Clinical Investigational Plan (CIP) INFORMATION	
Title:	Evaluation of the bowel cleansing in hospitalized population using Pure-Vu System
CIP Number:	**CL00044**
Version Date:	January 30, 2019
Version:	4.0
Sponsor:	Motus GI Medical Technologies LTD. Address: Keren Hayesod 22, Tirat Carmel, ZIP 3902638, Israel Tel: +972-4-6214446 Fax: +972-4-6214442

Summary of Changes to CIP			
Version	**Section**	**Description of Change**	**Reason for Change**
1.0	NA	• NA	NA -Initial
2.0	All	• Overall changes to wording • Changed from Patient to Subject • Changed to study design to exclude bowel prep as part of the study • Updated study diagram	

		• Case Report Forms have been taken out and will remain standalone documents	
3.0	All	• Updates to the inclusion and exclusion criteria • Updates on wording	Updates based on Interim Analysis
4.0	Study design	• Expanded enrollment per site from 25 to 35	Due to enrollment delays

1.0 Signature Page

Investigator Signature Page

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I, the undersigned, have read and understood the protocol specified above and agree on its content. I agree to perform and conduct the study as described in the protocol and in accordance with the relevant laws/regulations and standards.

Name	Signature	Date

2.0 Table of Contents

3.0 Protocol Synopsis

Study Summary	
Study Purpose	The aim of this study is to evaluate the potential improvement in colonoscopy procedure's outcomes when using the Pure-Vu System in hospitalized subjects who are indicated for colonoscopy procedure.
Objective	The primary objective of this study is to evaluate the bowel cleansing after Pure-Vu use in hospitalized subjects, which may increase the likelihood of a successful colonoscopy examination.
Study procedures	❖ Eligible subjects will be consented and enrolled ❖ Following standard bowel preparation, the nurse or study coordinator will be asked to complete a questionnaire about the subjects' baseline preparation condition prior to the colonoscopy procedure. ❖ Subjects will undergo colonoscopy procedure with Pure-Vu System. ❖ In case of inadequate bowel preparation as defined as BBPS < 2 in at least one of the colon segments, prior Pure-Vu use, the physician will complete a questionnaire on the patient's management standard of care assuming the absence of Pure-Vu.
Protocol Number	CL00044
Protocol Title	Evaluation of the bowel cleansing in hospitalized population using Pure-Vu System **Ver. 4.0**

Study Sponsor	Motus GI Medical Technologies, Keren Hayesod 22, Tirat Carmel, ZIP 3902638, Israel Tel: +972 (4) 6214446/103 Fax: +972 (4) 6214442
Sponsor Representative	Hagit Ephrath VP Health Economics, Regulatory and Clinical Affairs
Study Type	**Multicenter, prospective, feasibility study**
Study Product	Pure-Vu System
Study Phase	Post-market
510 (k) Number	K181437 Class II
Study Location	United States and Europe
Study Duration	Study period will last approx. 12 months
Planned Follow-Up	Follow-up will be conducted at 2 working days post-procedure to assess subject well-being and capture any adverse events.
Subject Population	Hospitalized subjects who are indicated for standard colonoscopy procedure and meet the eligibility criteria.
Determination of Sample Size	This is a pilot study that will include up to 100 subjects; no statistical considerations were made to determine the sample size.
Planned # of Sites	Up to 6 clinical sites
Primary Endpoint	The rate of improved cleansing level per segment will be evaluated by the Boston Bowel Preparation Score (BBPS) index.

Secondary Outcomes	The following secondary outcomes will be determined: • Type, incidence, severity, relationship and duration of adverse events. • Cecum intubation rate • Proportion of subjects with successful colonoscopy for the intended indication in the first attempt.
Randomization	NA- single arm
Eligibility Criteria	**Inclusion Criteria** 1. Hospitalized subjects who are indicated for a screening, diagnostic, surveillance or therapeutic colonoscopy 2. Subjects' age > 22 years 3. Subject has signed the informed consent **Exclusion Criteria** 1. Subjects with known Inflammatory Bowel Disease and / or active Colitis 2. Subjects with active diverticulitis 3. Subjects with known or detected (during colonoscopy) bowel obstruction 4. Subjects with ascites Child Pugh C 5. Subjects who are 30 days post-transplant 6. Subjects under active IV inotropic medications 7. Subjects with LVAD 8. Subjects with known coagulation disorder (INR ≥ 2 or platelets <50,000)

	9. Subjects with medical and/or hemodynamic instability. 10. Pregnancy (as stated by subject) or breast feeding 11. Subjects with altered mental status/inability to provide informed consent 12. Subjects who have participated in another interventional clinical study in the last 2 months
Interim analyses	Interim analysis will be done after first 45 subjects enrolled

4.0 Acronyms and Definitions

ADE	adverse device effect
ADL	activities of daily living
AE	adverse event
CRF	case report form
EC	Ethics Committee
FDA	Food and Drug Administration
GCP	good clinical practice
GI	gastrointestinal
ICF	informed consent form
IFU	Instruction for use
ICH	International Conference on Harmonisation
IRB	institutional review board
ISO	International Organization for Standardization
OC	optical colonoscopy
DCBE	double contrast barium enema

CT	computed tomography
MagC	Magnesium Citrate
SAE	serious adverse event
SADE	serious adverse device effect
USADE	unanticipated serious adverse device effect
WS	Workstation
WSC	Workstation Connector
BBPS	Boston Bowel Preparation Scale

5.0 Introduction

This document is a protocol for human research study. This study will be conducted in accordance with local government regulations, and applicable international standard of Good Clinical Practice, and institutional research policies and procedures.

5.1 Background

Colorectal cancer is the third most common cancer in men and the second most common cancer in women worldwide (2). In the United States, approximately 134,490 new cases are estimated for 2016 with approximately 49,190 deaths (8.0% of all cancer deaths) (3). Because colorectal cancer tends to develop slowly, screening and early detection can significantly reduce both the incidence and associated mortality of the disease (4).

