T-DOC® NXT Clinical Study

STUDY NUMBER:

TDOC-NXT-01

STUDY NAME:

T-DOC® NXT Clinical Investigation:

Assessing the Performance, Safety and Usability of our Next Generation T-DOC® NXT Catheter for Performing Urodynamic Studies

DOCUMENT:

CLINICAL STUDY PROTOCOL

NCT NUMBER:

NCT03615001

DOCUMENT VERSION & DATE:

Version 1.0

June 26, 2018

CLINICAL STUDY PROTOCOL

DEVICE:

T-DOC® NXT Air-Charged Urodynamic Catheters

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KEY SPONSOR STUDY TEAM

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[redacted]	[redacted]
[redacted]	[redacted]

TDOC-NXT-01

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CLINICAL STUDY PROTOCOL **PREPARED BY**	PRINT NAME: [redacted] Job function: [redacted]

In signing the box below the approver signifies that they have reviewed the protocol and approve it on the basis that it meets the following requirements

1. *The protocol is consistent with the clinical plan*
2. *Adequacy of sample size and appropriateness of proposed statistical analysis*
3. *Accuracy of device description, efficacy and performance characteristics*
4. *Biological safety of Investigational and control devices and their appropriateness for human use*
5. *Conformance to all applicable regulations*
6. *Adequacy in meeting business needs*

CLINICAL STUDY PROTOCOL **APPROVED BY**	PRINT NAME: [redacted] Job function: [redacted]

TDOC-NXT-01

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INVESTIGATOR(S)

Principal Investigator

[redacted]

PARTICIPATING SITE(S)

[redacted]

INSTITUTION(S)

[redacted]

TDOC-NXT-01

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"CONFIDENTIAL INFORMATION"

Will mean all information provided by one party to the other and clearly identified as "CONFIDENTIAL" by the transmitting party at the time of disclosure. If such transmittal occurs orally, the transmitting party will promptly reduce such transmittal in writing, mark and identify it as confidential, and provide such record to the other party.

Specifically excepted from this is all information that

1. was previously known by the receiving party
2. is publicly disclosed except by breach of this AGREEMENT either before or subsequent to the receiving party's receipt of such information
3. is rightfully received by the receiving party without an express obligation of confidence
4. is independently developed by personnel of the receiving party without use of or reliance upon information from the other party
5. is disclosed pursuant to any judicial or government request, requirement or order, provided that the disclosing party takes reasonable steps to provide the other party with sufficient prior notice in order to allow the other party to contest such request, requirement or order.

The receiving party will not disclose CONFIDENTIAL INFORMATION without authorization from the disclosing party. This provision shall remain in effect for five (5) years following completion of this study. COMPANY shall be provided with patient information as allowed by law and will maintain the confidentiality of all such patient information, unless specifically required to disclose such information by law.

INVESTIGATOR STATEMENT

I fully understand the requirements of this study and my role as Investigator. I agree to participate and to comply with the requirements presented to me by Laborie. I agree to follow the protocol laid out before me and to not deviate from it in any way. I also agree to document all the required information as fully as I can.

ACCEPTED BY **PRINCIPAL INVESTIGATOR**	PRINT NAME TITLE Signature	[redacted]

TDOC-NXT-01

T-DOC® NXT Clinical Investigation:

Assessing the Performance, Safety and Usability of our Next Generation T-DOC® *NXT Catheter for Performing Urodynamic Studies*

Document History

	Version	Date Effective	Changes	Rationale for Change
Creation	**1.0**	**June 26, 2018**	**-**	**First Release**
Amendments				

This is a premarket clinical research protocol. This study is conducted in accordance with the clinical protocol, Good Clinical Practice, and FDA 21 CFR Parts 50, 812 – Investigational Device Exemptions. This study is conducted in accordance with ethical principles that have their origin in the Declaration of Helsinki.

Table of Contents

1 List of abbreviations

ACC	Air-Charged Catheter
CRF	Case Report Form
IRB	Institutional Review Board
ERP	Enterprise Resource Planning
FDA	Food and Drug Administration
LUT	Lower Urinary Tract
LUTS	Lower Urinary Tract Symptoms
T-DOC®	Commercial name for the LABORIE air-charged catheters
T-DOC® NXT	Next Generation T-DOC® air-charged catheter
UDS	Urodynamics
NGM	Next Generation Modular
PIM	Patient Interface Module
USA	United States of America
WFC	Water-Filled Catheter
Pves	Vesical Pressure (Single sensor bladder catheter)
Pabd	Abdominal Pressure (Abdominal catheter)
Pura	Urethral Pressure (Dual sensor bladder catheter)

2 INTRODUCTION

2.1 Clinical Study Summary

Number of Sites	1
Number of Subjects	Minimum 20 and Maximum 40
Objective	The primary objective of this premarket study is to gather clinical data as follows: • Confirm that the T-DOC® NXT 7Fr vesical and abdominal catheters are safe and effective for measuring urodynamic pressure measurements in adults. The exploratory objective of this study is to gather user and patient impressions of device performance as follows:

