Clinical Investigational Plan

CHANGE HISTORY		
Rev. number	**Change Owner**	**Change description**
01	Shlomo Lewkowicz	DCO0023 Initial Release
02	Michal Nachmanovich	DCO0039 Sponsor Address. Exclusion Criteria update. Low X-ray body dose revision. Anticipated Adverse events revision
03	Shlomo Lewkowicz	ECO-19-000031 US Pilot study lowering BMI 19

AUTHORIZATION				
	Name	**Title**	**Date**	**Signature**
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Reviewer	Shlomo Lewkowicz	Clinical Affairs Director	See Arena	See Arena
Approver	Israel Hershko	Q&R Director	See Arena	See Arena

Clinical Investigational Plan
Study: CL-SY-02-0096
Study Protocol DOC. No.: **DOC001593**

EVALUATION OF SAFETY, USABILITY AND SUBJECT COMPLIANCE WHILE USING CHECK-CAP'S C-SCAN SYSTEM FOR PROVIDING STRUCTURAL INFORMATION ON COLONIC POLYPOID LESIONS AND MASSES

Study device: C-Scan® System
Check Cap study #: CL-SY-02-0096
Phase: Clinical evaluation: pre-market safety, usability, and subject compliance

Sponsor: Check-Cap US Inc
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2 STATEMENT OF COMPLIANCE

This study will be conducted in accordance with the Code of Federal Regulations on the Protection of Human Subjects (45 CFR Part 46), 21 CFR Parts 50, 56, 312, and 812 as applicable, any other applicable US government research regulations, and institutional research policies and procedures. The International Conference on Harmonization ("ICH") Guideline for Good Clinical Practice ("GCP") (sometimes referred to as "ICH-GCP" or "E6") will be applied only to the extent that it is compatible with FDA and DHHS regulations. The Principal Investigator will assure that no deviation from, or changes to the protocol will take place without prior agreement from the sponsor and documented approval from the Institutional Review Board (IRB), except where necessary to eliminate an immediate hazard(s) to the trial participants. All personnel involved in the conduct of this study have completed Human Subjects Protection Training.

3 CLINICAL INVESTIGATION PLAN APPROVAL

The undersigned confirm that they agree to conduct the study under the conditions described in this protocol. The investigator agrees to conduct this study in a manner that is consistent with good clinical practices and applicable laws and regulations for conducting clinical research.

Investigator Signature	Date
Investigator Name (Printed)	Investigator email

4 CLINICAL INVESTIGATION SUMMARY

Protocol Title	Evaluation of safety, usability and subject compliance while using Check- Cap's C-Scan System for providing structural information on colonic polypoid lesions and masses
Study Number	CL-SY-02-0096
Sponsor	Check-Cap, Inc.
Study Design	Prospective, Multi-center, Single-arm, safety study
Purpose	To demonstrate the safety of the Check-Cap C-Scan System
Study Centers	Up to two (2) centers located in the United States
Number of Participants	45 healthy subjects
Investigational Device	Check-Cap's C-Scan System comprises C-Scan Capsule, C-Scan Track and C-Scan View.
Intended use	The Check-Cap ***C-SCAN System*** is an ingestible capsule system intended to provide structural information on the endoluminal surface of the colon for the detection of colon polyps. It is intended for use in adults at average-risk for CRC who are not candidates for colonoscopy or who decline colonoscopy, or patients who had an incomplete optical colonoscopy.
Primary Objective	To evaluate the safety of the Check-Cap C-Scan System.
Secondary Objectives	• To evaluate subject's compliance • To evaluate subject's satisfaction • To collect data to improve the product's algorithm
Primary Safety Outcome Measure	Incidence of device and procedure related Serious Adverse Events (SAE)
Secondary Outcome Measures	• Subject compliance • Subject satisfaction • Procedure related data for improvement of algorithm: • Battery life Assessment • Device performance
Inclusion Criteria	1. Patients age 40 years or older 2. Able to provide a signed informed consent. 3. Willing and able to comply with the specified study requirements and follow-up evaluations, and can be contacted by telephone. 4. Able and agrees to undergo colonoscopy procedure. 5. Body Mass Index (BMI) > 19 and ≤ 35. 6. Maximum body (abdominal) circumference < 120 cm. 7. A colonoscopy procedure is pre-scheduled within 60 days
Exclusion Criteria	1. Subject who is not a suitable candidate for a colonoscopy (i.e., moderate sedation) 2. Known history of dysphagia or other swallowing disorders. 3. History of the followings: Inflammatory Bowel Disease (IBD) including Crohn's disease or Ulcerative, Colitis, Meckel's Diverticulum, Bowen Hernia, known fistulas or strictures (doctors' discretion), or a history of small bowel obstruction. 4. Known motility disorders: a. Chronic Constipation: less than 3 bowel movements/week, w/out the use of laxatives. b. Delayed gastric emptying. c. Narcotic use 5. Prior history of abdominal surgery that might cause bowel strictures leading to capsule retention, as determined by physician discretion with the exception of appendectomy, cholecystectomy and hysterectomy 6. Any condition believed to have an increased risk for capsule retention, strictures,

