A feasibility pilot study of the efficacy, reliability, safety and patient experience of the JiffyStent ureteric stent inserter.

Protocol Number JSI001
Version: 2.0
Date: 26 Feb 2024

Sponsor:
JiffyStent Pty Ltd

Statement of Compliance

This document is a protocol for a research project. This study will be conducted in compliance with all stipulation of this protocol, the conditions of the ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007) and the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95).

SPONSOR SIGNATURE PAGE

Clinical investigation title: A feasibility pilot study of the efficacy, reliability, safety and patient experience of the JiffyStent ureteric stent inserter.

Protocol No: JSI001

Sponsor's statement

I, the Sponsor, have reviewed this clinical investigation plan describing the design and specific provisions of the clinical investigation. I agree with the content of this document.

Cyril Dixon	Chief Operating Officer
Sponsor representative name (print)	Title
	3rd May 2024
Signature	Date

INVESTIGATOR SIGNATURE PAGE

Clinical investigation title: A feasibility pilot study of the efficacy, reliability, safety and patient experience of the JiffyStent ureteric stent inserter.

Protocol No: JSI001

Investigator's statement

I agree to conduct this clinical investigation in accordance with the design and specific provisions of this clinical investigation plan; modifications to the clinical investigation are only acceptable with a mutually agreed upon clinical investigation plan amendment as approved by the Sponsor and involved Ethics Committee(s).

I agree to await Ethics Committee approval of the clinical investigation plan and informed consent form before initiating the clinical investigation, to obtain consent from subjects prior to their enrolment, to collect and record data as required by the clinical investigation plan and associated case report forms, and to maintain documents related to the clinical investigation for the period of time required.

Confidential

This document contains confidential information belonging to JiffyStent Pty Ltd. Except as may be otherwise agreed to in writing, by accepting or reviewing these materials, I agree to hold such information in confidence and not to disclose it to others (except where required by applicable law), nor use it for unauthorised purposes.

Investigator name (print)

Signature Date

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1 ABBREVIATIONS

AE	Adverse event
ADE	Adverse device effects
CRF	Case report form
CRO	Contract research organisation
DD	Device deficiency
eCRF	Electronic case report form
ED-SSU	Emergency Department - Short Stay Unit
GCP	Good clinical practice
HREC	Human Research Ethics Committee
IFU	Instruction For Use
JSI	JiffyStent Inserter
KUB	Kidney, ureter and bladder
LTFU	Lost to follow-up
NHMRC	National Health and Medical Research Council
PI	Principal Investigator
QMS	Quality management system
SAE	Serious adverse event
SSI	Significant Safety Issue
TGA	Therapeutic Goods Administration
USADE	Unanticipated Serious Adverse Device Effect
USM	Urgent Safety Measure

2 REVISION HISTORY

Version Number	Version Date	Revisions
1.0	22 Jan 2024	N/A – initial document

3 SYNOPSIS

Clinical investigation plan	
Title	A feasibility pilot study of the efficacy, reliability, safety and patient experience of the JiffyStent ureteric stent inserter.
Short title	Evaluation of the JiffyStent Inserter in patients requiring a ureteric stent.
Protocol No.	JSI001
Investigational device	
Name	JiffyStent Inserter
Description	The JiffyStent Inserter is a single-use device which allows visualization of the ureteric orifice and subsequent insertion of a ureteric stent, which is pre-loaded by the health professional, into the ureter.
Indication for use	The JiffyStent Inserter enables temporary stenting of the ureter in adult patients with ureteral or renal obstruction due to an acute ureteric stone or ureteric stricture.
Clinical investigation design	
Background	The incidence of renal colic, or pain caused by a blockage in the urinary tract, varies depending on the population studied. In general, it is estimated to affect around 10-15% of the population at some point in their lives. The intention is to perform a proof-of-concept pilot study where the JiffyStent Inserter (JSI) will be used to insert a stent into participants who require a stent or have kidney blockage and pain from a stone in the ureter. A positive outcome of the proposed study will lead to a pivotal clinical trial suitable for regulatory approval for the JSI. The main objectives of the proposed trial are to evaluate the safety, feasibility and clinical efficacy of the JiffyStent Inserter. The study will: • Ensure that the JSI device works reliably. • Ensure JSI successfully inserts a ureteric stent in the ureter of participants. • Obtain preliminary evidence of safety. • Evaluate participant recruitment rate. • Assess participant experience and satisfaction with the JSI.

Aim	This study aims to evaluate the reliability, safety, clinical efficacy, and participant satisfaction using the JiffyStent Inserter.
Design	Single centre, first-in-human feasibility and safety pilot trial.
Hypothesis	The JiffyStent ureteric stent inserter can reliably, safely, quickly, effectively and to the participant's and doctor's satisfaction, insert a ureteric stent into the ureter of a participant with renal colic.
Methods	Eligible participants will be enrolled and have a ureteric stent inserted by the JiffyStent Inserter.
Endpoints	Primary endpoint The ability of the JiffyStent Inserter to correctly insert a stent into the ureter of a suitable participant as determined by a post-stenting kidney, ureter, and bladder (KUB) plain X-ray. Secondary endpoints • The mechanical reliability of the JSI to perform its function as expected. • The clinical safety of the JSI • Time taken to insert the ureteric stent using JSI. • Feasibility- evaluation of participant recruitment rate • Participant experience and satisfaction with the JSI User satisfaction for urological doctor/study researcher • Impact on workflow data • Impact on health economics
Trial Registration	ACTRN12623000264684p
Arms and interventions	Single arm: participants receiving treatment with JiffyStent Inserter.
Follow-up visits	Follow up visit for definitive stone treatment operation (usually within 14-21 days).
Study duration	Study duration for participant: 14-21 days. Encompasses screening, consent, intervention and ceasing at definitive stone treatment operation visit. Total study duration: six (6) months
Clinical investigation population	
Sample size	Up to 15 participants ≥ 18 years old
Key Inclusion criteria	• Consenting adult patient male or female, age ≥ 18 years old. • Patient about to undergo stent insertion as part of their routine urological care.

	• Ability to provide informed consent signed by study participant. • Willingness and ability to comply with study-related procedures/assessments
Key Exclusion criteria	• Age <18 years • Known allergy to local anaesthetic lubricating gel, Penthrox "green whistle" inhaler anaesthetic • Stone larger than 1cm • Stone impacted in ureter. • Men with prostate larger than 100cc in size • Patient with severe sepsis requiring nephrostomy or stabilisation in an operating room
Statistical analysis	
Analysis sets	N/A
Statistical design	This is an initial feasibility study. Outcomes will be summarized using descriptive statistics. There is no pre-specified power calculation

4 STUDY ADMINISTRATION STRUCTURE

4.1 Study Sponsor

JiffyStent Pty Ltd

5/210 Burgundy St

Heidelberg, Victoria 3084

AUSTRALIA

4.2 Contact Details

4.2.1 Trial Site

Site No. AU01

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4.2.2 Contract Research Organisation (CRO)

Avania Pty Ltd

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AUSTRALIA

Phone +61 2 9460 6688

4.3 Roles And Responsibility

This clinical investigation is sponsored by JiffyStent Pty Ltd (sponsor), located in Heidelberg, Victoria. An agreement between the involved site and the Sponsor will be set in place before the start of the study. This agreement details the specific roles and obligations of the site and the Sponsor, processing of data, confidentiality, insurance policy, publication policy, termination policy, applicable laws, and financial provisions.

The Sponsor is responsible for selecting qualified investigators and will provide information to the investigators to conduct the clinical investigation properly, which includes training on the device. The sponsor will further ensure proper monitoring and ensures the study is being conducted in accordance with this CIP. The Sponsor may delegate responsibilities, such as study management and monitoring, to a contract research organization (CRO).

The principal investigator (PI) will be a legally qualified clinician, trained in urology. Their qualification and experience will be assessed during a site feasibility visit. As study investigator, they are further responsible to protect the rights, safety, and welfare of subjects in the clinical investigation, ensure that informed consent is properly obtained and to ensure that the investigation is conducted appropriately. As principal investigator, they will act as team leader and will make sure that the involved team of co-investigators and study coordinators are appropriately trained on the protocol and procedures.

5 BACKGROUND

5.1 Lay Summary

A common presentation to the emergency department is a patient in excruciating pain from a kidney stone obstructing the ureter and kidney. Many of these patients will require a ureteric stent to relieve the obstruction and their pain. The current best treatment is to admit these patients to the operating room and insert a ureteric stent with the patient under general anaesthetic. This process can take 24 hours or more. The JiffyStent Inserter (JSI) is an innovative single use medical device that allows the Urologist or Emergency Department Physician to insert a ureteric stent while the patient is in the emergency room. This is a proof-of-concept study to show that the JSI works as desired by correctly inserting a stent into the ureters of participants, initially under controlled conditions in the operating room, and then in the emergency department. It is anticipated that use of the device will take 3-5 mins. If a stent cannot be inserted with the JSI after the first attempt, then a stent will be inserted in the operating room by the standard procedure. The outcome of every JSI and the success of the stent insertion will be recorded by the trial team by medical record review and discussion with the treating doctor. The study will involve up to 15 participants under controlled conditions. Of the 15 total participants, five (5) will be individuals who require a stent as a standard part of their urological procedure and 5-10 participants will be individuals who present to the emergency room with acute renal colic from a kidney stone and require a ureteric stent insertion. A successful outcome will lead to a pivotal multicentre clinical trial necessary for regulatory approval thereby making the JiffyStent Inserter available for widespread use.