	• Assess subjective patient feedback regarding the discomfort and pain levels • Assess user impressions of device performances by evaluating the following subjective measures: ease of use, ease of insertion, presence of artefacts, presence of coughs/valsalva response, measurements and tracings of urethral pressure profiles, stability of the tracing, perceived time savings, ease of voiding around catheter, presence of use errors, and overall satisfaction
Inclusion criteria	- Male and Female (Adult age 21+) - Patients with clinical indication for urodynamics (UDS) testing, for any medically necessary reason as per the physician.
Exclusion criteria	- Patients who suffer from bladder infections (not including patients with asymptomatic bacteriuria) - Patients who are pregnant - Patients with recent (less than 2 weeks) pelvic floor surgery - Patients who require the use of a suprapubic catheter - Patients with significant cognitive deficiency that prevent the patient from giving informed consent
Anticipated Study duration	The proposed recruitment phase following site initiation is 8 weeks (first subject in to last subject out). Patients will come to the clinic for one visit, the UDS procedure, where data pertaining to the safety, efficacy and usability aspects of catheter will be collected. Test duration may be slightly longer than a standard test while assessment of the study materials is being made, and so discomfort and inconvenience associated with an extended test duration may occur.
Follow-up	No patient follow-up different than a usual UDS study will be required. There is no required follow-up for the study unless there is an adverse event.
Study end point	Once the minimum subject recruitment goal is met, the sponsor will be informed. The site will have an option to continue recruitment until the maximum is reached, or the 8 week recruitment period closes, whichever occurs first. There will be a site monitoring visit(s) as per the monitoring plan

2.2 Primary Hypothesis

The primary objective of this premarket study is to gather clinical data as follows:

- Confirm that the T-DOC® NXT vesical and abdominal catheters are safe and effective for measuring urodynamic(UDS) pressure measurements in adults.

2.2.1 Primary Safety and Effectiveness Endpoints

Primary Effectiveness Endpoint

The primary effectiveness endpoint is a binary clinician response after each UDS study using the T-DOC® NXT Catheter to determine whether the ability to measure UDS pressure was clinically adequate (success) or inadequate (failure). The primary effectiveness hypothesis is a comparison of the lower bound for the estimate of the success rate to a minimally acceptable target value of 75%:

H_0: Effectiveness Success Rate is ≤ 75%

versus

H_A: Effectiveness Success Rate is > 75%

This hypothesis will be evaluated by comparing the lower limit of the 1-sided 95% Clopper-Pearson confidence interval to 75%. The null hypothesis will be rejected if the lower limit of the 1-sided 95% Clopper-Pearson confidence interval is > 75%, which indicates that a rate ≤75% would be inconsistent with the trial findings.

Primary Safety Endpoint

The primary safety endpoint is a binary clinician response after each UDS study using the T-DOC® NXT Catheter to determine whether the safety of the device was clinically adequate (success) or inadequate (failure). The primary safety hypothesis is a comparison of the lower bound for the estimate of the success rate to a minimally acceptable target value of 75%:

H_0: Safety Success Rate is ≤ 75%

versus

H_A: Safety Success Rate is > 75%

This hypothesis will be evaluated by comparing the lower limit of the 1-sided 95% Clopper-Pearson confidence interval to 75%. The null hypothesis will be rejected if the lower limit of the 1-sided 95% Clopper-Pearson confidence interval is > 75%, which indicates that a rate ≤75% would be inconsistent with the trial findings.

2.4 Exploratory Analyses

The following exploratory objectives of this study are to gather data on the following:

- Assess subjective patient feedback regarding the discomfort and pain levels
- Assess user impressions of device performances based on their individual experience with existing ACC catheters by evaluating the following subjective measures: ease of use, ease of insertion, presence of artefacts, presence of coughs/valsalva response, measurements and tracings of urethral pressure profiles, stability of the tracing,

perceived time savings, ease of voiding around catheter, presence of use errors, and overall satisfaction

3 BACKGROUND

3.1 Medical Device

Initially, water-filled catheters (WFC) were the only UDS catheter technology available and only intravesical pressure was assessed (Perez & Webster, 1992). However, with the demand for different ways to better assess LUT dysfunction, multiple catheters types have been developed. Currently, there are four different UDS catheter-based technologies available: WFC, air-charged catheters (ACC), microtip catheters, and fiberoptic catheters. It is generally known that minimal tracings artefacts and non-physiological changes in pressure are desired for a reliable UDS tracing (Couri *et al.,* 2017). It has been noted that ACC are less likely to be influenced by movement, thus decreasing the occurrence of artefacts (Cooper *et al.,* 2011, Gammie *et al.,* 2014). The Sponsor views this as a great advantage in the adult population since movement artefact can be a common issue affecting interpretation of the UDS tracing (Cooper *et al.,* 2011). The study is designed to test a new generation of UDS equipment and ACC catheters.

The existing T-DOC® 7 French UDS ACC line was first introduced to the market in the early 2000s. The design comprises a patent-protected catheter balloon charging mechanism (US6447462/EP1255485) that facilitates the pressure transfer medium for recording UDS pressure and detection of UDS events. The device is provided as a sterile, single-use catheter.

[redacted]

The catheters under review in this clinical investigation are the next iteration of the T-DOC® G1 catheters called T-DOC® NXT, and are intended for use on adult populations for measuring UDS pressures.

There are two T-DOC® NXT catheter configurations under assessment. The first will be a combination of a single sensor vesical (bladder) catheter, and an abdominal/rectal catheter. The second configuration will include a dual sensor bladder (urethral) catheter and an abdominal/rectal catheter. T-DOC® NXT catheters have gone through extensive design changes to provide improved performance and efficiency to our customers. Furthermore, the design has been improved with a new catheter-connector for easier connectivity, a modified balloon, and increased catheter length for better performance. Furthermore, the new design offers an easier

and effective workflow due to our new catheter-connect mechanism, which provides an audible and tactile feedback not present in our existing line of T-DOC® G1 catheters

Table 1. Dimensional changes and operational data comparison between existing T-DOC® G1 catheters and T-DOC® NXT.

