A Prospective, Pre-Market, Multicenter, Non-significant Risk Study to Validate the Performance of the Poseidon™ System for Fluid Management During Water-aided Colonoscopy.

The Poseidon Trial

CLIN-0100

Rev. B

8/18/2022

CLINICAL INVESTIGATION PLAN

Sponsored By

WAE Design, LLC.

200 Commerce Drive

Northbridge, Massachusetts, USA 01588

STUDY CONTACT INFORMATION

Role	Contact
Clinical Contact	Alexis L. James Director of Clinical Affairs WAE Design, LLC 200 Commerce Drive Northbridge, MA USA 01534 Tel: +1-508-847-9478 Email: alexis.james@waemedical.com
Coordinating Principal Investigator	Andrew Nett, MD Department of Gastroenterology & Hepatology California Pacific Medical Center Sutter Health Department of Gastroenterology & Hepatology San Francisco, CA Tel: +1-415-871-4551 Email: NettAS@sutterhealth.org

SPONSOR PROTOCOL APPROVAL PAGE

Jeffery Ryan Director WAE Design, LLC.	
	Date:
Alexis L. James Director of Clinical Affairs WAE Design, LLC.	
	Date:

STUDY TITLE:	**A Prospective, Pre-Market, Multicenter, Non-significant Risk Study to Validate the Performance of the Poseidon™ System for Fluid Management During Water-aided Colonoscopy.**
PROTOCOL NUMBER:	**CLIN-0100**
VERSION:	**B**

We, the undersigned, have read and approve the protocol specified above and agree on its content.

INVESTIGATOR PROTOCOL SIGNATURE PAGE

A Prospective, Pre-Market, Multicenter, Non-significant Risk Study to Validate the Performance of the Poseidon™ System for Fluid Management During Water-aided Colonoscopy.

CLIN-0100

Protocol Version B

I hereby agree to participate in the above noted study which evaluates the **Poseidon® System** and is Sponsored by WAE Design, LLC. (hereinafter the "Study Sponsor"). I agree to conduct this investigation according to the requirements of the protocol provided by the Study Sponsor, in accordance with all applicable local regulations, and in accordance with the conditions imposed by the reviewing Institutional Review Board (IRB) or Ethics Committee (EC). I agree to supervise all use of the study devices and to ensure appropriate informed consent is obtained from all subjects prior to inclusion in this study.

I understand that this investigation will be monitored by the Study Sponsor and/or a designee employed by the Study Sponsor. This monitoring will involve periodic inspection of my investigational site and ongoing review of the data that are submitted by me to the Study Sponsor.

I am aware that the Study Sponsor reserves the right to discontinue this investigation at any time.

I understand this study protocol and trial results are confidential, and I agree not to disclose any such information to any person other than a representative of the Study Sponsor, the IRB/EC, or regulatory authorities without the prior written consent of the Study Sponsor.

Accepted by:

Investigator Printed Name	Investigator Signature
Institution Name	Date (dd-MMM-yyyy)

PROTOCOL SYNOPSIS

A Prospective, Pre-Market, Multicenter, Non-significant Risk Study to Validate the Performance of the Poseidon™ System for Fluid Management During Water-aided Colonoscopy.	
Study Design	A prospective, pre-market, non-significant risk, multicenter trial
Study Objective	To validate the performance of the Poseidon System™ for fluid management during water-aided endoscopic procedures in the colon.
Study Device and Indication for Use	The Poseidon™ System (WAE Design, LLC Northbridge, MA USA) consists of the following components: • Poseidon Device (100001) (Single-use) • Waste bags Poseidon Device (100006) (Single-use) The Poseidon System is investigationally indicated to provide a pathway to control waste fluid during irrigation of the colon.
Planned Number of Subjects	Up to 30 subjects Fifteen subjects will be enrolled in this study and undergo water-aided colonoscopy with the Poseidon System. If the Primary Endpoint and Secondary Endpoint 1 are achieved in the first 15 subjects, the study will be complete. If the Primary Endpoint or Secondary Endpoint 1 are not achieved, changes to the device design will be made and this protocol will be conducted again in a second group of 15 subjects with updated device.
Planned Number of Investigational Sites	1-2 sites in the United States (US)
Primary Endpoint	1. The design of the Poseidon System meets all acceptance criteria for design validation. a. User is able to operate device per the instructions for use. This criterion will be assessed in a pass/fail manner with an allowance of only 1 failure in the first 15 subjects and 1 failure in the second 15 subjects (if applicable).

	b. User shall not adversely influence typical actuation of a scope during colonoscopy procedure as assessed using a 5-point Likert scale. c. User assessment of functional acceptability of Poseidon device ratchet location as assessed using a 5-point Likert scale. d. User assessment of functional acceptability of Poseidon device intergluteal cleft fit as assessed using a 5-point Likert scale e. The Poseidon System shall minimize passage of fluids through and around the scope lumen when a scope is in the device, as assessed using a 5-point Likert scale. **NOTE:** Criteria B – E must have a mean Likert score of >3 to pass.
Secondary Endpoints	1. Safety defined as the occurrence of all adverse events measured from the Index Procedure through the 2 Week Post Procedure Follow-up Visit. a. The occurrence of > 2 device-related serious adverse events (SAE) is considered a failure 15 subjects and 1 failure in the second 15 subjects (if applicable). 2. Procedure time measured in minutes from the point of scope insertion to the point of scope removal (scope-in / scope-out). 3. Device deficiencies defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance including malfunctions, use errors, and inadequate labelling.
Follow-up Schedule	• Screening Visit a. Informed consent process b. Selection criteria • Index Procedure Visit (May be Combined with Screening) (≤10 Days of Index Procedure) a. Demographic information:

i. Age at time of visit (years)
ii. Gender
iii. Height (cm)
iv. Weight (kg)
v. Race
vi. Ethnicity

b. Device information
   i. Device lot number
c. Type of anesthesia
   i. MAC
   ii. General anesthesia
d. Scope-in time (24-hour clock)
e. Acceptance criteria for design validation
f. Scope-out time (24-hour clock)
g. Adverse events
h. Device deficiencies

- Immediate Post Procedure Assessment
  a. Adverse events
- Discharge
  a. Date of discharge
- Unscheduled Visit
  a. Date of Unscheduled Visit
  b. Reason for Unscheduled Visit
  c. Adverse events
- 2 Week Post Procedure Follow-up (-3/+3 Days) (Telephone or Hospital)
  a. Adverse events
- End of Study

A Prospective, Pre-Market, Multicenter, Non-significant Risk Study to Validate the Performance of the Poseidon™ System for Fluid Management During Water-aided Colonoscopy.	
	a. End of study is defined as the completion of the 2-Week Post Procedure Follow-up Visit, withdrawal or lost-to-follow-up.
Study Duration	Each subject will participate in this study for approximately 2 weeks. Enrollment of 30 subjects is anticipated to 2 months. Following enrollment of the final subject the follow-up period will last approximately 2 weeks. The entire study is anticipated to last a total of 3 months.
Key Inclusion Criteria	1. Patients 18 years of age or greater. 2. Patients that have an indication to undergo water-aided colonoscopy. 3. Subjects with the ability to understand the requirements of the study, who have provided written informed consent, and who are willing and able to return for the required follow-up assessments.
Key Exclusion Criteria	1. Subject unable or unwilling to provide informed consent. 2. Subjects with prolapsing hemorrhoids that require intervention or hemorrhoids that have been treated within last 3 months. 3. Prior TAMIS (Trans-anal minimally invasive surgery) or TEMS (Trans-anal micro endoscopic surgery). 4. Any condition that in the opinion of the Investigator would create an unsafe clinical situation that would not allow the patient to safely undergo an endoscopic procedure. 5. Pregnant or lactating women or women of childbearing potential who do not employ a reliable method of contraception as judged by the Investigator, and/or are not willing to use reliable contraception for the duration of study participation. 6. Patient is enrolled in another trial that could interfere with the endpoint analyses of this trial.
Statistical Methods	This study is not powered and is being conducted by WAE Medical to validate certain aspects of the Poseidon System design that are not assessable in a bench or animal model. Descriptive statistics will be used to analyze the Primary and Secondary Endpoints. Data will be presented using means and standard deviations, median, quartiles, and minimum and maximum, as applicable.