Optical colonoscopy (OC) is considered the gold standard method for the evaluation of subjects with suspected colonic disease. A key factor for ensuring high quality colonoscopy and successful screening is good colon preparation. Bowel preparation prior to colonoscopy is one of the major barriers to patient compliance estimated as many as 38% of patients do not complete the bowel preparation due to palatability and/or intolerance to the large volume. Inadequate preparation is a major obstacle for achieving a high-quality colonoscopy (6).

Inpatient status is one of several factors associated with poor bowel preparation leading to incomplete colonoscopy procedures, which in turn may cause increased patient morbidity, missed pathology, prolonged hospital stay and increased cost. According to results from a

prospective study by Ness et al. (7) involving a cohort of 649 subjects, inpatient status is a risk factor for bowel preparation failure. Bowel preparation for hospitalized patients can be challenging due to the presence of ongoing acute illnesses, dehydration, comorbidities, and newly prescribed medications. Failure of bowel cleansing typically leads to aborting and re-scheduling procedures after better preparation is achieved, which in turn leads to prolonged hospitalizations.

Pure-Vu System enables colon cleansing during standard colonoscopy using a standard colonoscope with a length of 1630mm – 1710mm and a The Oversleeve, which fits over the colonoscope, is connected to an external workstation, generates fluid jets to break up the feces. The fecal matter & fluids are removed through the evacuation channels of the Oversleeve device into an external waste receptacle.

This study is designed to evaluate the potential improvements in colonoscopy procedure outcomes when using the Pure-Vu System in hospitalized subjects who are indicated for colonoscopy procedure.

6.0 Study Device

6.1 General Description

The Pure-Vu System is Food and Drug Administration (FDA) cleared device, intended to connect to standard colonoscopes to help facilitate intra-procedural cleaning of a poorly prepared colon by irrigating or cleaning the colon and evacuating the irrigation fluid (water), feces and other bodily fluids and matter, e.g. blood.

The Pure-Vu System comprises the following components:

- The Pure-Vu Workstation (WS) - controls the flow of gas (e.g. air) and water or saline to the Oversleeve device and the evacuation of fecal matter and fluids out of the body.
- The disposable Oversleeve is mounted on top of the colonoscope allowing the physician to clean the colon. The Oversleeve is connected to WS via the WS Connector (WSC).
- The disposable WS Connector is mounted onto the front panel of the WS and connects to the irrigation and sensing lines of the Oversleeve.

- The loading fixture is an ancillary device that is used to aid in loading the device on the colonoscope.
- External reservoir for collecting the evacuated fecal matter and fluids
- External foot pedals 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.

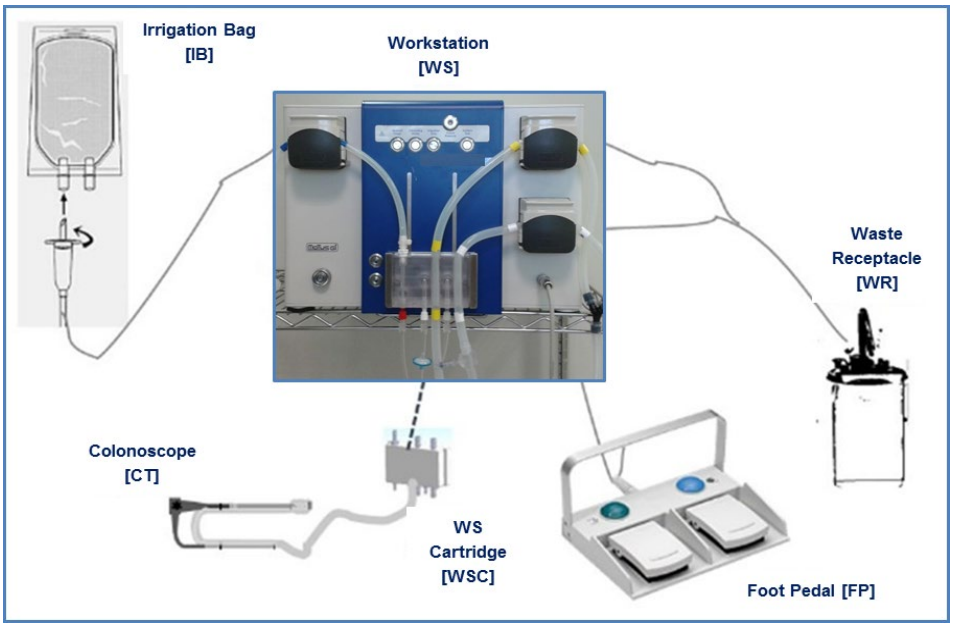


Figure 1: Pure-Vu Workstation – General design & components

A detailed description of the system components, its principles of operation, dimensions and packaging is elaborated in the Instruction for use (IFU).

6.1.1 Work Station (WS)

The WS controls the flow of gas (e.g. air) and water or saline to the Oversleeve device and the evacuation of fecal matter and fluids out of the body. The WS has the following main functions:

- Cleansing: Creates an irrigation stream, which is a mixture of liquid (water or saline) and air into the colon to break up fecal matter. The irrigation of air and liquid (water or saline) is referred to as "cleansing jets". The cleansing has three modes, high, medium and low with medium being the default setting. The physician can operate the system as per his clinical judgment. It is important to note that the evacuation function noted below is active during cleansing so that fluid is input and removed from the colon simultaneously.
- Evacuation: Removes fecal matter and fluids out of the colon. The evacuation function is active during the cleansing as previously noted and can also be used independently. During evacuation the system senses the pressure in the evacuation channel of the Oversleeve and if the pressure goes below pre-set limits will automatically reverse the flow to purge a potential blockage and then switch back to continue evacuation. The user also has the ability to manually purge the evacuation channel as well.
- User interface: Consists of actuators and indicators on the WS itself as well as a foot pedal to activate the main functions of the system so that users' hands are free to manipulate the colonoscope in a standard fashion.

6.1.2 Oversleeve

The Oversleeve is mounted on top of the colonoscope and is connected to WS via the WS Connector. The Oversleeve includes the following main components:

- Tubing: Six (6) tubes (2 Pebax and 4 PVC) that support the irrigation, evacuation and sensing functions of the system.
- Cleansing and Evacuation head: The Oversleeve's distal part which contains irrigation ports, evacuation openings, and colon sensing port.
- Inner sleeve: This sleeve attaches the Oversleeve to the colonoscope along its length. This sleeve is inflated to allow the colonoscope to be inserted through it and then deflated

to hold onto the colonoscope when it is navigated through the colon. The inner sleeve is also attached to the outer sleeve noted below on one side.