5.2 The burden of ureteric stones and acute renal colic

Acute renal colic is the sudden onset of severe flank pain originating over the costovertebral angle and radiating to the groin or testicles. It is associated with nausea, vomiting, and in some cases, visible haematuria.

5.2.1 Incidence

Acute renal colic is mainly caused by the obstruction of the urinary tract by the presence of a stone. Nephrolithiasis or kidney stones is a common condition with prevalence rates of 5% - 15% in the population. Yearly incidence of acute renal in North America and Europe is in the range of 0.2% to 0.5%. It is most likely (>70%) to occur in patients between the ages of 20 and 50. More likely in men than women by a factor of 2:1[1-4]. Risk factors include obesity, hypertension, family history, IBS, and diabetes.

5.2.2 Causes

Pain is often caused by a combination of ureteral muscle spasms, increased proximal peristalsis, localized inflammatory changes, renal swelling with capsular stretching, edema, and irritation. These, in turn, stimulate submucosal stretch

receptors in the ureter, renal pelvis, and capsule. Stimulation of the renal pelvis, peri pelvic renal capsule, and calices from stretching most closely mimic renal colic.

Patients often report dull constant pain with colicky episodes. While constant pain is linked to stretching of the renal capsule due to obstruction, colicky pain can be attributed to peristalsis of the ureteral smooth muscle.

5.2.3 Factors Associated with Surgical Intervention

Factors associated with earlier surgical intervention are - severe hydronephrosis; ureteral stone ≥ 9mm; >700 Hounsfield units stone density; ≥ 0.2 cc stone volume; >2mm ureteral wall thickness; extrarenal pelvis; anterior-posterior diameter of renal pelvis >18mm.[5, 6]

Up to 95% of stones >8mm require intervention to pass. Patients with infected stones need operative intervention to prevent severe and life-threatening sepsis.

5.2.4 Current Standard of Care

The current standard treatment for participants presenting to the emergency department-short stay unit with acute renal colic due to an obstructing ureteric stone is to give them pain relief, admit them to hospital, and then find a time in the operating room to insert a stent. This operating slot may be on a regular list or on the emergency operating list. Patients will often wait over 24 hours to have their stent inserted in the operating room with all the burden of prolonged fasting, recurrent pain, prolonged obstruction of the kidney with risk of kidney impairment, infection, and time away from home.

6 INVESTIGATIONAL DEVICE

6.1 Manufacturer

JiffyStent Pty Ltd (Victoria, Australia) is the legal manufacturer of the JiffyStent Inserter.

6.2 JiffyStent Inserter

The all-in-one single use JiffyStent Inserter allows visualization of the ureteric orifice and subsequent insertion of a pre-loaded ureteric stent into the ureter for the purpose of alleviating ureteric or renal obstruction due to an acute ureteric stone. The value of the JSI is that it will rapidly alleviate the participants pain without the need to go to the operating room. This will significantly reduce the time the participants experience pain; reduce burden on emergency department waiting times for hospital beds; reduce opportunity costs for emergency operating lists; reduce the inconvenience to surgeons waiting prolonged periods for emergency operating slots (often very late at night); markedly reduce the cost of treating ureteric stones for the health system. The system will be in contact with the body

(i.e., urinary tract system).

Additional information about the identification and description of the investigational device may be found in the current version of the Investigator Brochure EDIB-20100106-01_00. The JSI does not contain medicinal substances, human, or animal tissues or their derivatives of other biologically active substances.

6.3 Regulatory Classification

The JiffyStent Inserter is considered a class IIA device according to the *Therapeutic Goods (Medical Devices) Regulations 2002* (Australia), based on the following rule:

- Rule 3.2 (1): Surgically invasive medical devices intended for transient use.
  (1) This clause applies to a surgically invasive medical device that is intended for transient use.
- (2) Subject to subclauses (3) to (5), the device is classified as **Class IIa.**

6.4 Identification of Investigational Device

JiffyStent Inserter device number JSI-03_03 will be used for the purposes of this study.

6.5 Intended purpose in the clinical investigation

In this clinical investigation, the intended purpose of the JiffyStent Inserter is to allow visualisation of the ureteric orifice in participants who are about to undergo stent insertion as part of their routine urological care.

6.6 Intended populations and indications

The intended populations are adults ≥ 18 years who are about to undergo stent insertion as part of their routine urological care or have presented to the Emergency Department - Short Stay Unit (ED-SSU) with acute renal colic requiring admission to hospital for a ureteric stent.

6.7 Required training and experience

Investigators will be trained to use the investigational device (JiffyStent Inserter). The investigators working with the JSI will be legally qualified clinicians (e.g., urologists) trained in performing endoscopic ureteric procedures The investigators will be trained prior to the use of the investigational device (JiffyStent Inserter) by the Sponsor, JiffyStent, on the Instructions for Use (IFU) and the study protocol. Training will also include a demonstration of the device. All investigators will receive the same amount of virtual and in-person training.

Additionally, investigators shall have adequate qualifications with regards to the project specificities, including:

- Experience and training in clinical studies, particularly clinical studies involving medical devices, and Good Clinical Practices for Medical Devices (ISO 14155:2020);
- Able to read and understand English.
- On-site initiation visits will be organised, in which full training will be given to all appropriate staff members participating in the clinical investigation, including principal investigators, study coordinators, and any other site personnel pivotal to the conduct of the clinical investigation. This training will include at least the following: instructions on the functions and use of the investigational device, procedure outlines in the clinical investigation plan, main principles of Good Clinical Practices for Medical Devices (ISO 14144:2020), instructions on completion of case report forms, content of the investigator site file, and management of device deficiencies.

6.8 Device traceability

Access to investigational devices will be controlled and the investigational devices will be used only in the clinical investigation and according to the clinical investigation plan. The sponsor will keep records to document the physical location of all investigational devices from shipment of investigational devices to the investigation sites until return or disposal. The sponsor shall have instructions in place and make packaging materials available, if applicable, for the safe return or disposal of investigational devices, including potentially hazardous devices. The devices will be identified by a serial number and expiry date. One device will be used per participant.

6.9 Investigational device and comparator

One (1) JiffyStent Inserter device will be used per participant. There will be no comparator device.

6.10 Medical/Surgical procedures

Participant is positioned in supine position following adequate analgesia, sterile prep and drape is applied to the perineum. JiffyStent Inserter settings are adjusted to individual participant measurements (pre-determined by abdominal imaging) and ureteric stent loaded into investigational device. JiffyStent Inserter is powered on and connected to smart device. The JiffyStent Inserter proboscis is inserted into the urethra and advanced to the bladder. The ureteric orifice is visualised via the smart device and the wire with ureteric stent is inserted into the ureteric orifice. The spool is rotated thereby advancing the wire and stent up the ureter. This rotation is continued until its limit and then the JSI guidewire spool is rewound to its limit and the stent is seen curling in the bladder. The JSI is removed from the urethra and participant leaving the ureteric stent insitu. A kidney, ureter and bladder (KUB) x-ray is performed to confirm stent positioning.

7 JUSTIFICATION FOR CLINICAL INVESTIGATION DESIGN

7.1 Pre-clinical testing

In conducting our pre-clinical testing procedure, we were able to successfully demonstrate the key functions in dummy models. We successfully loaded the stent into the JSI and inserted the battery, switching the camera on without a hitch. The device was synced up to Wi-Fi, displaying clear vision from the camera on the connected app. Saline fluid was flawlessly affixed and running optimally.

Our researchers then proceeded to insert the apparatus into the bladder via the urethra. The ureter opening was swiftly located and clearly visible throughout the process. Utilizing cutting-edge technology, we were able to visualize both the guide wire and the stent entering the ureter opening accurately. Subsequently, the stent was advanced fully, and the guide wire was retracted entirely without any challenges.

During the entire procedure, the camera remained reliably connected while the stent placement within the bladder was clearly visualized. The JSI was subsequently removed without any complications. Post-procedure, an (visual/imaging by opening/removing the lid of the model) validated the correct positioning of the stent. The JSI was disposed of following all standard guidelines.

The duration to complete the sequence of this particular experiment averaged between 3-6 minutes. This streamlined process, allied with meticulous attention to procedure, ensured the successful completion of every task. For further information see document “Investigator Brochure EDIB-20100106-01_00.docx”

Physical Simulation Model

A specialized ureteral anatomy model has been used to test the JSI. This model offers a comprehensive representation of the entire urinary tract from the external urethral meatus at the tip of the penis to the ureter connecting to the bladder and its vital connection with the kidney.

Non-clinical pharmacology

No non- clinical pharmacology has been undertaken.

7.2 Clinical development stage

This clinical investigation is a first-in-human, feasibility study. It is used to capture preliminary safety and performance information on the final design of the JiffyStent Inserter.

7.3 Evaluation of clinical data

As this clinical investigation is a first-in-human, feasibility study there is no clinical data for evaluation.

