Clinical Investigational Plan:

Evaluation of the Performance of the Motus Cleansing System

Name/Trade name of the medical device:

Motus Cleansing System (MCS) **ver. 3.0**

Study Sponsor / Manufacturer:

Motus GI Medical Technologies LTD.

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Revision History:

Version	Description	Date
1.0	Not submitted	22 Feb 2015
2.0	Not submitted	25 may 2015
3.0	Not submitted	22 June 2015
4.0	Original submitted	21 July 2015
4.1	Following BfArM's requirement	24 Aug 2015
5	Following BfArM's and CMO requirements	27 Nov 2015
6	Following CMO requirements	27 June 2016

PROTOCOL SIGNATURE PAGE

Investigator Signature

I have read and understand the contents of the protocol # CL00016 and I agree to follow and abide by the guidelines set forth in this document. I agree to conduct the study in accordance with the signed clinical study agreement, European Standard ISO 14155, and any applicable country law / regulations. I also have read and understand the device Instruction for Use and the Investigator Brochure.

_____ Institution (print)	
_____ Principal Investigator Name (print)	
_____ Signature	_____ Date (dd/mmm(yy)

The Principal Investigator may delegate one or more of the above functions to an associate or co-investigator However, the Principal Investigator retains overall responsibility for Ethics Committee approval and proper conduct of the study, including obtaining and documenting subject informed consent, compliance with the study protocol, signing Clinical Study Agreement, collection of all required data, and the training of any additional co-investigator.

Sponsor representative signature

_____Ravit Peled_____ Name (print)	_____Clinical Director_____ Title
_____ Signature	_____ Date (dd/mmm(yy)
_____Hagit Ephrath_____ Name (print)	_____VP QA, RA and Clinical_____ Title
_____ Signature	_____ Date (dd/mmm(yy)

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1. PROTOCOL SYNOPSIS

Document ID:	CL00016
Title:	Evaluation of the performance of the Motus Cleansing System (MCS)
Study Sponsor	Motus GI Medical Technologies, Keren Hayesod 22, Tirat Carmel, ZIP 3902638, Israel Tel: +972 (4) 6214446/103 Fax: +972 (4) 6214442 Israel
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Investigational Device:	Motus Cleansing System (MCS)
Indication for use	The MCS is intended to facilitate intra-procedural cleaning of a poorly prepared colon by irrigating the colon and evacuating the irrigation fluid and feces
Regulatory status	The MCS is a non CE marked, class IIa medical device.
Study Period	Study period will last approx. 6 months
Duration of Participation	The duration of subject participation in the study is expected to be a maximum of 16-19 days (i.e. 1-3 preparation days + colonoscopy procedure day + 14 days post procedure)
Study Design	Prospective, multi-center, single-arm, open-label study
Randomization	No randomization will be applied.
Sample Size	sample size of 47 patients is required to achieve improvement of 60 % in the rate of adequate cleansing rate between the pre and post procedure for the primary hypothesis.
Number of Subjects	Up to 47 eligible subjects (15-16 subjects per site)
Study Population	Subjects allocated for a screening, diagnostic or surveillance colonoscopy
Objectives	The main objective of the study is to demonstrate the performance of the Motus GI system used in conjunction with screening, diagnostic or surveillance colonoscopy
Study Endpoints and Measures	Primary Endpoint Pre and Post procedure adequate cleansing rate per subject Secondary Endpoint: Type, incidence, severity, and duration of adverse events

2. LIST OF ABBREVIATIONS AND DEFINITIONS:

Abbreviations:	Description:
MCS	Motus Cleansing System
WS	Workstation
WSC	Workstation Cartridge
AE	Adverse Event
BBPS	Boston Bowel Preparation Scale
CRC	Colorectal Cancer
CRF	Case Report Form
CIP	Clinical Investigational Plan
EC	Ethics Committee
ICF	Informed Consent Form
IFU	Instructions For Use
SAE	Serious Adverse Event
SD	Standard Deviation
SADE	Safety Adverse Device Effect
DSMB	Data Safety Monitoring Board

3. INTRODUCTION

3.1. BACKGROUND

Colonoscopy is an endoscopic examination of the colonic mucosa. The procedure is considered the "gold standard" for detecting, diagnosing and treating abnormalities in the colon and is widely used for various clinical indications. High-quality colonoscopy is imperative for enhancing efficacy of and for decreasing the costs associated with the procedure. A key factor for ensuring high-quality colon visualization using colonoscopy is a good colon preparation.

Despite the importance of good preparation, many patients do not or are not able to adequately prepare themselves prior to the colonoscopy procedure. It is estimated that as many as 33% of colonoscopy patients arrive for their colonoscopy with inadequate colon preparation[1]. Factors that contribute to poor preparation include inconvenience and discomfort of ingesting cleansing agents (laxatives), concerns about lost work days, contraindication to cleansing agents, obesity and immobility due to medical condition or old age. Achieving a good level of colon preparation is one of the major barriers to successful and cost effective colonoscopy for colorectal cancer screening as well as for diagnosis of other gastrointestinal conditions.

Motus Cleansing System (MCS) facilitates a thoroughly-cleansed bowel for subjects with a poorly prepared colon. By providing intra-procedural mechanical colon cleansing, the MCS reduces reliance on subject pre-procedure colon preparation for ensuring high quality colonoscopy. By offering simple, fast, safe and effective intra-procedural cleansing, the MCS is expected to improve the quality of colonoscopy, to reduce the need for repeat colonoscopies, to increase the patient compliance to colonoscopy procedure and to reduce the patient dependency on the quality of the procedure.

3.2. PRE-CLINICAL & CLINICAL TESTING

Pre-clinical testing, including electrical and mechanical design testing, biocompatibility, reliability tests, software validation and animal studies were conducted in compliance with the applicable international standards and the essential requirement of the Medical Device Directive 93/42/EEC (MDD) to the MCS (Please refer to the Investigator's Brochure section "Pre-clinical Testing" for more information). To date, clinical trials were performed using various versions of the MCS (including the current version) and demonstrated 95%-100% cleansing capabilities in poorly prepped subjects. The

[1] Adenoma Detection on Repeat Colonoscopy after Previous Inadequate Preparation, Colin L Smith, Journal of Gastroenterology and Hepatology research, Vol 2, No 12 (2013)

subjects were prepped with reduced preparation doses relatively to those that are standardly used, including the same preparation regime that is described in this protocol. Detailed information on the pre-clinical & clinical testing is provided in the Investigator's Brochure, section "Pre-Clinical & Clinical experience with the device".

4. RISKS AND BENEFITS OF THE INVESTIGATIONAL SYSTEM

Risk-Benefit analysis and steps to control or mitigate the risks are included in the Instruction for use and the Investigator's Brochure section "Risk Management" and "Risk Analysis Report".

4.1. ANTICIPATED CLINICAL BENEFITS

MCS utilizes a cleaning technology which is expected to improve the quality of colonoscopy, to reduce reliance on subject pre-procedure colon preparation for ensuring high quality colonoscopy, to increase the subject compliance to colonoscopy procedure and to reduce the need for repeated colonoscopies required due to insufficient colon preparation, these consequently may reduce pain, discomfort, risk and cost.

In addition to these benefits, as the MCS is attached to the colonoscope and is used during the standard colonoscopy procedure, additional potential benefits of the MCS in conjunction with a standard colonoscope includes the ability to screen the entire colon for any abnormalities that may lead to colorectal cancer and the ability to perform therapeutic procedures such as polyp/ tumor removal or biopsies, when necessary.

4.2. ANTICIPATED ADVERSE DEVICE EFFECTS

The potential complications associated with the MCS device are:

- Perforation
- Laceration
- Mild tissue trauma
- Patient infection/biologic reaction

Several steps to mitigate those risks were made (see section 4.3) , following those mitigations the use of the MSC do not increase the risk to the patient.

However as the MCS is used in conjunction with a standard colonoscope during a colonoscopy procedure the complications associated with using the MCS cannot be differentiated from those associated with the colonoscopy procedure.

The risks associated with the colonoscopy procedure along with the procedure itself (i.e., preparation and sedation) as reported in the literature are:

- Colonoscopy-related risk such as bowel perforation, tissue trauma, abdominal pain, bleeding, fever, and infection.
- preparation related risks (lasting >24 hours following colonoscopy) are: Changes in bowel habits, Nausea and vomiting, Dehydration and Renal dysfunction (rare).
- Sedation-related are: cardiovascular disorder, hypotension, and hypoxia
- Death

4.3. RESIDUAL RISK ASSOCIATED WITH THE INVESTIGATIONAL DEVICE

The Residual risk is the risk remaining after the risk controls have been implemented.

The residual risk is evaluated according to the following:

- Acceptable Residual risk includes all RPN ≤ 9.
- Risks rated 10-16 will be acceptable if the risk benefit ratio justifies it.

All risks of using MCS were mitigated by risk management process according to EN ISO 14971:2012.

The mitigation to the risks associated with the investigational device includes but is not limited to the followings:

- Smooth head shape that contains lumens for cleansing jets and evacuation. The lumens' size were optimized to ensure the safety of the patients along with effective cleansing.
- The MCS sleeves are made from a flexible and low friction material to allow ease advancement through the colon and to minimize any impact to the steering angle of the colonoscope.
- Hydrophilic coating at the distal 30cm of the outer sleeve to create a lubricious surface to allow ease insertion and advancement.
- Cleansing procedure can be operated in 3 modes (low, medium, high), where the physician can control the intensity of cleansing jets to ensure the safety of the patients along with effective cleansing.

All the risks and mitigations associated with the investigational device can be found in: *"RD00002 – FMEA Appendix to RA Report 03 11 2015.xlsx"*

The potential residual risk following the mitigations are all acceptable (for more details please refer to "Risk analysis report").

Considering the residual risks and the risk against benefit assessment, it can be concluded that the system may offer potential benefit to the patients along with no significant risk increase compared to the standard of care procedure.

4.4. RISK ASSOCIATED WITH THE PARTICIPATION IN THE CLINICAL INVESTIGATION

The potential risks associated with the participation in the clinical investigation may include a repeated colonoscopy procedure as the subjects enrolled to the study are required to undergo a limited prep as compared to the preparation given prior to standard colonoscopy procedure to mimic a poor colon preparation.