	Distributions of each continuous variable will be assessed prior to analysis and examined for normality. Data with interval or ratio scales to be analyzed that are not normally distributed will be analyzed using non-parametric statistics.
Primary Analysis and Passing Validation	Primary Analysis: The Primary Endpoint for this study is the assessment that the Poseidon™ System meets all acceptance criteria for design validation. a. User is able to operate device per the instructions for use. This criterion will be assessed in a pass/fail manner with an allowance of only 1 failure in the first 15 subjects and 1 failure in the second 15 subjects (if applicable). b. User shall not adversely influence typical actuation of a scope during colonoscopy procedure as assessed using a 5-point Likert scale. c. User assessment of functional acceptability of Poseidon device ratchet location as assessed using a 5-point Likert scale. d. User assessment of functional acceptability of Poseidon device intergluteal cleft fit as assessed using a 5-point Likert scale e. The Poseidon System shall minimize passage of fluids through and around the scope lumen when a scope is in the device, as assessed using a 5-point Likert scale. To assess whether the Primary Endpoint is met in each group of 15 subjects (as applicable), Criteria A-E must all pass receive a passing score. The questionnaire attached in Appendix A will be answer during each case to document performance of the Poseidon System relative to Criteria A-E As defined above, criterion A will be assessed on a pass/fail basis. Only 1 failure in each group of 15 will be allowed; >1 failure will result in failure of criterion A. Criteria B – E will be assessed using a Likert-scale. After 15 each criterion has been assessed in all subjects, scores will be compiled by calculating a mean Likert-score. To pass, each criterion must have a

	mean Likert score of >3. A score ≤ 3 is considered a failure. The rating of the Likert scale will be as follows: • A value of 1 = Strongly Disagree • A value of 2 = Disagree • A value of 3 = Neutral • A value of 4 = Agree • A value of 5 = Strongly Agree <u>Passing Validation:</u> To pass overall validation in the first 15 subjects, the Primary Endpoint and Secondary Endpoint 1 must receive passing scores. If this is achieved in the first 15 subjects the Poseidon System has passed validation and the study is considered complete. If this is not achieved, design changes to the device are warranted. Once the design changes are made, the new device will be tested in an additional 15 subjects. The Primary Endpoint and Secondary Endpoint 1 must receive passing scores. If this is achieved in the second 15 subjects, the Poseidon System has passed the validation. If this is not achieved in the second group of 15 subjects the Poseidon System has failed validation.
Regulatory Status	The Poseidon System is a pre-market investigational device that does not have regulatory clearance in the United States.

TABLE OF CONTENTS

Tables and Figures:

1. Introduction

Colonoscopy for the management of colorectal polyps is the standard of care in the United States with over 15-million procedures performed annually.[1] For polyps greater than 10 mm, endoscopic mucosal resection (EMR) is performed to remove the tissue in a piece-meal fashion. Although effective, EMR presents challenges when perfomed during conventional colonoscopy such as high rates of polyp recurrance and low en-bloc resection, especially in polyps greater than 20mm.[2]

The emergence of water-aided, or "underwater", colonoscopy to combat the challenges experiened during EMR with conventional procedures was first described by Binmoeller et al in 2012.[3] During the procedure, the colon is filled with distilled water or a saline solution instead of air or carbon dioxide, which decreases tension in the colon wall and allows for a natural separation of the mucosal and submucosa from the muscularis propria.[2] Light from the endoscope is refracted in the water which enhances magnification and visualization of tissue. Furthermore, the water or saline solution facilitates maneuverability of the endoscope and causes sessile or flat mucosal lesions to become more contracted and polypoid. All of this combined allows for improved yields during EMR resulting in higher rates of en bloc resection. A recent meta-analysis including 11 studies concluded that underwater EMR outperformed EMR during conventional colonoscopy for en-bloc resection and reported similar rates of intra-procedural and delayed bleeding.[4]

Despite this evidence, there is low adoption of water-aided colonoscopy in everyday practice. A common reason for this is the management of fluid within the colon. There is no standard way to retain, exchange, or collect fluid during the procedure which inevitably results in excess fluid and bio waste leaking from the colon and collecting on the stretcher bed, under and around the patient.

The Poseidon™ System developed by WAE Medical to address the fluid management issues experienced during water-aided colonoscopy. The Poseidon device is inserted into the anal canal before the endoscope. A ratchet mechanism allows for adjustment of the introducer length due to variation in patient anatomy. Once the intruducer is secure a balloon is inflated to prevent fluid from passing out of the patient during a water aided endoscopy. Valves within the device faciliate controlled fluid drainage into an attached waste bag. The endoscope is then inserted into the Poseidon device to begin the colonoscopy. The aim of this study is to validatethe performance of the Poseidon System™ for fluid management during water-aided endoscopic procedures in the colon. .

2. Device Description

The Poseidon System is a fluid management system that is investigationally indicated to provide a pathway to control waste fluid during irrigation of the colon. The Poseidon device is a manually placed and controlled device that provides support and sealing on the perimeter of an endoscope while managing fluids naturally exiting the anus, during a colonoscopy procedure. The device consists of a introducer and hand piece that allows for passage of an endoscope with valves and a retention balloon that minimize fluid passage with a single-use

waste bag for collecting fluid and debris. The Poseidon™ System is not yet FDA 510(k) cleared.

2.1. *Device Components*

The Poseidon System is comprised of the following components:

- **Poseidon Device (100001) (Single-Use):** The device consists of the introducer and balloon cuff insufflator. Once the introducer is lubricated on the balloon it is then inserted into the rectum and locked into place. The balloon is then inflated to stabilize the device before the endoscope is inserted. (**Figure 1**)
- **Poseidon Waste bag (Single-use):** The waste bag is attached to the vacuum line outside the subject allowing for fluid to be drained into the bag. It is regulated with a relief valve. (**Figure 2**)

Figure 1: Poseidon Device:

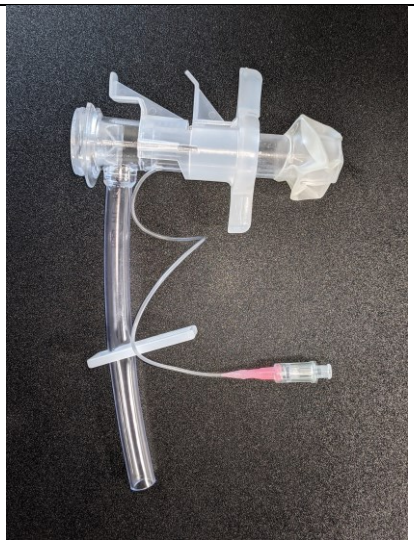
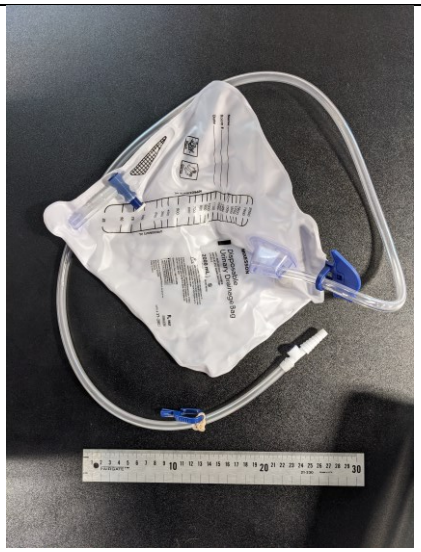


Figure 2: Poseidon Waste Bag:



2.2. *Pre-clinical Testing*

The following is a list of completed testing to support a future the IRB submission and possible 510(k):

- Sterility: Validation results are not required for the submission. Sterilization method is hydrogen peroxide (H_2O_2)
- Shelf Life: Including device performance, package integrity testing after simulated distribution and accelerated aging to support an expiration date. Shelf life is 6 months.
- Biocompatibility: Testing per 10993-1 for all patient contacting materials

- Verification: Testing as determined by Risk Management and design requirements including includes tensile, dimensional, stiffness or other testing of product attributes
- Simulated use: In a bench top model demonstrating intended user can use the device as intended and device performs to specification.

3. Study Objectives

To validate the performance of the Poseidon™ System for fluid management during water-aided endoscopic procedures in the colon.

4. Study Endpoints

4.1. *Primary Endpoint*

The primary endpoint for this study is the assessment that the Poseidon device meets all acceptance criteria for design validation.

1. The design of the Poseidon System meets all acceptance criteria for design validation.
    a. User is able to operate device per the instructions for use. This criterion will be assessed in a pass/fail manner with an allowance of only 1 failure in the first 15 subjects and 1 failure in the second 15 subjects (if applicable).
    b. User shall not adversely influence typical actuation of a scope during colonoscopy procedure as assessed using a 5-point Likert scale.
    c. User assessment of functional acceptability of Poseidon device ratchet location as assessed using a 5-point Likert scale.
    d. User assessment of functional acceptability of Poseidon device intergluteal cleft fit as assessed using a 5-point Likert scale
    e. The Poseidon System shall minimize passage of fluids through and around the scope lumen when a scope is in the device, as assessed using a 5-point Likert scale.

    NOTE: Criteria B – E must have a mean Likert score of >3 to pass. The rating of the Likert scale will be as follows:

    - A value of 1 = Strongly Disagree
    - A value of 2 = Disagree
    - A value of 3 = Neutral
    - A value of 4 = Agree
    - A value of 5 = Strongly Agree

The questionnaire that will be used to assess the Primary Endpoint is attached in Appendix A.

4.2. *Secondary Endpoints*

The secondary endpoints for this study are as follows:

1. Safety defined as the occurrence of all adverse events measured from the Index Procedure through the 2 Week Post Procedure Follow-up Visit.
    a. The occurrence of > 2 device-related serious adverse events (SAE) is considered a failure 15 subjects and 1 failure in the second 15 subjects (if applicable).
2. Procedure time measured in minutes from the point of scope insertion to the point of scope removal (scope-in / scope-out).
3. Device deficiencies defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance including malfunctions, use errors, and inadequate labelling.

5. Study Design

This study is a prospective, pre-market, non-significant risk, multicenter trial.

5.1. *Scale and Duration*

Up to 30 subjects will be enrolled in this study.

Initially 15 subjects will be enrolled in this study and undergo water-aided colonoscopy with the Poseidon™ System. If the Primary Endpoint and Secondary Endpoint 1 are achieved in the first 15 subjects, the study will be complete.

If the Primary Endpoint or Secondary Endpoint 1 are not achieved, changes to the device design will be made and this protocol will be conducted again in a second group of 15 subjects with updated device. All studies sites and associated IRBs will be notified if the second group of 15 subjects will need to be enrolled.

It is anticipated that enrollment of the first 15 subject will take a period of 2 month. If enrollment of the second 15 subjects is required, it is estimated that device design changes will take 1-2 months, and enrollment of the second group of 15 subjects will take a period of 2 months.

Each subject will be followed for approximately 2 weeks following the procedure. Overall the study take 3-7 months to complete.

5.2. *Study Devices*

All subjects enrolled in this study will undergo water-aided colonoscopy with fluid management performed by the Poseidon™ System. All devices used during the procedure be captured on the applicable case report form (CRF).

5.3. *Non-significant Risk Justification*

Per 21 CFR 812.3, a significant risk device means an investigational device that:

- Is intended as an implant and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is purported or represented to be for use supporting or sustaining human life and presents a potential for serious risk to the health, safety, or welfare of a subject;
- Is for a use of substantial importance in diagnosing, curing, mitigating, or treating disease, or otherwise preventing impairment of human health and presents a potential for serious risk to the health, safety, or welfare of a subject; or
- Otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.

The Poseidon System does not meet any of the above criteria of a significant risk device and therefore can be categorized as a non-significant risk (NSR) device.

5.4. *Justification for Study Design*

WAE Medical is conducting this NSR study to validate certain aspects of the Poseidon System design that are not assessable in a bench or animal model. The study will be conducted according to abbreviated IDE regulations as per 21 CFR 812.2(b) and will require the approval of NSR status by all participating IRBs.

6. Subject Selection

Patients who meet all of the inclusion criteria and none of the exclusion criteria will be considered for enrollment in this study.

6.1. *Inclusion Criteria*

1. Patients 18 years of age or greater.
2. Patients that have an indication to undergo water-aided colonoscopy.
3. Subjects with the ability to understand the requirements of the study, who have provided written informed consent, and who are willing and able to return for the required follow-up assessments.

6.2. *Exclusion Criteria*

1. Subject unable or unwilling to provide informed consent.
2. Subjects with prolapsing hemorrhoids that require intervention or hemorrhoids that have been treated within last 3 months.
3. Prior TAMIS (Trans anal minimally invasive surgery) or TEMS (Trans anal micro endoscopic surgery).
4. Any condition that in the opinion of the Investigator would create an unsafe clinical situation that would not allow the patient to safely undergo an endoscopic procedure.
5. Pregnant or lactating women or women of childbearing potential who do not employ a reliable method of contraception as judged by the Investigator, and/or are not willing to use reliable contraception for the duration of study participation.
6. Patient is enrolled in another trial that could interfere with the endpoint analyses of this trial.

7. Subject Accountability

7.1. *Point of Enrollment*

Subjects may be enrolled in this study if they sign and date the informed consent form (ICF) and meet all of the selection criteria noted in Section 6 of this protocol. No study-related activity can take place until the subject is considered enrolled.

7.2. *Screen Failure*

Patients that do not meet the selection criteria noted in Section 6 of this protocol will be considered Screen Failures. Subjects that are enrolled in the study may screen out of the study up to, and during the index procedure if any of the selection criteria noted in Section 6 of the protocol are found not to be met. Screen failures will not be counted towards enrollment and will be replaced. Screen failures will be accounted for on the applicable case report form (CRF).