8 OBJECTIVES

8.1 Aim

This study aims to evaluate the reliability, safety, clinical efficacy, and participant satisfaction using the JSI.

8.2 Hypothesis

That the JiffyStent Inserter can reliably, safely, quickly, effectively and to the participant's and doctor's satisfaction, insert a ureteric stent into the ureter of a participant with renal colic.

8.3 STUDY OUTCOME MEASURES

8.3.1 Primary endpoint:

- The ability of the JSI to correctly insert a stent into the ureter of a suitable participant as determined by post-stenting KUB plain X-ray.
    - Timepoint: Immediately post-stent insertion with KUB Xray
    - Measure: Investigator's assessment of position of superior part of stent within kidney collecting system on KUB plain X-ray performed after stent insertion (Yes/No/Unsure)
        - If "Unsure"- proceed to renal ultrasound to confirm.
        - If "No" or still "Unsure" then proceed to standard stent insertion in operating room

8.3.2 Secondary endpoints:

- The mechanical reliability of the JSI to perform its function correctly as determined by the treating doctor as noted on a global doctor satisfaction score.
    - Timepoint: Immediately post-device usage
    - Measure: Rating of device reliability, i.e. correct mechanical function to work as intended on global doctor satisfaction score.
- The clinical safety of the JSI.
    - Timepoint: Immediately post-intervention commencement through to final follow up visit.
    - Measure: Assessed using reported adverse events, device deficiencies and participant questionnaire.
- Time taken to insert the ureteric stent using JSI (measures stent insertion procedure time only, workflow data assesses overall workflow and will be assessed separately).
    - Timepoint: Immediately post-intervention commencement.
    - Measure: Use of stopwatch or calculated from start and end times and recorded on a

case report form.

- Feasibility- evaluation of participant recruitment rate.
    - Timepoint- At study completion. To be completed within 6 months of study commencement.
    - Measure: A log will be kept of all participants invited to the study and if applicable, their reasons for refusal noted. Feasibility will be assessed using recruitment/withdrawal data and an audit of study enrolment and withdrawal logs.
- Participant experience and satisfaction with the JSI.
    - Timepoint: Prior to stent insertion (within 2 hours), Post stent insertion (within 1 hour), and at follow up visit for definitive stone management surgery (within 14-21 days)
    - Measure: Participants will receive a Patient Satisfaction Questionnaire regarding their experience of ureteric stent insertion with the JiffyStent Inserter.
- User satisfaction for urological doctor/study researcher.
    - Timepoint- Immediately after stent-insertion.
    - Measure: Investigators will receive a User Questionnaire regarding their experience of using the JSI. Collated data will be analysed 3-6 months post-intervention commencement.
- Impact on workflow data
    - Measure: Analysis of improvements in workflow including time in the ED-SSU, total length of stay, time utilisation by urology doctors.
    - Timepoint: At follow up visit for definitive stone management surgery (within 14-21 days)
- Impact on health economics
    - Measure: Comparison of costings related to length of stay, admission, operating room utilisation, staffing, equipment.
    - Timepoint: At study completion. A health economist will be engaged to help perform the analysis.

9 OVERALL STUDY DESIGN

9.1 Study design

Single centre, first-in-human pilot study of a novel medical device. The study will involve two groups up to 15 participants under controlled conditions. Of the 15 total participants, five (5) will be individuals who require a stent as a standard part of their urological procedure (Group 1) and 5-10 participants will be individuals who present to the ED-SSU with acute renal colic from a kidney stone and require a ureteric stent insertion (Group 2).

- Participants requiring a stent as part of standard urological procedure will be placed under general anaesthetic

in the operating room as per standard of care. The ureteric stent will then be inserted using the JSI under standard controlled conditions.

- In participants who present to the emergency room, a stent will be inserted in the ED-SSU cubicle using the JSI by an experienced urological doctor who is skilled in inserting ureteric stents. Analgesia for the procedure will include the local topical anaesthetic gel (i.e. Instillagel®) injected into the urethra prior to device insertion and a Penthrox "green whistle" temporary inhaled anaesthetic. A post-stent insertion KUB X-ray will then be performed to confirm position of the stent.

9.2 Schedule of Assessment

Assessments	Screening *(Day -7 to Day 1)*	Procedure *(Day 1)*	Follow Up Visit *(14 to 21 Days Post Tx)*
Informed consent	X		
Inclusion/Exclusion Criteria	X		
Medical History	X		
Demographics	X		
CT Scan / MRI	X[a]		
KUB X-Ray		X[b]	
Renal Ultrasound		(X) [c]	
User Questionnaire		X[d]	
Participant Questionnaire		X[e]	X
Device Deficiencies		X	
Adverse Events	X	X	X
Concomitant Medications	X	X	X
Stone Management			X[f]

a. Prior imaging may be collected up to 30 days prior to treatment
b. Performed after stent insertion for confirmation of position of the stent.
c. If unable to confirm stent positioning via X-Ray, then proceed to perform renal ultrasound
d. Performed 'Immediately after stent-insertion'
e. Performed 'Prior Insertion' and 'Post Insertion'
f. As per standard practice

9.3 Informed Consent

Potential participants will be informed of the risks and requirements of the study, and during the study, participants will be given any new information that may affect their decision to continue participation. They will be told that their consent to participate in the study is voluntary and may be withdrawn at any time with no reason given and without penalty or loss of benefits to which they would otherwise be entitled. Only participants who are fully able to understand the risks, benefits and potential AEs of the study, and provide their consent voluntarily will be enrolled. Participants must sign an informed consent form (ICF). Where a subject is unable give informed consent, they will not be considered for inclusion in the study.

9.4 Inclusion criteria

1. Consenting adult participant male or female, age ≥ 18 years old.
2. Participant about to undergo stent insertion as part of their routine urological care or
3. Patient who has presented to the emergency department with acute renal colic requiring admission to hospital for a ureteric stent.
4. Ability to provide informed consent by study participant.
5. Willingness and ability to comply with study-related procedures/assessments.

9.5 Exclusion criteria

1. Age <18.
2. Known allergy to local anaesthetic lubricating gel, Penthrox “green whistle” inhaler anaesthetic.
3. Stone larger than 1cm.
4. Stone impacted in ureter.
5. Men with prostate larger than 100cc in size.
6. Participant with severe sepsis requiring nephrostomy or stabilisation in an operating room.

9.6 Representativeness of included population

The investigation population represents the intended target population in terms of age (adult population) and gender (any gender). Subjects about to undergo stent insertion as part of their routine urological care or have presented to the emergency department-short stay unit with acute renal colic requiring admission to hospital for a ureteric stent will be treated with the JSI. Therefore, the included population is considered a representative sample for the intended use of JSI.

9.7 Definition of enrolment

Time at which, following recruitment and before any clinical investigation-related procedures are undertaken, a participant who meets the eligibility criteria signs and dates the informed consent form.

9.8 End of treatment

The end of treatment is defined as the day the decision was made to permanently discontinue all study treatment and participant engagement. End of treatment is the date of final participant survey completion and definitive stone

management surgery (14-21 days post enrolment). Each participant will be followed through to the end of treatment, unless he/she has died or withdrawn consent, or the study is terminated.

9.9 Follow up phase

Participants will attend one follow-up visit which will occur approx. 14 to 21 days post-stent insertion with JiffyStent Inserter.

The following assessments will be performed:

- Completion of participant survey
- Definitive stone management surgery (Standard of Care)
- Recording adverse events (via medical record review and participant assessment)

Ongoing standard of care medical evaluation/follow up will continue at the site following final trial visit and follow up.

9.10 End of study

The clinical investigation will be considered complete six (6) months after the last participant is enrolled in the study.

9.11 Activities by sponsor representatives

Procedures related to the clinical investigation will be performed by the principal investigator, study coordinators, and/or other authorised study staff, as applicable. A sponsor representative may be present during investigational procedures for technical support.

The following activities are performed by the Sponsor and/or its representative:

- Provision of instructional advice regarding JSI set up, procedure, use and disposal.
- The sponsor and/or its representative will provide technical support only and will not physically partake in device use or implementation.
- Participants will be consulted, and verbal consent obtained prior to sponsor and/or it's representative entering participant and treatment location.

9.12 Potential confounding factors

Potential confounding factors that may compromise the outcome of the clinical investigation include:

- Misuse of the device by the investigator.
- Misevaluation of the eligibility criteria by the investigator.
- Misevaluation of SAE in relation to the device by the investigator.

As to minimise these potential confounding factors, appropriate control measures are implemented by design and with the investigators before the study start and carefully monitored throughout the study.

9.13 Monitoring plan

Avania (Contract Research Organization (CRO)) has designed and implemented a comprehensive monitoring plan. This plan is essential to ensure that the trial adheres to ethical and regulatory standards, maintains data integrity, and ultimately generates reliable results. The CRO will perform a risk assessment to identify potential challenges and risks associated with the trial. Based on this assessment, Avania has designed a monitoring strategy that includes the frequency and type of site visits. In a pilot trial, close monitoring is essential to evaluate the trial's feasibility, identify operational issues, and ensure participant safety. The CRO's monitoring team will conduct both remote and on-site visits to assess source data verification, informed consent processes, and compliance with the study protocol. The CRO will ensure proper documentation, data accuracy, and timely query resolution. The CRO will outline the qualifications and responsibilities of the monitors, as well as the communication and reporting mechanisms to keep all stakeholders informed of trial progress.