Based on previous clinical data an excellent cleansing effectiveness was demonstrated following the use of the MCS device ; MCS improved the cleansing level from 30% at baseline to 93% after the cleansing was operated, where the preparation in these studies were identical to the preparation in current study, for further detailed please refer to the "clinical evaluation report" (see pages 5-8 of the Risk Benefit assessment document).

Therefore, it is expected that the risk of a repeated colonoscopy procedure is low.

4.5. POSSIBLE INTERACTION WITH CONCOMITANT MEDICAL TREATMENT

The Bowel preparation agent used in this study is generic bisacodyl tablets , and is approved in U.S and in Europe. Bisacodyl belongs to a group of medicines known as stimulant laxatives that increases bowel movements and is considered to be safe with negligible risk of complications.

The anticipated risks associated with this agent are:

- Changes in bowel habits (e.g. Diarrhea, Constipation)
- Nausea & Vomiting
- Dehydration

The preparation in this study is less intensive compared to the standard preparation done prior to colonoscopy procedure, by using only Bisacodyl without the split dose of 4 liter polyethylene glycol (PEG) that is normally required prior to standard colonoscopy procedure.

As the subjects to be enrolled in this study are eligible and referred to standard colonoscopy procedure (I.e., CRC /Surveillance/ diagnostic) we expect that the risks related to the preparation agent will be similar or even lower than the risks following a standard preparation to colonoscopy procedure.

4.6. STEPS THAT WILL BE TAKEN TO CONTROL/ MITIGATE THE RISK

In order to ensure the safety of the MCS device for subjects enrolled in the study an independent group of experts chosen by the sponsor will constitute the Data and Safety Monitoring Board (DSMB). The DSMB will evaluate every Adverse Event. All Adverse Events will be reported as per the standard clinical practices as detailed in section 16.3. All adverse event incidence rates will be summarized by anticipation, severity and relationship to the investigational device.

In addition, in case of occurrence of a SAE at least possibly related to the MCS the study will terminated immediately and until completion of the DSMB investigation.

4.7. RISK/BENEFIT RATIONALE

The MCS is used in conjunction with a standard colonoscope during a colonoscopy procedure. Hence, the complications associated with using the MCS are anticipated to be similar to those associated with the colonoscopy procedure. As with any colonoscopy procedure, when using the MCS there is some risk of bowel perforation, pain, infection and bleeding. Although the risks of the procedure with the MCS is expected to be comparable to conventional colonoscope (0.35%), the device is an add-on to a standard colonoscope. Hence, diameter is bigger, and the cleansing time may add some minutes to the procedure time. In contrast, a disadvantage that is presented in standard colonoscopy and can possibly be decreased when using the MCS is that of stopping the colonoscopy procedure due to improper preparation of the colon by the subject.

The potential benefits of the MCS are utilization of a cleaning technology that may improve the standard colonoscopy visualization, reduce reliance on subject pre-procedure colon preparation for ensuring high quality colonoscopy, increase the subject compliance to colonoscopy procedure and reduce the need for repeated colonoscopies required due to insufficient colon preparation, these consequently may reduce pain, discomfort, risk and cost.

The latest MCS version was tested in an animal study including 35 pigs and two preliminary clinical studies including 30 subjects. No major complication or serious adverse events occurred within the course of those studies, and only 2 mild adverse events were reported .

In addition, these clinical studies demonstrated an excellent cleansing effectiveness; MCS improved the cleansing level from 30% at baseline to 93% after the cleansing was operated, where preparation was identical to the current study. Efficacy results support the study design rationale that decreases the risks associated with the preparation without increasing the risk related to incomplete colonoscopy procedure.

Lastly, patients to be enrolled to this study shall be eligible to colonoscopy, thus the risks detailed above covers all the population intended to participate in the study (i.e., screening, surveillance and diagnostic).

Considering the residual risks and the potential and the risk against benefit assessment, it can be concluded that the system may offer potential benefit to the patients along with no significant risk increase.

5. THE INVESTIGATIONAL SYSTEM

The MCS offers a simple, fast, safe and effective intra-procedural cleansing , the MCS is expected to improve the quality of colonoscopy, to reduce reliance on subject pre-procedure colon preparation for ensuring high quality colonoscopy ,to reduce the need for repeat colonoscopy and to increase the subject compliance to colonoscopy procedure.

5.1. NAME AND INTENDED USE

The MCS is intended to facilitate intra-procedural cleaning of a poorly prepared colon by irrigating the colon and evacuating the irrigation fluid and feces.

This is an experimental study aimed to evaluate the MCS performance in subjects with poor prepared colon. To ensure poor colon preparation in the subjects to be enrolled in the study, the subject is required to follow a specific prep instructions which include use of a limited prep as compared to standard of care preparation given prior to colonoscopy procedure.

Based on previous clinical data, a poor cleaning will be found in about 60% of the subject following the regimen preparation that is proposed in this protocol, this will allow a thorough investigation of the MSC performance in cleaning a poor prepared colon.

For further details please refer to the :" clinical evaluation report" (see pages 5-8 of the Risk Benefit assessment document).

5.2. SYSTEM DESCRIPTION

The MCS enables colon cleansing during standard colonoscopy using a standard colonoscope. The cleansing device, which is attached to the tip of the colonoscope and is connected to an external workstation, generates fluid jets within the colon thus dissolving the feces into small parts. The fecal matter & fluids are drained through the evacuation pipe of the cleansing device into a collecting reservoir.

The MCS ver. 3.0 that will be use in this clinical trial comprises the following components:

- The disposable add-on cleansing device (MCS Add-on) ver. 3.0 that attaches to the colonoscope and is connected to the external workstation , using the WS Cartridge (WSC).
- The MCS Workstation that supplies gas and liquids to the device. The workstation includes:
    - Pressure sensors to continuously monitor pressure levels within the colon Inlet Module that includes a pump to enable liquids (e.g. water or saline) & gas (e.g. air) flow in to the cleansing device.
    - Outlet Module that contacts to a suction pump\source and evacuates fecal matter and fluids from the colon.
- The loading fixture ver. 1.0 is an ancillary device that is used to aid the nurse in loading the device on the colonoscope. The loading fixture consists of a pressure source to inflate the inner sleeve of the device and keep the colonoscope properly aligned with the Add-on to allow easy insertion of the colonoscope into the Add-on.
- External reservoir ver. 1.0 for collecting the evacuated fecal matter and fluids
- External foot pedals ver. 3.0 that operate the cleansing and evacuation process to be used by the investigator.

Below is a drawing showing the various components of the system and where they connect to each other.

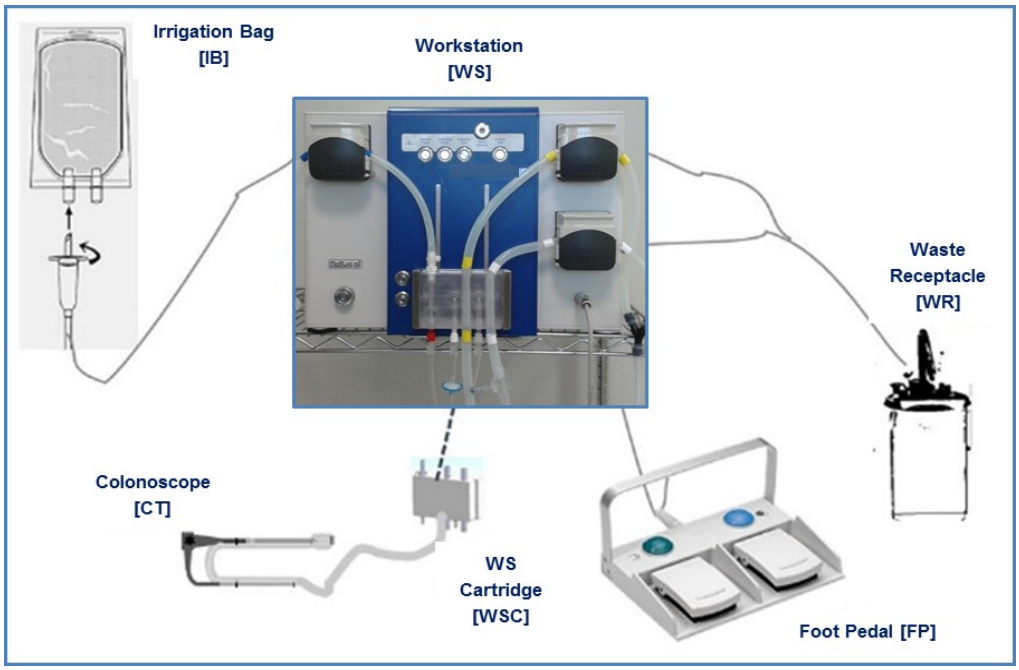


Figure 1: MCS Workstation – General design & components

5.3. SYSTEM WORKSTATION

The workstation is intended to provide irrigating water or saline & air, and to drain fecal matter & fluids out of the body during the cleansing \ colonoscopic procedure.

5.3.1. WORKSTATION COMPONENTS:

The workstation [WS] includes the following components:

- Monitoring & Control Unit (Software ver. 2.10) that controls the irrigation fluids and gas into the colon, evacuation of fluids and feces out of the colon.
- External receptacle containing irrigation liquid (saline or water) which is connected to the irrigation line. (Please note this is a consumable not supplied by Motus GI).
- External waste receptacle for the fecal material & fluids that are evacuated out of the colon throughout the evacuation line.
- External foot pedals that operate the irrigation, evacuation, cleansing modes and manual-purging processes used by the investigator.

The Add-on device assembled on the colonoscope is connected to the WS by the WS Cartridge (WSC).