7.3. *Withdrawal*

Study participation is voluntary and a subject may decide to withdraw their consent at any time with or without reason and without impact on their continued medical care.

A study Investigator may withdraw a subject form the study without the subject's consent. If this occurs, the Investigator will inform the subject. Reasons for subject withdrawal by an Investigator may include, but are not limited to:

- The Investigator decides it is in a subject's best interest not to continue participating in the study.
- The Investigator decides that it may be harmful for a subject to continue participating in the study.

- The subject is not compliant with study required follow-up.
- The study Sponsor (WAE Medical, Inc.) terminates the study early.
- The IRB, EC, or a regulatory agency decides to terminate the study early.
- The subject is considered lost-to-follow-up.

If a subject withdraws from the clinical study or if they are withdrawn by an Investigator, their status and reason for withdrawal will be documented on the applicable study CRF.

Subjects that withdraw or are withdrawn by the Investigator from the study after undergoing treatment with the study or control device will not be replaced for enrollment. Subjects who withdraw or are withdrawn from the study prior to undergoing treatment with the study or control device will be replaced for enrollment.

All applicable CRFs up to the point of withdrawal must be completed and will be used for analysis.

7.4. *Lost-to-Follow-up*

In order to consider a subject lost-to-follow-up, site personnel should first make all reasonable efforts to locate and communicate with the subject. All attempts to contact the subject must be recorded in the subject's study file including the date, time and name of site personnel who have attempted to contact the subject. Subjects who are deemed lost-to-follow-up will not be replaced for enrollment and will be accounted for on the applicable study CRF.

All applicable CRFs up to the point of lost-to-follow-up status must be completed and will be used for analysis.

7.5. *Enrollment Controls*

8. The Sponsor will closely monitor enrollment for this study. Sites will be asked to notify the Sponsor regarding each new subject to be screened and enrolled. Sites will be notified when overall enrollment is close to reaching 15 and when enrollment is complete. If the Primary Endpoint and Secondary Endpoint 1 are not achieved, Sites and associated IRBs will be informed that device design changes will be made (which will take approximately 1-2 months). When it is time to begin enrollment of the second group of 15 subjects, sites and associated IRBs will be notified. Once again, the Sponsor will closely monitor enrollment and sites as was done with the first 15 subject.Study Methods

8.1. *Data Collection Schedule*

Table 1.0 below provides a schedule of required study visits as well as assessments. Details regarding each study visit are provided in the following sections.

Table 1: Schedule of Required Visits and Assessments

Procedure/Assessment	Screening* (≤10 Days of Index Procedure)	Index Procedure (0 Days)	Discharge	Follow-up Visits	
				2 Weeks× (± 7 Days)	Unscheduled Visit
Informed Consent	X				
Inclusion / Exclusion	X				
Enrollment	X				
Demographics		X			
Medical History		X			
Device Information		X			
Anesthesia Information		X			
Acceptance Criteria for Design Validation		X			
Total Procedure Time (Scope-in / Scope-out)		X			
Adverse Events		X	X	X	X
Device Deficiencies		X			
End of Study §				X	

* May be combined with the Index Procedure Visit.
§ End of study is defined as completion of the 2-week Post Procedure Follow-up Visit, withdrawal, lost-to-follow-up, or death; whichever occurs first.
×The 2 Week Post Procedure Follow-up Visit may be performed as a telephone all or in-hospital visit.

8.2. *Source Documentation*

A source document is the first place where data is recorded for a clinical study. Source documents may include a subject's original medical record, source worksheets provided by the Sponsor for a specific clinical study, procedure and follow-up notes, clinical or office charts, imaging and imaging reports, etc. Source documents may be hard copy or electronic. All source documentation for this study must be maintained at the study site and made available for monitoring by the Sponsor and/or their representatives. Data from source documentation will be used by the clinical site to complete the CRFs for this study.

8.3. *Screening (Within 10 Days of Index Procedure) (Hospital/Clinic Visit)*

The Screening Visit may be performed at the same time as the Index Procedure. During the Screening Visit the following data collection and assessments will be performed:

1. Date of visit
2. Informed consent process
3. Inclusion/Exclusion criteria (refer to Section 6 of this protocol)
4. Enrollment (refer to Section 7 of this protocol)

8.3.1. *Informed Consent Process*

All subjects taking part in this clinical study must undergo the informed consent process. Subjects must be allowed adequate time to review the consent, raise questions, and make a voluntary decision to participate in the clinical study. Each subject must sign and date the IRB/EC approved ICF before any clinical study-related procedures are performed. A copy of signed ICF will be provided to the subject for his/her records. Study personnel should explain to the subject that even if the subject agrees to participate in the study and signs the ICF, during the procedure they demonstrate not to be a suitable candidate for the study and screen out.

8.4. *Index Procedure*

8.4.1. *Poseidon Procedure*

All enrolled subjects will undergo water-aided colonoscopy using the Poseidon System for fluid management. The operator of the Poseidon device must be a physician and must have received sufficient training in clinical endoscopic technique.

Investigators will assemble and place the Poseidon System prior to initiating colonoscopy according to the investigational instructions for use .

8.4.2. *Data Collection*

During the Index Procedure Visit, the following data collection and assessments will be performed for both study arms:

- Date of Index Procedure
- Demographic information including:
    - Age at the time of the visit (years)
    - Gender
    - Height (cm)
    - Weight (kg)
    - Race
    - Ethnicity
- Device information
- Type of anesthesia:
    - MAC
    - General
- Scope-in time (24 hour clock)
- Acceptance Criteria for Design Validation
- Scope-out time (24 hour clock)
- Adverse events
- Device deficiencies

8.5. *Immediate Post Procedure Visit*

- Adverse events

8.6. *Discharge*

At the point of Discharge the following data collection and assessments will be performed for both study arms:

- Date of discharge

8.7. *2 Week Post Procedure Follow-up Visit (Telephone or Hospital) (+/- 3 day window)*

The 2 Week Post Procedure may be performed over the phone or in the hospital. The following data will be collected during this visit:

- Date of Follow-up Visit
- Adverse events

8.8. *Unscheduled Visit*

Unscheduled Visits are visits where study subjects are seen in person or over the phone between protocol required follow-up visits. If an Unscheduled Visit occurs the following data will be collected for both study arms:

- Date of Unscheduled Visit
- Reason for Unscheduled Visit
- Adverse events

8.9. *End of Study*

End of study is defined as the completion of the 2-Week Post Procedure Follow-up Visit, withdrawal, lost-to-follow-up, or death; whichever occurs first. At this point, a subject's participation in the study will end.

9. Statistical Considerations

9.1. *Endpoints*

9.1.1. *Primary Endpoint*

The Primary Endpoint for this study is the assessment that the Poseidon™ System meets all acceptance criteria for design validation.

f. User is able to operate device per the instructions for use. This criterion will be assessed in a pass/fail manner with an allowance of only 1 failure in the first 15 subjects and 1 failure in the second 15 subjects (if applicable).

g. User shall not adversely influence typical actuation of a scope during colonoscopy procedure as assessed using a 5-point Likert scale.

h. User assessment of functional acceptability of Poseidon device ratchet location as assessed using a 5-point Likert scale.

i. User assessment of functional acceptability of Poseidon device intergluteal cleft fit as assessed using a 5-point Likert scale

j. The Poseidon System shall minimize passage of fluids through and around the scope lumen when a scope is in the device, as assessed using a 5-point Likert scale.