10 ETHICS

10.1 Guiding Principles

This study is to be performed in accordance with the ethical principles of the Declaration of Helsinki (June 1964 and amended 1975, 1983, 1989, 1996, 2000, 2008 and Note of Clarification 2002 and 2004), ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95) annotated with Therapeutic Goods Administration comments, NHMRC National Statement on Ethical Conduct in Research Involving Humans 2007 (Updated 2018) and ICH GCP Notes for Guidance on Good Clinical Practice (CPMP/ICH/135/95).

10.2 Ethical considerations of recruitment

All potential participants in this study will be adults over 18 years of age, sound of mind, and able to be fully informed of the requirements and risks of the study. Participants presenting to the ED-SSU unit may be experiencing pain and the hope of having this pain relieved immediately might limit their ability to comprehend the risks, although they be minimal, involved in taking part in this study. Doctors in urology are skilled at managing patients under extreme stress such as those suffering renal colic or prior to surgery. Careful consideration will be given to ensuring that patients understand that their immediate pain relief is of utmost importance and not related to their participation in the study.

10.3 Ethical considerations of consent

The ethical considerations related to consent will be minimal in this project. This is primarily because eligible participants all require a ureteric stent. This stent can be inserted with the JSI or by the standard procedure in an operating room. Therefore, the consent is no different to the usual consent process for having a stent inserted apart from the fact that this is a new technique with a novel medical device. Only fully informed participant who can understand English or have it carefully explained to them by an interpreter we be eligible to participate in the study. There are no cultural issues that may affect this consent process.

10.4 Management of participant's expectation of the perceived benefit of participating in the research

Participants expectations will be managed by a careful and adequate fully informed consent process. This will involve explaining to the participant that the JSI is currently an experimental medical device. They will be informed that the insertion of a correctly placed stent is identical to that achieved by the standard procedure in an operating room. It will also be explained that we expect there to be a 5 to 10% failure rate that will require going to theatre for insertion of a stent via the standard procedure. It will also be carefully explained that there is a risk of incorrect placement and potential damage to the ureter that maybe more easily recognised in the operating room with the benefit of real-time image intensifier X-ray.

10.5 Ethical considerations relating to the collection and/or use of the information/data in this project

Participants will be allocated a unique study number. The site research coordinator will compile an enrolment log, including the participant's name, date of birth, hospital identification number, unique study number and date and time of procedure. Subsequent data will be identified by the unique study number only. The enrolment log and study data will be kept separately. Study data will be entered into a password protected REDCap database managed by the principal investigator. No identifying data will be entered into the database.

Similarly, hard copies of study data collected on paper source worksheets will be stored separately in the locked office of the principal investigator. Only the PI and research team will have access to this information, and they will not disclose this information to any other person or entity.

When archiving, the study site investigator will take all appropriate measures to safeguard and prevent access to this data by any unauthorised third party.

The investigator will maintain the confidentiality of all study documentation and take measures to prevent accidental or premature destruction of these documents. The investigator will retain the study documents at least 15 years after

the completion or discontinuation of the study. The investigator must notify the study management committee prior to destroying any essential study documents following the study completion or discontinuation.

If any investigator retires, relocates, or otherwise withdraws from conducting a study, the responsibility for maintaining records may be transferred to the coordinating centre or another investigator. The coordinating centre must be notified of and agree to the change. All associated documentation must also be updated.

Austin Health medical records will be approached to allow the investigators access to electronic medical records of participants. We aim to have this permission granted as soon as possible. Medical records will be accessed to collect data regarding the participant's previous medical treatments in Austin Health.

10.6 Confidentiality of participant data

Participant confidentiality will be maintained throughout the clinical investigation in a way that ensures the information can always be tracked back to the source data. For this purpose, a unique participant identification code will be used that allows identification of all data reported for each participant. Data relating to the clinical investigation might be made available to third parties (for example in case of an audit performed by regulatory authorities) provided the data are treated confidentially and that the participant’s privacy is guaranteed.

When archiving, the study site investigators will take all appropriate measures to safeguard and prevent access to this data by any unauthorised third party. The investigator will maintain the confidentiality of all study documentation and take measures to prevent accidental or premature destruction of these documents. The investigator will retain the study documents at least 15 years after the completion or discontinuation of the study. The investigator must notify the study management committee prior to destroying any essential study documents following the study completion or discontinuation.

If any investigator retires, relocates, or otherwise withdraws from conducting a study, the responsibility for maintaining records may be transferred to the coordinating centre or another investigator. The coordinating centre must be notified of and agree to the change. All associated documentation must also be updated

10.7 Ethics Committee Approval

The trial site will submit this protocol and any other relevant study documentation to the responsible local or national constituted Human Research and Ethics Committee (or equivalent). Approval of the protocol plans for obtaining consent and related documents will be obtained prior to the start of the study at the site. It is the principal investigator’s responsibility to ensure that all conditions for approval of the study are met and that amendments to

the protocol or serious adverse events are also reported to the HREC (or equivalent) as required by that committee

11 RISKS AND BENEFITS OF THE INVESTIGATIONAL DEVICE, CLINICAL PROCEDURE AND CLINICAL INVESTIGATION

11.1 Anticipated clinical benefits

The JiffyStent Inserter is a new medical technology which inserts a standard ureteric stent into the ureter of a participant with acute renal colic without the need for an operating theatre. The JSI proposes multiple benefits including:

- Reduced time to stent insertion.
- Less pain for the participant
- Less pain management required.
- Eliminates need for general anaesthetic.
- Reduced length of stay
- Reduced use of resources – operating room, anaesthetist, radiologist, urologist time.
- Improved workflow with less disruption to normal surgical activities
- Reduced cost of inserting ureteric stents in suitable participant

11.2 Anticipated adverse device effects

The JSI is a new medical technology which inserts a standard ureteric stent into the ureter of a participant with acute renal colic. The risks of inserting the stent with the JSI are similar to those experienced during the standard stent insertion procedure in an operating room.

11.2.1 Clinical risks

Hazard	Risk	Mitigation and residual risk
Guidewire perforates the ureter which is unrecognised while using the device. **Probability: Likely** **Severity: Serious** **See Appendix A for scores at bottom of sheet**	The stent will be inserted outside of the ureter. Consequences: Obstruction not relieved Pain not relieved Increased risk of infection Risk of long-term ureteric stricture The risk of a 1.67 millimetre diameter hole in the ureter is minimal. There is a small risk of long-term ureteric stricture which may be related to the perforation or more likely the impacted stone causing inflammation and scarring at this point in the ureter. Despite optimal conditions, this can sometimes happen during the standard procedure in an operating room but may be recognised with the benefit of the in-theatre imaging intensifier X ray machine.	A post-stent insertion KUB X-ray will be performed to confirm position of stent. Patients with incorrectly placed stents will be taken to the operating room for removal of the stent and insertion of a new stent under image intensifier guidance.
Guidewire does a U-turn in the ureter **Probability: Possible** **Severity: minor**	The stent will be in the ureter below the level of obstruction. Consequences: Obstruction not relieved Pain not relieved This will cause no permanent harm to the participant.	A post-stent insertion KUB X-ray will be performed to confirm position of stent. This risk can be mitigated by careful participant selection as per our indications of a stone <1cm in size and in stones that are not impacted. Participants with incorrectly placed stents will be taken to the operating room for removal of the stent and insertion of a new stent under image intensifier guidance.

Use of JiffyStent Inserter or insertion of stent causes pain or discomfort **Probability: Almost Certain** **Severity: Serious**	Participant discomfort or pain in urethra or bladder due to insertion of JSI into the bladder without general anaesthetic. Patient discomfort or pain in flank or abdomen due to the insertion of the stent up the ureter.	Readily available local anaesthetic gel and lubricating jelly inserted into the urethra prior to insertion of the device. Further analgesia may include Penthrox green whistle device, oral medications, or intravenous medications such as midazolam, fentanyl, or ketamine.
Participant infection **Probability: Possible** **Severity: Serious**	Patient develops a urinary tract infection related to the use of the device. This risk should be no greater than the usual risks of infection with the standard procedure in the operating room.	Standard sterile preparation and drape as per usual set up prior to insertion of a urinary catheter. Single dose of oral or intravenous antibiotics could be given at the time of the device use and stent insertion.
Patient experiences blood in urine. **Probability: Likely** **Severity: Serious**	Patient may experience blood in urine following use of device and insertion of stent. This is usually mild and self-limiting. In very rare instances it can be very heavy bleeding with clots that may require admission to hospital and further operations. This risk should be no greater with use of the device compared to standard procedure in an operating room.	Appropriately qualified doctor performing the procedure. Fully informed consent regarding possibility of blood in urine after procedure. Good instructions to participant about staying well hydrated following the procedure and represent to the hospital or contact their doctor if heavy bleeding persists.
Stent migration **Probability: unlikely** **Severity: Serious**	The stent may migrate after initial correct positioning. This risk is unchanged from the standard procedure when inserted in an operating room.	Routine post stent insertion follow-up includes proceeding to definitive management of the stone or possibly a repeat CT of the ureter to see if the stone has passed spontaneously.
Stone formation on stent. **Probability: Possible** **Severity: Serious**	Stones may form on stents in the urinary tract if left for a prolonged time or in rapid stone formers. This risk is unchanged from the standard procedure of inserting the stent in the operating room.	Routine follow-up of a stent insertion includes proceeding to definitive management of the stone or possibly a repeat CT of the ureter to see if the stone has passed spontaneously.
Forgotten stent. **Probability: Possible** **Severity: Serious**	Stent is left in the body and participant forgets or is not invited back for definitive management of stone. Stent can become heavily encrusted requiring complex and sometimes invasive surgery to remove. This risk is only slightly greater than if performed in an operating room due to	Adequate routine follow-up for definitive management of stone within an acceptable time period. The JiffyStent Inserter packaging will include a participant information sheet reminding them of the need for definitive follow-up of their kidney stone. Ultimately, there may be an