	Existing T-DOC® G1	**Proposed T-DOC® NXT**
[redacted]	[redacted]	[redacted]
[redacted]	[redacted]	[redacted]
Pves Balloon Sensor Location	1” from the tip	1” from the tip
Pabd Balloon Sensor Location	1” from the tip	1” from the tip
Pura Balloon Sensor Location (If Applicable)	2.36” from Pves	2.36” from Pves
[redacted]	[redacted]	[redacted]
Catheter Length	23.5”	Abdominal: 31.4" Single/Dual sensor urethral catheter: 37.4"
Flow Rate Specification	Maximum 70mL/min	70 mL / min
Sensor Balloon Measurement Error	Maximum 4.0% of applied pressure at 0 – 250 cmH_20 (system level)	Maximum 4.0% of applied pressure at 0 – 250 cmH_20 (system level) *
Operational Pressure Range	0 to 250 cmH_20	0 to 250 cmH_20

**Design feasibility test results indicate <3% balloon measurement error*

3.2 Prior Literature & Studies

The T-DOC® ACCs have been regarded as simple to use, easy to insert, set-up, and zero to atmospheric pressure (Internal Doc #PD-TR-151-01). This has been supported by clinical literature indicating that air-charged catheters are gaining popularity due to their simple handling and set-up (Chapple, MacDiarmid & Patel, 2009). Several studies have been published that examine the accuracy and behaviour of ACCs, both in non-clinical (Cooper *et al.*, 2011,

Couri *et al., 2007*), and clinical (T. McKinney, 2015, Gammie *et al.,* 2016, Digesu *et al.*, 2014) settings. Since this is a new investigational device, there is no prior literature examining the safety and effectiveness of the T-DOC® NXT catheter in patients.

Please refer to Section 5 of the Investigator Brochure (TDOC-NXT-01-IB) for a more detailed review of the available published literature.

3.3 Rationale

The next generation T-DOC® catheter (T-DOC® NXT) is based on our previous Air-Charged Catheter (ACC) technology, that has undergone design changes to provide improved performance and efficiency to our customers. The design has been improved with a new catheter-connector for easier connectivity, a modified balloon and increased catheter length for better performance. Since T-DOC® NXT is based on an existing design, there is published data supporting the safety, performance and usability of the principle aspects of the design. T-DOC® ACCs have been on the market over 10 years (>6MM sold catheters) and have collected significant amount of data in adults. However, due to the design changes, further evidence is required to confirm the safety and effectiveness of the next generation catheter prior to market release. The aim of this pre-market study is to collect data of the catheters' performance and confirm they are safe and effective for UDS. Furthermore, the new design offers an easy and effective workflow due to the new catheter-connect mechanism, which provides an audible and tactile feedback not present in the existing line of T-DOC® catheters. Summative usability testing will be conducted in a simulated environment, and will be confirmed in this pre-market study. A limitation to this study is that it will be conducted with the Aquarius NGM unit with a modified cable to allow the catheters to connect with the new catheter-connect system. This modification is necessary because the NXT UDS machine with new T-DOC® NXT Patient Interface Module (PIM) will not be available. This study will gather data to support concurrent design validation activities while establishing clinical safety and effectiveness of the device in the adult population.

Finally, there will be no control arm, blinding, or treatment/intervention component to this study. This is based on the trial design and the fact that this is a non-comparative study; inclusion of a sham or placebo is not feasible nor necessary, and the device under evaluation is not a treatment or intervention.

For the purposes of this study, decisions regarding timing for prescribing UDS testing will be at the discretion of the Investigators.

4 STUDY OBJECTIVES

4.1 Primary Objectives

The primary objective of this premarket study is to gather clinical data as follows:

- Confirm that the T-DOC® NXT 7Fr vesical and abdominal catheters are safe and effective for measuring UDS pressure measurements in adults.

4.2 Exploratory Objectives

The exploratory objective of this study is to gather user impressions of device performance as follows:

- Assess subjective patient feedback regarding the discomfort and pain levels
- Assess user impressions of device performances based on their individual experience with existing ACC catheters evaluating the following subjective measures: ease of use, ease of insertion, presence of artefacts, presence of coughs/Valsalva response, measurements and tracings of urethral pressure profiles, stability of the tracing, perceived time savings, ease of voiding around catheter, presence of use errors and overall satisfaction

4.3 Claims and Intended Performance

- The T-DOC® NXT catheter causes minimal discomfort during insertion, during the test, and removal
- Adverse Event Claims as per results
- Subjective claims:
    - The T-DOC® NXT catheters are safe and effective for use on adult patients
    - The T-DOC® NXT catheters are easy to use
    - The T-DOC® NXT catheters are easy to set-up / zero
    - The T-DOC® NXT catheters are easy to insert
    - The T-DOC® NXT catheters have consistent/stable tracings
    - The T-DOC® NXT catheter has adequate subtracted pressures

4.4 Assessment of Risks and Adverse Device Effects

Risks to the subject will be no greater than those of a standard UDS test. Subjects may experience temporary discomfort upon insertion of the catheters. Test duration may be slightly longer than a standard test while assessment of the study materials is being made, and so discomfort and inconvenience associated with an extended test duration may occur.

UDS testing exposes subjects to risks of urethral instrumentation which can result in infection, urethral trauma and pain (Winters *et al.* 2012). Other risks can include transient discomfort during or following the procedure, transient dysuria or bleeding (hematuria) following the procedure, or urinary tract infection, which occurs in 2-4% of subjects (Chapple, MacDiarmid & Patel, 2009).

In conclusion, the overall residual risks associated with the use of T-DOC® NXT catheters within this study set-up, are acceptable when weighed against the benefits, and are no different than the risks when using other UDS catheter technologies. The sponsor team has also established that patients are subjected to no more than minimal risk since an IDE is not required for this study (Ref: TDOC-NXT-01 - Risk Determination). Lastly, UDS is a widely-performed procedure on subjects requiring specialized management for urinary incontinence/retention problems, as

recommended by the ICS (Abrams *et al.,* 2013), and is useful in characterizing LUT function, identifying causes of symptoms and quantifying related pathophysiological processes (Rosier PF., 2013). Thus, the clinician must weigh the risks and benefits as to whether the UDS test offers additional diagnostic value beyond symptom assessment, physical examination and other diagnostic testing (Winters *et al.,* 2012).