	bowel adhesion or 'obstacles' to free passage of the capsule (such as intestinal tumors, radiation enteritis) or incomplete colonoscopies(e.g. due to obstructions or non-steroidal anti-inflammatory drugs (NSAID) enteropathy) as determined by physician discretion. 7. Has a cardiac device (e.g. pacemaker or Implantable Cardioinverter Defibrillator (ICD)) or any other implanted active device 8. Known sensitivity to iodine, or with known kidney failure. 9. Known condition which precludes compliance or is contraindicated with study and/or device instructions. 10. Has a Magnetic Image Resonance (MRI) procedure scheduled within 1 month 11. Known condition of drug abuse and/or alcoholism. 12. Women who are either pregnant or nursing at the time of screening (to be verified by urine or serum pregnancy test for woman of child- bearing potential who are not post-menopausal or undergone surgical sterilization. 13. Concurrent participation in another clinical trial using any investigational drug or device.
Study Duration	The total study duration across all patients is expected to be approximately 6 months, dependent upon subject recruitment rate.
Participant Duration	The duration of study participation for each subject is expected to be approximately 8-10 weeks.

5 SCHEDULE OF STUDY ASSESSMENTS

Assessments	Pre-screening	Visit 1: Baseline and C-Scan	Follow-up 1: C-Scan - During Procedure follow-up	Follow-Up 2: C-Scan Procedure End follow-up Call	Follow-up 3: Colonoscopy Post Procedure follow-up Call
Visit Window	-30-0 days	0 days	0- As required days	1-3 days post procedure	1-3 days post procedure
Questionnaire	X				
Informed Consent		X			
Inclusion/ Exclusion Criteria		X			
Demographics		X			
Medical History		X			
Concomitant Medications		X			
Pregnancy test[1]		X			
C-Scan procedure		X			
Connect to C-Scan		X			
C-Scan capsule		X			
Ingest contrast		X	X		
FIT test			X		
Follow up phone calls[2]			X		
Capsule Excretion				X	
Abdominal x-ray[3]				X	
Subject Satisfaction Survey				X	X
Colonoscopy Report	X[4]				X
Follow up visit call				X	X
Adverse Events		X	X	X	
Study Exit					X

[1]Urine pregnancy test for women of childbearing potential
[2]Minimum of two phone calls per day until capsule excretion
[3]Abdominal x-ray ONLY if suspected that capsule has not been excreted (subject will come to office/unscheduled visit)
[4] Collection of a previous colonoscopy report, if available

6 ABBREVIATIONS

AE	Adverse Event
AR	Adverse Reaction
BMI	Body Mass Index
CFR	Code of Federal Regulations
CI	Chief Investigator
CIP	Clinical Investigation Plan
CMT	Compton backscattering
CPS	Capsule Positioning System
CRA	Clinical Research Associate
CRC	Colorectal Cancer
CRF	Case Report Form
CRO	Clinical Research Organization
CT	Computerized tomography
EC	Ethics Committee (see REC)
FDA	Food and Drug Administration
FIT	Fecal Immunochemical Test
FOBT	Fecal Occult Blood Test
GCP	Good Clinical Practice
GI	Gastrointestinal
GLP	Good Laboratory Practice
IB	Investigator Brochure
IBD	Inflammatory bowel disease
ICD	Implantable Cardioinverter Defibrillator
ICF	Informed Consent Form
ICH	International Conference of Harmonization
IFU	Instructions for Use
IRB	Institutional Review Board
Max	Maximum
Min	Minimum
MRI	Magnetic Resonance Imaging
NAMSA	North American Scientific Associates
NSAID	non-steroidal anti-inflammatory drugs
PI	Principle Investigator
RA	Radioactive
RF	Radio frequency
SAE	Serious Adverse Event
SCA	Scan Control Algorithm
StD	Standard deviation
SOP	Standard Operating Procedure
TMF	Clinical investigation Master File
TTT	Total Transit Time
UADE	Unanticipated Adverse Device Effect
XRF	X-ray Florescence