5.4. THE WORKSTATION FRONT PANEL AND INTERFACES

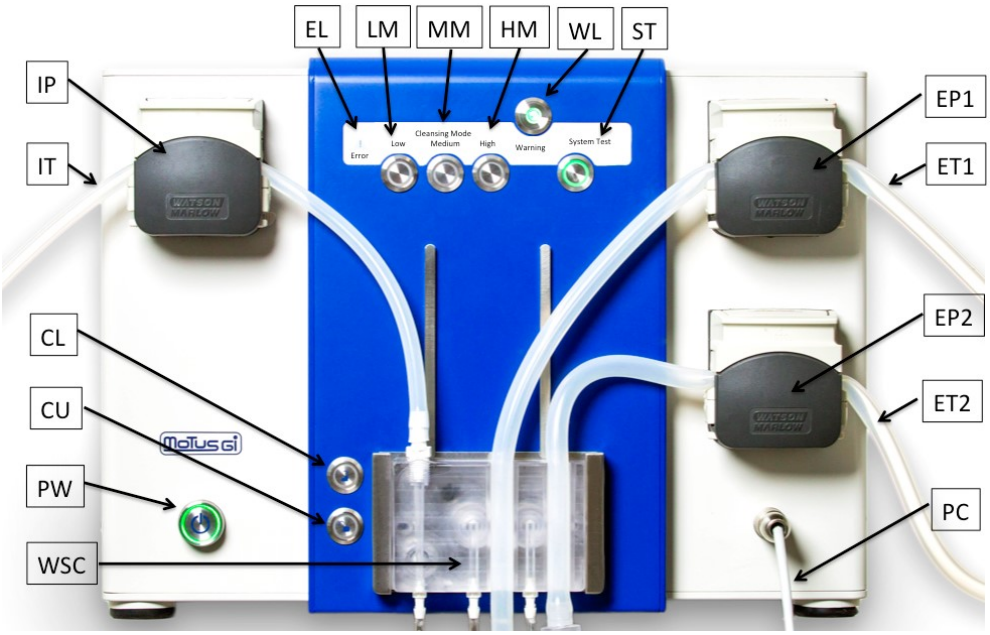


Figure 2: The Workstation

The WS contains the following main components: On/Off power button [PW] that turns on and off the power. Irrigation pump (IP) that pumps room temperature saline (not shown in this figure) and air into the MCS Add-on (shown in figure 4) via the irrigation tubing [IT]. The fecal material & fluids are removed from the colon, using the evacuation pumps [EP1, EP2] via the evacuation tubing [ET1, ET2], into the waste receptacle (not shown in this figure). The WS cartridge [WSC] connects the Add-on device to the Workstation. The WS cartridge slides into place in the front of the workstation and has lock/unlock buttons [CL, CU] to lock & unlock the WS Cartridge into place.

The cleansing/evacuation mode is controlled by the foot pedal (shown in figure 3) which connects to the pedal connector [PC]. The MCS undergoes a System Test when the System Test button [ST] is activated. The system test ensures the MCS is functioning properly prior to procedure commencement. The system can be operated in three cleansing modes; low, medium (default mode) and high. The mode selection is activated by the three cleansing mode buttons [LM, MM, HM] on the WS or by using the cleansing mode selector button [CMS] on the foot pedal. The warning indication light [WL] will indicate when an assembly related issue or system malfunction occurs. This warning indication is both visual and audible. For warning indication, handlings see troubleshooting in the IFU

(section 8 page 22). The error light (EL) will indicate when a non-recoverable error occurs, necessitating an intervention by Motus GI personnel.

5.5. THE FOOT PEDAL UNIT

The foot pedal allows the physician to choose each of the operating modes during the procedure. The operating modes are as follows (Figure 3: MCS Foot Pedal Unit (optional scheme)):

- Cleansing – simultaneous irrigation and evacuation, activated by the right foot pedal.
- Evacuation only mode – Activated by the left pedal.
- Manual Purge – Activated by the left button [MP].
- Cleansing Mode Selector – Activated by the right button. User can switch between three cleansing modes; low, medium (default mode) and high.

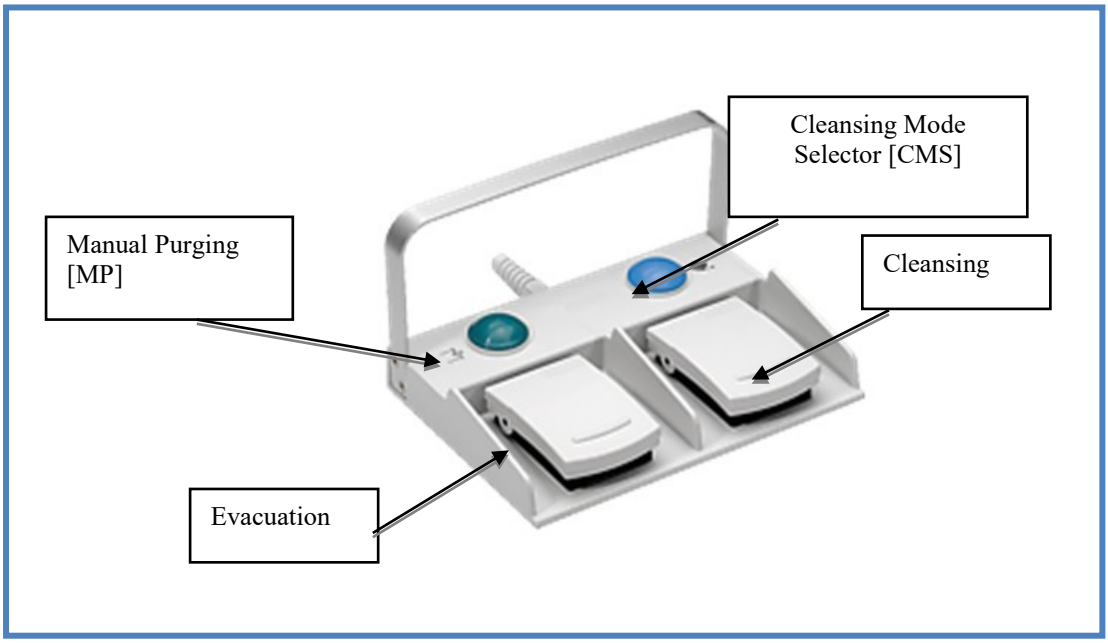


Figure 3: MCS Foot Pedal Unit (optional scheme)

5.6. MCS ADD-ON DEVICE

5.6.1. THE ADD-ON DEVICE

The MCS Add-on device is a single use disposable, which slips over a standard colonoscope with a maximum outer diameter of 21.2mm. The device consists of multiple irrigation and evacuation

conduits as well as channels for the sensing capabilities of the system. The Add-on device has an outer sleeve to provide a smooth surface while inside the colon and an inner sleeve to provide the proper connection to the colonoscope. At the distal end of the Add-on device is the insertion port for the colonoscope, which also includes an inflation connector that is attached to an air compressor. The insertion port is loaded into the loading fixture, which aids insertion of the colonoscope into the Add-on device. Proximal to the insertion port all of the add-on device's conduits branch off and extend to the WS cartridge [WSC]. The WS cartridge [WSC] is an integrated cartridge that connects the MCS Add-on device to the Workstation.

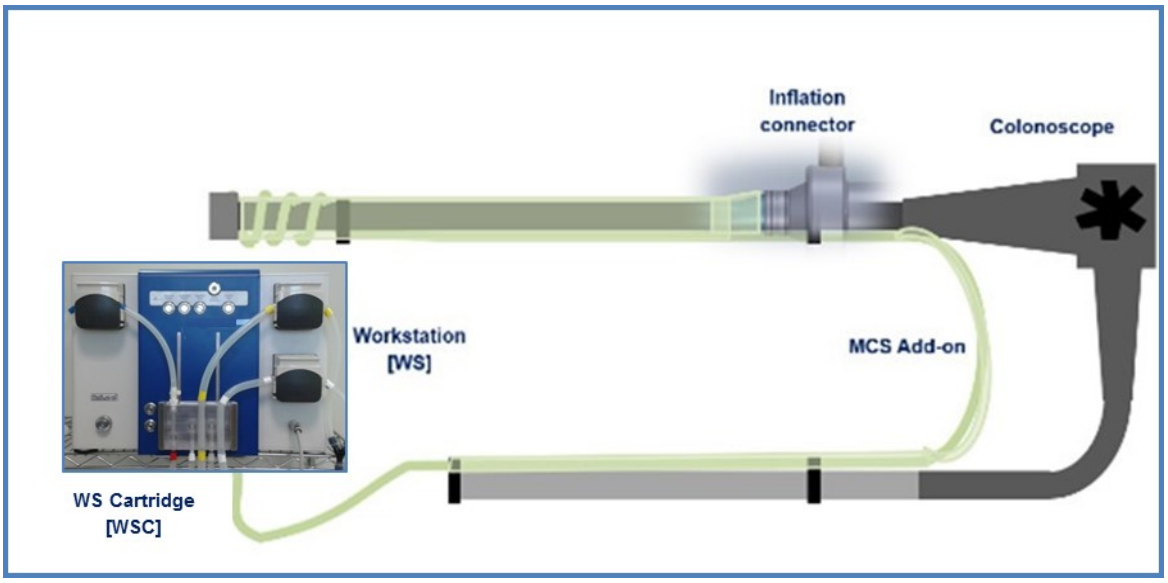


Figure 4 – MCS Add-on device- General Design

5.6.2. The irrigation & Evacuation Head [CEH]:

The irrigation and evacuation head (Figure 5) comprise a fluid supply pipes that supply fluids via a manifold to 4 cleansing jets [JT]. The head is attached to the colonoscope's distal end. The sensor pipes are connected to the irrigation and evacuation head [CEH] on one end, and to the WS via the cartridge in their other end.

The irrigation and evacuation head also comprises openings [WI] through which fecal matter & fluids are being drained out of the colon via the evacuation pipes.

Following is a schematic

zoom on the head and its functions.

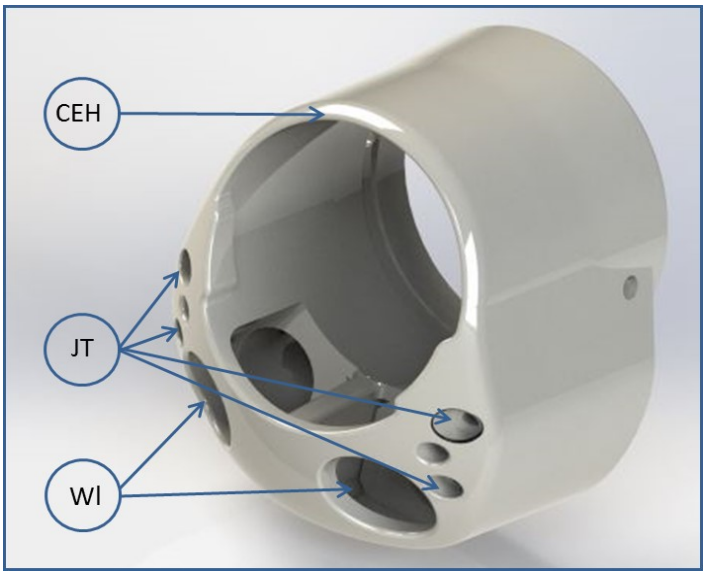


Figure 5 – MCS Add-on device – Zoom on The Irrigation & Eva

A detailed description of the system components, its principles of operation, dimensions and packaging is elaborated in the Investigator's Brochure.

