T-DOC® 5 French Clinical Study

STUDY NUMBER:

TDOC5Fr-PEDS-01

STUDY NAME:

T-DOC® 5 Fr Pediatric Clinical Investigation:

A Pivotal Study to Assess the Performance, Safety and Usability of a New 5 French Air-Charged Catheter for Performing Urodynamic Studies on Pediatric Subjects

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STATISTICAL ANALYSIS PLAN

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Version 1.0

July 9, 2018

CLINICAL STUDY STATISTICAL ANALYSIS PLAN

DEVICE:

T-DOC® 5 French Air-Charged Vesical and Abdominal Urodynamic Catheters

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Statistician	Print Name	[redacted]	Date	18 July 2018
	Signature			

This document has been reviewed by LABORIE (Refer to Entropy PRC# 022385).

Contents

Introduction

The purpose of this statistical analysis plan (SAP) is to provide clarification about the statistical considerations and methods to be implemented for the analysis of data from the TDOC5Fr clinical study. This statistical analysis plan is based on protocol version 2.02 (TDOC5Fr-PEDS-01-PR-V2.02). The protocol clearly describes the study endpoints, but the hypothesis testing procedures and criteria for study success is requires additional details. The SAP is written by an independent statistician [redacted] with no access to or knowledge of accumulating trial data. Any revisions to the SAP will be made prior to database lock and reasons for such revisions will be described in the final clinical study report.

Study Objectives and Endpoints

The following are the objectives and endpoints of the TDOC5Fr-PEDS-01 clinical study:

OBJECTIVES	ENDPOINTS
Primary	
To confirm the T-DOC® 5Fr vesical and abdominal catheters as a safe and effective means of measuring urodynamic pressure in pediatric subjects 12 years of age and younger.	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® 5 Fr vesical and abdominal catheters are safe and effective for measuring urodynamics pressure in patients who enrolled and completed the urodynamic procedure.
Secondary	
To evaluate the usability of the device by collecting clinical user feedback and evaluating the following subjective measures using defined ordinal scales: ease of use, ease of insertion, presence of artefacts, stability of the tracing, perceived time savings, ease of voiding around catheter, presence of use errors and overall satisfaction.	The usability performance endpoint will be captured in a questionnaire format. The trained clinical users will rate the T-DOC® 5 Fr performance on a scale of 1-5 on the study outcome questionnaire.
Exploratory	
To explore whether the newly designed, smaller sized T-DOC® 5 Fr catheters causes undue discomfort based on subjective subject feedback regarding the discomfort and pain level, for those able to communicate such feedback.	This exploratory endpoint will be measured by collecting patient feedback (within the abilities of the child) regarding the level of discomfort and pain experienced during their Urodynamic test using the Wong-Baker visual analogue scale. Patients capable of providing feedback on a Visual Analogue Scale, will grade their discomfort/pain at 5 or lower, on the Wong-Baker scale from 0 ("No Hurt") to 10 ("Hurts worst").
To explore the effect of several factors (e.g., age, gender, weight, height) on optimal insertion depth of the T-DOC® 5 Fr catheters.	Subjects' age, gender, weight, and height will be recorded on TDOC5Fr-PEDS-01-CRF1. These data will be analysed to determine a subject stratification approach to be used in examining further hypotheses for later research regarding optimal insertion depth.

Analysis revisions from the protocol

All subjects enrolled and completed the urodynamic procedure will be considered in the final analysis. Enrolled subjects who do not undergo the urodynamic procedure or begin the urodynamic procedure but do not complete it (for any reason determined by the investigator to be unrelated to the T-DOC® 5 Fr catheters) will not be included in the final analysis and can be replaced.

Primary Endpoint

In the statistical analysis plan, the null hypotheses for the safety and effectiveness endpoints are designed to rule out success rates ≤ 75%. The hypotheses as stated in the protocol are based on obtaining a point estimate of ≥ 95% rather than bounding the lowest rate that would be consistent with the observed data.

The allowable Type I error (α) for each hypothesis will be 5% (1-sided), and the Type II error is calculated to be 10% (90% power).

Safety and effectiveness will be evaluated separately via the following sets of hypotheses:

Primary Hypothesis for Safety

- H_0: Clinicians rate T-DOC® 5 Fr vesical and abdominal catheter as safe for measuring urodynamic pressure in ≤ 75% of enrolled pediatric subjects who complete the urodynamic procedure
- H_A: Clinicians rate T-DOC® 5 Fr vesical and abdominal catheter as safe for measuring urodynamic pressure in > 75% of enrolled pediatric subjects who complete the urodynamic procedure

Primary Hypothesis for Effectiveness

- H_0: Clinicians rate T-DOC® 5 Fr vesical and abdominal catheter as effective for measuring urodynamic pressure in ≤ 75% of enrolled pediatric subjects who complete the urodynamic procedure
- H_A: Clinicians rate T-DOC® 5 Fr vesical and abdominal catheter as effective for measuring urodynamic pressure in > 75% of enrolled pediatric subjects who complete the urodynamic procedure

The study will be declared a success if both null hypotheses for safety and efficacy are ruled out.

Secondary Endpoint

In the statistical analysis plan, adjustments are made to the approach that will be followed to evaluate the secondary endpoint to reflect that the goal is to qualitatively describe users' interactions with a device as described in regulatory guidance for usability testing (*FDA's guidance- 'Applying Human Factors and Usability Engineering to Medical Device's, 2016*). Clinical users who have performed three or more procedures with the T-DOC® 5 Fr catheters, shall rate the T-DOC® 5 Fr catheter usability performance on a scale of 1-5 for the clinical user questionnaire, comparing their experience with use of their currently used urodynamics catheter. Responses of 3, 4, or 5 will be tallied as a positive result while responses of 1 or 2 will be tallied as a negative result.

Since there will be 5 responses at most for each of the questions for the secondary endpoint, and the results are thus not well-suited to statistical analysis, hypothesis testing is not appropriate. Instead, the proportions of positive and negative results will be summarized and analysed using descriptive statistics.

Exploratory Analysis

Exploratory Analysis for Discomfort/Pain

To satisfy the first exploratory endpoint (subject experience), a categorical response variable using the Wong-Baker scale from 0 ("No Hurt") to 10 ("Hurts worst") will be used. Subjects will grade their discomfort/pain on the Wong-Baker scale from 0 ("No Hurt") to 10 ("Hurts worst"). of 1, 2, 3, 4, or 5 will be tallied as a positive result while responses of 6, 7, 8, 9, or 10 will be tallied as a negative result.

Because the subjects range in age from 2-12 years, the number of subjects capable of providing feedback on the Wong-Baker scale is anticipated to be limited (≤ 10 is expected). Due to this uncertainty, no formal hypothesis testing will be performed. However, the binary endpoint described above as well as the mode and frequency distribution of the Wong-Baker scale will be used to summarize the results.

Exploratory Analysis for Insertion Depth

To satisfy the second exploratory endpoint, subject data including gender, age, height, weight, adverse events during or immediately following the test and 5-7 days follow-up, catheter insertion depth will be collected as objective evidence on each patient's CRF, where insertion depth is considered the response variable and assumed to be influenced by gender, age, height, weight and/or BMI.

Regression testing can be used to examine the relationship between the insertion depth and collected data (gender, age, height, weight and BMI). The collected data will also be reported using graphical tools based on gender, age, height, weight and BMI. T-tests for differences in insertion depth based on subgroups (male and female, above and below the median height, weight and BMI) will be performed if appropriate.