7 INTRODUCTION

7.1 Colorectal Cancer Screening

Colorectal cancer (CRC) is the third leading cause of cancer death according to the American Cancer Society but is largely preventable. Approximately 97,000 new cases of colon cancer will be detected in the United States annually, with over 50,000 deaths. Studies published in the early 1990s, showing that screening for CRC can reduce CRC -related mortality, led many organizations to recommend screening in asymptomatic, average-risk adults older than 50 years. Since then, however, national screening rates remain low in most countries. For example, in the United States for adults age 50 and older, colorectal cancer screening was 63% in 2015, Canada 16% (2011), Spain 49.2% (2014) and the Netherlands 68.2% (2014), including the United States and Europe. Several important studies published over the past four years have refined our understanding of existing screening tools and explored novel means of screening and prevention

In an attempt to reduce this cancer related death, legislation was passed in both the US and Germany in 2002, which establishes by law, reimbursement for screening colonoscopy in the population 50 years and older in the US, and 55 and older in Germany. This has increased the potential number of screening colonoscopies in these 2 countries alone to 15 million colonoscopies a year.

Current strategies to prevent CRC vary considerably with regard to effectiveness, up-front costs, risks, and invasiveness. New CRC screening tests such as Fecal Occult Blood Test (FOBT) and Fecal Immunochemical Test (FIT) detect blood in the stool, where fresh or occult is a sensitive indicator for the presence of an advanced adenoma or cancerous tumor which are typically bleeding due by angiogenesis – a proliferation of blood vessels in the polyp. FOBT and FIT do not provide structural information of the colon and by that fail to diagnose non-cancerous as well as adenomatic polyps They are one mechanism to improve adherence. Screening of the colon can be performed by Sigmoidoscopy, endoscopic colonoscopy and virtual colonoscopy. Sigmoidoscopy, endoscopic colonoscopy and virtual colonoscopy are invasive and require cleansing of the colon. Patients are required to conduct a rigorous preparation for cleansing of the colon. Stool DNA (ColoGuard) is another recently added test for detecting CRC by identifying specific DNA markers which were carried by the Stool from a cancerous tumor in the colon.

The colon preparation process is regarded as one of the main objections of patients, and many choose to forgo completion of a scoping procedure as a result. Additionally, for patients with advanced cardiac disease, undergoing antithrombotic therapy, considered at high risk to undergo sedation or who have kidney diseases which might be compromised by cleansing preparations, scope procedures may pose a problem to the patient, Therefore, a technology whereby structural information could be provided, yet does not require rigorous cleansing of the colon and is not considered invasive would be beneficial to patients.

7.2 C-Scan Technology

The technology of the Check-Cap Imaging System is based on a low dose radioactive (RA) sealed source embedded in the C-Scan capsule which radiates X-Rays through a collimator to all directions. The capsule is designed to start scanning once it reaches the cecum and the X-ray is emitted when the capsule is propagating along the colon during contraction of the walls. While stationary (which is most of the time) the capsule is set at an idle mode and the radiation X-ray source is blocked by the collimator. The transit time of the capsule in the colon might vary from 24-100 hours, pending the typical bowel activity of the subject. The capsule is powered by onboard batteries and is designed to operate up to 100 hours.

The C-Scan is designed to be ingested without any cleansing of the colon and travel through the gastrointestinal (GI) tract naturally while the subject continues daily activities, including eating normally. During C-Scan procedure the subject swallows a capsule and capsule travels painlessly through the gastrointestinal tract, identifying polyps, the precursors of colorectal cancer. In order to increase the contrast of the colon's walls and to differentiate them from their content, it is essential to increase the stool's contrast by ingesting radio-opaque material. It is a standard procedure using approved Iodine based liquids, contrast agents such as (Telebrix or Omnipaque) at the discretion of the hospital similar to the preparation to abdominal computerized tomography (CT).