6. OBJECTIVES

6.1. PRIMARY OBJECTIVE

To evaluate the performance of MCS in cleansing a poorly prepared colon.

6.2. SECONDARY OBJECTIVES:

To evaluate the safety related to the MCS.

6.3. EXPLORATORY OBJECTIVES:

- To evaluate the net time to Cecum in MCS procedures.
- To evaluate the net procedure time in MCS procedures.
- To evaluate the cecal intubation rate in MCS procedures.
- To evaluative user (physicians and nurses) satisfaction.

7. STUDY ENDPOINTS

7.1. PRIMARY ENDPOINTS

The rate of adequate cleansing level per subject will be evaluated by the BBPS[2] scoring index pre- and post the cleansing operation.

7.2. SECONDARY ENDPOINTS

Type, incidence, severity, and duration of adverse events

7.3. EXPLORATORY ENDPOINTS

1. Net time until cecum is visualized
2. Net time of the entire colonoscopy procedure
3. Rate of procedures where the cecum was visualized .
4. User satisfaction will be evaluated by a questionnaire filled-in by the physicians and nurses who conduct the procedures and assemble the MCS.

8. DURATION OF STUDY

The study will begin after the approval by the competent Ethics Committees and the Competent Regulatory Authorities. Enrollment period is anticipated to be up to 6 months. Study duration for subject will be 16-19 days.

The study duration is therefore estimated to be 6 months.

9. PARTICIPATING CENTERS

The chosen investigators have documented experience in conducting clinical investigations and in performing colonoscopy procedures, and are able to recruit the desired number of subjects into the study.

[2] Lai E.J. et al," The Boston Bowel Preparation Scale: A valid and reliable instrument for colonoscopy-oriented research", Gastrointestinal Endosc. ,2009: 69(3 Pt 2): 620–625

10. STUDY DESIGN

The study is multicenter study ,planned as a single arm, open trial, aimed at evaluating the performance and safety of a colon cleansing device during a colonoscopy procedure in a poorly prepared colons.

Subjects are planned to be enrolled at 3 clinical sites (1 in Germany and 2 in the NL).

Subjects who meet the eligibility criteria will be screened for study participation at a baseline visit(visit 1). Subject who is eligible to the study will required to follow a specific preparation instruction starting 2 days prior to the colonoscopy with the MSC procedure.

Following the procedure a telephone follow-up will be conducted at 48 hours (± 24 hours) and 14 days (± 3 days) post MCS procedure to assess patient well-being and capture any AEs.

The study design can be seen in the following figure and is detailed in the study procedure section

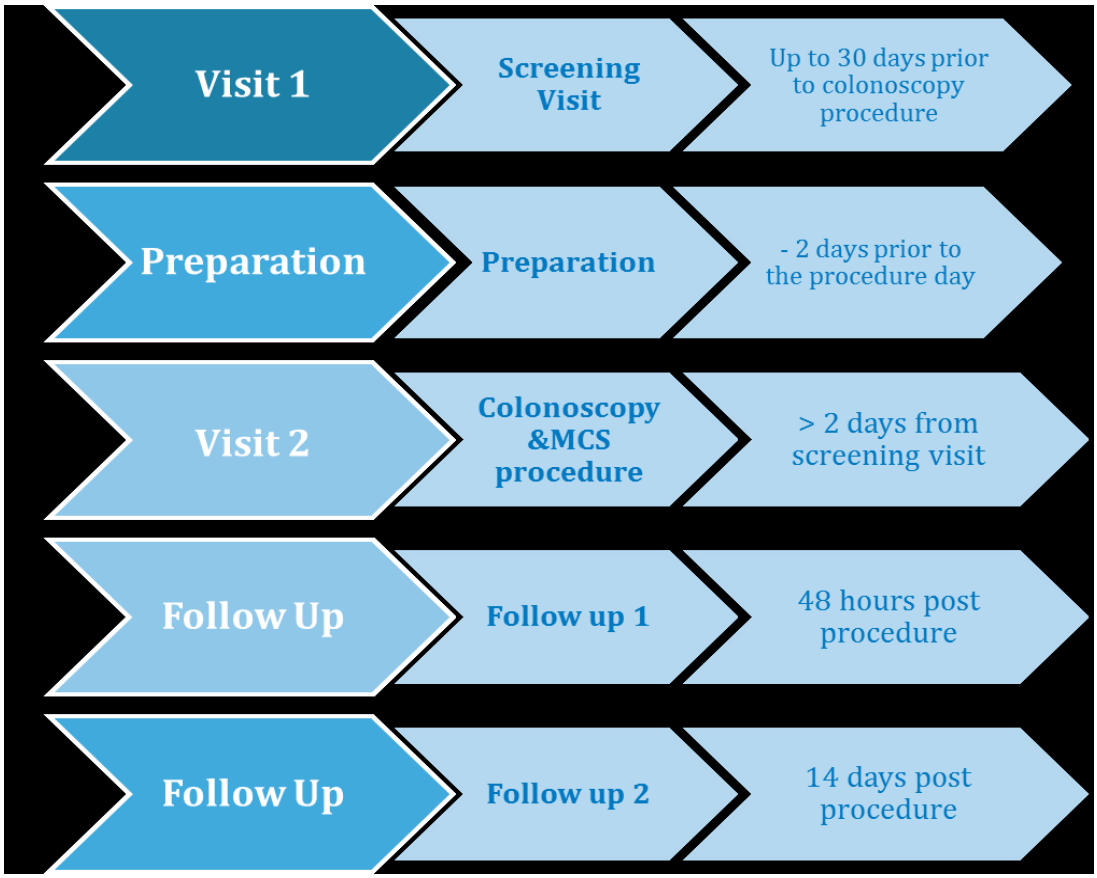


Figure 6: Study design scheme

The detailed study design and scheduled of assessments table can be found in the appendix B.

11. SUBJECT POPULATION

11.1. NUMBER OF SUBJECTS

Up to 47 eligible subjects (up to 15-16 adult eligible subjects per site) that are candidates for diagnostic, screening or surveillance colonoscopy procedure will be enrolled in the study.

Subjects will be considered for the study if they meet the specific inclusion/exclusion criteria.

The criteria for enrollment must be strictly followed.

At least 15% from the entire population will be included in each of the sub groups (i.e., Screening, Surveillance, diagnostic)

11.2. INCLUSION CRITERIA

1. Subjects being considered for diagnostic, screening or surveillance colonoscopy
2. Subjects in the age range of 18-75 years inclusive
3. Subjects with BodyMass Index (BMI) within the range of 18.5-35 inclusive
4. Subject has signed the informed consent

11.3. EXCLUSION CRITERIA

1. Subjects with known Inflammatory Bowel Disease
2. Subjects with known diverticulitis disease or with prior incomplete colonoscopy due to diverticular disease
3. Subjects with known or detected (during colonoscopy) bowel obstruction
4. History of prior surgery to colon and/or rectum
5. ASA≥IV
6. Renal insufficiency (Creatinine ≥ 1.5mg /dL) (based on medical history)
7. Abnormal Liver enzymes (ALT/AST ≥ 2 times upper limits of normal) (based on medical history)
8. Subjects taking anticoagulants drugs (excluding aspirin) or dual antiplatelet therapy
9. Subjects with known coagulation disorder (INR >1.5).
10. Subjects treated with H2 receptor antagonists or proton pump inhibitors within the 72 hours prior to consuming the Bisacodyl

11. Subjects with active, ongoing lower GI bleeding with hemodynamic instability.
12. Subjects with known Mega Colon
13. Pregnancy (as stated by patient) or breast feeding
14. Subjects with altered mental status/inability to provide informed consent
15. Patients who have participated in another interventional clinical study in the last 2 months

12. STUDY PROCEDURES

12.1. SELECTION OF INVESTIGATORS AND TRAINING

The physicians that will be participate in this trial are experienced colonoscopists.

Each Investigator participating in the clinical trial and the associated clinical study staff will receive training on the clinical protocol. This includes training related to the cleansing evaluation according to the BBPS scoring index, training on AE reporting, case report form (CRF) completion, as well as the device and system (including instruction for use, procedural use, device characteristics, warnings, precautions, and contraindications).

Investigators will be trained in accountability procedures for the investigational products. All experimental devices and materials will be used in accordance with the investigational plan by the clinical staff that have been granted appropriate qualifications and training. Unused devices will be returned to the sponsor.

In addition to the above all study Principal investigators (i.e., Prof. Siersema, Prof. Neumann and Dr. Spaander) were trained on the MCS system in an animal model. The training was performed at "Medanex" Clinic , Belgium on July 2015.

12.2. SUBJECT ASSIGNMENT

The study-center will be identified by a single digit number (e.g., 01). The center will assign to enrolled subjects a number in sequence to coincide with the sequence of enrollment. Therefore each subject will be unequivocally identified by a 2-digit center identifier followed by a three digit subject identifier (eg 01-001). Once enrolled at the eligibility assessment visit, the subject will be requested to follow study procedures.

12.3. PRE-ENROLLMENT AND ELIGIBILITY ASSESSMENT (VISIT 1)

Subjects participating in the study may be recruited from investigator's patients pool.

Eligibility assessment shall be conducted prior to the scheduled colonoscopy by phone call and based on the subject's medical history. Candidates who were found to be potentially eligible to participate in the study, will be approached by the investigator to obtain written informed consent prior to any study specific procedures being performed. An explanation on the study purpose, procedures, possible risk and benefits and subject responsibilities to the potential participant will be provided. The subjects will be given the opportunity to evaluate any information about the study in detail and will be allowed to ask the investigator any question regarding the study. The subject's willingness and ability to meet the study requirements will be determined. The investigator must obtain written informed consent prior to subjecting the patient to any study related activity.

Visit 1- Screening visit

Subjects will be assessed for eligibility to participate based on the inclusion and exclusion criteria.

When it has been established that the subject is potentially eligible , written informed consent will be obtained during the visit. The subject will sign and date the consent form. The Investigator will also sign and date the consent form. The original of the informed consent form will be retained with the subject records and a copy will be provided to the subject.

The subject will be recorded on the Subject Enrollment and Visit Log and his/her eligibility will be confirmed.