5 MEDICAL DEVICE

5.1 Description

The catheters used in this study will be design verified, sterilized and appropriately labelled before the clinical investigation can begin.

The catheter device models to be evaluated as part of this study include:

1. T-DOC® NXT vesical single sensor catheter (blue)
2. T-DOC® NXT abdominal single sensor catheters (red)
3. T-DOC® NXT Vesicle, dual sensor catheter available for optional urethral measurement studies (blue and yellow)

Traceability of investigational study materials will be maintained via the Inventory Control Log (Q905-FRM-17). Any remaining investigational material stock after study close-out will be returned to the study sponsor at the sponsors' expense.

The T-DOC® NXT catheters are manufactured using equivalent materials to the existing T-DOC® G1 catheters [redacted], and are verified biocompatible in accordance with the standards EN ISO 10993-5 and -10 and -18 – Biological evaluation of medical devices.

None of the materials being used in this study contain biologically active substances or pharmacological agents.

From a Regulatory standpoint, the following medical device classification rules apply in Europe, the United States and Canada, respectively:

For the European Union, Class IIa

For the United States, Class II as per FDA

For Canada, Class II as per Health Canada Medical Device Regulations

5.2 Purpose & Use

Intended Use: The Air-charged Urodynamic Catheters are intended for measuring Urodynamic pressures. The Air-charged Urodynamic Catheters are intended to be connected to Urodynamics Analyzer systems using a reusable electronic component.

Indications for Use: The UDS Catheters are sterile and intended for single use on adult patient population requiring UDS pressure monitoring through the measurement of bladder, urethral, and rectal (or vaginal) pressures.

5.3 Summary of Non-Clinical Safety & Performance Data

The T-DOC® NXT family of UDS catheters has been tested per ISO 10993 and must meet all biocompatibility requirements for acute tissue contacting devices which includes Cytotoxicity, Sensitization, and Irritation. Furthermore, design verification studies will be undertaken to verify that Level 2 design requirements are met. Please refer to the Investigator Brochure for further details.

5.4 Summary of Clinical Safety & Performance Data

Please refer to Section 5 of the Investigator Brochure (TDOC-NXT-01-IB) for detailed review of relevant previous clinical safety and performance data. In all literature presented, the T-DOC® air-charged catheters are safe and effective for measuring UDS pressures further justifying the study rationale.

5.5 Risks and Benefits

Risks to the subject will be no greater than those of a standard UDS test. Physicians are responsible for determining whether subjects are normally indicated, and who would benefit from UDS testing. Subjects must meet all inclusion criteria to be eligible for recruitment into this study. There is no direct subject benefit for participating other than to gather objective evidence of T-DOC® NXT 7 Fr ACC clinical use. Please refer also to Section 4.5 above (Assessment of Risks and Adverse Device Effects), and Section 6 of the Investigator Brochure (TDOC-NXT-01-IB).

The sponsor has also established that patients are subjected to no more than minimal risk since an IDE is not required for this study (Ref: TDOC-NXT-01 - Risk Determination). Lastly, UDS is already a widely performed procedure on subjects requiring specialized management for urinary incontinence issues, as recommended by the ICS (Abrams *et al.,* 2013), and is useful in characterizing LUT function, identifying causes of symptoms and quantifying related pathophysiological processes (Rosier P.F., 2013). In conclusion, the overall residual risks associated with the use of T-DOC® NXT catheters within this study set-up, are acceptable when weighed against the benefits.

6 STUDY DESIGN

6.1 Description

This premarket study will be conducted where a minimum number of subjects will undergo a conventional UDS study that will be conducted according to Good UDS Practices (Rosier *et al*., 2016). Subject data including age, medical history, height, weight, adverse events during or immediately following the test, catheter insertion depth etc., will be collected on each patient's CRF. There will be no control arm, blinding, or treatment/intervention component to this study.

The following steps gives a high-level overview of the study design and subject flow-through based on number of patients enrolled:

- Adult patients are referred for UDS testing
- Patient are approached to enrol in the study during their UDS visit and give informed consent
- Urodynamic testing is conducted, and case report forms are completed
- Adverse events are followed for closure

6.2 Duration

The expected duration of each subject's participation is one clinic visit to receive their already prescribed UDS test. Once ethics board approval is received, site training and initiation is expected to take 1-2 weeks, whereas the estimated duration of active recruitment for this study is estimated at 2 months. Database lockout and study report completion is estimated at less than 1 month after the last subject is recruited.

7 PATIENT SELECTION

7.1 Inclusion Criteria

- Male and Female (Adult age 21+)
- Patients who are scheduled and indicated for UDS testing, for any medically necessary reason as per the physician.

7.2 Exclusion Criteria

- Patients who suffer from bladder infections (not including patients with asymptomatic bacteriuria)
- Patients who are pregnant
- Patients with recent (less than 2 weeks) pelvic floor surgery
- Patients who require the use of a suprapubic catheter
- Patients with significant cognitive deficiency that prevent the patient from giving informed consent

7.3 Vulnerable Populations

The targeted subject group is not a vulnerable population

7.4 Recruitment Plans

The target enrolment is a minimum of 20 patients (maximum 40).

Subjects who are visiting the UDS clinic for their medically-indicated UDS test will be approached regarding participation in this study. It is estimated that recruitment should take approximately 2 months. Recruitment will be monitored through scheduled meetings with the site co-ordinator. If the subject signs the informed consent, this will be treated as the point of enrolment.

7.5 Informed Consent

The Investigator (according to applicable regulatory requirements), or a person designated by the Investigator, and under the Investigator's responsibility, should fully inform the subject of all pertinent aspects of this clinical trial, including the written information giving a favourable opinion by the IRB. New information regarding the study will be provided to the subject by the Site.