- Outer sleeve: This sleeve covers the entire portion of the device that goes inside the colon keeping the tubes in position and providing a smooth surface to interface with the wall of the colon. The distal 28 cm of the sleeve is coated with hydrophilic coating to provide a lubricious surface to aid in advancing the system through the colon.
- Inflation connector: Provides the port to pressurize the inner sleeve during the loading of the colonoscope and provides the entry location for the colonoscope to be inserted into the Oversleeve.

6.1.3 WS Connector

The disposable WS Connector is mounted onto the front panel of the WS and connects to the irrigation and sensing lines of the Oversleeve.

The WS Connector slides into the groves on the WS and once in place the user activates the locking mechanism to hold the WS Connector in place and align the connections to the two sensors and the air source for the irrigation. The user will then place the tubing that is on the proximal side of the WS Connector into for irrigation. The evacuation tubing will form the Oversleeve will be placed into the channels on the WS Connector and then into the pump heads according to its color-coding. Last the user will connect a standard bag of saline or water to the irrigation line and the evacuation line to the recommended waste tank.

6.1.4 Ancillary Apparatus

The final part of the system is ancillary apparatus to aid in loading the device on a colonoscope.

- The loading apparatus consists of a pressure source and a distal sealing plug to facilitate inflation of the inner sleeve of the device as well as a base to keep the Oversleeve in a stable position to allow insertion of the colonoscope through the inner sleeve.

6.2 Pre-clinical data

The Pure-Vu system was used by four experienced gastroenterologists in 35 Yorkshire cross swine (66% female) that received a reduced bowel preparation to ensure an inadequate bowel preparation at baseline. Prior to the colonoscopy the Pure-Vu was attached to the colonoscope and the baseline prep was assessed during insertion. The Pure-Vu system was then employed to cleanse the colon and the prep was then assessed post-Pure-Vu use.

No adverse effects and no failed or prematurely terminated cases were noted. Fourteen percent of the swine colons were adequately prepped at baseline (mean BBPS score 0.5 ± 0.7) and improved to 100% after use of Pure-Vu ($p < 0.001$) (mean BBPS score 3.0 ± 0.0). The physicians found Pure-Vu easy and intuitive to operate. The Pure-Vu system effectively cleaned inadequately prepped swine colons and found to be easy to use.

6.3 Clinical data to Date

The Pure-Vu System was evaluated in ninety-seven subjects (54% males) from five sites using similar protocol.

Pure-Vu was used in subjects indicated for a screening, diagnostic or surveillance colonoscopy. To ensure an inadequately prepped colon, subjects underwent a reduced preparation consisting of dietary restrictions (no dried fruit, seeds or nuts) starting 2 days prior to the colonoscopy, an 18 to 24 hour clear liquid diet and a split dose of 20mg Bisacodyl.

The cleansing quality was evaluated before and after use of the Pure-Vu System with the Boston Bowel Preparation Score (BBPS) (1).

Two subjects were excluded from the analysis due to the followings: One subject had breakfast on day of procedure and therefore was excluded from the cleansing efficacy and usability analysis due to non-compliance with the pre-procedural prep regimen. The other subject was excluded because the device could not reach beyond the sigmoid colon due to the subject's

anatomy, thus the physician used a slim colonoscope to complete the procedure and indicated that only a slim colonoscope would be able to advance past the sigmoid and into the cecum.

The Pure-Vu significantly increased the number of subjects with an adequate cleansing level (BBPS >= 2 for all 3 colon segments) from 25%; CI 95% [17%, 35%] at baseline to 99%; CI 95% [94%, 100%] after Pure-Vu. Cecum intubation rate was 98%; CI 95% [94%, 100%]). Mean post-treatment BBPS score was 8.7 ± 1.0 vs. 3.9 ± 2.2 prior to Pure-Vu use. Physicians were satisfied with the device's use. No major difficulties were experienced when performing polypectomy and no serious adverse events were reported.

7.0 Risk/Benefit Analysis

7.1 Anticipated Risks Associated with Pure-Vu System conjunction with a standard colonoscope

The Pure-Vu is used in conjunction with a standard colonoscope during a colonoscopy procedure. Hence, the complications associated with using the Pure-Vu are anticipated to be similar to those associated with the colonoscopy procedure. As with any colonoscopy procedure, when using the Pure-Vu there is some risk of bowel perforation, pain, infection or bleeding. Although the risks of the procedure with the Pure-Vu System are expected to be comparable to conventional colonoscope (0.35%), the device is an add-on to a standard colonoscope.

The Pure-Vu system was tested in an animal study including 35 pigs and in preliminary clinical studies including 97 subjects.

No major complication or serious adverse events occurred within the course of those studies.

In addition, these clinical studies demonstrated an excellent cleansing effectiveness; Pure-Vu improved the cleansing level from 25% at baseline to 99% after the cleansing was operated and in 98% of the subjects the cecum was reached and the procedures completed successfully.

Lastly, subjects 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.

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 subjects along with no significant risk increase.

7.2 Anticipated Risks Associated with bowel preparation agents

The Bowel preparation agent used in this study follows the current practice used in US hospitals.

The main anticipated risks associated with the bowel preparation agents including nausea with or without vomiting, abdominal pain and dehydration.

7.3 Residual risk associated with the study 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 Pure-Vu 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' sizes were optimized to ensure the safety of the subjects along with effective cleansing.
- The Pure-Vu Oversleeves are made from a flexible and low friction material to allow ease of advancement through the colon and to minimize any impact to the steering angle of the colonoscope.

- Hydrophilic coating at the distal 28cm of the outer sleeve to create a lubricious surface to aid in 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 effective cleansing.

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

7.4 Potential Benefits to the Subject

The potential benefits of the Pure-Vu System 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.

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

8.0 Study Objectives

8.1 Primary objective

To evaluate the improvement of bowel cleansing after Pure-Vu use in hospitalized subjects which may increase the likelihood of a successful colonoscopy examination.