After eligibility is confirmed, the subject's baseline condition will be assessed and entered to the CRF to include: subject population group, age, gender, race, height, weight, medical records/history and reason for referral.

The colonoscopy procedure will be scheduled to be at least 2 days ahead but no later than 30 days.

In the event that the screening and eligibility assessment takes place more than 30 days prior to the planned procedure date, the investigator should contact the subject prior to the procedure date to assure there is no change in the subject's medical condition.

Subjects will be instructed regarding the preparation regime and will be given the diaries which are needed to be filled out during the preparation phase.

The Physician will instruct the subject to bring the diaries to the scheduled colonoscopy.

Subjects who were found to be not eligible for the study following signature of the Informed Consent Form , will be withdrawn from the study. The following procedures will not be performed in these

subjects, the Subject Enrollment and Visit Log will be completed and the subject eligibility section in visit 1 as well as a "Study Completion" form will be completed in the CRF.

12.4. COLON PREPARATION PROTOCOL

In a trial to mimic poorly prepped subjects, the subjects will be instructed to follow a limited preparation regimen. An example of proposed bowel preparation regimen is detailed below:

- Split dosing of Bisacodyl* (2 tablets of 5mg in each dose):
  - First dose: 2 tablets Bisacodyl either in:
    - the early afternoon 1 day prior to colonoscopy (for morning procedures)

      OR
    - the evening 1 day prior to colonoscopy (for afternoon procedures)
  - Second dose: 2 tablets Bisacodyl either in:
    - the evening 1 day prior to colonoscopy (for morning procedures)

      OR
    - the early morning on the day of procedure (for afternoon procedures)

The following diet requirements will apply:

- From 2 days prior to colonoscopy until colonoscopy procedure: no dried fruits, seeds, nuts, legumes and a like.
- Up to 24 hours prior to colonoscopy: clear liquid diet
- Colonoscopy day: 3 hours before the procedure – no food/liquids

  * Generic Bisacodyl will be used in the study as routinely used in the participating sites according to the indications of use but following the dosing regime shown above.

The bisacodyl should be use as detailed in the ICF and per the physicians instruction.

- Bisacodyl is taking whole ,by mouth with a full glass of water (8 oz/240 mL), with or without food.
- Drinking extra fluids while taking bisacodyl is recommended.
- Taking Bisacodyl within 1 hour after taking an antacid or milk is not allowed.

An example of the bowel preparation regimen for the subjects can be found in the Appendix C and in the ICF.

12.5. COLONOSCOPY PROCEDURE (VISIT 2)

Pre-Examination Procedures

- Verify eligibility checked and informed consent was obtained after explaining all risks, benefits, and alternatives to the candidate.
- Verify that the research assistant has collected completed diaries from the subject.
- Verify all background/clinical information, demographic and medical history was documented
    - Note: Subjects that did not take the bowel preparation or failed to complete the bowel preparation will not undergo the procedure and will be excluded from the study.
- Verify all connections and assembles are properly attached (see Instructions for Use "Setup and Interconnections" section and sections 5.4 and 5.5. in this protocol)
- Verify device works properly (see Instructions for Use "System Operation" section and sections 5.4 and 5.5. in this protocol)
- Place and prepare the subject for the procedure as per standard colonoscopy.
- Perform a digital rectal exam as per standard colonoscopy , evaluate the adequate level of the preparation and start the colonoscopy procedure as per standard of care.

Colonoscopy procedures

- The procedure will be performed by the clinical investigator(s), experienced in GI endoscopy according to local standard of care. Anesthesia will be applied as well per the standard of care. In order to ensure correct operation of the MCS a Motus GI representative may attend the procedure. Using the MCS, requires specific training with the MCS that will be provided by the sponsor prior to the study. MCS operation is described in the Instruction For Use.
- The MCS will be operated according to section "Operating the MCS workstation" in the IFUs. The colon preparation level for each segment of the colon (Left, Transverse, Right) before the cleansing operation during the insertion phase and post the cleansing operation during withdrawal will be evaluated using the BBPS (Appendix A – Scoring method).
- Once the procedure is completed, relevant data will be recorded on the CRF in addition, findings, diagnosis as well as Physician questionnaire will be recorded/completed.

Specific situations occurring during colonoscopy

- If the attempt to reach the cecum is failed, the investigator shall perform the procedure with a pediatric or any other colonoscope he/she may choose without the MCS. The subject will complete the study as planned.
- If a medical condition requiring treatment is detected during colonoscopy, the subject will be treated as per the standard care.

Post-Examination

Subjects will be transferred to recovery room for observation per standard colonoscopy protocol. Subjects will be contacted by phone 48 hours after the procedure to verify that there has been no change in their well-being.

Follow-up

Fourteen days after the procedure, each subject will be contacted by phone to verify that there has been no change in their well-being following the procedure. Any AE will be documented in the CRF. Before a subject is considered "lost to follow-up", there must be at least two documented attempts to contact the subject.

The company may have the option to match the diagnostic and therapeutic interventions performed during the study with the pathologic results from the lab when obtained.

12.6. DIARIES:

Subject diaries are provided to the subject at visit 1 to be filled by the subjects during the preparation phase. This will include diet and bowel movement information. The subject is instructed to bring the diary with him/her to the scheduled colonoscopy.

Additional questions regarding basic demographic information, and health assessment will be filled out in the CRF by the study team.

All subjective assessment questions recorded in the CRF may be used in future studies.

13. STUDY COMPLETION PROCEDURES

13.1. SUBJECT COMPLETION OF STUDY

Subjects are considered to have completed the study if they have completed all study requirements up to the 14 day follow up call. All subjects enrolled in the clinical investigation (including those withdrawn and those who were screened failure) shall be accounted for and documented.

13.2. SUBJECT WITHDRAWAL

Subjects will be withdrawn from the study if one of the following occurs;

- The subject voluntarily discontinues his or her participation in the study.
- Continuation of the course of the study would jeopardize the subject's health and/or welfare (at the discretion of the Investigator)
- There is a concurrent illness (unrelated to treatment) that prevents the subject from complying with the study requirements
- The subject is unwilling or unable to comply with the protocol
- The subject was found to be not-eligible following signature of the Informed Consent Form .

The reasons for the subject's withdrawal from the study must be recorded in the subject's CRF and captured on the Subject Enrollment and Visit Log. All withdrawn subjects having performed the colonoscopy procedure with MCS, will be followed up to 14 days post procedure to verify that there have been no changes in their well-being for the entire period of the study.

THE SPONSOR OR ITS DESIGNEE MUST BE NOTIFIED OF A SUBJECT WITHDRAWAL.

13.3. SUBJECT EXIT

Subject exit and termination forms must be completed for all subjects who signed informed consent and either complete the study, discontinue participating in the study, are considered lost to follow-up, or are withdrawn from the study. Before a subject is considered "lost to follow-up", there must be at least two documented attempts to contact the subject.

14. ASSESSMENTS OF MOTUS CLEANSING SYSTEM (MCS)

The first 3 subjects of each physician will be excluded from the MCS performance evaluation in order to compensate for the system operation learning curve. Those subjects however will be included in the safety evaluation.

14.1. PERFORMANCE ASSESSMENT

The rate of adequate cleansing level before and after the cleansing operation will be evaluated.

The rating of the cleansing quality will be evaluated by using the Boston Bowel Preparation Scale (BBPS) (Appendix A). Segment score of 0-3 given to each of the 3 segments of the colon (Left side, Transverse and right side).

BBPS* scores will be rated by the colonoscopies, on the basis of three segment scores summed for maximum score of 9, where:

- 0 = unprepared
- 9 = completely clean (in completed to Cecum procedures)

An adequate cleansing procedure will be considered when all the colon segments will be graded as 2 or above.

Note: the above is applicable also for an incomplete procedures.

* Detailed information is provided in Appendix A.

14.1.1. PRE- PROCEDURE CLEANSING PER SUBJECT

Evaluating the cleansing (preparation) rate while inserting the device, prior to the cleaning procedure, for the entire colon.

This measurement will serve as the subjects' baseline condition with regards to colon cleansing.

14.1.2. POST PROCEDURE CLEANSING PER SUBJECT

Evaluting the cleansing rate of the MCS while withdrawing colonoscope, post the cleaning procedure, for the entire colon.

14.2. SAFETY ASSESSMENT

An independent group of experts chosen by the sponsor will constitute the Data and Safety Monitoring Board (DSMB). The DSMB will evaluate every Adverse Event. All Adverse Events will be reported as per the standard clinical practices, according to section 16.3. All adverse event incidence rates will be summarized by anticipation, severity and relationship to the investigational device.

The incidence of major complications using the MCS and the Standard Optical Colonoscopy will be presented.

The safety of the MCS in terms of rate of MCS -related severe adverse events as compared to standard colonoscopy procedure will be evaluated. Overall, routine colonoscopy is considered to be a safe procedure with an overall low risk of major complications of approximately 0.35 percent[3,4]. Expected (non-severe) adverse events which is under estimated due to the lack of monitoring those events in literature, include device related mucosal trauma, changes in bowel habits, nausea, bloating, abdominal discomfort, gas and in some cases bleeding.

Mild anticipated incidents, seen also in a standard colonoscopy with no clinical significant meaning, will be reported as per the direction of the DSMB.

14.3. PROCEDURE AND CECUM REACHED TIME

Time to cecum is defined as the net duration from insertion of the colonoscope to visualization of the cecum.

Time of the whole procedure is defined as the net duration from insertion of the colonoscope until removing of the whole instrument (guide: >6min withdrawal time).

Start & end time of any diagnostic or therapeutic intervention which will be performed during the insertion or retrograde phase, will be calculated and reduced from the total time.

14.4. CECAL INTUBATION

Completion of colonoscopy with the MCS is defined from insertion of colonoscope to visualization of the cecum, confirmed by a snapshot.

Cecal intubation will be evaluated by the number of colonoscopy procedures that reached the cecum.

14.5. USER SATISFACTION

User satisfaction will be evaluated by a questionnaire (specified in the CRF). The physicians who will conduct the procedures and the nurse who assists the procedure and assembles the MCS will be asked to fill-in a dedicated questionnaire in the CRF and include their feedback on the system.