Prior to a subject's participation in the clinical trial, the written Informed Consent Form should be signed, name filled in and personally dated by the subject and by the person who conducted the informed consent discussion. A copy of the signed and dated written Informed Consent will be provided to the subject. The date of the informed consent should be recorded on the subject's CRF.

The Informed Consent Form used by the Investigator for obtaining the subject's informed consent must be reviewed and approved by the Sponsor prior to submission to the appropriate IRB for approval/favourable opinion.

The study sponsor does not foresee any circumstances where emergency enrolment would occur due to the device indication (it is not used in emergency situations), and the fact that patients being recruited are attending their UDS appointment as a pre-scheduled visit.

7.6 Subject Withdrawal

Subjects may withdraw voluntarily from the study or the investigator may terminate a subject's participation (see below). The Investigator will notify the sponsor when a subject is withdrawn from the study (and if possible why), and this will be recorded on the subject's CRF and withdrawal form. Subjects who withdraw from the trial will be allowed to be replaced by another subject.

7.7 Suspension or Premature Termination

The study may be terminated prematurely if the Sponsor or the Investigator feel that the equipment is not producing results as expected which could be due to inappropriate operator handling or faulty equipment. The Investigator and/or sponsor would determine termination by observing unanticipated problems, design defects, evidence of noncompliance, or serious

and/or continuing noncompliance which could affect any of subject safety, device performance or integrity of study data.

8 MANAGEMENT OF MEDICAL DEVICE

8.1 Description

The following devices and equipment will be required for each patient. Those indicated by asterisk (*) are to be sourced and provided by the site:

- Laborie UDS equipment already in use
- Computer/laptop with Laborie UDS-120 UDS software already loaded and in use by each site
- Infusion transducer (optional)
- Uroflowmetry/Urocap device configured with the UDS equipment and computer for pressure-flow studies, already in use by each site (optional)
- T-DOC® transducer backwards compatibility cables:
    - Pabd (red) – Abdominal channel reusable cable
    - Pves (blue) – Bladder channel reusable cable
    - Pura (yellow)- Urethral channel reusable cable (optional)
- One (1) air-charged T-DOC® NXT abdominal single sensor catheter per subject
- One (1) air-charged T-DOC® NXT single sensor catheter or one (1) air-charged T-DOC® NXT dual sensor catheter per subject
- EMG cable (optional component at the discretion of the site)
- EMG patches (optional component at the discretion of the site)
- Laborie UDS pump tubing infusion line per subject (must be Laborie part number: TUB500)
- 1000 mL beaker* (whatever is currently in use at the site) (optional)
- Weight of 500g provided by Laborie (optional?)
- One (1) sterile saline bag per subject*
- Tape*
- Lubricant*
- Gloves*
- Any other supplies deemed necessary for conducting a UDS study*

The study agreement will further specify the equipment and disposables that will be required and provided by Laborie.

8.2 Regimen

N/A – there is no treatment regimen required as part of this study.

8.3 Assignment to Groups

No stratification of subjects will be utilized based on study design.

8.4 Preparation and Handling

The Urodynamic system and air-charged catheters will be prepared, and maintained by the physician.

8.5 Packaging and Labelling

Investigational device labelling will appear on all investigational materials under FDA 21 CRF Subpart 812.5. A copy of the investigational label is shown the Investigator's Brochure.

8.6 Device Accountability

All devices used directly for testing subjects must be recorded using the device LOT number on the subjects CRF form.

8.6.1 Laborie to Study Site:

All investigational devices or equipment transferred between Laborie and the study site must be recorded through the Inventory Control Log. This includes postal deliveries and any deliveries made in person by Laborie. Any equipment or devices that are not used and are returned to Laborie must be recorded on the Inventory Control Log as well. It is Laborie's responsibility to ensure that all inventory both at Laborie and the study site correlate. All investigational device accountability will be recorded through the Inventory Control Form.

8.6.2 Study Site Usage:

All devices used directly for testing subject samples must be recorded on the Inventory Control Form. All devices used by the study site that are not directly used for the testing of subject samples must be recorded on the Inventory Control Form. This includes any devices used for training or demonstration or any devices which are noted to be defective when opened.

8.6.3 Study Site to Laborie:

Any equipment or devices that are not used and are returned to Laborie must be recorded on the Inventory Control Form.

When the devices have been received by Laborie, it is Laborie's responsibility to ensure that all inventory control forms both at Laborie and the study site correlate.

8.7 Concomitant Treatment

Not applicable in this study

8.8 Subject Compliance Monitoring

Not applicable in this study.

9 ASSESSMENT OF INVESTIGATIONAL DEVICE

9.1 Endpoints

OBJECTIVES	ENDPOINTS	JUSTIFICATION FOR ENDPOINTS
Primary		
To confirm the T-DOC® NXT vesical and abdominal catheters are a safe and effective means of measuring UDS pressure in adults.	The primary endpoint will be measured by recording the clinician safety and effectiveness rating for each patient on their CRF. The clinician will indicate whether the T-DOC® NXT vesical and abdominal catheters are safe and effective for measuring UDS pressure in at least 20 of patients enrolled.	Given the intended use of the device, and the fact that there is no single or combination of objective measures generated from the UDS test that can establish the safety and effectiveness, it is justified to obtain clinician feedback via a binary response whether the device was safe and/or effective for measuring UDS pressure.

9.2 Methods of Assessment

A T-DOC® NXT air-charged catheter will be used to assess and record bladder and abdominal pressures which are in turn used by the clinician to identify UDS events. These measurements will be recorded using a LABORIE UDS system. The resulting interpretations regarding safety, effectiveness, and usability will be made by the physician overseeing the subject's case.

All study outcome data captured will be compiled and analysed by the LABORIE study team to determine if the endpoints were successfully achieved based on whether the null hypotheses were accepted or rejected.