During the passage of the capsule in the gastrointestinal tract, it transmits information to a recorder attached to the back. In order to collect data about the instantaneous localization of the capsule traveling in the colon additional sensors are embedded in the recorder on the back side. A commercial wrist watch is supplied (optional) with the C-Scan system for use by the subject during the procedure. The watch is tuned to 'listen' and display the information transmitted from the capsule to the Track. The watch is a monitoring tool to optimize data interpretation during the clinical study and is not an integral part of the C-Scan system.

After the capsule is expelled, the data from the recorder is downloaded to an acquisition workstation. Later, the data is transferred to a processing workstation and analyzed to create a map of the colon. The current C-Scan system is designed to operate for up to 100 hours. The average radiation dose calculated from these procedures is 52 uSV (typical results from last study: StD 38, Min. 19, Max. 165 uSV) – this is equivalent to one chest X-ray radiation.

8 PREVIOUS STUDIES

More than 220 volunteers have ingested the C-Scan capsule in its various versions. Three subjects failed to ingest the capsule due to Acataposis. All capsules except four were captured and returned by the subjects. All returned capsules were tested in Check-Cap laboratories and their sealing and structure were verified.

The average transit time estimated from the last 63 procedures (CE study) was ~52 hours with 32h StD. In most cases the capsule arrived to the caecum within 24 hours (average 16 hrs.) and the motility through the colon was 16 hours (with 32h StD).

Some subjects reported mild diarrhea or mild discomfort, all events resolved within few hours w/out any intervention. No capsule retention (more than 300 hours per protocol) had been reported to date. In one case the capsule was retrieved by colonoscopy after 100+ hours in the caecum. The 'post' colonoscopy was rescheduled earlier according to the request of the participant. Three serious adverse events were reported, although, none were device or procedure related. All events were resolved without the need of medical intervention.

8.1 Clinical Study Protocol C-SY 00093

A multicenter clinical study was conducted at four sites in Israel in 2017. Sixty-Six subjects were enrolled (40 Men (61%) and 26 Women (39%), BMI <40), of which three failed to ingest the capsule, including one subject with a known swallowing disorder which was not disclosed to the study team during screening. Forty-Three had polyp(s) (65%) as indicated by their prior recent colonoscopy reports and the other 23 were considered as average risk population without any prior information about their colon.

All study procedures were completed and feedback from most subjects was positive and reassuring that the procedure was well-tolerated.
All capsules (except one) were collected and retrieved for QA inspection. They were all found to be intact and hermetically sealed.

The total transit time (TTT) is measured in hours between capsule ingestion to excretion. The TTT is the sum of 3 distinct sections:

a. Time until reaching the caecum
b. Time capsule dwells in the caecum
c. Time of colon passage until excretion

The following table is the summary of all 63 cases in whom the study was completed (3 did not ingest). The standard deviation (STD) is quite high due to the considerable variability in bowel motility.

	Total Transit Time	Time to Caecum	Time in Caecum	Passage in colon
Average *(hours)*	52.3	15.9	16.8	16.5
STD	32.9	13.7	18.8	12.1

Table 2: Average transit time of the 3 sections of the GI tract and the standard deviation in each one.

There were no cases of C-Scan capsule retention (medical definition of Capsule retention is when TTT is longer than 300 hours – about 13 days).
The C-Scan is designed to operate continuously for 100 hours. There was one case in which the capsule was retained for 100-200 hours and then removed during the follow-up colonoscopy procedure

and in another case it was initiated by the sponsor since the batteries in the capsule were already depleted and no additional benefit was expected from the procedure. In two other cases, drugs (*Picolax*) were used to expedite the expulsion of faulty capsules (that stopped working). In all four cases the total time was less than 200 hours. In one case the capsule was not retrieved by the patient at the end of the procedure and. probably lost in the sewage system. Abdominal X-ray on the following day confirmed that the capsule was expelled with no residual in the GI tract images. All cases were completed uneventfully.