	the usual safeguards to ensure adequate follow-up for admitted participants coming through the operating room.	app that could generate an e-mail and follow up or communication with the hospital emergency medical record to ensure definitive management of the stone and the stent is not forgotten.
Ureteric orifice cannot be seen **Probability: Unlikely** **Severity: Minor**	Ureteric orifice may not be seen due to excessive bleeding, a very large prostate, or failure to be able to visualize the ureteric orifice within the bladder due to abnormal anatomy or user inexperience. Stent unable to be deployed. No harm to participant apart from slight increased risk of infection and participant discomfort associated with procedure.	Indications for device use include prostates smaller than 100g in size or without a large medium lobe. Device will be designed to ensure that there is adequate flow to ensure good vision through the camera. Adequate online training modules to help non-urologists identify the ureteric orifice. If unable to find ureteric orifice, then JiffyStent Inserter can be removed with minimal harm to participant. Procedure abandoned and take to theatre as per standard procedure for removal of stent and insertion of new stent.

11.2.2 Device Mechanical Risks

Hazard	Risk	Mitigation and residual risk
Device failure or Spools get jammed and fail to work correctly- no stent inserted **Probability: Possible** **Severity: negligible**	Stent is unable to be inserted. Minimal harm to participant.	Quality design and manufacture processes and strict adherence to best practice QMS. Procedure abandoned and take to theatre as per standard procedure for stent insertion.
Spools get jammed and fail to work correctly- partial stent insertion **Probability: Possible** **Severity: minor**	Procedure not completed successfully. Stent half hanging out and may be across urinary sphincter leading to temporary incontinence.	Quality design and manufacture processes and strict adherence to best practice QMS. Procedure abandoned and take to theatre as per standard procedure for removal of stent and insertion of new stent.

Incorrect guidewire length set-too long **Probability: Possible** **Severity: serious**	Guidewire inserts too far. Usually, guidewire has floppy end that will curl up in collecting system of kidney. Stent still inserted correctly. Very rarely, guidewire will pierce top of kidney collecting system and stent may be inserted outside of kidney.	Device has a failproof stop so that the guidewire cannot be inserted more than 33cm. We will use a guidewire with a 3cm floppy tip that will curl if it hits end of collecting system. Device has variable length settings for shorter ureters. These will be related to the height of participant and clearly marked on the device. instructional online video will provide education around ureteric length determination. In the case of no length being set, the guard wire will be limited at 33 centimetres which will be safe in nearly all instances. Post procedure KUB X-ray will confirm correct position of upper end of stent within the kidney collecting system.
Incorrect guidewire length set-too short **Probability: Possible** **Severity: serious**	Guidewire does not insert far enough. This might cause the stent to curl inferior to the renal stone or pelvis. This may be below the level of the stone and therefore the obstruction is not relieved, and participant's pain is not relieved.	A post-stent insertion KUB X-ray will be performed to confirm position of stent. Participants with incorrectly placed stents will be taken to the operating room for removal of the stent and insertion of a new stent under image intensifier guidance.

11.2.3 Device Electrical Risks

Hazard	Risk	Mitigation and residual risk
Smart device will not connect with JiffyStent Inserter Wi-Fi **Probability: Possible** **Severity: negligible**	Procedure cannot be commenced. No harm to participant.	Quality design and manufacture principles of board and WIFI components. Extensive mechanical, electrical and aging/transport testing. participant goes to theatre for standard procedure. Careful instructions on smart devices that can be used with device.

Smart device disconnects from JiffyStent Inserter Wi-Fi **Probability: Possible** **Severity: negligible**	Procedure cannot be completed. Minimal harm to participant. Financial risk with single use device.	Quality design and manufacture principles of board and WIFI components. Extensive mechanical, electrical and aging/transport testing. Device can be removed without injury to participant. If stent is partially deployed, it can be removed or if in urethra then the only downside is temporary incontinence. Participant taken to theatre for stent removal and insertion of new stent.
Battery runs out on JiffyStent Inserter **Probability: Possible** **Severity: negligible**	Loss of vision on smart device screen. No harm to patient. Financial risk with single use device.	Device can be removed without injury to patient. If stent is partially deployed, it can be removed or if in urethra then the only downside is temporary incontinence. Patient taken to theatre for stent removal and insertion of new stent. Battery will have a minimum 30 min run time. This would be considered well beyond a reasonable time to successfully complete a stent insertion outside of the operating room.
Smart device runs out of battery during procedure **Probability: Possible** **Severity: minor**	loss of vision on smart device screen. No harm to participant. Financial risk with single use device.	Educational material and online course could state the importance of having adequate battery life before commencing procedure. Replace battery or replace device or take to operating room as per standard procedure.
LED lights fail to illuminate **Probability: Possible** **Severity: minor**	Procedure cannot be started or completed. Minimal harm to participant. Financial risk with single use device.	Quality design and manufacture principles of board and WIFI components. Extensive mechanical, electrical and aging/transport testing. Device can be removed without injury to participant. If stent is partially deployed, it can be removed or if in urethra then the only downside is temporary incontinence. Participant taken to theatre for stent removal and insertion of new stent.
Camera does not work. **Probability: Possible** **Severity: minor**	Procedure cannot be started or completed. No to minimal harm to participant. Financial risk with single use device.	Quality design and manufacture principles of board and WIFI components. Extensive mechanical, electrical and aging/transport testing. Device can be removed without injury to participant. If stent is partially deployed, it can be removed or if in urethra then the only downside is temporary incontinence. Participant taken to theatre for stent removal and insertion of new stent.

		Use new device or take to operating room as per standard procedure.
Electronic board faults **Probability: Possible** **Severity: minor**	Procedure cannot be started or completed. No to minimal harm to participant. Financial risk with single use device.	Use new device or take to operating room as per standard procedure.
Battery faults **Probability: Possible** **Severity: minor**	Procedure cannot be started or completed. No to minimal harm to participant. Financial risk with single use device.	Use new device or take to operating room as per standard procedure.
Privacy of Wi-Fi connection. **Probability: Unlikely** **Severity: serious**	Participant's face and or genitals may be seen before inserting proboscis. Minimal risk of identification or harm once inside bladder.	Extremely private and secure connection that cannot be viewed by anyone else. De-identified so minimal harm of view of inside of bladder. No data is transmitted. Video is only real-time and not recorded or saved. Only one connection can be made to Wi-Fi.
Smart device image quality unsuitable for successfully complete procedure **Probability: possible** **Severity: minor**	Smart device screen resolution or image is too poor to identify ureteric orifice. Procedure cannot be completed due to poor image. Minimal harm to participant.	Online module educational material will cover the specs of suitable smart devices. Swap to suitable smart device. Device can be removed without insertion of stent and participant taken to theatre for standard insertion of stent procedure.

Appendix A: Risk Score Matrix

Probability Scorings:		
No.	**Harm**	**Value**
Almost Certain	100%	5
Likely	10%	4
Possible	1%	3

Unlikely	0.10%	2
Rare	0.01%	1

Severity:		
Rating	**Definition**	**Value**
Catastrophic	Results in death	5
Critical	Results in permanent impairment or life-threatening injury	4
Serious	Results in injury or impairment requiring professional medical intervention	3
Minor	Results in temporary injury or impairment not requiring professional medical intervention	2
Negligible	Inconvenience or temporary discomfort	1

11.3 Risks associated with participation in the clinical investigation

The risks that are anticipated for participation in the clinical investigation are:

- Anticipated adverse device effect for the use of JSI as provided in Section 11.2.2 and 11.2.3
- Procedure related adverse events are similar to the standard of care as provided in Section 11.2.1
- There are no known possible interactions between the use of the JSI and concomitant medical treatments

11.4 Risk mitigation

The potential risks associated with the use of JSI have been identified in the Risk Assessment Report in Section 11.2. Potential risks were mitigated to an acceptable level through verification testing, validation activities, inclusion of warning/precautions in the IFU, instructional materials, and healthcare professional training. Where possible, design verification, design validation, process verification, and process validation activities were conducted to further mitigate risks. Any residual risks were documented in the Risk Benefit Analysis, which declared that the potential benefits of the JSI outweigh the risks. Furthermore, potential risks associated with participation in this investigation will be minimised and managed in accordance with ISO 14155:2020, and requirements of the approving Ethics Committee(s).