[3] ASGE, Complications of colonoscopy, Gastrointestinal Endoscopy, Volume 74, No. 4 : 2011

[4] Dominitz J. A., et al., "Complications of Colonsocopy", Gastrointestinal Endosc.2003: 57(4): 441-445

15. STATISTICAL CONSIDERATIONS

15.1. DETERMINATION OF SAMPLE SIZE

The primary objective of the study is to evaluate the effectiveness of MCS in cleansing a poorly prepared colon.

Based on previous study data (pre-clinical and clinical), 36% and 96% success rates of good/excellent cleansing levels are have been found for pre procedure and post procedure, respectively.

A sample size of 47 patients is required as per McNemar test to determine that the paired discordant proportion are significantly different under the followings assumptions:

Probability of Type I Error (α) = 0.05

Power (1 - β) = 0.8

Proportion switching from + to - = 0

Proportion switching from - to + = 0.6

Sample size required (number of pairs) = 11

This pilot study will include 3 sites (i.e., 2 sites in NL and 1 site in Germany). As per McNemar sample size calculation 11 subjects will be recruited per site.

Adding 10% of drop out (i.e. 4 cases) and additional 9 cases (The first 3 subjects of each physician) that will be excluded from the secondary analysis in order to compensate the system operation learning curve.

The overall sample size is as follows:

3 subjects per site for training - overall 9 subjects

11 subjects per site - overall 33 subjects

Addition of 10% of withdrawn subjects - 4 subjects

Therefore , up to 47 subjects (15-16 subjects per site) are planned to be enrolled to this study.

15.2. DESCRIPTION OF STATISTICAL METHODS

Demographic and other baseline characteristics will be provided for all subject.

Summary statistics (arithmetic mean, standard deviation, median, minimum and maximum for quantitative variables) will be presented for the total study population. Frequency tables for qualitative data will be provided.

Any deviation from specified statistical plan will be in addition to "per protocol" analysis and will be reported as such. Post-hoc analysis will be conducted according to the existing data gathered, if necessary.

15.2.1. ANALYSIS OF POPULATION

Subjects will be excluded from the efficacy analysis as missing/invalid data by the following:

- Subject withdraws
- Unprepared subjects (not taken the preparation or had a partial bowel preparation)
- System technical failure

Individual listings of withdrawal / failure including descriptive information will be provided.

In addition, in cases of incomplete procedure (i.e., the entire colon is not visualized); the overall BBPS per patient will be evaluated based on the colon segments that were visualized.

15.2.2. PRIMARY END POINT HYPOTHESIS ANALYSIS

The primary endpoint is the bowel cleansing level, as determined by BBPS scoring index, assessed in total and by segment (cecum, ascending, transverse, descending/sigmoid, and rectum).

The primary statistical hypothesis is that the rate of adequate cleansing level (i.e., BBPS>1) post MCS procedure will significantly improve as compared to the rate of adequate cleansing level pre procedure (prior the MCS use) , assuming 60% chance for improvement (P01).

The primary performance assessment will be based on data from all colon segments observed during the colonoscopy procedure.

Chi-square or Fisher's exact test, as appropriate, will be performed in order to compare proportions of good or excellent cleansing level (i.e., BBPS>1) pre and post MCS procedure.

In addition, frequency counts, percentages, and 95% confidence intervals will be provided.

15.2.3. SECONDARY SAFETY ANALYSIS

The secondary endpoint is to evaluate the Device related adverse event and the overall adverse events rate.

The safety analysis set will consist of all subjects who were enrolled into the study.

Individual listings of adverse events including type of device, adverse events (reported term), seriousness, duration, relationship to the study device, severity and the adverse events outcome will be provided for the total population and per population group.

AEs will be summarized using frequency counts and percentages.

15.2.4. Exploratory Measures Analysis

Time to cecum

Net duration from insertion of the colonoscope to visualization of the cecum will be summarized a table by the following time categories:

- ≤10 min
- 11-20 min
- 21-30 min
- ≥31 min

Count and percentage will be provided for time category.

In addition a descriptive statistics for continuance variable, including number of subjects, mean, median, standard deviation, minimum, and maximum will be provided..

Start & end time of any diagnostic or therapeutic intervention which will be performed during the insertion phase, will be calculated and reduced from the total time to Cecum.

Total examination time

Net duration from insertion of the colonoscope removing of the whole instrument (Guide: >6min withdrawal time) will be summarized in a table by the following time categories:

- ≤30 min
- 31-40 min
- 41-50 min
- ≥51 min

The analysis will include only procedures that were completed to the cecum.

Count and percentage will be provided for time category.

In addition a descriptive statistics for continuance variable, including number of subjects, mean, median, standard deviation, minimum, and maximum will be provided.

Start & end time of any diagnostic or therapeutic intervention which will be performed during the procedure, will be calculated and reduced from the total time to Cecum.

Cecal intubation

The count and percentage of subjects for which cecum could be reached by the colonoscope with the MCS will be presented together with 95% confidence intervals.

User satisfaction

Will be summarized in a table via descriptive statistics by data type. The questionnaire will be filled in by the physicians who will conduct the procedures and the nurse who assists in the procedure and assembles the MCS and includes their feedback on the system

15.3. BLINDING AND RANDOMIZATION

Blinding and randomization are not applicable in this study.

15.4. POOLING

In addition to generating clinical reports from this study, data from the sites in this multi-center study and possibly from additional studies performed in other clinical centers following the same study design and using a common protocol may be pooled. In such a case the study data may be pooled and subgroup analysis of the primary endpoint by center will be used to evaluate the poolability of the results. The safety and clean rate by center interaction will be tested with appropriate standard statistical methods. Data from the user satisfaction questionnaires may be pooled later as well to be used in a future usability study.

15.5. HANDLING OF MISSING DATA

Dropouts and subjects lost to follow will be treated as missing values and therefore dropped from analysis of performance variables. A subject for whom the procedure was not performed to due to no or partial bowel preparation will not be entered into this analysis**.** No imputation of missing data will be performed.

15.6. INTERIM ANALYSIS

An Interim analysis related to pre-procedure cleansing will be conducted after 10 subjects per site or 50 cases overall, whatever comes first. Interim analysis will primarily assess the subjects' pre-

procedure cleansing in order to ensure enough poorly prepped cases for the evaluation of the device capabilities. Preparation procedure may be adjusted as per interim results direction.

16. ADVERSE EVENTS

16.1. DEFINITION

An adverse event (AE) is any untoward medical occurrence, unintended disease or injury, or untoward clinical signs (including abnormal laboratory findings) in subjects, users or third persons, whether or not related to the investigational medical device.

Abnormal results of diagnostic procedures are considered to be adverse events if the abnormality:

- Is considered by the investigator to be of clinical significance

A serious adverse event (SAE) is defined as any undesired adverse event in a clinical study or performance evaluation study occurring to a subject , users or third persons whether or not related to the investigational medical device that led directly or indirectly to the following:

- Leads to death;
- Results in a life-threatening illness or injury;
- Results in a permanent impairment of a body structure or a body function;
- Requires in-patient hospitalization or prolongation of existing hospitalization;
- Results in medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function;
- Led to foetal distress, foetal death or a congenital abnormality or birth defect

This includes device deficiencies 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. Planned hospitalization for a pre-existing condition, or a procedure required by the CIP, without serious deterioration in health, is not considered a serious adverse event.

An adverse device effect (ADE) is any adverse event related to the use of an investigational medical device. This definition includes any event resulting from insufficiencies or inadequacies in the instructions for use or the deployment of the device, or any event that is a result of a user error, or from intentional misuse of the investigational device.

A Serious Adverse Device Effect (SADE) is an adverse device effect that has resulted in any of the consequences characteristics of a serious adverse event or that might have led to any of these

consequences if suitable action had not been taken or intervention had not been made or if circumstances had been less fortunate.

An Unanticipated Serious Adverse Device Effect (USADE) is a serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current version of the risk analysis report

A Device Deficiency is any inadequacy of a medical device with respect to its identity, quality, durability, reliability, safety or performance (device deficiencies include malfunctions, use errors, and inadequate labelling).

Anticipated Adverse Events, A list of anticipated adverse events is provided in "Anticipate Risks" section of this study protocol.

16.2. ADVERSE EVENTS CLASSIFICATION

The severity of adverse events will be rated as follows:

- Mild: An AE which is transient or mild in nature, which does not limit the subject's activity, and which does not require medical intervention
- Moderate: An AE which has mild-moderate impact on the subject's activity or requires minimal medical intervention or monitoring
- Severe: An AE which has marked impact on the subject's activity or requires medical care

Each AE will be classified as SAE or non-SAE as follows:

- A serious adverse event (SAE) is any adverse event that is fatal or life threatening, or results in permanent impairment of a body structure or function, or in-patient or prolonged hospitalization, or requires medical or surgical intervention to prevent life-threatening illness or injury, or led to foetal distress, foetal death or congenital abnormality or birth defect.

The relationship of the AE and SAE to the treatments or procedures is defined as follows:

- Unrelated: Any event that does not follow a reasonable temporal sequence from administration of study treatment AND that is likely to have been produced by the subject's clinical state or other modes of therapy administered to the subject.
- Unlikely: Any event that does not follow a reasonable temporal sequence from administration of study treatment OR that is likely to have been produced by the subject's clinical state or other modes of therapy administered to the subject OR that does not follow a known pattern

of response to suspected device OR does not reappear or worsen when the device is re-administered

- Possibly: Any reaction that follows a reasonable temporal sequence from administration of study treatment OR that follows a known response pattern to the suspected device AND that could not be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.
- Related: Any reaction that follows a reasonable temporal sequence from administration of study treatment AND that follows a known response pattern to the suspected device AND that recurs with re-challenge, AND/OR is improved by stopping the use of the device.

16.3. ADVERSE EVENTS REPORTING

Throughout the course of the study, all efforts will be made to capture and evaluate adverse events. If an adverse event occurs, the first concern is for the safety and welfare of the subject. Appropriate medical intervention will be made. All adverse events observed by the Investigator or reported by the subject, whether or not related to the MCS or to a study-procedure, have to be recorded in the appropriate section of the subject's CRF. CRFs will be collected throughout the study. Information about AEs will include as a minimum the description of the event, date of onset, date the event was noticed by Investigator, an evaluation of the relatedness of the adverse event to the MCS and /or study procedure, medical assessment for seriousness, actions taken and whether study participation was discontinued.

A pre-existing condition, which is a condition that is present at the beginning of the study, should be recorded as an adverse event if the frequency, intensity, or the character of the condition worsens during the study period.