8.2 Secondary objectives:

- To evaluate the safety related to the Pure-Vu System.
- To evaluate the potential improvement in hospitalized subjects' outcomes when using the Pure-Vu System.

9.0 Study Endpoints

9.1 Primary endpoints

The rate of improved cleansing level per segment will be evaluated by the BBPS (1) scoring index pre- and post- Pure-Vu use during a colonoscopy examination.

9.2 Secondary endpoints

The following endpoints will be evaluated per study arm:

- Type, incidence, severity, and duration of adverse events.
- Cecum intubation rate
- Proportion of subjects with successful colonoscopy with Pure-Vu for the intended indication in the first attempt.

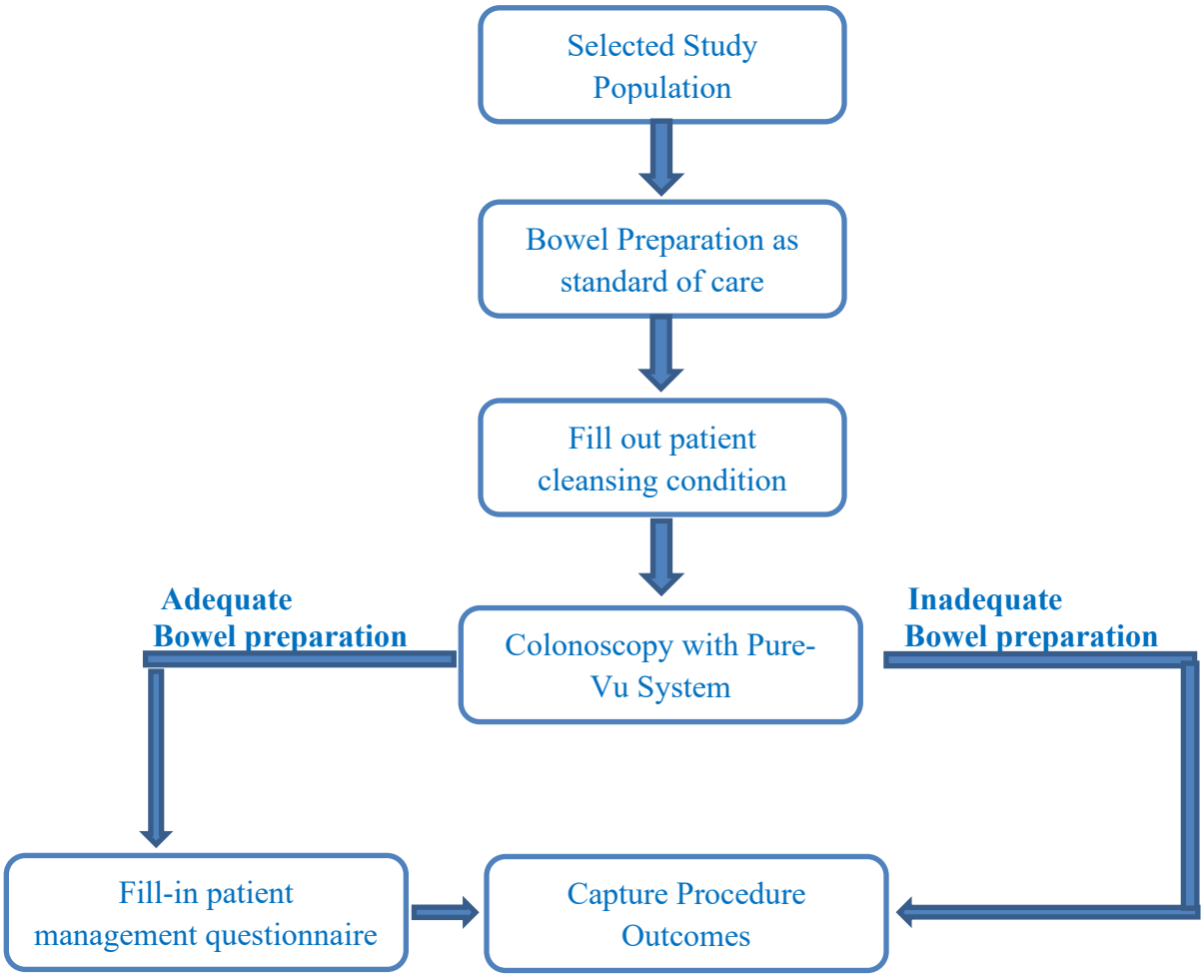
10.0 Study Design

This multicenter, prospective, single arm study will include up to 100 subjects (up to 35 subjects per site), aimed at evaluating the performance of the Pure-Vu System in cleansing hospitalized subjects' colon who are indicated for standard colonoscopy procedure. Subjects will be enrolled at up to 6 clinical sites in the United States and Europe

- Subject consent will be obtained
- Prior to the colonoscopy procedure, the nurse or study coordinator will be asked to complete a questionnaire including the subjects' bowel preparation type, volume, duration and overall preparation condition.
- The subject will undergo the colonoscopy procedure with the Pure-Vu system.
- In case of inadequate bowel preparation defined as BBPS score less than 2 in at least one of the colon segments prior Pure-Vu use, the physician will complete a questionnaire on the patient's management standard of care assuming the absence of Pure-Vu.

- Following the colonoscopy with Pure-Vu a follow-up evaluation will be conducted at 48 hours (± 48 hours) to assess subject's well-being and capture any adverse events. If the subject is no longer hospitalized, the follow up will be conducted by a telephone call.

Study Flowchart



11.0 Subject Selection and Enrollment

After being informed of the study, the subject will sign the sites' designated IRB approved informed consent form (ICF). Enrollment of up to 100 subjects is planned.

Subjects' participation in the study will last approximately 3 days, including the procedure day, and the follow up period.

Subjects will be considered for the study if they meet the specific inclusion/exclusion criteria. The criteria for enrollment must be followed explicitly.