10 PATIENT SAFETY

10.1 Definitions

10.1.1 Adverse Events:

Any untoward medical occurrence in a subject, whether or not related to the investigational medical device.

10.1.2 Adverse Device Effect:

Any adverse event related to the use of an investigation medical device.

10.1.3 Device Deficiency:

Inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance

10.1.4 Serious Adverse Event:

An adverse event that:

1. Led to a death;
2. Led to a serious deterioration in health of a patient, user, or others that:
    a. Results in a life-threatening illness or injury;
    b. Results in a permanent impairment of a body structure or body function;
    c. Requires in patient hospitalization or prolongation of existing hospitalization;
    d. Results in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to body structure or a body function;
3. Led to foetal distress, foetal death or a congenital abnormality/birth defect.

10.1.5 Unanticipated Adverse Device Effect:

Any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigation protocol or application, or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

10.1.6 Unanticipated Serious Adverse Device Effect (USADE):

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

10.2 Data Collection

Adverse events, device deficiencies, serious adverse events, and unanticipated adverse device effect shall be recorded on the CRF.

10.3 Reporting

All serious adverse events and unanticipated adverse device effects occurring during the investigation will be reported as soon as possible, but no later than 10 working days after the

Investigator/Laborie first learns of the effect. This information will be submitted to Laborie/investigator and the IRB.

10.4 Foreseeable Events

For a complete Risk Management Report please refer to the Risk Management File. The residual risks have been deemed acceptable and the benefits overweighs the risks. Please also refer to Section 4.5 above Assessment of Risks and Adverse Device Effects

10.5 Contact Information

In the event of a serious adverse event and serious adverse device event please contact:

[redacted]

10.6 Follow-Up

If an adverse event occurs, any follow-up intervention prescribed is at the discretion of the Investigator, and the site must notify Laborie of the outcome of the follow-up. The study safety endpoint will be measured by capturing adverse event data both during the study visit.

11 STUDY PROCEDURE

11.1 Visit Schedule

Evaluation	Screening & Clinic Visit	
	Part 1*	Part 2
Informed Consent	X	
Inclusion Criteria		X
Exclusion Criteria		X
UDS Study		X
Record any Adverse Events		X
Complete CRF		X

*Part 1 and Part 2 may be combined into 1 visit

11.2 Screening for Eligibility

Subjects may be screened for eligibility for this study by referencing the inclusion criteria. No special testing is required in order to determine eligibility.

11.3 Part 1 (Informed Consent)

1. Conduct Informed Consent discussion with the subject and sign

11.4 Part 2 (Urodynamic Clinic Visit)

1. Determine if the subject is eligible for this study.
2. Conduct Informed Consent discussion with the subject and sign.
3. Collect medical history and record in case report form (TDOC-NXT-01- CRF2).
4. Collect and record other patient details as required on TDOC-NXT-01- CRF1 [weight (lbs), height (‘,”), date of birth, sex, etc].
5. Site personnel will explain what will happen during the UDS test to the subject/parent or caregiver.
6. Site personnel will prepare UDS equipment, study materials, other sterile disposables and supplies as required for the UDS study and record catheter lot number information on TDOC-NXT-01- CRF1.
7. Follow the investigational device instructions for use for placing the catheters. Record all the necessary data on TDOC-NXT-01- CRF1.
8. Conduct UDS study according to ICS Good UDS Practice recommendations, including regular cough checking to ensure good pressure transmission and catheter positioning wherever possible (Rosier *et al.,* 2016). Record all the necessary data on TDOC-NXT-01- CRF1.
9. Site personnel to ask patients to answer questions on urodynamic experience and record all data on TDOC-NXT-01- CRF4.
10. After completing a day of urodynamics, the user is to fill out a questionnaire and record all necessary data on TDOC-NXT-01- CRF3.

NOTE: If an adverse event occurs during this study, any follow-up intervention prescribed is at the discretion of the Investigator. This information should also be recorded on the subject’s CRF (TDOC-NXT-01- CRF1-) and the AE form (TDOC-NXT-01- CRF5).

11.5 End of Study (EOS)

At the conclusion of the UDS test, the subject is no longer required to undergo any further study-related procedures.

Once a site has completed its target recruitment, the sponsor (Laborie) will schedule a time to close-out the site, either in person or by telephone as per the monitoring plan. All study related files will be collected and reviewed for completeness. The EOS is considered the point when all subjects have been followed-up and data collection completed.

12 STATISTICAL CONSIDERATIONS

12.1 Primary Safety and effectiveness Endpoints

12.1.1 Primary Effectiveness Endpoint

The primary effectiveness endpoint is a binary clinician response after each UDS study using the T-DOC® NXT Catheter to determine whether the ability to measure UDS pressure was clinically adequate (success) or inadequate (failure). The primary effectiveness hypothesis is a comparison of the lower bound for the estimate of the success rate to a minimally acceptable target value of 75%:

H_0: Effectiveness Success Rate is ≤ 75%

versus

H_A: Effectiveness Success Rate is > 75%

This hypothesis will be evaluated by comparing the lower limit of the 1-sided 95% Clopper-Pearson confidence interval to 75%. The null hypothesis will be rejected if the lower limit of the 1-sided 95% Clopper-Pearson confidence interval is > 75%, which indicates that a rate ≤75% would be inconsistent with the trial findings.

12.1.2 Primary Safety Endpoint

The primary safety endpoint is a binary clinician response after each UDS study using the T-DOC® NXT Catheter to determine whether the safety of the device was clinically adequate (success) or inadequate (failure). The primary safety hypothesis is a comparison of the lower bound for the estimate of the success rate to a minimally acceptable target value of 75%:

H_0: Safety Success Rate is ≤ 75%

versus

H_A: Safety Success Rate is > 75%

This hypothesis will be evaluated by comparing the lower limit of the 1-sided 97.5% Clopper-Pearson confidence interval to 75%. The null hypothesis will be rejected if the lower limit of the 1-sided 97.5% Clopper-Pearson confidence interval is > 75%, which indicates that a rate ≤75% would be inconsistent with the trial findings.