To assess whether the Primary Endpoint is met in each group of 15 subjects (as applicable), Criteria A-E must all pass receive a passing score. The questionnaire attached in Appendix A will be answer during each case to document performance of the Poseidon System relative to Criteria A-E

As defined above, criterion A will be assessed on a pass/fail basis. Only 1 failure in each group of 15 will be allowed; >1 failure will result in failure of criterion A.

Criteria B – E will be assessed using a Likert-scale. After 15 each criterion has been assessed in all subjects, scores will be compiled by calculating a mean Likert-score. To pass, each criterion must have a mean Likert score of >3. A score ≤ 3 is considered a failure. The rating of the Likert scale will be as follows:

- A value of 1 = Strongly Disagree
- A value of 2 = Disagree
- A value of 3 = Neutral
- A value of 4 = Agree
- A value of 5 = Strongly Agree

9.1.2. *Secondary Endpoints*

The secondary endpoints for this study are as follows:

1. Safety defined as the occurrence of all adverse events measured from the Index Procedure through the 2 Week Post Procedure Follow-up Visit.
    a. The occurrence of > 2 device-related serious adverse events (SAE) is considered a failure 15 subjects and 1 failure in the second 15 subjects (if applicable).
2. Procedure time measured in minutes from the point of scope insertion to the point of scope removal (scope-in / scope-out).
3. Device deficiencies defined as an inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance including malfunctions, use errors, and inadequate labelling.

9.2. *General Statistical Methods*

Descriptive statistics will be used to analyze the Primary and Secondary Endpoints. Data will be presented using means and standard deviations, median, quartiles, and minimum and maximum, as applicable..

Distributions of each continuous variable will be assessed prior to analysis and examined for normality. Data with interval or ratio scales to be analyzed that are not normally distributed will be analyzed using non-parametric statistics..

9.2.1. *Number of Subjects per Investigative Site*

If one clinical site is used for this study, it will enroll up to 30 subjects. If two clinical sites are used for this study an effort to have similar enrollment at each center will be made (i.e. 7 or 8 subjects at each site for each group of 15).

9.3. *Sample Size*

This study will enroll up to 30 subjects. Sample size determination is based on WAE Design Control and Validation Procedures.

9.4. *Data Analyses*

To assess whether the Primary Endpoint is met in each group of 15 subjects (as applicable), Criteria A-E must all pass receive a passing score. The questionnaire attached in Appendix A will be answer during each case to document performance of the Poseidon System relative to Criteria A-E

As defined above, criterion A will be assessed on a pass/fail basis. Only 1 failure in each group of 15 will be allowed; >1 failure will result in failure of criterion A.

Criteria B – E will be assessed using a Likert-scale. After 15 each criterion has been assessed in all subjects, scores will be compiled by calculating a mean Likert-score. To pass, each criterion must have a mean Likert score of >3. A score ≤ 3 is considered a failure. The rating of the Likert scale will be as follows:

- A value of 1 = Strongly Disagree
- A value of 2 = Disagree
- A value of 3 = Neutral
- A value of 4 = Agree
- A value of 5 = Strongly Agree

Secondary Endpoints will be analyzed as follows:

1. Safety: All adverse events will be collected and assessed for relationship to the study device and/or study procedure, seriousness, and severity. Adverse events will be grouped by type and presented in frequencies. If >2 device related SAEs occur, the endpoint will fail.
2. Overall Procedure Time: The mean of all procedure times will be taken. There are no pass/fail criteria for this endpoint.
3. Device Deficiencies: All device deficiencies will be collected, grouped by type, relationship to adverse events, and presented in frequencies. There are no pass/fail criteria for this endpoint.

9.5. *Passing Overall Validation*

To pass overall validation in the first 15 subjects, the Primary Endpoint and Secondary Endpoint 1 must receive passing scores. If this is achieved in the first 15 subjects the Poseidon System has passed validation and the study is considered complete. If this is not achieved, design changes to the device are warranted.

Once the design changes are made, the new device will be tested in an additional 15 subjects. The Primary Endpoint and Secondary Endpoint 1 must receive passing scores. If this is achieved in the second 15 subjects, the Poseidon System has passed the validation. If this is not achieved in the second group of 15 subjects the Poseidon System has failed validation.

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9.5.1. *Interim Analyses*

No interim analyses are planned for this study.

9.5.2. *Changes to Planned Analyses*

Any changes to the planned statistical analyses made prior to performing the analysis will be documented and approved in this protocol. Changes from the planned statistical methods after performing the final analysis will be documented in the clinical study report along with a reason for the deviation.

10. Data Management

10.1. *Data Collection, Processing, and Review*

Subject data will be recorded using electronic CRFs (eCRFs) in a web-based, limited access, electronic data capture (EDC) system.

The clinical database will reside on a production server hosted by the EDC System. All changes made to the clinical data will be captured in an electronic audit trail and available for review by the Sponsor or its representative. The associated software and database have been designed to meet regulatory compliance for deployment as part of a validated system compliant with laws and regulations applicable to the conduct of clinical studies pertaining to the use of electronic records and signatures. Database backups are performed regularly.

The Investigator provides his/her electronic signature on the appropriate electronic case report forms (eCRFs) in compliance with local regulations. Changes to data previously submitted to the Sponsor require a new electronic signature by the Investigator acknowledging and approving the changes.

The Sponsor will perform visual and/or electronic data review to identify possible data discrepancies. Manual and/or automatic queries will be created in the EDC system and will be issued to the site for appropriate response. Site staff will be responsible for resolving all queries in the database.

10.2. *Data Retention*

The Principal Investigator or his/her designee or Investigational site will maintain, at the clinical site, all essential study documents and source documentation that support the data collected on the study subjects in compliance with ICH/GCP guidelines. Documents must be retained for at least 2 years after the last approval of a marketing application or until at least 2 years have elapsed since the formal discontinuation of the clinical investigation of the

product. These documents will be retained for a longer period of time by agreement with WAE Medical or in compliance with other country/regional/local regulations.

The Principal Investigator or his/her designee will take measures to ensure that these essential documents are not accidentally damaged or destroyed. If for any reason the Principal Investigator or his/her designee withdraws responsibility for maintaining these essential documents, custody must be transferred to an individual who will assume responsibility and WAE Medical must receive written notification of this custodial change. Sites are required to inform WAE Medical in writing where paper or electronic files are maintained in case files are stored off site and are not readily available.

11. Amendments

If a protocol revision is necessary which affects the rights, safety or welfare of the subject or scientific integrity of the data, an amendment is required. Appropriate approvals of the revised protocol must be obtained prior to implementation.

12. Protocol Deviations

An Investigator must not make any changes or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency. An Investigator shall notify the Sponsor and the reviewing IRB/EC of any deviation from the investigational plan to protect the life or physical well-being of a subject in an emergency, and those deviations which affect the scientific integrity of the clinical investigation. Such notice shall be given as soon as possible, but no later than 5 working days after the emergency occurred, or per prevailing local requirements, if sooner than 5 working days.

All deviations from the investigational plan, with the reason for the deviation and the date of occurrence, must be documented and reported to the Sponsor. Sites may also be required to report deviations to the IRB/EC, per local guidelines and regulations.

Deviations will be reviewed and evaluated on an ongoing basis and, as necessary, appropriate corrective and preventive actions such as site re-training, site enrollment hold or site discontinuation will be put into place by the Sponsor.