11.1 Inclusion Criteria

1. Hospitalized subjects who are indicated for a screening, diagnostic, surveillance or therapeutic colonoscopy
2. Subjects' age > 22 years
3. Subject has signed the informed consent

11.2 Exclusion Criteria

1. Subjects with known Inflammatory Bowel Disease and / or active Colitis
2. Subjects with active diverticulitis
3. Subjects with known or detected (during colonoscopy) bowel obstruction
4. Subjects with ascites Child Pugh C
5. Subjects who are 30 days post-transplant
6. Subjects under active IV inotropic medications
7. Subjects with LVAD
8. Subjects with known coagulation disorder (INR ≥ 2 or platelets <50,000)
9. Subjects with medical and/or hemodynamic instability.
10. Pregnancy (as stated by Subject) or breast feeding

11. Subjects with altered mental status/inability to provide informed consent
12. Subjects who have participated in another interventional clinical study in the last 2 months

11.3 Withdrawal Criteria

Subjects may withdraw from the study at their own request or at the request of their legally acceptable representative. The investigator may withdraw a subject from the study at any time for the following reasons:

- Severe side effects clearly related to the study device.
- Presence or appearance of exclusion criteria.
- Appearance of accompanying diseases rendering further participation in the study impossible.
- A significant protocol violation, as determined either by the sponsor or the investigator
- Subject noncompliant with investigational procedures

The sponsor must be informed in each withdrawal case. The reason for withdrawal must be recorded in the CRF and in the subject's study file.

11.4 Selection of Investigators and Training

Board-certified gastroenterologists in accordance with US and hospital guidelines will be considered for participation as investigators in this study. Physicians in training (residents, fellows) and physician assistants may assist the Study Investigator in any aspect of the procedure as per standard procedures and practices at his/her institution.

Each Investigator participating in the clinical trial and the associated clinical study staff will receive training on the clinical protocol. This includes training on AE reporting, case report form (CRF) completion, and Good Clinical Practice (GCP), as well as the device and system (including procedural use, device characteristics, shelf life and storage requirements, warnings, and precautions).

12.0 Study Procedures

12.1 Screening and Informed Consent

A screening/baseline assessment will be performed prior to the scheduled Pure-Vu procedure to ensure subject's eligibility and willingness to participate in the study.

At the screening visit, subjects will be approached to obtain written informed consent prior to any study specific procedures being performed. The purpose of the study and the benefits and risks of the procedures will be explained to the subject and the consent process must be documented accordingly in the medical records. Subjects who agree to study participation must sign an IRB-approved ICF. Subjects will be informed that their participation in this study is voluntary and they may refuse to participate or discontinue from the study at any time. Subjects will be given the opportunity to ask the investigator questions so that they are adequately informed about the research. A copy of the signed informed consent must be provided to the subject and the informed consent process will be documented in source documents.

If new information becomes available that may affect a subject's decision to continue to take part in the study, this information will be discussed with the subject by the investigator.

The following assessments will be performed prior to the scheduled procedure and the results recorded on the appropriate subject CRFs:

- Verification of eligibility criteria and subject risk per guidelines
- Demographics (age, gender, height, weight)
- Surgical and medical history (prior abdominal surgery, GI symptoms)
- General medical history will be assessed based on the subject's clinical condition

Subjects who were found to be ineligible for the study following signature of the Informed Consent Form will be withdrawn from the study and no further follow up will be performed.

12.2 Randomization

NA –Single study arm

12.3 Screen Failures

A subject is considered enrolled in the study when the ICF is signed. Only subjects who undergo the colonoscopy procedure with Pure Vu will be followed. Subjects who provide study consent, but then are determined to be ineligible will be considered screening failures and will not require additional study follow-up. The reason for the screening failure will be clearly documented, 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

As standard practice in the hospitalized population setting, bowel preparation is prescribed for individuals undergoing a colonoscopy procedure. The typical and recommended bowel prep is the 4 Liters of GoLytly as a split dose. Although this bowel prep is widely prescribed, it is not a requirement that the subject completes the bowel prep prior to the colonoscopy procedure for the study.

12.5 Colonoscopy procedure

Pre-Examination Procedures

- Verify eligibility checked and informed consent was obtained after explaining all risks, benefits, and alternatives to the subject.
- Verify that the study coordinator/nurse has completed the questionnaire regarding the subject's bowel cleansing condition.
- Verify all background/clinical information, demographic and medical history was documented

- Verify all connections and assembles are properly attached (see Instructions for Use)
- Verify device works properly (see Instructions for Use)
- Place and prepare the subject for the colonoscopy procedure.

Colonoscopy Procedures

The insertion during the colonoscopy procedure will be performed by the clinical study investigator(s), experienced in GI endoscopy according to local standard of care. The withdrawal part of the colonoscopy procedure will be performed as per the clinical investigator(s) direction. Physicians in training (residents, fellows) and physician assistants may assist the Study Investigator in any aspect of this part of the procedure as per standard procedures and practices at his/her institution. In cases where upper endoscopy is planned, it will be conducted per the physician's discretion. Anesthesia will be applied as well per the standard of care. In order to ensure correct operation of the Pure-Vu System a Motus GI representative may attend the procedure. Pure-Vu System operation is described in the Instruction for Use.

The colon preparation level for each colorectal segment (ascending, transverse and descending) before the cleansing operation during the insertion phase will be evaluated using the BBPS scoring index (Appendix B).

In case of inadequate bowel preparation defined as BBPS less than 2 in at least one of the colon segments prior Pure-Vu use, the physician will complete a questionnaire as it relates to the subjects management standard of care assuming absence of the Pure-Vu System.

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.

The colonoscopy examination with the Pure-Vu will be recorded on digital media. Only the subject study ID and initials should appear in the recorded video.

The cecum will be documented in a picture, if applicable.

All optical colonoscopy still pictures will be saved in a digital format. Quality copies of the pictures taken during optical colonoscopy will be provided to the sponsor and the optical colonoscopy report will be reviewed as part of the monitoring process.
These videos and pictures will be archived and may be used in future analyses to, for example, provide further information about observed lesions or to assess study quality.

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 Pure-Vu. 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 Follow-up

Subjects will be transferred to recovery room for observation per clinical site's colonoscopy protocol and will continue his/her medical flow as per the standard of care. Follow-up will be conducted 2 business days (+/- 48 hours) after the procedure to verify that there has been no change in their well-being. 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.