All Adverse Events still on-going at the end of the study period need to be followed until resolution.

Serious Adverse Events will be reported by the Investigator to the sponsor with no delay, and anyway not later than 2 days after the Investigator learned about the event. The sponsor will notify the DSMB members on the event immediately , and no later than 72 hours after the sponsor learned about the event. The Investigator will use the study specific CRF reporting form. SAEs will be processed and reported by Sponsor to Competent Authorities and Ethics Committees according to the applicable

local regulations. Serious adverse events that are still on-going at the end of the study period must be followed up to determine the final outcome.

The investigator is responsible for the classification of adverse events and together with the sponsor for the ongoing safety evaluation of the clinical investigation. The sponsor shall:

- Forward all AE records and the investigator's assessment to the DSMB. The DSMB will fulfill its responsibility to monitor the safety of patients by conducting formal reviews of the accumulated safety data. These reviews will normally occur at regular intervals, however, in case of specific concerns, ad-hoc meetings can be set up.

  A DSMB will evaluate AEs for their relatedness to the investigational device and will make recommendation regarding reporting, continuation, modification, or termination of the trial. The DSMB will determine and document in writing their seriousness and relationship to the investigational device.
- Review all device deficiencies and determine and document in writing whether they could have led to a serious adverse device effect;
- Report or ensure the reporting, to the EC by the principal investigator(s), of all serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by national regulations or by the EC. The investigator must inform the sponsor and the local EC about any serious adverse effects and serious adverse device effects as soon as becoming aware of the occurrence by Fax/Telephone.
- Report to regulatory authorities, within the required time period, all serious adverse events and device deficiencies that could have led to a serious adverse device effect, if required by national regulations
- In the case of a multi-center study, inform all principal investigators in writing of all the serious adverse events at all investigation sites that have been reported to the sponsor, and ensure that they are reported to their EC, if required by national regulations; this information shall be sent to all the principal investigators within a time frame established based on the perceived risk as defined in the risk analysis report
- Ensure that the EC and the regulatory authorities are informed of significant new information about the clinical investigation.

- In case of serious adverse device effects and device deficiencies that could have led to serious adverse device effects, determine whether the risk analysis needs to be updated and assess whether corrective or preventive action is required.

For further details about responsibilities, operative procedures and applicable local regulations please refer to the "Serious Adverse Events Reporting Plan" signed by sponsor and delegated CRO, current version.

16.4. DEVICE TECHNICAL FAILURES

Device deficiencies occurred within the colonoscopy procedure will be reported.

17. INVESTIGATION ADMINISTRATION

The investigation will be conducted according to this protocol and according to the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with Good Clinical Practice, EN ISO 14155:2011(E) and the applicable national laws and regulations.

This may include an inspection by Motus representatives and/or Regulatory Authority representatives at any time. The investigator must agree to the inspection of study-related records by the Regulatory Authority/Motus representatives, and must allow direct access to source documents to the Regulatory Authority/Motus representatives.

Regulatory Authority approvals/authorizations/notifications, when required, will also be in place and fully documented prior to study start.

17.1. ETHICAL COMMITTEE (EC) AND COMPETENT AUTHORITY (CA) INFORMATION

This protocol and the informed consent (IC) form must be reviewed and approved by the appropriate EC where the study is to be conducted before enrollment of subjects. Study start will also require approval by the relevant CA in each participating country. Changes to the protocol that may increase the risk or present new risks to the subject, or may adversely affect the validity of the trial, must be approved in writing by the sponsor and by the EC and the CA before the change is implemented

17.2. EC/CA APPROVAL LETTER

EC approval to participate in this trial is required from each institution participating in this investigation. CA approval to participate in this trial is required from each country participating in this investigation. Prior to subject enrollment, a signed copy of the EC and CA approval letters addressed to the investigator must be submitted to the sponsor certifying study approval. Investigators are responsible for submitting and obtaining review of the study by their EC according to the national rules and regulations. CA notification in each country will be performed by the study sponsor.

18. RESPONSIBILITIES OF SPONSOR AND INVESTIGATOR

18.1. PRINCIPAL RESPONSIBILITIES OF SPONSOR

Sponsors are responsible for selecting qualified investigators and providing them with the information they need to conduct the investigation properly, ensuring proper monitoring of the investigation, ensuring that EC and CA review and approval are obtained. Additionally, the sponsor is responsible in ensuring that any reviewing EC, and relevant competent authorities are promptly informed of significant new information about the investigation. The sponsor is responsible to comply with applicable governmental regulations.

18.2. PRINCIPAL RESPONSIBILITIES OF CLINICAL INVESTIGATOR

The role of the principal investigator is to implement and manage the day-to-day conduct of the clinical investigation as well as ensure data integrity and the rights, safety and well-being of the subjects involved in the clinical investigation.

Each Investigator agrees to comply with all applicable governmental regulations and the requirements of this study. Investigators who do not comply with the protocol, or conditions included in approvals granted by the reviewing committee, will have their participation in the study terminated.

19. STUDY RECORD RETENTION AT STUDY SITE

The investigator shall organize the conservation of study documents until the end of it, respecting all regulations and specific recommendations concerning the preservation of medical records in clinical trials.

To facilitate assessments and / or audits/ or inspections of health and regulatory authorities, the investigator undertakes to maintain records, including the identity of all subjects (enough information to link the records, e.g., the CRF and hospital records) and all original signed informed consent forms. The investigator should retain records for a minimum period of 5 years (or longer period than the period indicated in Directive 93/42/EEC or local regulations). Study records shall be stored under strict security and be available for review for authorized personnel only.

20. RESPONSIBILITIES AND DUTIES OF MONITOR

20.1. GENERAL

The sponsor will conduct investigational site monitoring to ensure that all investigators are in compliance with the protocol, regulatory requirements and the Investigator's agreement.

The sponsor will review significant new information, including unanticipated adverse events and ensure that such information is provided to the study investigators and all reviewing EC

20.2. STUDY MONITOR RESPONSIBILITIES

Site visits will be conducted by an authorized Motus GI representative after having received training on the study protocol, regulatory framework and the medical device function and use.

Visit tasks, preparation and follow up are described in detail in the study specific Monitoring Plan.

During study conduct the following visits will be performed:

- Site Evaluation Visit:

were conducted by the Sponsor to select qualified Investigators and to determine the investigative site's ability to conduct the clinical investigation prior to commencement of the study.

- Site Opening Visit

will be conducted to train site staff on the study protocol, patient selection, study procedures and data recording processes.

- Monitoring Visits

will be conducted to inspect study data, subjects' medical records, and CRFs in accordance with ISO14155 and the respective local and national government regulations and guidelines (if applicable).

The Study Investigator and the investigating site will permit authorized clinical research personnel and clinical monitors from Motus and/or designee(s) employed by Motus to review completed CRFs, EC/CA decisions, clinical site records, and facilities relevant to this study at regular intervals throughout the study.. Additionally, subject charts and clinical records will be requested and reviewed so that protocol adherence and source documentation can be verified. The accuracy and quality of the data obtained from the investigator and maintained by Motus will be confirmed through a structured program of clinical field auditing and internal review detailed in the monitoring plan. In instances where data protection regulations prohibit the direct examination of hospital records by the study Sponsor or designee(s), the Investigator will cooperate in a system of source data verification with the Sponsor. Monitoring may be performed with in person visits or remotely, when applicable.

To ensure the rights, safety, and welfare of study subjects are being maintained, the monitor will review training records to ensure all study staff are trained on the study protocol and use of the study devices. If the monitor discovers that an investigator is not complying with the signed Investigator Agreement, the investigational plan, applicable laws, or any conditions of approval imposed by the reviewing EC and CA, the monitor will report to the Sponsor and take such steps necessary to promptly secure compliance. If compliance cannot be secured, device shipments to the investigator may be discontinued and the investigator's participation in the investigation terminated. The monitor shall also require such an investigator to dispose of or return the device, unless this action would jeopardize the rights, safety, or welfare of a subject.

- Site Close-Out Visit:

After last patient completed last visit, CRF is completed and all queries are resolved, a closing visit will be performed for a final review of CRF, queries resolved, Investigator Site File and to ensure correct archiving (see section 19).

21. DATA COLLECTING AND QUALITY CONTROL

This study will utilize an electronic database and eCRF (a web based system , that is provided by "TechnoSTAT Ltd") All data requested on the eCRF are considered mandatory . Data points not collected and/or recorded will be considered deviations unless otherwise specified.

The Principal Investigator must ensure the accuracy and completeness of the recorded data that will be recorded in compliance with local regulations. Changes to data previously submitted to the sponsor will require a new signature by the Investigator to acknowledge/approve the changes.

Visual and/or computer data review will be performed to identify possible data discrepancies. Manual and/or automatic queries will be created and will be issued to the site for appropriate response. The site staff will be responsible for resolving all queries in the database.

- This study will be using a ISO 14155 compliant electronic data capture system that will ensure: Attributability, completeness, reliability, consistency and logic of the data entered,
- Data changes are documented and that there is no deletion of entered data (audit trail)
- Maintenance of a security system that prevents unauthorized access to the data
- Maintenance of a list of individuals who have access to the electronic data system as well as the dates of access
- Signature of all completed CRFs by the principal investigator or authorized designee,
- Maintenance of an adequate backup and data retention system.

22. SUBJECT CONFIDENTIALITY

All reports and communications relating to study subjects will identify the subject only by his/her initials and case number. The investigator will complete subject identification on a confidential site log, which will be used for the purposes of traceability and follow-up. This will be treated with strict adherence to professional standards of confidentiality, and will be filed under adequate security and restricted accessibility.

23. SUBJECT INFORMED CONSENT FORM

The Principal Investigator, or his designee, in accordance with institutional policy, will obtain an Informed Consent that is reviewed and accepted by the Ethics Committee. A written consent form bearing the full name, date and signature of the subject and the local investigator will be obtained from each subject. The signed Informed Consent constitutes a confidential document and therefore should be archived in the study binder. A copy of the consent should be given to the subject.

24. INVESTIGATOR/STUDY DISCONTINUATION

Any investigator will be removed from the study if he/she demonstrates a pattern of non-adherence to the study protocol and/or unethical behavior.

The study may be discontinued if at any time, in the opinion of the hospital ethics committee and the principle investigator, the study represents an unreasonable medical risk to subjects. The list of reasons for the study termination can be found in the ICF and in the site Investigator Agreement (IA).

