
SAE	Sponsor	Within 10 working days of knowledge
	EC/IRB, if required	Per IRB requirement
Device malfunction with clinical sequelae	Sponsor EC/IRB, if required	Within 48 hours via written communication. Return the device to sponsor within 48 hours.
Serious protocol deviations (e.g., ICF not obtained, to protect the life or physical well-being of a subject in an emergency)	Sponsor EC/IRB, if required	Within 5 working days of knowledge Per IRB requirement
Withdrawal of EC/IRB approval	Sponsor	Within 5 working days of knowledge
Annual progress report	Sponsor, EC/IRB	Annually
Final report	Sponsor, EC/IRB	Within 3 months of study completion or termination
Note: Each IRB/EC may require more stringent reporting requirements that those listed in this table.		

14.8 Sponsor Responsibilities

Spinal Singularity, Inc. is the Sponsor of this study. The Sponsor's responsibilities in the study include:

- Selecting the Principal Investigator(s), all clinical investigators and study sites, and other consultants or personnel (e.g., monitors) who participate in the study.
- Provide study protocol, device, and GCP training to participating study sites, in quantities sufficient to support study activities, per agreements executed with the study sites.
- Select all qualified clinical Investigators and study sites and other consultants or personnel (e.g., monitor) who participate in the study.
- Provide financial support to each study site.
- Follow/promote all regulatory standards per appropriate regulations for study sites, core laboratories, and other participants, and ensure compliance by periodically monitoring sites.
- Ensure completion of site monitoring of clinical data at each clinical study site.
- Retain ownership of all clinical data generated in this study, and control the use of the data for appropriate purposes only.
- Review and approve publication of study results in the literature.

14.8.1 Confidentiality

All information and data sent to the Sponsor concerning subjects or their participation in this study will be considered confidential according to HIPAA regulations. Data used in the analysis and reporting of this evaluation will be used in a manner without identifiable reference to the subject. Investigators will consent to visits by Sponsor's staff and its authorized representatives, as well as by the U.S. FDA or any other local governmental body, to review the study subjects' medical records, including any test or laboratory data that might have been recorded on diagnostic test media.

14.8.2 Amending the Investigational Study Protocol

Neither any Investigator nor the Sponsor will modify this Clinical Investigational Protocol without first obtaining concurrence of the other in writing. All changes to the Clinical Investigational Protocol must be submitted to the EC/IRB for review and approval. Any change that would require alteration to the ICF must receive approval from the applicable EC/IRB prior to implementation. Following approval, any Investigational Protocol amendment must be distributed to all protocol recipients at the site.

14.8.3 Protocol Deviations

A protocol deviation/violation is generally an unplanned excursion from the protocol that is not implemented or intended as a systematic change. An Investigator failed to perform tests or examinations as required by the protocol or failures on the part of study subjects to complete scheduled visits as required by the protocol, would be considered protocol deviations. These types

of deviations are reported to the sponsor and in accordance with the IRB policy.

A Protocol Deviation CRF must be completed by the site for each study protocol deviation (e.g., failure to obtain informed consent, enrolling a subject who does not meet inclusion / exclusion criteria, not performing required testing, missed follow-up window, etc.). An Investigator must notify the Sponsor and the reviewing EC/IRB of any deviation from the Study Protocol that was done to protect the life or physical well-being of a subject. Such notice should be given as soon as possible, but no later than five (5) working days after the emergency occurred.

14.8.4 Site Noncompliance and Nonperformance

Repeat serious protocol deviations will be closely monitored. If excessive deviations or a failure to reduce deviations are noted, the Sponsor reserves the right to suspend study enrollment at that site until a sufficient system is in place at the site to reduce further deviations.

After a site completes all required approvals and training, a Site Initiation Visit (SIV) will be conducted as a final check of the site readiness. If a site is not able to enroll its first subject 3 months after "Ready to Enroll" status, the Sponsor may elect to terminate the investigational site and allocate the slot to another candidate site.

The Sponsor reserves the right to terminate an investigational site from the study for any of the following reasons including, but not limited to:

1. Failure to obtain Informed Consent
2. Failure to report safety events (i.e. Adverse events)
3. Repeated protocol violations
4. Repeated failure to complete Electronic Case Report Forms
5. Failure to enroll an adequate number of subjects

14.8.5 Device Accountability

The Gen 2 Connected Catheter Systems allocated for investigational site use will be stored in a secured area until use. Each site will be responsible for tracking the receipt and disposition of all investigational Gen 2 Connected Catheter System devices. The unused Gen 2 Connected Catheter Systems must be returned to the Sponsor at the end of the study.

14.8.6 Sponsor Reporting Responsibilities

Table 14-2 lists those reports that are the Sponsor's responsibility and timelines to report to the IRB. If applicable regulations or IRB requirements mandate stricter reporting requirements than those listed, the stricter requirements must be followed.