13. Device Accountability

Investigational devices from the Sponsor, the devices will only be used for the purpose of this clinical study and they will be maintained in a secure, limited-access area. All investigational devices provided to a clinical site will be labeled with the wording "CAUTION -- Investigational device. Limited by Federal (or United States) law to investigational use." As required by 21 CFR 812.5. Receipt and disposition of these devices shall be kept in the device accountability log for this study.

The Sponsor shall keep records to document the physical location of all study devices from the point of shipment until use, return, or disposal.

Clinical sites that use their own commercial equipment must still track the devices used for the purpose of the study on the device accountability log.

The Principal Investigator or an authorized designee will maintain the device accountability log for this study. The following information will be required for every device:

- Date of receipt (if provided by Sponsor for purpose of clinical study)
- Product ID number
- Serial number of capital equipment
- Lot number of disposable devices
- Expiration date (as applicable)
- Date of device use
- Subject ID number in which the device was used
- Date device was returned to Sponsor (as applicable)
- Reason device was returned to Sponsor (as applicable)

14. Compliance

14.1. *Statement of Compliance*

This post market study will be conducted in accordance with this protocol, ISO 14155, The Declaration of Helsinki, ICH Guidelines for Good Clinical Practices, applicable parts of the US Code of Federal Regulations, and pertinent individual country laws and regulations. The study shall not begin until the required approval/favorable opinion from the IRB/EC is obtained. Any additional requirements imposed by the IRB/EC shall be followed, if appropriate.

14.2. *Investigator Responsibilities*

The Principal Investigator of an investigational site is responsible for ensuring that the study is conducted in accordance with the Clinical Trial Agreement, the protocol, ISO 14155, ethical principles that have their origins in the Declaration of Helsinki, any conditions of approval imposed by the reviewing IRB/EC, and prevailing local and/or country laws and/or regulations, whichever affords the greater protection to the subject.

The Principal Investigator's responsibilities include, but are not limited to, the following.

- Prior to beginning the study, sign the Clinical Trial Agreement and comply with the Investigator responsibilities as described in such Agreement.
- Prior to beginning the study, sign the Protocol Signature page documenting his/her agreement to conduct the study in accordance with the protocol.
- Provide his/her qualifications and experience to assume responsibility for the proper conduct of the study and that of key members of the site team through up-to-date

curriculum vitae or other relevant documentation and disclose potential conflicts of interest, including financial, that may interfere with the conduct of the clinical study or interpretation of results.

- Make no changes in, or deviate from this protocol, except to protect the life and physical well-being of a subject in an emergency; document and explain any deviation from the approved protocol that occurred during the course of the clinical investigation.
- Create and maintain source documents throughout the clinical study and ensure their availability with direct access during monitoring visits or audits; ensure that all clinical-investigation-related records are retained per requirements.
- Ensure the accuracy, completeness, legibility, and timeliness of the data reported to the Sponsor in the CRFs and in all required reports.
- Record, report (Sponsor, IRB/EC as applicable), and assess the relationship and seriousness of adverse events to the device and procedure, as applicable per the protocol.
- Record and report (Sponsor, IRB/EC as applicable) all device deficiencies.
- Report to Sponsor, per the protocol requirements, all Serious Adverse Events (SAEs) and device deficiencies that could have led to a Serious Adverse Device Effect (SADE) and potential/Unanticipated Serious Adverse Device Effect (USADE) or Unanticipated Adverse Device Effect (UADE).
- Report to the IRB/EC and regulatory authorities any SAEs and device deficiencies that could have led to a SADE and potential/USADE or UADE, if required by the national regulations or this protocol or by the IRB/EC, and supply WAE Medical with any additional requested information related to the safety reporting of a particular event.
- Maintain the device accountability records and control of the device, ensuring that the study device is used only by authorized/designated users and in accordance with this protocol and instructions/directions for use.
- Allow the Sponsor to perform monitoring and auditing activities and be accessible to the clinical research monitor or auditor and respond to questions during monitoring visits or audit(s).
- Allow and support regulatory authorities and the IRB/EC when performing auditing activities.
- Ensure that informed consent is obtained from all subjects in accordance with applicable laws, this protocol and local IRB/EC requirements.
- Provide adequate medical care to a subject during and after a subject's participation in a clinical study in the case of adverse events, as described in the ICF.
- Inform the subject of the nature and possible cause of any adverse events experienced.
- As applicable, provide the subject with necessary instructions on proper use, handling, storage, and return of the study device when it is used/operated by the subject.

- Inform the subject of any new significant findings occurring during the clinical investigation, including the need for additional medical care that may be required.
- Provide the subject with well-defined procedures for possible emergency situations related to the clinical study, and make the necessary arrangements for emergency treatment, including decoding procedures for blinded/masked clinical investigations, as needed.
- Ensure that clinical medical records are clearly marked to indicate that the subject is enrolled in this clinical study.
- Ensure that, if appropriate, subjects enrolled in the clinical investigation are provided with some means of showing their participation in the clinical investigation, together with identification and compliance information for concomitant treatment measures (contact address and telephone numbers shall be provided).
- Inform, with the subject's approval or when required by national regulations, the subject's personal physician about the subject's participation in the clinical investigation.
- Make all reasonable efforts to ascertain the reason(s) for a subject's premature withdrawal from clinical investigation while fully respecting the subject's rights.
- Ensure that an adequate investigation site team and facilities exist and are maintained and documented during the clinical investigation.
- Ensure that maintenance and calibration of the equipment relevant for the assessment of the clinical investigation is appropriately performed and documented, where applicable.

14.2.1. ***Delegation of Authority***

When specific tasks are delegated by an Investigator, including but not limited to conducting the informed consent process, the Principal Investigator is responsible for providing appropriate training and adequate supervision of those to whom tasks are delegated. The Investigator is accountable for regulatory violations resulting from failure to adequately supervise the conduct of the clinical study.

14.3. ***Institutional Review Board/Ethics Committee***

The protocol and ICF must have the approval of a properly constituted committee ("Institutional Review Board" / "Ethics Committee") responsible for approving clinical trials. The signed IRB/EC approval letter must identify the documents approved (i.e., list the Investigator 's name, the protocol title, and date of approval, and informed consent document). A copy of the approval of the protocol (or permission to conduct the study) and ICF, must be received by the Sponsor before recruitment of subjects into the study and shipment of investigational product/equipment. Prior approval must also be obtained for other materials related to subject recruitment or which will be provided to the subject.

Annual IRB/EC approval and renewals will be obtained throughout the duration of the study as required by local/country or IRB/EC requirements. Copies of the Investigator's reports and the IRB/EC continuance of approval must be provided to the Sponsor.