11.5 Benefit-risk rationale

JiffyStent Pty Ltd believes that any potential risk presented by this clinical investigation has been minimised and that adequate testing, safeguards, and safety monitoring have been incorporated into the clinical investigation to further minimise and mitigate the risks. JiffyStent Pty Ltd believes that the benefits of the JSI outweigh the potential risks posed to participating subjects.

This clinical investigation has been designed to involve as little pain, discomfort, fear and any other foreseeable risks as possible of the subjects. The risk threshold and the degree of distress are mitigated to as low as possible and is monitored throughout the clinical investigation (see Section 14). Overall, risk management activities shall be performed throughout the clinical investigation. The risk management approach is provided in the Risk Management Plan < Risk assessment TDRA-20100109-01_00.docx>

12 PARTICIPANT DISCONTINUATION/WITHDRAWAL

A participant will be discontinued from the study for any of the following reasons:

- Withdrawal of consent
- Lost to follow-up (LTFU)

When a participant withdraws before study completion, the reason for withdrawal is to be documented in both the

eCRF and in the source document. If the reason for withdrawal from the study is withdrawal of consent, then no additional study assessments are allowed. In the situation where a study participant has an indwelling ureteric stent, arrangements will be made for the participants to return to the study site for definitive stone management and stent removal.

12.1 Withdrawal of consent

A participant may withdraw from the study at any time at his/her or own request or may be withdrawn at any time at the discretion of the investigator for safety behavioural compliance or administrative reasons. This is expected to be uncommon.

If a participant notifies an investigator that he/she would like to withdraw consent from the study, the investigator should discuss any potential medical risks of withdrawal and must schedule definitive stone management surgery and stent removal (if required), and ongoing medical evaluation/follow up at site.

If the participant withdraws consent for disclosure of future information, the sponsor may retain and continue to use any data collected before such a withdrawal of consent.

When a participant withdraws before study completion the reason for withdrawal is to be documented in the eCRF and in the source document. If the reason for withdrawal from the study is withdrawal of consent, then no additional assessments are allowed. If a participant withdraws the subject can be replaced to achieve targeted enrolment numbers.

12.2 Lost to follow up

A participant will be considered LTFU if he or she repeatedly fails to return for protocol-specified scheduled visits and is unable to be contacted by the study site. A participant cannot be deemed LTFU until all reasonable efforts made by the study site personnel to contact the participants are deemed futile. Should the participant continue to be unreachable, they will be considered LTFU and withdrawn from the study. If a participant is withdrawn the subject can be replaced to achieve targeted enrolment numbers.

12.3 Procedure for the replacement of subjects

Participants who screen fail are not considered enrolled in the study, therefore do not count towards the maximum total enrolment. Participants who are enrolled and treated in the study but withdraw their consent will not be replaced. Replacement subjects will be screened and recruited as outlined in Section 9.

13 DATA MANAGEMENT

13.1 Procedures for verification, validation and securing of electronic clinical data systems

Data will be collected and recorded using a validated EDC system that meets all requirements as set forth in the TGA guidelines and ISO standards. An audit trail is available for tracking all information that the EDC user enters, modifies or deletes.

13.2 Data entry and collection

All data will be collected by trained staff from all study procedures and assessments and documented on the appropriate Case Report Forms (CRFs) for the study. Data collection will be restricted primarily to those variables necessary to define clinical participant characteristics including baseline demographics, primary diagnoses, physiological parameters, therapeutic interventions and documentation of adverse events.

13.3 Case report forms

The investigators shall ensure the accuracy, completeness, legibility and timelines of the data reported in eCRF and in all required documentation. Data reported on the eCRF shall be supported by the source documents with any discrepancies being explained. Any corrections made to documents will be done according to ISO 14155:2020. If an item is not available or is not applicable, this fact should be indicated; no space is to be left blank. The investigator who has signed the clinical investigation plan signature page or his/her authorised designee is to personally sign the eCRFs to validate that the observations and findings are recorded on the eCRFs correctly and completely. The eCRFs are to be completed in a timely manner after the subject's visit. Failure to meet the documentation requirements may lead to the disqualification of an investigator.

13.4 Data retention

The investigator maintains all clinical investigation records for the minimum time required in the country in which the clinical investigation is conducted (Australia). Records to be retained may include: all correspondence, documentation of device receipt and disposition, each subject's case history and record of exposure to the device, the clinical investigation plan and amendments, Investigator Brochure, and dates and reasons for any deviations to the clinical investigation plan or as otherwise specified by the applicable laws and regulations.
Furthermore, the documentation will be kept by JiffyStent Pty Ltd for a period of at least 15 years after the clinical investigation with the device in question has ended, or, if the device is subsequently placed on the market, at least 10 years after the last device has been placed on the market.

13.5 Data variables collected

Data collection will include:

13.5.1 Participant demographics

- Participant unique identifier number (UIN)
- Age (years)
- Sex (Male/Female)
- Indication for stent insertion
- Stone characteristics
    - Size (in mm)
    - Position (Proximal/Mid/Distal ureter)
    - Estimated length of participant's ureter from imaging (in cms)
- Past Urological History including Past stent insertions (& ease), past stones and previous procedures (collected via medical history review and participant assessment).

13.5.2 Procedure Information

- Device serial number
- Duration of procedure (mins:secs) including:
    - Set-up time (opening sterile JSI packaging to the connection of the sterile saline IV to JSI)
    - Instrumentation time (time from insertion to removal of JSI)
- Environment procedure performed in
- Equipment utilised
- Guidewire setting length

13.5.3 Investigator Experience

- Rate each of the following (1-5) upon ease of
    - Opening of sterile package
    - Setting of estimated ureter length on guidewire spool using adjustable pin
    - Loading of ureteric stent onto guidewire and into ready position (including use of provided pusher)
    - Winding action of guidewire spool
    - Connection of JSI to Smart device utilising QR codes
    - Visual/connection quality of Smart device video feed
    - Connection of irrigation fluids
    - Ergonomics of JSI insertion into urethra
    - Insertion of JSI into urethra
    - Aligning guidewire with desired ureteric orifice
    - Advancement of guidewire & stent along ureter to desired position
    - Ability to maintain visualisation of ureteric orifice during GW advancement & retraction
    - Disconnection of stent
    - Removal of JSI from urethra

- Analgesia/sedation utilised.
- Perceived participant tolerance of procedure (very poorly, poorly, tolerated, well tolerated)
- Difficulties encountered.
- Complications
- Overall rating of JSI procedure
- Other comments

13.5.4 Participant experience

- Measurement of pain before during and after treatment
- Rate of experience and satisfaction
- Other comments

13.6 Source data requirements

The investigator or its delegate will perform primary data collection drawn from original documents (printed, optical or electronic document containing source data). Data to be collected for purposes of the clinical investigation must not be entered directly into the eCRF before being recorded first in the source documents. All source documentation must be available for review by the study monitor during monitor visits. Source data is defined as all information in original records, certified copies of original records of clinical findings, observations, or other activities in a clinical investigation, necessary for the reconstruction and evaluation of the clinical investigation. This includes source data initially recorded in an electronic format.

13.7 Data quality and monitoring

Several procedures to ensure data quality and protocol standardisation will help to minimise bias and to optimise data quality. These include:

- Study design
- Use of specific inclusion and exclusion criteria
- A site initiation training will be conducted before the start of the trial to ensure consistency in procedures.
- A detailed data dictionary will define the data to be collected and entered into the eCRF
- The management committee will perform timely validation of data entered into the eCRF, queries and corrections.

The sponsor will use a combination of monitoring techniques: central, remote, or on-site monitoring, to monitor this study. The sponsor will perform on site monitoring visits as frequently as necessary. The monitor will record dates of the visit in a study visit log that will be kept at the study site stop direct access to source documents (medical records) must be allowed for the purpose of verifying that the recorded data are consistent with the original source data.

Findings from this review will be discussed with the study site personnel. The sponsor expects that, during monitoring visits, the relevant study site personnel will be available, the source documents will be accessible, and a suitable environment will be provided for review of study related documents. The monitor will meet with the investigator on a regular basis during the study to provide feedback on the study conduct.

14 STATISTICAL CONSIDERATIONS

14.1 Power calculation and sample size

This is a first-in-human, proof-of-principle pilot study to determine feasibility of a human trial therefore, analysis of the study endpoints will be done using descriptive statistics. Descriptive statistical variables will include the mean (with two-sided 95% confidence intervals), standard deviation, median, minimum, and maximum for continuous variables and frequency and percentage (with two-sided exact 97%confidence intervals) for categorical variables. Descriptive tables will be produced for baseline characteristics including demographics and medical history, procedure, adverse events, medications, physical exams, protocol deviations and outcomes The study has an exploratory nature and, as such, no formal sample size estimation has been performed. A sample size of 5-15 participants is expected to provide meaningful data for future design and development considerations.

14.2 Statistical Design & Methods

This study has a single arm design in which all participants followed will have received a JiffyStent Inserter treatment. Participants will be unblinded to their treatment, and no participants will be randomised to a parallel group receiving a control treatment.