Table 14-2: Sponsor Reporting Responsibilities

Type of Report Report Prepared For	Sponsor Reporting Responsibilities	
	Reporting Time Frame	**Report Prepared For**
Unanticipated Adverse Device Effect (UADE)	Investigators, IRBs	Written - Within 10 working days from the time the Sponsor first learns of the effect.
Withdrawal of IRB Approval or other action on part of the IRB that affects the study	Investigators, IRBs	Written – Within 5 working days.
Device Recall	Investigators, IRBs	Written – Within 30 working days.
Inappropriate Informed Consent	IRB	Investigator's report submitted within 5 working days of notification
Study Closure	Investigators, IRBs	Within 10 days
Final Report	Investigators, IRBs	Final report - within 6 months of study closure

15 STUDY ADMINISTRATION

15.1 Monitoring Procedures

It is the responsibility of the study Sponsor to ensure that proper monitoring of this investigation is conducted. Appropriately trained personnel, appointed by the study Sponsor, will complete any monitoring that is done. The monitoring will be the responsibility of Sponsor study personnel with an address as listed in the title page of this document. Monitor(s) will ensure that the investigation is conducted in accordance with:

- The signed Investigator's Agreement
- The Investigational Plan
- Appropriate laws and regulations
- Any conditions of approval imposed by the reviewing EC/IRB and/or other regulatory agencies

The clinical study will be monitored according to the guidelines summarized below. The Sponsor may choose to perform random inspections throughout the study as an element of quality assurance. Investigators will allow auditing of their clinical investigation procedures.

A study specific Monitoring Plan is created and implemented to standardize monitoring activities across centers and ensure human subject protection and verify data integrity. The monitors will receive study specific and SOP training prior to conducting any monitoring visits. Study monitors are selected based on their training, qualifications and experience to monitor the progress of an investigation. Study monitors may be Sponsor's employees or representatives. This study monitoring will include a site qualification, study initiation, interim, and close out visits. All study monitors will be required to follow the Sponsor's monitoring plan and monitoring standard operating procedures (SOPs).

The study monitoring will be executed by a Sponsor representative.

15.1.1 Monitoring Visit

The following factors will be taken into account when determining the frequency of the monitoring visits: subject accrual rate at each center, total number of subjects enrolled at each center, and Clinical Investigation Protocol compliance at each center. It is anticipated each site will be monitored at least once upon the completion of the follow-up visits for all enrolled subjects at the study site. Monitors will require direct access to subjects' medical records pertinent to the study (and study inclusion criteria), study management documents, regulatory documents and Subject Informed Consent documents, as well as other potential applicable records not listed here.

Monitors may ensure the clinical investigators have and continue to have staff and facilities to conduct the clinical investigation safely and effectively. Monitors may conduct the following monitoring activities throughout the study:

- Verification that the current IRB-approved informed consent was signed and dated by each subject prior to participating in the study required procedures.
- Verification of documentation in the subject's record that informed consent was signed prior to initiation of the study procedures and that a copy of the signed and dated consent was provided to the subject.
- Source documentation verification by reviewing the eCRFs against source documentation for accuracy and completeness of information.
- Verification that the Investigational Devices are being used according to the Clinical Investigation Protocol, Instructions for Use and, all malfunctions / IFU deficiencies are reported. as required.
- Verification that subjects met study enrollment criteria.
- Confirmation that the study is being conducted according to the Clinical Investigation Protocol and applicable regulations.
- Verification that study deviations are documented and reported.
- Verification that the procedures for recording and reporting adverse events to the sponsor are followed.
- Ensuring proper error correction.
- Verification of training documentation of all study personnel participating in study related activities.

- Reviewing all correspondence and regulatory documents, including confirmation of IRB-approved Clinical Investigation Protocol or amendments.
- Resolution of outstanding issues and completion of assigned tasks will be documented by the monitors.

Each monitoring visit will be documented via a monitoring report and follow-up letter. The follow up visit letter will be sent to the Investigator to document issues identified, corrective actions and if applicable preventive actions. At subsequent visits the issues resolved will be documented in this letter to demonstrate resolution. Monitoring visits will be conducted by trained monitors and designees. The Monitoring Plan identifies the frequency of monitoring and training requirements of the monitors.

15.1.2 Study Closure

Study closure is defined as a specific date that is determined by study completion and/or regulatory requirements have been satisfied per the Clinical Investigation Protocol (CIP) and/or by decision of the Sponsor or IRB. Study closure visits will be conducted at all enrolling clinical sites in order to review record retention requirements with site personnel. A telephone contact may take the place of a study closure visit if appropriate (e.g., low subject enrollment, recent monitoring visit, etc.)

16 CLINICAL TRIAL OVERSIGHT

16.1 Safety Monitoring

Evaluation and adjudication of safety data (e.g. serious adverse events, all deaths, etc.) will be performed on an ongoing basis by the Independent Research Monitor. The Independent Research Monitor for this study will be Dr. Jaime Landman, MD. Data and reports will be reviewed and adjudicated pursuant to the guidelines outlined in this clinical investigation protocol and Dr. Landman will have full authority to stop the study in accordance with ethical practices and stopping rules.

In addition to these reports, data will be aggregated for review and analysis periodically. These reports will be shared with the Independent Research Monitor and the monitor will be offered the opportunity to provide insight or input into any observable trends in the data.

17 POTENTIAL DEVICE CHANGE

Future product line extensions or design changes may be introduced into the study in a controlled manner based on feedback from Investigators. In addition, manufacturing changes may be introduced in a controlled manner. All design and manufacturing process changes will be performed under the Sponsor's design control and other relevant processes and will be fully tested to ensure that it meets specifications prior to introduction to the study.

18 PUBLICATION POLICY

The results of the clinical study maybe used by the Sponsor (and its subsidiaries and affiliates) for the purposes of national and international registration, publication and information for medical professionals. If necessary, regulatory authorities will be notified of the Investigator's name,

address, qualifications and extent of involvement. The Sponsor and the Investigators are committed to the publication of the results of this study in a peer-reviewed journal.

All publications and presentations related to this study will be developed per the latest publication policy by the Sponsor.

19 REIMBURSEMENT

Spinal Singularity, Inc. will not receive payment or reimbursement for any devices used during execution of this clinical study. All investigational devices utilized will be provided to patients / clinics at no cost.

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