14.4. ***Sponsor Responsibilities***

- As the study Sponsor, WAE Medical, Inc. is responsible for the overall conduct and quality of the study, including the assurance that the study complies with the appropriate standards and regulations that apply to medical device clinical investigations. WAE Medical will also ensure adherence to the Sponsor general duties as outlined by GCP standards, the US FDA, and as required pertinent individual country laws and regulations. Additionally, the WAE Medical study management will ensure that qualified monitors are monitoring the study according to the protocol, GCP standards and study regulations, and that the Informed Consent process is followed per each site's local and US FDA requirements.
- WAE Medical will ensure the study is registered at a minimum on clinicaltrials.gov as per applicable regulations.
- WAE Medical will select qualified and experienced Investigators and clinical sites to participate in the study and will obtain financial disclosure of participating Investigators.
- The Sponsor will ensure all Investigators and clinical study staff are trained to the study protocol, applicable study specific documentation, and other study specific requirements. Documentation of training will be maintained.
- WAE Medical will select or designate clinical monitors who are qualified by training and experience, to monitor and oversee the conduct of the study.
- WAE Medical will ensure all information and data received regarding study subjects or their participation in this study is kept confidential. Only authorized WAE Medical personnel or an WAE Medical representative including, but not limited to, monitors and a Contract Research Organization (CRO) will have access to these confidential records. WAE Medical may have access to a subject's identifiable health information but will keep this information confidential in accordance with all applicable laws and regulations. WAE Medical may use subjects' health information to conduct this research, as well as for additional purposes, such as overseeing and improving the performance of its device, new medical research and proposals for developing new medical products or procedures, and other business purposes. Information received during the study will not be used to market to subjects; subject names will not be placed on any mailing lists or sold to anyone for marketing purposes.
- Sponsor or CRO representative may request access to all study records, including source documents, for inspection and duplication. In the event that an Investigator is contacted by a regulatory agency or local IRB in relation to this study, the Investigator will notify the Sponsor or designated monitor/CRO as soon as possible. Authorized regulatory personnel have the right to inspect and copy all records pertinent to this study.
- Study data collected during this study may be used by WAE Medical for the purposes of this study, publication, and to support future research and/or other business purposes. All data used in the analysis and reporting of this study will be without identifiable reference to specific subject name.

- The Sponsor will maintain records of the clinical study for a minimum of 2 years after the final study report is completed, or longer if required by local or national regulatory agencies.
- The Sponsor will ensure safety reporting to regulatory authorities, as appropriate, according to local/country specific regulations.
- WAE Medical will ensure a final study report is provided to all IRBs/ECs and regulatory authorities (as applicable).

14.4.1. ***Role of WAE Medical Representatives in Procedures***

WAE Medical personnel can provide technical support to the Investigator and other health care personnel (collectively HCP) as needed during an Poseidon Device procedure. Support may include HCP training, product troubleshooting, addressing HCP questions, or providing clarifications to HCPs concerning the operation of WAE Medical equipment/devices.

In addition, WAE Medical personnel may perform certain activities to ensure study quality. These activities may include the following.

- Observing procedures to provide information relevant to protocol compliance
- Reviewing collected data and study documentation for completeness and accuracy

WAE Medical **personnel will not do the following.**

- Practice medicine
- Provide medical diagnosis or treatment to subjects
- Make suggestions or offer opinions regarding the manner in which the Investigator or site staff performs or should not perform any particular aspect of the study procedure, other than ensuring that the device is being used appropriately and safely
- Discuss a subject's condition or treatment with a subject without the approval and presence of the Investigator
- Independently collect critical study data (defined as primary or secondary endpoint data)
- Enter data in EDC systems or on paper CRFs

14.5. ***Insurance***

Where required by local/country regulation, proof and type of insurance coverage, by WAE Medical for subjects in the study will be obtained.

15. Monitoring

On site and/or remote monitoring will be performed during the study to assess continued compliance with the protocol and applicable regulations. In addition, the clinical research monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Principal

Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively. The Principal Investigator /institution guarantees direct access to original source documents by WAE Medical personnel, their designees, and appropriate regulatory authorities. The frequency of monitoring visits will be determined by the Sponsor. The Sponsor will contact a clinical site ahead of time to schedule monitoring visits on a date agreeable to both parties.

The study may also be subject to a quality assurance audit by WAE Medical or its designees, as well as inspection by appropriate regulatory authorities. Notice regarding audit dates/scheduling will be provided to a site ahead of time. It is important that the Principal Investigator and relevant study personnel be available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

16. Potential Risks and Benefits

16.1. *Risks Associated with the Poseidon Device*

Use of the Poseidon™ System during water-aided endoscopy procedures poses no new risks to the patient than the risks of the colorectal intubation. Risks associated with the Poseidon device or procedure include but are not limited to:

- Anal canal Irritation
- Tissue abrasion from cuff over inflation

In addition to the risks listed above, the risks related to endoscopy and anesthesia should be explained to the subject.

Risks related to anesthesia include:

- Postoperative confusion
- Heart attack
- Pneumonia
- Stroke

16.2. *Risk Minimization Actions*

All efforts will be made to minimize these potential risks by:

- Selection of qualified Investigators and qualified investigational centers;
- Training the Investigators on proper technique for the Poseidon Device;
- Training the Investigators and on adherence to the study protocol and system IFU;
- Observation of procedures by the WAE Medical, Inc. and/or clinical personnel, as needed;

- Defining clear inclusion/exclusion criteria that ensure only appropriate subjects are enrolled and treated;
- Scheduled monitoring visits to the investigational site; and
- Regular communication with Investigator(s) and staff.

16.3. ***Anticipated Benefits***

Benefits of undergoing water aided endoscopy with the Poseidon device as compared to without may include:

- Potentially improved waste fluid management during water aided procedures
- Potentially less procedural time associated with improving colonoscope control
- Potentially lower risk for transmission of communicable bacteria/viruses

17. Safety Reporting

17.1. ***Adverse Event Definitions***

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

- **NOTE 1:** This includes events related to the investigational medical device.
- **NOTE 2**: This definition includes events related to the procedures involved.
- **NOTE 3:** For users or other persons, this definition is restricted to events related to the investigational medical device.

- **Serious Adverse Event (SAE):** An adverse event that meets one or more of the following criteria:
  - led to death,
  - led to serious deterioration in the health of the subject, that either resulted in
    - a life-threatening illness or injury, or
    - a permanent impairment of a body structure or a body function, or
    - in-patient or prolonged hospitalization, or
    - medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
  - led to fetal distress, fetal death or a congenital abnormality or birth defect
  - **NOTE 1:** Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without a serious deterioration in health, is not considered a serious adverse event.

- **Unanticipated Adverse Device Effect (UADE):** Any serious adverse event caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the investigational plan or application (including a supplementary plan or application), or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects.

- **Device Deficiency:** An inadequacy of an investigational medical device related to its identity, quality, durability, reliability, safety, or performance. This may include malfunctions, use error, or inadequacy in the information supplied by the manufacturer.
    - **NOTE 1:** Any device deficiency that might have led to a serious adverse event if a) suitable action had not been taken or b) intervention had not been made or c) if circumstances had been less fortunate is considered a reportable event.

17.2. ***Adverse Event Relationship Definitions***

All adverse events must be assessed for relationship to the study or control device (as applicable) and procedure by the Investigator. Relationship definitions are as provided below:

- **Not Related:** The event is due to an underlying or concurrent illness or effect of another device, drug or intervention and is not related to the investigational device, procedure or general surgery.
- **Possible:** The event has a strong temporal relationship to the use of the investigational device, procedure or general surgery, and an alternative etiology is equally or less likely.
- **Probable:** The event has a strong temporal relationship to the use of the investigational device, procedure or general surgery and another etiology is unlikely or significantly less likely.
- **Definite:** An event that can only be attributed to the use of the investigational device, procedure or general surgery.
- **Not Assessable:** The event's relationship to the use of the investigational device, procedure or general surgery cannot be assessed.
    - **NOTE 1:** Adverse events with a definite or probable relationship to the device or procedure are considered **"related"** events.