25. PROTOCOL COMPLIANCE/PROTOCOL DEVIATIONS

A deviation is defined as an event where the exact instructions contained in this protocol, the clinical trial agreement or the applicable regulations have not been followed. Deviations are classified by occurrence, i.e., sporadic vs. repeated and seriousness, i.e., major vs. minor.

Major deviations may impact subject safety, alter the risk/benefit ratio, compromise the integrity of the study data, and/or affect subjects' willingness to participate in the study. Minor deviations do not impact subject safety, compromise the integrity of the study data, or affect subjects' willingness to participate in the study.

Protocol deviations will be reported to the sponsor using suitable forms, regardless of whether medically justifiable, pre-approved by the sponsor or taken to protect the subject in an emergency.

The instructions and procedures specified in this protocol require diligent attention to their execution. Except for an emergency situation in which proper care for the protection, safety and wellbeing of the study subject requires alternative treatment, the study shall be conducted exactly as described in the approved protocol. No alterations or changes to this protocol will be permitted. However, should there be question or consideration of deviation from the protocol, clarification must be sought from the sponsor. Any subject treated in a manner that deviates from the protocol, or who is admitted into the study but is not qualified according to the protocol, may be ineligible for analysis and thereby compromises the study. The investigator and research team must comply with all applicable international and national laws.

25.1. PROTOCOL AMENDMENTS

The protocol cannot be amended by the investigators, or study personnel, without first obtaining review and the agreement of the sponsor. Medically significant amendments to the protocol (e.g., affecting the rights, safety, or wellbeing of the human subjects involved in the investigation, the scientific soundness of the investigational plan, the validity of data or information resulting from the completion of an approved protocol, or the relationship of the likely subject risk/ benefit relied upon to approve a protocol or if there are otherwise significant inclusion of new categories of subjects, etc.) may not be instituted prior to approval by the relevant Ethics Committee and regulatory approval by relevant Competent Authorities,.

26. PACKAGING

The shelf life of the MCS Add-on is 12 months. In this clinical trial, the system and its accessories will be manufactured and then shipped to the clinical sites following all study regulatory approvals and prior the initiation of the study. The Add-on devices are packed and transported for the clinical investigation from the company storage to the medical center by the Motus GI team in an appropriate environmental condition. The Motus GI team or designee is responsible to verify adequate transportation and to ensure that the package is not being compromised prior to the trial. At the clinical site the Add-on device is assembled on top of the colonoscope and then being connected to the WS according to the applicable instructions, detailed in the IFU.

26.1. LABELING

All equipment associated with the clinical trial will be identified with visible markings stating "Exclusively for clinical investigation ".

All packages are labeled in conformance to Motus GI Packaging Best Practice, which are applicable to Single Use, Limited Shelf Life, Lot produced items. Examples of the main system and packaging label as well as operation instructions, precautions and warnings are defined in the "Instructions For Use".

26.2. INVENTORY CONTROL

The sponsor will initiate shipment of the product from the sponsor to the site upon receiving all required documents (e.g., approval/favorable opinion from EC and regulatory authorities where required). The sponsor will maintain tracking for all shipment documentation. Prior to any shipment, the site will be informed by the sponsor of the upcoming shipment, expected arrival date, and content of the shipment. The site should confirm receipt of the shipment. The site will file the Sponsor's Shipping Receipt in the Sponsor's Study File.

An Investigator's Device Accountability form will be conducted under the Regulatory Binder at each site and will be monitored by the site's clinical research associate (CRA).

In case of technical failure, the site will approach the technical support team which will help solve the problem and will notify the site's CRA.

For each dispensed MCS add- on, the following information should be recorded:

- The subject study number
- Date dispensed
- Disposables' ID number

At the termination of the study, all unused study material must be returned with the corresponding documentation as directed by Motus GI.

27. USE OF DATA AND PUBLICATIONS

All data and results and all intellectual property rights in the data and results derived from the study will be the property of Motus GI Medical Technologies, who may utilize the data in various ways, such as for submission to government regulatory authorities or disclosure to other investigators, educational, further product development and marketing uses.

Publication of the Study results in scientific literature is encouraged, but the Company reserves the right to review any paper written utilizing data generated from the Study before such paper is presented (including by poster presentation, invited speaker or guest lecturer presentation, etc.) or submitted for publication. The Institution and the investigator shall provide the Company with a copy of all such manuscripts and materials , and allow the Company a reasonable time to review and comment.

The Institution and the Investigator further agree to delay the publication for an additional ninety (90) days from first submission for review to ccompany, at the request of the Company, where the ccompany considers such delay necessary for the protection of its Intellectual Property Rights.

28. APPENDIX A –SCORING METHOD

The system performance & cleansing quality can undergo a intra procedural evaluation using the 0-3 BBPS[5] scoring method per segment. Since the BBPS cleansing scoring method is subjective by nature, and the scale is influenced by the physician experience and the work load during the procedure, there might be a variance between the scoring evaluation of performing physicians. In this case the recorded video/images may undergo a blinded off-line re-evaluation using independent trained gastroenterologists which will act as a central readers for all procedures.

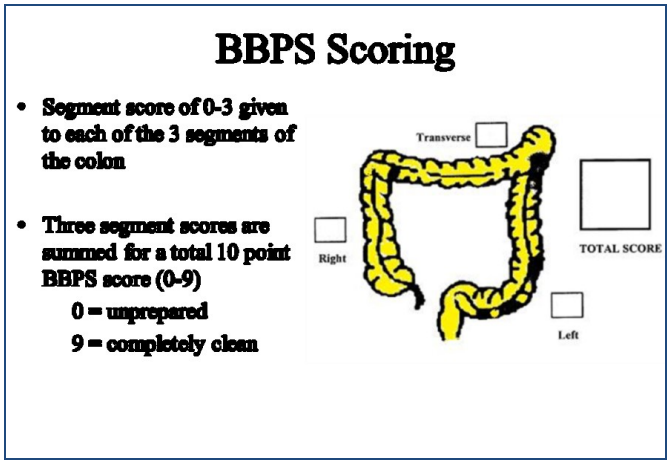
The points assigned according to the Boston Bowel Preparation Scale (BBPS) are as follows:

0 = Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.

1 = Portion of mucosa of the colon segment seen, but other areas of the colon segment not well seen due to staining, residual stool and/or opaque liquid.

2 = Minor amount of residual staining, small fragments of stool and/or opaque liquid, but mucosa of colon segment seen well.

3 = Entire mucosa of colon segment seen well with no residual staining, small fragments of stool or opaque liquid. The wording of the scale was finalized after incorporating feedback from three colleagues experienced in colonoscopy.



[5] Lai E.J. et al," The Boston Bowel Preparation Scale: A valid and reliable instrument for colonoscopy-oriented research", Gastrointestinal Endosc. ,2009: 69(3 Pt 2): 620–625

29. APPENDIX B – STUDY DESIGN AND SCHEDULE OF ASSESSMENT

Visit	Visit 1 Screening Visit	Colon Preparation	Visit 2 Colonoscopy ≥ 2 days and ≤ 30 days after visit 1	Follow up 1	Follow up 2
Days	**>-2days**	**-2 to 0 days**	**0**	**48 hours ±24 hours**	**14 day ±3 days**
Informed Consent*	X				
Eligibility assessment	X				
Colon Preparation Instructions	X				
Medical History, Concomitant Medications, Demographic details	X				
Diaries	X (providing)	X (by the subjects)			
Bowel Preparation		X (by the subjects)			
Colonoscopy Procedure			X		
Follow Up			X **	X	X
Adverse Events Reporting		X			

*Informed consent will be obtained prior to the conduct of any study procedures
**Before discharge from the hospital

30. APPENDIX C –COLON PREPARATION INSTRUCTIONS FOR THE SUBJECT

Morning procedures **Two days prior to colonoscopy procedure day: Date _____**		
All day	No hard food	No dried fruits, seeds, nuts, legume and alike
The day before the colonoscopy procedure day: Date _____ • **Last solid meal at: Date_____ Time_____ PM/AM**		
Starting time: _____ PM/AM	Clear liquid diet – No solid foods, milk products or alcoholic beverages are allowed.	*Approved Clear liquid diet: Water, clear fruit juices (no pulp), clear cordials, soft drinks, jelly (yellow or orange), sports drinks. Black tea or coffee sweetened to taste without milk, soy or whiteners. Clear soups, chicken or beef broth. A combination of these clear fluids will give a variety of fluid intake. Do not have anything colored red or purple. Barley sugar is allowed.
Bowel preparation - First Dose:		
_____PM/AM	2 pills of 5mg Bisacodyl	Early afternoon
Bowel preparation - Second Dose:		
_____PM	2 pills of 5mg Bisacodyl	Evening
Colonoscopy procedure day: Date _____		
Diet: starting-		
_____PM/AM	Clear liquids	up to 3 hours prior to the colonoscopy procedure
_____PM/AM	No Food/liquids	3 hours prior to the colonoscopy procedure
_____PM/AM	Colonoscopy Procedure	

- Please Bring your diaries to the colonoscopy procedure

Afternoon procedures • **Two days prior to colonoscopy procedure day: Date _____**		
All day	No hard food	No dried fruits, seeds, nuts, legume and alike
The day before the colonoscopy procedure day: Date _____		
Starting time: _____ PM/AM	Clear liquid diet – No solid foods, milk products or alcoholic beverages are allowed.	*Approved Clear liquid diet: Water, clear fruit juices (no pulp), clear cordials, soft drinks, jelly (yellow or orange), sports drinks. Black tea or coffee sweetened to taste without milk, soy or whiteners. Clear soups, chicken or beef broth. A combination of these clear fluids will give a variety of fluid intake. Do not have anything colored red or purple. Barley sugar is allowed.
Bowel preparation - First Dose:		
_____PM	2 pills of 5mg Bisacodyl	Evening
Last solid meal at: Date_____ Time_____ PM/AM		
Colonoscopy procedure day: Date _____		
Bowel preparation - Second Dose:		
_____ AM	2 pills of 5mg Bisacodyl	Early morning
Diet: starting-		
_____PM/AM	Clear liquids	up to 3 hours prior to the colonoscopy procedure
_____PM/AM	No Food/liquids	3 hours prior to the colonoscopy procedure
_____PM/AM	Colonoscopy Procedure	

- Please Bring your diaries to the colonoscopy procedure