13.0 Statistical Analysis

13.1 Sample Size Determination

This is a pilot study that will include up to 100 subjects; no statistical considerations were made to determine the sample size.

13.2 Description of statistical methods

Basic demographic and other baseline characteristics will be collected and analyzed for all subjects. Summary statistics (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. Intent-To-Treat and Post-hoc analysis will be conducted according to the existing data gathered, if necessary.

13.3 Primary Endpoint Analysis

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

The primary statistical hypothesis is that the cleansing level post Pure-Vu procedure will be significantly improved as compared to the cleansing level pre procedure (prior the Pure-Vu use).

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

The count and percentage of segments and subjects with improved BBPS after the Pure-Vu cleansing procedure will be presented together with 95% confidence intervals.

13.4 Secondary Endpoints Analysis

13.4.1 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, reported term, seriousness, duration, relationship to the study device, severity and the adverse events outcome will be provided for the total population. AEs will be summarized using frequency counts and percentages.

13.4.2 Efficacy Analysis

Cecal Intubation Rate

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

Proportion of subjects with successful colonoscopy at first attempt

Successful colonoscopy at first attempt is defined as complete procedure conducted as scheduled for the intended indication.

Frequency counts, percentages, and 95% confidence intervals will be provided. In addition, the above proportion will be compared vs. the proportion of subjects that would have underwent a complete procedure at first attempt assuming absence of the Pure-Vu System (as per the data to be captured by the Patient Management Direction). Chi-square or Fisher's exact test, as appropriate, will be performed to evaluate the difference between the two clinical set-ups.

13.5 Analysis Populations

Cases withdrawn prior to the Pure-Vu procedure and those with technical failures will be excluded from the primary analysis. Cases with failure to reach the desired colon segment per the intended indication, which cannot be conducted with Pure-Vu, will be excluded from the primary analysis. All subjects who have the Pure-Vu inserted will be included in the safety analysis.

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

13.6 Interim Analyses

An interim analysis is planned after procedure completion of 45 subjects aims to verify the recruitment pace and the study flow.

14.0 Adverse Events (AEs) and Complications

AE and AE subcategories are defined per ISO14155:2011, as described below.

14.1 Adverse Event (AE)

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

This definition includes events related to the investigational medical device or the comparator and the procedures involved.

AEs will be collected starting from the time subject is enrolled until the follow-up period is completed.

14.2 Serious Adverse Event (SAE)

A Serious AE (SAE) is an AE that has

a) Led to death,

b) Led to serious deterioration in the health of the subject, that either resulted in

1) A life-threatening illness or injury, or

2) A permanent impairment of a body structure or a body function, or

3) In-patient or prolonged hospitalization, or

4) Medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,

c) Led to fetal distress, fetal death or a congenital abnormality or birth defect

NOTE: Planned hospitalization for a pre-existing condition, or a procedure required by the clinical investigational plan, without serious deterioration in health, is not considered an SAE.

Some important medical events, although they may not result in death, be life-threatening, or require hospitalization may still be considered SAEs when, based upon appropriate medical judgment, they are felt to jeopardize the subject and may require medical or surgical intervention to prevent one of the outcomes listed above.

Life threatening means that the subject was, in the view of the investigator, at immediate risk of death from the reaction as it occurred. This does not include an AE that, if more severe, might have caused death.

Disability means a substantial disruption of a person's ability to conduct normal life's functions.

14.3 Adverse Device Effect (ADE)

An Adverse Device Effect (ADE) is an AE related to the use of an investigational medical device.

This definition includes AEs resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.

This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.

14.4 Serious Adverse Device Effect (SADE)

A Serious Adverse Device Effect is an adverse device effect that has resulted in any of the consequences characteristic of an SAE.

14.5 Unanticipated Serious Adverse Device Effect (USADE)

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

14.6 Adverse Event Severity Classification

Severity will be defined according to the following criteria:

Mild	Awareness of event, but easily tolerated
Moderate	Discomfort enough to cause some interference with activities of daily living (ADL)
Severe	Incapacitating, with an inability to perform ADL

An AE can be classified as severe and not deemed a SAE. Similarly, a SAE is not automatically severe in nature.

14.7 Adverse Event Relationship Classification

Relationship to study product administration will be determined as follows:

- *No Relationship*: No relationship between the AE and the administration of study treatment and a known relationship to other etiologies such as concomitant medications, procedure, or subject's clinical state.
- *Possible Relationship:* An AE that follows a reasonable temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment but could have been produced by the participant's clinical state or by other therapies.
- *Probable Relationship:* An AE that follows a reasonable temporal sequence from administration of the study treatment; follows a known response pattern to the study treatment; and cannot be reasonably explained by the known characteristics of the participant's clinical state or by other therapies.

- *Definite Relationship:* An AE that follows a plausible temporal sequence from administration of the study treatment and follows a known response pattern to the study treatment. The reaction cannot be reasonably explained by the known characteristics of the subject's clinical state or other modes of therapy administered to the subject.
- *Unknown/Impossible to Determine:* Given the information available, sequence and timing of events, it is unknown or impossible to determine the relationship of the AE with the study treatment.

14.8 Adverse Event Outcome Classification

Outcome of the event will be defined according to the following:

- *Resolved:* The event has fully resolved at the end of the study.
- *Resolved with sequelae*: The event has resolved, but retained pathological conditions resulting from the prior disease or injury.
- *Continuing:* The event is ongoing at the end of the study.
- *Death:* This event is determined to be the cause of death.

14.9 Device Deficiencies

A device deficiency is an inadequacy of a medical device related to its identity, quality, durability, reliability, safety, or performance, such as malfunction, misuse or use error and inadequate labeling.

All device deficiencies will be documented and the device should be returned to Motus GI for analysis, if possible. Instructions for returning the investigational device will be provided. Device deficiencies should also be documented in the subject's medical record.

Device deficiencies are NOT to be reported as AEs. However, if there is an AE that results from a device deficiency, that specific event would be recorded on the appropriate CRF.