12.2 Exploratory Analyses

- Assess subjective patient feedback regarding the discomfort and pain levels
- Assess user impressions of device performances based on their individual experience with existing ACC catheters by evaluating the following subjective measures: ease of use, ease of insertion, presence of artefacts, presence of cough/valsalva response, measurements and tracings of urethral pressure profiles, stability of the tracing, perceived time savings, ease of voiding around catheter, presence of use errors and overall satisfaction

12.3 Sample Size Determination & Power

The null hypotheses for the primary safety and the primary effectiveness endpoints are designed to rule out success rates ≤ 75%. There will be no type I error adjustment for simultaneous testing of these endpoints within the same trial. Based on clinical judgement and previous testing, the true success rate for both safety and efficacy is assumed to exceed 95%. Thus, the power calculation is identical for the safety and effectiveness endpoints, and a true success rate of 96% is assumed for each endpoint.

Analysis of 20 subjects would provide 81% power to rule out a success rate ≤ 75% when the true success rate is assumed to be 96%, based on a 1-sided test with type I error rate of 5%. This study requires a minimum of 20 subjects to ensure adequate power, but the final sample size will be based on site enrolment capabilities. If 30 subjects or 40 subjects are enrolled, the power to rule out a success rate ≤ 75% will be 96% and 99%, respectively (Fleiss, J.L. *et al.,* 2003).

12.4 Randomization / Blinding

Randomization and/or blinding is not utilized in this study based on study design.

12.5 Analysis Plan

A Statistical Analysis Plan containing the details of the analyses and hypothesis testing will be finalized prior to database lock. All subjects who complete the UDS study will be considered in the final analysis. Data will be analysed as discussed in Section 12.1 above.

If any CRFs are found to be incomplete, the study monitor will follow-up as to the reasoning. If for some reason a clinical user is unable to complete their questionnaire, the questions they have completed will be included in the analysis. Data will be monitored as the study progresses, please refer to Section 7.7 for details about suspension or premature termination.

12.6 Deviations

In any event there are deviations from the original statistical plan, they will be described and justified in the final report.

12.7 Early Stopping

An informal interim data analysis will be conducted once 20 subjects have been recruited in order validate the product design meets the user requirements.

There are currently no criteria for stopping the study early on statistical grounds, however please refer to Section 7.7 for details about suspension or premature termination.

13 DATA HANDLING & RECORD KEEPING

13.1 Direct Access

The Investigator/Institution will permit trial-related monitoring, audits, IRB review, and regulatory inspections by providing direct access to the source data/documents as needed.

13.2 Confidentiality & Security

All information disclosed or provided by the Sponsor (or any company/institution acting on their behalf), or produced during the study, including, but not limited to, the Study Protocol, the CRFs, the Instructions for Use and the results obtained during the course of the study, is confidential. The Investigator or any person under his/her authority agrees to undertake to keep confidential and not to disclose the information to any third party without the prior written approval of the Sponsor.

However, the submission of this Study Protocol and other necessary documentation to the Ethics Committee (IRB) is expressly permitted, the IRB members having the same obligation of confidentiality.

The Sub-Investigators, if employed, shall be bound by the same obligation as the Investigator. The Investigator shall inform the Sub-Investigators of the confidential nature of the Usability Study.

The Investigator and the Sub-Investigators shall use the information solely for the purposes of the Study, to the exclusion of any use for their own or for a third party's account.

All data to Laborie will be confidential and all subject identifiers will be blacked out before being sent to Laborie. Documents will be kept in a secure location and all digital information will be kept following HIPAA and local government regulations.

13.3 Data Handling

A list of individuals will be maintained who are authorized to make any changes to the data. Data will be reviewed by the Sponsor (outside of monitoring personnel), and requests for clarification and/or corrections will be made through the monitor. Once the review is conducted, the database will be considered clean and ready for analysis. Missing values will remain missing, i.e. no attempt will be made to input missing values and only observed values will be used in data analyses and presentations.

13.4 Case Report Form (CRF) & Source Documents

All study staff will be trained on the protocol requirements and questionnaire completion. It is the responsibility of the Investigator to maintain adequate and accurate questionnaires and CRFs designed by Laborie to record all observations and other data pertinent to the clinical investigation. All questionnaires and CRFs should be completed in their entirety in a neat, legible manner to ensure accurate integration of data. Should a correction be made, the information to be modified must not be overwritten. The corrected information will be transcribed by the authorized person on the questionnaire. Source document worksheets for recording data will be created as agreed upon by the sponsor or the site as required. Data from the source documents should be entered into the CRF after each subject's visit. The anonymized UDS data files (DTA files) requested by the sponsor for each patient, to confirm the quality of the study. A unique subject code will be assigned to each subject based on the site number (100) and sequential subject number (i.e. 100-001). The investigator is responsible for maintaining subject identifying information. CRF's will be treated as source data in the event

that the original information is entered in the CRF first (and no source document worksheet is utilized for that data point).

13.5 Record Retention

An investigator or sponsor shall maintain the records required by 21 CFR Part 812.140 during the investigation and for a period of 2 years after the latter of the following two dates: The date on which the investigation is terminated or completed, or the date that the records are no longer required for purposes of supporting a premarket approval application or a notice of completion of a product development protocol. The Investigator must maintain confidential all study documentation, and take measures to prevent accidental or premature destruction of these documents. All essential documents from the Investigator will be kept in the Investigator binder. All sponsor essential documents will be kept in the study master file. The investigator and sponsor shall also maintain a record of their location of the respective essential documents. If the Investigator's personal situation is such that archiving can no longer be ensured by him/her, the Investigator shall inform the Sponsor and the relevant records shall be transferred to a mutually agreed upon designee.