Several adverse events were reported including one case of irritating sensation in the esophagus that lingered for hours after capsule ingestion, skin irritation (under the stickers), soft stool, abdominal pain, headache, radiation level (body dose) was significantly higher than the typical dose of 50 uSV and four cases in which the transit time was longer than 120 hours. Three SAE events occurred including one hemorrhage/hematoma seen on abdominal wall, one post-colonoscopy bleeding and one post-colonoscopy abdominal pain. All SAE were non-related to device or C-Scan procedure and resolved without medical intervention. Several technical malfunctions occurred during the study, none of which resulted in harm to the subject but did not provide any data regarding the performance of the C-Scan system. During the study, updates were made to the system software to continue to optimize the algorithm and the ability to collect additional physiological data.

This study demonstrated that the C-Scan procedure was safe as no device- related serious adverse event occurred in any *C-Scan* clinical trial and the procedure was well-tolerated by the participating volunteers. The primary end point of safety for the C-Scan system was demonstrated. The primary end point for performance in terms of Positive Percent Agreement resulted in 44% capsule vs 37% for FIT. The protocol target was set at 55%, hence superiority was demonstrated with a lower than expected result. The result of Negative Percent Agreement was 89% vs. a set target of 75%, hence target surpassed the expected result.

8.2 Laboratory Tests

Rigorous laboratory tests have been performed on the Check-Cap Ltd. C-Scan System

8.2.1 Image Reconstruction

Based on the laboratory tests performed with the current version of our imaging capsule, polyps of 6 mm and larger should be visible and 10 mm polyps and larger are expected to be detected at high sensitivity. To further enhance the visibility of 6 mm - 9 mm polyps, a new design of the collimator was successfully tested in a future version of our imaging capsule, which enables 2.5 times the number of photons to be detected on the detectors, allowing the implementation of image enhancement algorithm, which is expected to improve the imaging performance.

8.2.2 Polyp Detection

Laboratory tests were carried out to estimate the capsule's ability to detect polyps in phantoms and demonstrate sensitivity and specificity of such detection ("*Polyp Detection Analysis" in the Investigator's Brochure (IB)).* Fusion of CMT and XRF data contributed to noise reduction and enabled to demonstrate 100% true positive and 0% false positive.

8.2.3 Biocompatibility

Successful Biocompatibility test performed on Nov/2015 (NAMSA) stated there were no deviations to the provisions of the FDA Good Laboratory Practice (GLP) Regulations (21 CFR, Part 58) noted during the course of the study.

8.2.4 Animal Studies:

Raw data from an animal colon ("*Animal Testing and Tissue Equivalent Phantom Image Reconstruction" in the IB)* showing a decrease in X-ray florescence (XRF), photon signals and an increase in Compton backscattering, or CMT, signals corresponding to the position of a polyp that was detected when our imaging capsule passed over the polyp.

9 INVESTIGATIONAL DEVICE

9.1 Device Description

The C-Scan technology (Figure 1) is designed to provide structural information of the human colon without the need for fasting and prior bowel cleansing, eliminating the need to sedate subject and obviating the requirement for the insufflation of colon.

The system modality generates structural information on the colon, and is intended as a preliminary assessment of the colon which could assist in the detection of pre-cancerous polyps.

9.1.1 C-Scan System Components

Figure 1 : Components of the C-Scan System

- C-Scan® Cap: Ingestible capsule (C-Scan Cap) enabling intra-colon feature visualization, based on a radioactive source and an array of detectors.
- C-Scan® Track: External Capsule Positioning System (CPS) incorporated into the C-Scan Track attached to the subject's back, communicates with the C-Scan Cap, and stores all procedure data.
- C-Scan® View: A PC based Workstation (C-Scan View) that enables procedure data loading from the C-Scan Track, managing of subject information, 2D and 3D colon imaging, reports generation and printouts and storage/reload of procedure data to and from a CD. An Algorithm uses these subsystems to estimate the C-Scan Cap position (using electromagnetic signals generated within the C-Scan Cap and the C-Scan Track), identifies C-Scan Cap movements in the colon and correspondingly initiates C-Scan Cap scans using a dedicated Scan Control Algorithm (SCA)

At the beginning of C-Scan procedure, the subject is connected to the C-Scan Tracker and asked to ingest the C-Scan Capsule. In order to increase the contrast of the colon's walls and to differentiate them from their content, it is essential to increase the stool's contrast by ingesting radio-opaque material. It is a standard procedure using approved Iodine based liquids, contrast agents such as (Telebrix or Gastrografine) at the discretion of the hospital similar to the preparation to abdominal CT. After ingestion, the subject can go about his or her normal daily routine. The capsule travels painlessly through the gastrointestinal tract, seeking polyps.