14.10 Adverse Event Recording and Reporting

Assessment of the occurrence of an AE will be based on changes in the subject's signs and symptoms. AEs will be monitored until a subject completes the study unless the Investigator determines the event is related to the investigational device, in which case they will be monitored until resolution if possible. Medical care will be provided, as defined in the informed consent, for any AE related to study participation. AEs will be collected on an AE CRF and applicable source documentation.

The following should not be considered an AE:

- A condition requiring a preplanned procedure unless the condition worsened since screening
- A preexisting condition found as a result of screening, unless the condition has worsened since enrollment.

All AEs observed during the course of this study, regardless of severity or relationship to the investigational device will be recorded on the appropriate CRF.

14.11 Reporting Responsibilities

An investigator shall submit to the sponsor and to the reviewing IRB a report of any SAEs, ADEs, SADEs, USADEs, and device deficiencies that could have led to a serious adverse device effect occurring during an investigation within 24 hours of learning of the event, but in no event later than 10 working days after the investigator first learns of the effect.

A sponsor who conducts an evaluation of an unanticipated adverse device effect under 21 CFR Part 812.46(b) shall report the results of such evaluation to FDA and to all reviewing IRB's and participating investigators within 10 working days after the sponsor first receives notice of the effect. Thereafter the sponsor shall submit such additional reports concerning the effect as FDA requests (21 CFR Part 812.150).

15.0 Ethics and Compliance

15.1 Statement of Compliance

This clinical investigation will be conducted in accordance with the ethical principles that have their origin in the Declaration of Helsinki, ISO 14155:2011 (Clinical Investigation of Medical Devices for Human Subjects – Good Clinical Practice), ICH-GCP, and any regional or national regulations, as appropriate.

This may include an inspection by Motus GI 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 GI representatives and must allow direct access to source documents to the Regulatory Authority/ Motus GI representatives. Regulatory Authority approvals/authorizations/notifications, where required, will also be in place and fully documented prior to study start.

15.2 Protocol Compliance

No changes to the protocol will be permitted without the written approval from Motus GI and the IRB. The investigator must notify Motus GI and the reviewing IRB of any deviation from the Investigational Plan when specific to the protection of the life or physical well-being of a subject in an emergency. Such notice must be given as soon as possible, but in no event later than 5 working days after the emergency has occurred. Except in such an emergency, prior written approval by Motus GI is required for changes in or deviations from the Plan. If these changes or deviations affect the scientific soundness of the Plan or the rights, safety, or welfare of human subjects the IRB will also be notified. All other deviations will be reported per the site's IRB deviation policy. Should any deviations from the Investigational Plan occur, these will be reviewed by Motus GI for their clinical significance. If the event is performed without written approval from all parties, the investigator may be terminated from the study.

15.3 Institutional Review Board (IRB)/Ethics Committee (EC)

Documented approval from the appropriate Institutional Review Board (IRB) and Ethics Committee (EC) will be obtained for all participating centers prior to study start, according to ICH GCP, local laws, regulations, and organization. When necessary, an extension, amendment, or renewal of the IRB/EC approval must be obtained. The IRB/EC must supply to the sponsor a list of the IRB membership and a statement to confirm that the IRB/EC is organized and operates according to GCP and applicable laws and regulations.

15.4 Subject Informed Consent

Prior to the beginning of the trial, the investigator must have the IRB/EC written approval of the ICF and any other written information to be provided to subjects. The written approval of the IRB/EC together with the approved ICFs must be filed in the study files.

The process of obtaining informed consent must be in accordance with applicable regulatory requirement(s) and must adhere to GCP and to the ethical principles originating in the Declaration of Helsinki. Written informed consent must be obtained before any study specific procedure takes place. Participation in the trial and date of informed consent given by the subject should be documented appropriately in the subject files.

15.5 Insurance

All subjects participating in the trial will have insurance coverage by the Sponsor, which is in line with applicable local laws.

15.6 Confidentiality

All records identifying the subject will be kept confidential and, to the extent permitted by the applicable laws and/or regulations, will not be made publicly available.

Subject names will be kept confidential. Only the subject number and initials will be recorded in the CRF, and if the subject name appears on any other document, it must be obliterated. In cases were the local law does not allow using the subject initials serial number will be appointed (e.g. AAA, BBB). Study findings stored on a computer will be stored in accordance with local data protection laws. The subjects will be informed in writing that representatives of the sponsor, IRB/EC or Regulatory Authorities may inspect their medical records to verify the information collected, and that all personal information made available for inspection will be handled in strictest confidence and in accordance with local data protection laws. Subjects will also be informed that information regarding the study that does not include subject identifiers will be posted on clinicaltrials.gov.

If the results of the trial are published, the subject's identity will remain confidential.

The investigator will maintain a list to enable subjects' records to be identified.

15.7 Use of Data and Publications

Information regarding the study and study data will be made available via publication on clintrials.gov.

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, 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.

The investigator, while free to utilize data derived from the study for scientific purposes, must discuss any publication with the sponsor prior to release and obtain written consent of the sponsor on the intended publication. The sponsor recognizes the right of the investigator to publish the results upon completion of the study. However, the investigator must send a draft manuscript of the publication or abstract to the sponsor 45 days in advance of submission in

order to obtain approval prior to submission of the final version for publication. This will be reviewed promptly and approval will not be withheld unreasonably. In case of a difference of opinion between the sponsor and the investigator(s), the contents of the publication will be discussed in order to find a solution which satisfies both parties.

Disclosure of involvement in a publication (e.g., sponsor of the study; collection, analysis, and interpretation of data; professional writing assistance) must be as specified by journal-specific policies, submission requirements, and prevailing editorial standards, in addition to those specified by International Committee of Medical Journal Editors. Authors must ensure that an acknowledgement/disclosure statement is included in the body of the manuscript for Motus GI to review for accuracy. All authors must also disclose financial or personal affiliations that could be considered conflicts of interest as per journal requirements.

16.0 Monitoring Procedures

Site visits will be conducted by an authorized Motus GI representative to inspect study data, subjects' medical records, and CRFs in accordance with current ICH GCPs 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 GI and/or designee(s) employed by Motus GI to review completed CRFs, IRB decisions, and Investigator, clinical site records, and facilities relevant to this study at regular intervals throughout the study per the monitoring plan. 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 GI 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 provide another mechanism of access to allow source data verification by 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 IRB/EC, 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.