14.3 Analysis of the primary endpoint

Correct placement of the stent into the ureter as visualised on KUB plain x-ray post procedure.

14.4 Analysis of the secondary endpoints

- The mechanical reliability of the JSI to perform its function as expected.
- The clinical safety of the JSI
- Time taken to insert the ureteric stent using JSI
- Feasibility- evaluation of participant recruitment rate
- Participant experience and satisfaction with the JSI
- User satisfaction for urological doctor/study researcher.
- Engagement and acceptability to surgical, medical and nursing hospital staff

- Impact on workflow data
- Impact on health economics

14.5 Analysis Populations

Analysis of the primary objective will be conducted using the intent-to-treat sample including all participants treated with the JSI.

14.6 Statistical Deviations

Any post-hoc, or unplanned, analyses not identified in this CIP or in the SAP will be clearly identified in the clinical investigation report.

14.7 Interim Analysis

No interim analyses are planned for this clinical investigation.

14.8 Missing Data

Every effort will be made to collect all data points in the study. The Sponsor plans to minimise the amount of missing data by appropriate management of the prospective clinical study, proper screening of study participants, and training of participating investigators, monitors and study coordinators. All partial data that is available on participants who drop out during the course of the study will be included. No imputation will be performed for study outcomes.

15 SAFETY MONITORING AND REPORTING

15.1 Definitions

15.1.1 Adverse event (AE)

An adverse event is any untoward medical occurrence in a clinical trial participant undergoing a medical procedure that does not necessarily have a causal relationship with this treatment. These will not necessarily constitute an adverse event unless they are considered to be of concern or related to the study or the intervention in the investigator's clinical judgement. In all cases, the condition or disease underlying the symptom, sign or laboratory value should be reported.

15.1.2 *Adverse device effect (ADE)*

An adverse device effect is defined as an AE related to the use of an investigational medical device. This definition includes any adverse event resulting from insufficiencies or inadequacies in the instructions for use, the deployment, the implantation, the installation, the operation, or any malfunction of the investigational medical device as well as

any event that is a result of a use error or intentional misuse.

15.1.3 Serious adverse events (SAE)

Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigation plan, without serious deterioration in health, is not considered a serious adverse event.

A serious adverse event (SAE) or serious adverse reaction is defined as any adverse event/reaction that:

- Results in death
- Is life-threatening.
- Requires hospitalization or prolongation of current hospitalization.
- Results in persistent or significant disability or incapacity

Medical and scientific judgement will be exercised by the principal investigator in deciding whether an adverse event/ reaction will be classified as serious.

15.1.4 Device deficiency (DD)

A device deficiency is defined as an inadequacy in the identity, quality, durability, reliability, safety, or performance of an investigational device. Device deficiencies include malfunctions, use errors, or inadequacy in information supplied by the manufacturer, including labelling.

15.1.5 Serious Adverse Device Effect (SADE)

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

15.1.6 Unanticipated Serious Adverse Device Effect (USADE)

An unanticipated serious adverse device effect is a serious adverse device effect which by its nature, incidence, severity, or outcome has not been identified in the current risk assessment.

15.1.7 Significant Safety Issue (SSI)

SSI is defined by the NHMRC (2016) Guidance on safety monitoring and reporting in clinical trials involving therapeutic goods as:

A safety issue that could adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial.

15.1.8 Urgent Safety Measure (USM)

USM is defined by the NHMRC (2016) Guidance on safety monitoring and reporting in clinical trials involving therapeutic goods as:

A measure required to be taken to eliminate an immediate hazard to a participant's health or safety.

Note: This type of significant safety issue can be instigated by either the investigator or Sponsor and can be implemented before seeking approval from the Ethics Committee(s) or institutions.

15.2 Non-reportable adverse events

There are no non-reportable adverse events.

15.3 Causality

Each (serious) adverse event will be classified according to 4 different levels of causality:

- Unrelated
- Possibly
- Probably
- Definitively related

The Sponsor and the investigators will use the following definitions to assess the relationship of the (serious) adverse event to the investigational device or the investigation procedure.

Not related: relationship to the device, comparator or procedures can be excluded when:

- the event has no temporal relationship with the use of the investigational device or the procedures to application of the investigation device
- the (serious) adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible
- the discontinuation of medical device application or the reduction of the level of activation/exposure – when clinically feasible – and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event
- the event involves a body-site or an organ that cannot be affected
- the (serious) adverse event can be attributed to another cause (e.g., an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment, or other risk factors)
- harms to the participant are not clearly due to use error

Possibly: the relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

Probably: the relationship with the use of the investigational device or comparator, or the relationship with procedures, seems relevant and/or the event cannot reasonably be explained by another cause.

Definitely Related: the (serious) adverse event is associated with the investigational device, comparator, or with

procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures
- the event has a temporal relationship with investigational device use/application or procedures
- the event involves a body-site or organ that:
    - the investigational device or procedures are applied to
    - the investigational device or procedures have an effect on
- the event follows a known response pattern to the medical device (if the response pattern is previously known)
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious event (when clinically feasible)
- other possible causes (e.g., an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug, or treatment) have been adequately ruled out
- harm to the participant is due to error in use
- the event depends on a false result given by the investigational device used for diagnosis, when applicable

In order to establish the relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the serious event.

The Sponsor and the investigators will distinguish between the (serious) adverse events related to the investigational device and those related to the procedures (any procedure specific to the clinical investigation). An adverse event can be related both to procedure and the investigational device. Complications caused by concomitant treatments not imposed by the clinical investigation plan are considered not related. Similarly, several routine diagnostic or patient management procedures are applied to patients regardless of the clinical investigation plan. If routine procedures are not imposed by the clinical investigation plan, complications caused by them are also considered not related.

In some particular cases the event may be not adequately assessed because information is insufficient or contradictory and/or the data cannot be verified or supplemented. The Sponsor and the investigators will make the maximum effort to define and categorize the event and avoid these situations. Where an investigator assessment is not available and/or the Sponsor remains uncertain about classifying the (serious) adverse event, the sponsor should not exclude the relatedness; the event should be classified as “possible” and the reporting not be delayed.

Particular attention shall be given to the causality evaluation of unanticipated serious adverse events. The occurrence of unanticipated events related to the use of the device could suggest that the clinical investigation places subjects at increased risk of harm than was to be expected beforehand.

15.4 Severity

Each (serious) adverse event will be classified according to three (3) levels of severity. The Sponsor and the

investigators will use the following definitions to assess the severity of the (serious) adverse event:

Mild: Awareness of signs or symptoms, but easily tolerated and are of minor irritant type causing no loss of time from normal activities. Symptoms do not require therapy or a medical evaluation; signs and symptoms are transient.
Moderate: Events introduce a low level of inconvenience or concern to the participant and may interfere with daily activities, but are usually improved by simple therapeutic measures; moderate experiences may cause some interference with functioning.
Severe: Events interrupt the participant's normal daily activities and generally require systemic drug therapy or other treatment; they are usually incapacitating

15.5 Reporting Requirements

15.5.1 Reporting (Serious) Adverse Events

Adverse event reporting will start at the time of signing consent. Underlying diseases are not reported as adverse events, but any deterioration in severity will be reported.
Adverse event information will be collected for all participants. At every participant visit, the investigator will determine whether an adverse event has occurred since the last visit. All adverse events will be reported in the CRF. The date of the initial event and the subsequent treatment will be documented.

The Investigator will be required to report any and all Serious Adverse Events (SAEs) that occur throughout the course of the study, regardless of causality or expectedness, to the Sponsor or designee within 24 hours of knowledge of the event.

Minimum information on the case report form will include:

- Participant initials and study number
- Nature of the event
- Commencement and cessation of the event
- An investigator's opinion of the relationship between study involvement and the event (unrelated, possibly, probably or definitively related).
- Whether treatment was required for the event and what treatment was administered.

The Sponsor is responsible to assess whether the SAE meets requirements for expedited reporting.

15.5.2 Reporting Device Deficiencies

All device deficiencies related to the identity, quality, durability, reliability, safety, or performance of an investigational

medical device shall be documented throughout the clinical investigation and appropriately managed by the Sponsor. For device deficiencies the investigator will describe any action other than any corrective or remedial actions taken to prevent recurrence of the deficiency. A remedial action is any action other than routine maintenance or servicing of a medical device where such action is necessary to prevent recurrence of a device deficiency. This includes any amendment to the device design to prevent recurrence.

15.6 Expedited Reporting

15.6.1 Unexpected Serious Adverse Device Effects (USADEs)

The Sponsor is responsible for assessing safety information received from Investigators and must reporting all fatal or life threatening USADEs to the HREC and the TGA no later than 7 calendar days after being made aware of the case. Any follow-up information must be supplied within a further 8 calendar days.

For all other USADEs that are not fatal or life-threatening, the HREC and the TGA must be notified by the Sponsor no later than 15 calendar days after being made aware of the case.

15.6.2 Significant Safety Issues (SSI)

The Sponsor must notify the TGA, the HREC and Investigators of all significant safety issues (SSI) that adversely affect the safety of participants or materially impact on the continued ethical acceptability or conduct of the trial within 15 calendar days of the Sponsor being made aware of the issue.