13.6 Performance Monitoring

Monitors will periodically check questionnaire data to ensure all fields are entered as far as possible and inquire as to whether any usability issues are being encountered as the study progresses.

14 MONITORING, AUDITING, AND INSPECTING

14.1 Study Monitoring Plan

The Investigator agrees to provide reliable and accurate data, and all information requested by the study protocol (with the help of any questionnaire, other appropriate instruments) in an attributable, legible, contemptuous, original, accurate, and complete form according to the instructions provided and to ensure direct access to source documents to Sponsor representatives. Any changes to the soured data shall be traceable and not obscure the original entry.

The Sponsor of this Study is responsible to Health Authorities for taking all reasonable steps to ensure the proper conduct of this study protocol with regards to ethics, protocol compliance, integrity and validity of the data recorded on the CRF and questionnaires. Thus, the main duty of the Monitoring Team is to help the Investigator and the Sponsor maintain a high level of ethical, scientific, technical and regulatory quality in all aspects of the study.

At regular intervals during the study, the site will be contacted, through monitoring visits, letters or telephone calls, by a representative of the Monitoring Team to review study progress, Investigator and subject compliance with study protocol requirements, and any emergent problems. The monitoring plan will describe the frequency, extent, and nature of monitoring.

14.2 Auditing and Inspecting

For the purpose of ensuring compliance with the study protocol, Good Clinical Practice and regulatory requirements, the Investigator should permit inspection by applicable regulatory body authorities. This investigation will not include audits conducted by the Sponsor.

The Investigator agrees to allow the inspectors to have direct access to his/her study records for review, being understood that these personnel are bound by professional secrecy, and as such will not disclose any personal identity or personal medical information.

The Investigator will make every effort to help with the performance of the inspections, giving access to all necessary facilities, data, and documents.

As soon as the Investigator is notified of a future inspection by the authorities, he will inform the Sponsor and authorize the Sponsor to participate in this inspection.

The confidentiality of the data verified and the protection of the subjects should be respected during these inspections.

Any result and information arising from the inspections by the regulatory authorities will be immediately communicated by the Investigator to the Sponsor. The Investigator shall take appropriate measures required by the Sponsor to take corrective actions for all problems found during the inspections.

15 DEVIATIONS

All departures from the approved protocol shall be documented by the Investigator. All deviations will be recorded on the subject CRF, and a deviation report will be sent to Laborie and the ethics board, as required. Timelines for notification will be subject to ethics board standard operating procedures. Deviations will be reviewed and signed off by the sponsor. If deviations are observed/reported that significantly affect or have the potential to significantly affect human subject protection or reliability of the trial results, then LABORIE will conduct a root cause analysis and implement appropriate corrective and preventative actions.

16 AMENDMENTS

If there are any changes to the protocol during the application of the study or during the length of the clinical study in progress, the IRB will be notified for review. During an ongoing study if an amendment is made to the protocol the amended protocol will be sent to the applicable institution within the timelines required. The Investigator should not implement any deviation from, or changes to the clinical protocol without agreement by the sponsor and prior review and documented approval/favourable opinion from the IRB of an amendment, except when necessary to eliminate an immediate hazard(s) to a clinical study subject. In some instances, an amendment may require a change to the Informed Consent Form. The investigator must

receive an IRB approval/favourable opinion concerning the revised Informed Consent Form prior to implementation of the change.

17 STUDY ADMINSTRATION

17.1 Funding Source and Conflicts of Interest

Laborie will be the sponsor and the financial details are covered in the Investigator Agreement.

17.2 Subject Stipends or Payments

Subjects will be offered a $40 USD stipend for their participation in the study to offset the cost of parking and/or meals required during their clinic visit.

The Sponsor has covered this study by means of an insurance covering bodily injury or property damage arising out of the clinical trial. The certificate of insurance evidencing the coverage, insurance company, policy number and the sum insured are provided in the Study's File.

17.3 Committees

A Data Monitor Committee will not be utilized in this study based on the evaluation of the level of potential risks.

17.4 Study Timetable

PROPOSED STUDY TIMELINE	TOTAL DURATION (WEEKS)	ACTUAL DATES
PROPOSED SITE TRAINING & INITIATION PHASE	**1**	**July 2018**
PROPOSED RECRUITMENT (1st subject in to last subject out)	**8**	**July- September 2018**
PROPOSED DATABASE LOCKOUT	**1**	**October 2018**
PROPOSED STUDY REPORT COMPLETION	**3**	**October 2018**
TOTAL (WEEKS / MONTHS)	-	
ESTIMATED COMPLETION (QUARTER)	**Start Q4 FY2018**	**End of October 2018**

18 ETHICS AND REGULATORY APPROVAL

This study will not begin until the appropriate approvals from the IRB have been obtained. Any additional requirements imposed by the IRB will be followed. This study will be conducted in compliance with all international laws and regulations, and national laws and regulations of the countries in which the usability study is performed, as well as any applicable guidelines.

19 PUBLICATION POLICY

The results of the study may be submitted for publication, whether peer-reviewed or marketing materials. Publication rights and details are covered in the Investigator Agreement, there may be other authors involved in the creation of the publication.

20 ATTACHMENTS

20.1 Informed Consent Documents

- TDOC-NXT-01-ICF - Informed Consent Form

20.2 Investigator's Brochure

- TDOC-NXT-01-IB T-DOC NXT Investigator's Brochure

20.3 Case Report Forms

- TDOC-NXT-01- CRF1Case Report Form 1
- TDOC-NXT-01- CRF2Case Report Form 2
- TDOC-NXT-01- CRF3Case Report Form 3
- TDOC-NXT-01- CRF4Case Report Form 4
- TDOC-NXT-01- CRF5Case Report Form 5

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