16.1 Data Collection and Processing

This study will utilize a Case Report Form (CRFs). All data requested on the CRFs are considered required. 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 and then provide his/her signature on the appropriate CRFs and will be documented 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.

Data review will be performed to identify possible data discrepancies and queries will be created and issued to the site for correction. The site staff and site investigator will be responsible for resolving all data queries.

17.0 Study Supplies and Device Accountability

17.1 Packaging

The Pure Vu disposables are composed of biocompatible plastic parts and are supplied clean in a sealed package. The shelf life of the device was tested within the device verification and validation process to support shelf life period of 9 months.

17.2 Labeling

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.

17.3 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 IRB). 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 completed and filed in the Regulatory Binder at each site.

In case of technical failure, the site will inform the designated sponsor contact.

For each dispensed Pure-Vu Oversleeve and WS connector, the following information should be recorded:

- The subject study number

- Date dispensed
- Oversleeve Lot Number
- Work Station Connector Lot Number

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

17.4 Retention of Records

All source documents and CRFs will be kept for a period of no less than five years after the later of the following dates: the date of which the study is terminated or completed or; the date that the records are no longer required supporting marketing applications.

17.5 Study Completion/Termination of Study

Motus GI reserves the right to discontinue the study at any stage, with suitable written notice to all investigators and reviewing IRBs/ECs, following unforeseen events or other factors that do not permit continuation of the study. Similarly, investigators may withdraw from the study at any time, subject to providing written notification to Motus GI 30 days prior to the date they intend to withdraw. However, Motus GI and investigators will be bound by their obligation to complete the follow-up of subjects already participating in the study. The subjects must be followed according to the clinical protocol, and information obtained during subject follow-up shall be reported to Motus on the appropriate CRF.

The appropriate IRB/EC will be notified of discontinuation of the trial for any reason not later than 5 working days after the sponsor makes this determination and not later than 15 days after the sponsor receives a notice from the IRB/EC and/or regulatory authority.

18.0 General Information

18.1 Study Contact Information

Questions should be directed to Clinical Affairs.

Clinical Affairs
Hagit Ephrath VP of Health Economics, Regulatory and Clinical Affairs Motus GI Technologies LTD. Keren Ha'yesod 22 3902638 Tirat Carmel, Israel Phone: +972 (73) 3243824 Mobile: +972 (52) 314-2045 Email: hagit@motusgi.com

19.0 References

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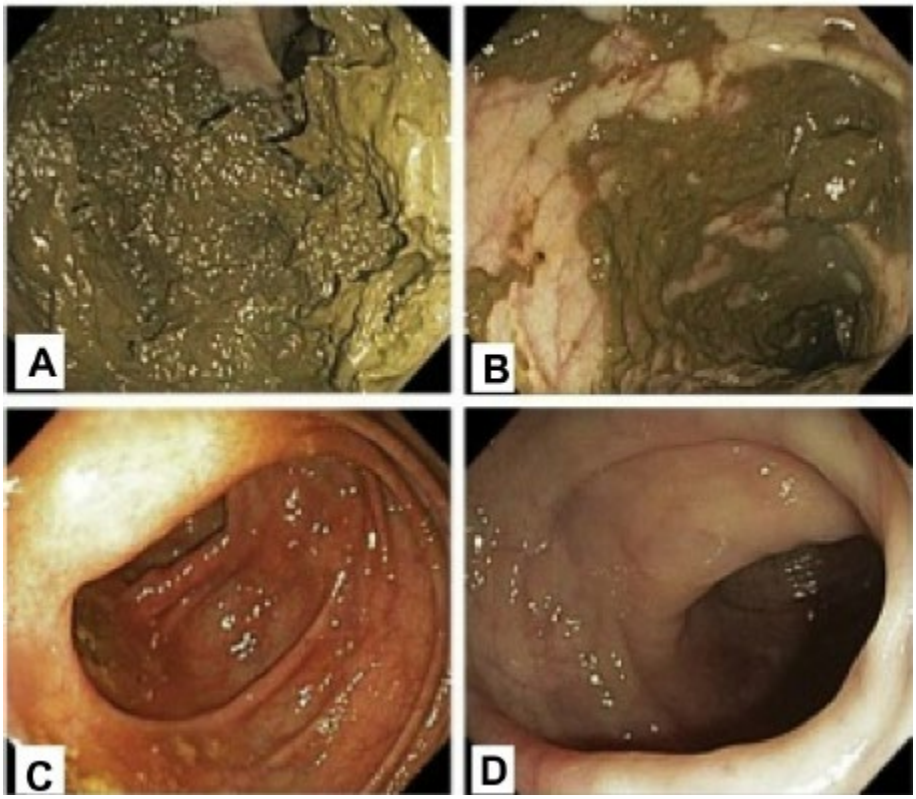
20.0 Appendixes A: Study Design and Schedule of Assessment

	Visit 1	**Follow Up**
Days	**0**	**2 Business Days** (± 48 hours)
Informed Consent	X	
Eligibility assessment (medical records, BMI, etc.)	X	
Medical History, Concomitant Medications, and Demographic details	X	
Assessment of patient's bowel preparation questionnaire	X	
*Assessment of patient's management Directions (filled-in by the physician)	X	
Colonoscopy Procedure	X	
Follow Up	X	X
Adverse Events Reporting	X	X

*for subjects with inadequate bowel cleansing level in at least one segment at baseline.

21.0 Appendix B: Boston Bowel Preparation Scale



- **A: Score 0-** Unprepared colon segment with mucosa not seen due to solid stool that cannot be cleared.
- **B: Score 1** - A portion of the mucosa of the colon segment is seen, but other areas of the colon segment are not seen well due to staining, residual stool, and/or opaque liquid.
- **C: Score 2-** A minor amount of residual staining, small fragments of stool, and/or opaque liquid are visible, but the mucosa of the colon segment are seen well.
- **D: Score 3-** The entire mucosa of the colon segment is seen well with no residual staining, small fragments of stool, or opaque liquid.