15.6.3 Urgent Safety Measure (USM)

The Sponsor must notify the TGA, the HREC and Investigators of all significant safety issues (SSI) that meet the definition of an urgent safety measure (USM) as soon as possible but must be within 72 hours.

15.7 Emergency Contacts:

Emergency contact details for the reporting of SAEs, device deficiencies, SADEs and USADEs are as follows:

	Sponsor	**Avania Pty Ltd**
Name	Cara Webb	Flora Yuen
Position	Clinical Trial Coordinator	Project Manager
Email	cara@jiffystent.com	flora.yuen@avaniaclinical.com
Phone	+61 3 409 704 857	+61 2 9460 6688 ext 3030

15.8 Safety Data Monitoring Committee

An independent Safety Data Monitoring Committee (SDMC) will be established to assess study outcome and safety

data at periodic points during study enrolment and recommend if the study should be continued, revised or closed. These reviews will provide assurance that the product is safe for use and will support continued investigation of the JSI. The SDMC will be compromised of group of independent medical clinicians and a biostatistician. SDMC members will not have any conflicts of interest which may affect objectivity. The SDMC's activities and responsibilities will be governed by the SDMC Charter.

After the first 5 participants are treated through the operating room, the SDMC will review the data for efficacy, reliability and safety outcomes prior to enrolling further participants.

15.9 Prior or Concomitant Medications

Administration of concomitant medications before, during and after the stent insertion shall be consistent with standard of care, usual practice, international guidelines and general recommendations, according to the participants' medical condition. All medications, including OTC medications, vitamins, and herbal supplements, and non-drug therapies taken or administered by participants during the study will be recorded in the eCRF.

16 AMENDMENTS, DEVIATIONS AND WAIVERS

16.1 Amendments

Investigators may not modify (amend) this clinical investigation plan without obtaining written concurrence of the Sponsor, involved Ethics Committee(s), and applicable regulatory authorities.

16.2 Deviations and Waivers

Investigators may not deviate from this clinical investigation plan without first receiving approval in writing from the Sponsor, involved Ethics Committee(s), and applicable regulatory authorities, except to protect the rights, safety and well-being of human subjects under emergency circumstances. All deviations will be documented on eCRFs.

The use of waivers from the Clinical Investigation Plan is prohibited.

16.2.1 Reporting

Investigators will also adhere to procedures for reporting deviations to the involved Ethics Committee(s) in accordance with their specific reporting policies and procedures.

Under emergency circumstances, deviations from the clinical investigation plan to protect the rights, safety and wellbeing of human subjects may proceed without prior approval of the sponsor and the Ethics Committee(s). Such deviations shall be documented and reported to the sponsor and the Ethics Committee(s) as soon as possible, but no later than 24 hours after the investigator had been made aware.

Deviations from the clinical investigation plan to the inclusion or exclusion criteria and deviations that affect the primary endpoints are considered major deviations. Deviations that may affect the secondary endpoints are considered minor deviations. All deviations will be reviewed by the medical monitor. The medical monitor is

responsible for major/minor classification of the deviations.

16.2.2 Corrective and preventive actions *code*

JiffyStent Pty Ltd or its representatives will evaluate deviations to the clinical investigation plan during monitoring visits. Individual event corrective and preventive actions may be recommended at that time. In addition, deviations occurring across investigational sites will be reviewed by JiffyStent Pty Ltd on a periodic basis to determine if more global preventive actions may be required.

16.2.3 Investigator disqualification criteria

JiffyStent Pty Ltd reserves the right to terminate an investigator/investigational site for any of the following reasons:

- Failure to secure subject informed consent including protection of personal data prior to enrolment.
- Failure to report safety events within 24 hours of discovery after learning of the event.
- Failure to report serious adverse device effects within 24 hours of discovery.
- Repeated investigational plan deviations.
- Repeated failure to appropriately complete case report forms.
- Failure to enrol an adequate number of subjects. Loss of or unaccounted for investigational product inventory

16.2.4 Follow-up management

Section 9 describes the procedures and precautions taken for participants following the end or early termination of the investigation or for participants who are lost to follow-up or withdraw their consent. Participants will receive standard of care in case a protocol deviation leads to the end, temporary halt, or early termination of the investigation. The standard of care is defined by the applicable treatment protocol(s) at the investigational site.

Any unresolved (S)AEs at a participants' final study visit must be marked unresolved on the eCRF AE form. Any (S)AE that is related to the study device and unresolved at the end of the study will be followed by the investigator until resolution or for 30 days after the last study visit if the treatment plan can be transferred to the primary physician or specialist or is determined to be irreversible.

Participants withdrawn due to an adverse event will be followed for 30 days or until resolution of the adverse event, whichever is the shorter time. After study end, participants will receive medical care according to standard of care.

17 DEVICE ACCOUNTABILITY

Access to investigational devices will be controlled and the investigational devices will be used only in the clinical investigation and according to the clinical investigation plan. The sponsor will keep records to document the physical location of all investigational devices from shipment of investigational devices to the investigation sites until return or disposal. The sponsor shall have instructions in place and make packaging materials available, if applicable, for the safe return or disposal of investigational devices, including potentially hazardous devices.

The principal investigator or an authorised designee shall keep records documenting the receipt, use, return and disposal of the investigational devices, which shall include:

a) name(s) of person(s) who received, used, returned or disposed the device,
b) the date of the receipt,
c) identification of each investigational device (batch number/serial number or unique code),
d) quantity of investigational devices,
e) the expiry date, if applicable,
f) the date or dates of use,
g) subject identification,
h) date on which the investigational device was returned/explanted from subject, if applicable,
i) the date of return of unused, expired or malfunctioning investigational devices, if applicable.
j) the date and documentation of disposal of the investigational devices as per instructions of the sponsor, if applicable.

Written procedures will be established for the entire process of device accountability.

18 VULNERABLE POPULATION

The subject population of this clinical investigation do not meet the criteria for a vulnerable population as defined in ISO 14155:2020, Section 3.55.

19 SUSPENSION OR PREMATURE TERMINATION OF THE CLINICAL INVESTIGATION

JiffyStent Pty Ltd reserves the right to terminate an investigator and/or investigational site for any of the reasons provided in Section 16.5.

In addition, JiffyStent Pty Ltd may choose to suspend or prematurely terminate the clinical investigation for the following reasons:

- Device deficiency or malfunction
- Production limitation

- Administrative decision

JiffyStent Pty Ltd will promptly notify the investigators, Ethics Committees and Regulatory Authorities in this event and provide for appropriate therapy and follow-up for the subjects.

20 STATEMENTS OF COMPLIANCE

This clinical investigation will be conducted in compliance with the principles that have their origin in the latest version of the Declaration of Helsinki, this clinical investigation plan, requirements of the approving Ethics Committee(s) and Regulating Authorities, ISO 14155:2020, and other applicable national and regional regulatory requirements whichever provides the greater protection of the individual.

This clinical investigation will not be initiated until approval has been obtained from the Ethics Committee(s) and the Regulating Authorities. Any additional requirements imposed by the Ethics Committee(s) or Regulating Authorities will be followed, as appropriate. No deviation from the clinical investigation plan will be implemented without the prior review and approval of the Ethics Committee(s) except where it may be necessary to eliminate an immediate hazard to a subject. In such case, the deviation will be reported to the Ethics Committee and applicable regulatory authorities as soon as possible. Clinical trial insurance will be secured prior to investigation initiation.

This clinical investigation is funded by JiffyStent Pty Ltd. The principal investigator at the study site will become a signatory on a study-specific Clinical Trial Agreement (CTA) which details the legal and regulatory roles and responsibilities of the Sponsor, investigator, and study site in carrying out the clinical investigation.

21 FUNDING

This study is funded by JiffyStent Pty Ltd

22 PUBLICATION POLICY

After closure of the clinical investigation, the results will be summarised in a Clinical Investigation Report, which will be submitted to the investigators, Ethics Committee(s) and appropriate regulatory authorities. This Clinical Investigation Report will include a summary of the results based on a statistical evaluation and clinical assessment. JiffyStent Pty Ltd may at any time publish the results of and information pertaining to the investigation subject only to compliance with regulatory requirements pertaining to participant protected health information. The conditions under which an investigator may publish results from this clinical investigation in any form are defined in detail in the clinical trial agreement.

The clinical investigation has been registered in the publicly accessible database The Australian New Zealand Clinical Trials Registry (www.anzctr.org.au) ACTRN 12623000264684P. Contents will be updated throughout study conduct

and results will be entered at study completion.

Irrespective of the outcome of the clinical investigation, within one year of the end of the clinical investigation or within three months of the early termination or temporary halt, JiffyStent Pty Ltd will submit a clinical investigation report to the approving Ethics Committee

23 REFERENCES

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3. Kutilek, S., I. Plasilova, and V. Chrobok, *Two Different Causes of Paediatric Hypercalcaemia.* Sultan Qaboos Univ Med J, 2018. **18**(3): p. e389-e392.
4. Nadav, G., et al., *Evaluation of the clinical significance of sonographic perinephric fluid in patients with renal colic.* Am J Emerg Med, 2019. **37**(10): p. 1823-1828.
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