During the passage of the capsule in the gastrointestinal tract, it transmits information to the C-Scan Tracker (recorder) attached to the patient's back. In order to collect data about the instantaneous localization of the capsule traveling in the colon, sensors are embedded in the recorder.

9.1.2 Radio Frequency (RF) Wrist Watch

The watch is an optional monitoring tool to optimize data interpretation during the clinical study and is not an integral part of the C-Scan system, as in Figure 2.

Figure 2: RF Wrist Watch

A commercial wrist watch (product of Texas Instruments) is supplied with the C-Scan system for use by the subject during the procedure. The watch incorporates a passive RF receiver which is tuned to 'listen' and display the information transmitted from the capsule to the Track. The added information is valuable for the subject to follow the progress of the capsule and to better understand messages from the system.

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10 STUDY OBJECTIVES

10.1 Primary Objectives

To evaluate the safety of the Check-Cap C-Scan System.

10.2 Secondary Objectives

- To evaluate subject's compliance
- To evaluate subject's satisfaction
- To collect data to improve the product's algorithm

10.3 Primary Safety Outcome Measure

The safety of the Check-Cap System will be evaluated by the incidence of device or procedure related Serious Adverse Events (SAE), as adjudicated by the Independent Physician Adjudicator.

10.4 Secondary Outcome Measures

- Subject compliance will be assessed by
  - Non-compliance rate throughout the study via diary completion by the subject
  Specific questionnaire. completed by remote subject monitoring (via telephone)

- Subject satisfaction will be established by:
  - Designated questionnaire that focuses on patient's impressions regarding tolerance and potential safety concerns. Acceptance criteria was defined as average score >3.5 (1- low satisfaction to 5- high satisfaction), which represent high satisfaction with the safety and tolerance of the C-scan system.
  - Comparing patient's satisfaction with colonoscopy procedure.

- Collecting procedure related data:
  - Technical performance in normal daily routine.
  - Segmental transit time.
  - Procedure duration.
  - Bowel movements.
  - Agreement between C-Scan and colonoscopy with respect to the presence/absence of colonic polyp(s) [Note: C-scan data not to be used for clinical decision making in the care of patients, for this clinical study].
  - Inter-observer variability in the detection of significant clinical findings on a 'per patient' decision
- Battery life Assessment
  - Assessing adequate power supply for complete scan of the colon: length of capsule operation lifetime with respect to the lifetime specification of 100 +/- 10% hours.
- Device performance
  - Assessing colon model by the physician reviewers as presented on C-Scan View (*e.g.*, normal, partial, right side missing, *etc.*).
  - Collecting data to improve the product's algorithm.

11 STUDY DESIGN

11.1 Overall Design

Up to 45 healthy subjects will participate in this study. Subjects to be enrolled in this study are indicated and scheduled to undergo optical colonoscopy based on the following symptoms or by being classified as higher than average risk based on one or more of the following:

- Surveillance - Significant findings in previous optical colonoscopy
- Diagnostic - Polyps detected in virtual colonoscopy referred for polypectomy
- Diagnostic - Polyps detected in previous optical colonoscopy (community setting) referred for polypectomy
- Diagnostic - Positive FIT test
- Diagnostic – one or more of the typical symptoms:
- abdominal pain
- Change in bowel habits
- Anemia or overt bleeding in stool
- Significant weight loss
- First degree relatives of CRC subjects

Alternatively, average risk based on their age and demographics referred for screening for polyps

Each subject will receive a comprehensive explanation regarding the study nature. During this process, and per ethical committee approval, subjects may be asked several questions (over the phone) regarding their medical background for preliminary assessment of eligibility. Once informed consent is obtained, a thorough evaluation of subject's eligibility will be performed based on inclusion / exclusion criteria. Eligible subjects will be required to undergo FIT procedure, per package insert instructions, within pre-defined timelines. All subjects will be scheduled to undergo capsule procedure, to be followed later on with optical colonoscopy procedure.