17.3. ***Adverse Event Severity Definitions***

All adverse events must be assessed for severity by the Investigator. Severity definitions are as provided below:

- **Mild:** Awareness of signs or symptoms, but easily tolerated; are of minor irritant type; causing no loss of time from normal activities; symptoms would not require medication or a medical evaluation; signs or symptoms are transient.
- **Moderate:** Interferes with the subject's usual activity and/or requires symptomatic treatment.
- **Severe:** Symptom(s) causing severe discomfort and significant impact of the subject's usual activity and requires treatment

17.4. ***Investigator Reportable Events and Timelines***

As part of this study all AEs, regardless of relationship to the device and/or procedure, will be captured on the applicable CRF and reported to the Sponsor. Event types and associated reporting timelines are listed below:

- All AEs regardless of the relationship to the device and/or procedure must be reported to the Sponsor within **10 business days** of first becoming aware.
- All SAEs regardless of relationship to the device and/or procedure must be reported to the Sponsor within **3 calendar days** of first becoming aware.
- All Device Deficiencies must be reported to the Sponsor withing **3 calendar days** of first becoming aware.
- All UADEs must be reported to the Sponsor within **1 business day** of first becoming aware of the event.

"Becoming aware" is the point at which a member of the study team has acquired information that reasonably suggests that a reportable AE has occurred. Adverse Event reporting for this study will begin at the point of the Index Procedure and will extend through end of study for each individual subject. Underlying diseases and pre-existing conditions are not considered AEs.

- **NOTE 1:** Intraprocedural bleeding that occurs during a procedure with the study or control device that can be managed endoscopically during the procedure is not considered an AE.

Reporting an AE or Device Deficiency to the Sponsor within the timeframes noted above can be done by submitting the Adverse Event or Device Deficiency CRF in the EDC system with as much event data as possible, by emailing the Sponsor, or by calling the Sponsor. For AEs, the medical diagnosis should be reported as the Event Term on the CRF instead of individual symptoms. Each individual AE or Device Deficiency should be reported on its own Adverse Event CRF.

17.5. ***WAE Medical Device Deficiencies and Device Return***

All device deficiencies (including but not limited to failures, malfunctions, use errors, product nonconformities, and inadequacy in the information supplied by the manufacturer) will be documented and reported to WAE Medical. If possible, the device(s) should be returned to WAE Medical for analysis. Instructions for returning the study device(s) will be provided as needed. If it is not possible to return the device, the Investigator should document why the deficient device was not returned and the final disposition of the device on the device accountability log (as applicable).

17.6. ***Reporting to Regulatory Authorities / IRBs / ECs / Investigators***

WAE Medical is responsible for reporting certain device related events and device deficiencies to the appropriate regulatory authority for complaint reporting purposes.

Furthermore, the Sponsor will ensure all SAEs and UADEs are provided to each participating Principal Investigator for review as applicable.

The Principal Investigator is responsible for informing the IRB/EC, and regulatory authorities of UADEs and SAEs as required by local/regional regulations.

18. Premature Termination of the Study

WAE Medical reserves the right to terminate the study at any stage but intends to exercise this right only for valid scientific or administrative reasons and for reasons related to the protection of study subjects. Investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing in the event of study termination.

18.1. *Criteria for Premature Termination of the Study by the Sponsor*

Possible reasons for premature study termination include, but are not limited to, the following.

- The frequency or occurrence of safety events that present unreasonable risk to participating subjects which cannot be mitigated
- An enrollment rate far below expectation that prejudices the conclusion of the study
- A decision on the part of WAE Medical to suspend or discontinue development of the device

18.2. *Termination of Study Participation by the Investigator or Withdrawal of IRB/ EC Approval*

Any Investigator, or IRB/ EC participating in this study may discontinue participation in the study or withdrawal approval of the study, respectively, with suitable written notice to WAE Medical. Investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing in the event of these occurrences.

18.3. *Requirements for Documentation and Subject Follow-up*

In the event of premature study termination a written statement as to why the premature termination has occurred will be provided to all participating sites by WAE Medical. The IRB/EC and regulatory authorities, as applicable, will be notified. Detailed information on how enrolled subjects will be managed thereafter will be provided.

In the event an IRB/EC terminates participation in the study, participating Investigators, associated IRBs/ECs, and regulatory authorities, as applicable, will be notified in writing. Detailed information on how enrolled subjects will be managed thereafter will be provided by WAE Medical.

In the event a Principal Investigator terminates participation in the study, study responsibility will be transferred to another Investigator, if possible. In the event there are no opportunities to transfer Principal Investigator responsibility; detailed information on how enrolled subjects will be managed thereafter will be provided by WAE Medical.

The Principal Investigator or his/her designee must return all study-related documents and investigational product to WAE Medical, unless this action would jeopardize the rights, safety, or welfare of the subjects.

18.4. ***Criteria for Suspending/Terminating a Study Site by the Sponsor***

WAE Medical reserves the right to stop the enrollment of study subjects at a study site at any time after the study initiation visit if no subjects have been enrolled for a period beyond 3 months after site initiation, or if the site has multiple or severe protocol violations/noncompliance without justification and/or fails to follow remedial actions.

In the event of termination of site participation, all study devices provided to the site by the Sponsor for the purpose of the study will be returned to WAE Medical. The IRB/EC and regulatory authorities, as applicable, will be notified. All subjects enrolled in the study at the site will continue to be followed through the end of follow-up. The Principal Investigator at the site must make provision for these follow-up visits unless WAE Medical notifies the investigational site otherwise.

19. Publication Policy

WAE Medical requires disclosure of its involvement as a Sponsor or financial supporter in any publication or presentation relating to a WAE Medical study or its results. WAE Medical will submit study results for publication (regardless of study outcome) following the conclusion or termination of the study. WAE Medical adheres to the Contributorship Criteria set forth in the Uniform Requirements of the International Committee of Medical Journal Editors (ICMJE; http://www.icmje.org). In order to ensure the public disclosure of study results in a timely manner, while maintaining an unbiased presentation of study outcomes, WAE Medical personnel may assist authors and Investigators in publication preparation provided the following guidelines are followed.

- All authorship and contributorship requirements as described above must be followed.
- WAE Medical involvement in publication preparation should be discussed with the Coordinating Principal Investigator(s) at the onset of the project.
- The First and Senior authors are the primary drivers of decisions regarding publication content, review, approval, and submission.

20. Bibliography

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3. Binmoeller KF, Weilert F, Shah J, et al. "Underwater" EMR without sub- mucosal injection for large sessile colorectal polyps (with video). Gastrointest Endosc 2012;75:1086-91.
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21. Abbreviations and Definitions

Abbreviation/Acronym	Term
AE	Adverse Event
CAP	Corrective Action Plan
CEC	Clinical Events Committee
CRF/eCRF	Case Report Form / Electronic Case Report Form
CRO	Clinical Research Organization
DSMB	Data Safety Monitoring Board
EC	Ethics Committee
FDA	Food & Drug Administration
GCP	Good Clinical Practice
HCP	Health Care Professional
ICF	Informed Consent Form
ICH	International Conference on Harmonization
IFU	Instructions for Use
IRB	Institutional Review Board
ISO	International Organization for Standardization
MAC	Monitored Anesthesia Care
PI	Principal Investigator
QOL	Quality of Life
SAE	Serious Adverse Event
SOC	Standard of Care
UADE	Unanticipated Adverse Device Effect