One to three days following end of C-Scan procedure the subjects will be contacted by phone by the clinical coordinator to follow-up on the subject well-being. Same follow-up procedures will be applied one to three days following Optical Colonoscopy procedure. Medical history and concomitant medication information will be collected for all subjects.

11.2 Study Duration

The duration of study participation for each subject is expected to be approximately 8-10 weeks. The total study duration across all patients is expected to be approximately 6 months, dependent upon subject recruitment rate.

12 SUBJECTS ELIGIBILITY

12.1 Study Population

The total Study population is up to 45 subjects at up to two investigational sites in the United States.

12.2 Inclusion Criteria

a. Male or female at the age of 40-80 years' old.
b. Subject provided signed informed consent.
c. Subject is willing and able to comply with the specified study requirements and follow-up evaluations, and can be contacted by telephone.
d. Subjects able and agrees to undergo colonoscopy procedure.
e. BMI ≥ 19 and ≤ 35.
f. Maximum body (abdominal) circumference < 120 cm.
g. Has at least 3 bowel movements per week
h. A colonoscopy procedure is pre-scheduled within 60 days

12.3 Exclusion Criteria

a. Subject who is not a suitable candidate for a colonoscopy (i.e., moderate sedation)
b. Known history of dysphagia or other swallowing disorders.
c. History of the followings: Inflammatory Bowel Disease (IBD) including Crohn's disease or Ulcerative, Colitis, Meckel's Diverticulum, Bowen Hernia, known fistulas or strictures (doctors' discretion), or a history of small bowel obstruction.
d. Known motility disorders:
    i. Chronic Constipation: less than 3 bowel movements/week, w/out the use of laxatives.
    ii. Delayed gastric emptying.
    iii. Narcotic use
e. Prior history of abdominal surgery that might cause bowel strictures leading to capsule retention, as determined by physician discretion with the exception of appendectomy, cholecystectomy and hysterectomy
f. Any condition believed to have an increased risk for capsule retention, strictures, bowel adhesion or other obstacles to free passage of the capsule (such as intestinal tumors, radiation enteritis) or incomplete colonoscopies (e.g. due to obstructions or NSAID enteropathy) as determined by physician discretion.
g. Has a cardiac device (e.g. pacemaker or ICD) or any other active implanted device
h. Known sensitivity to iodine, or with known kidney failure.
i. Known condition which precludes compliance or is contraindicated with study and/or device instructions.
j. Has a Magnetic Image Resonance (MRI) procedure scheduled within 1 month
k. Known condition of drug abuse and/or alcoholism.
l. Women who are either pregnant or nursing at the time of screening (to be verified by urine or serum pregnancy test for woman of child- bearing potential who are not post-menopausal or undergone surgical sterilization.
m. Concurrent participation in another clinical trial using any investigational drug or device.

12.4 Withdrawal Criteria

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

a. Severe side effects clearly related to the study device or procedure
b. Less than adequate compliance with the study routine
c. Presence or appearance of exclusion criteria
d. Refusal to undergo 'post' colonoscopy
e. A significant protocol violation
f. At the specific reasonable request of the sponsor

The sponsor must be informed in each withdrawal case within 24 hours. The reason for withdrawal has to be recorded in the subject's file.

13 STUDY PROCEDURES AND SCHEDULE

13.1 Study Procedures

The C-Scan study procedures and flow are outlined in Figure 3. The schedule of study assessments are listed in Table 1. The subjects are only required to attend two visits, but are expected to conduct phone assessments after ingestion but prior to expulsion of the capsule.

Table 1: Schedule of Assessments

Assessments	Pre-screening	Visit 1: Baseline and C-Scan	Follow-up 1: C-Scan - During Procedure follow-up	Follow-Up 2: C-Scan Procedure End follow-up Call	Follow-up 3: Colonoscopy Post Procedure follow-up Call
Visit Window	-30-0 days	0 days	0- As required days	1-3 days post procedure	1-3 days post procedure
Questionnaire	X				
Informed Consent		X			
Inclusion/ Exclusion Criteria		X			
Demographics		X			
Medical History		X			
Concomitant Medications		X			
Pregnancy test[1]		X			
C-Scan procedure		X			
Connect to C-Scan		X			
C-Scan capsule		X			
Ingest contrast		X	X		
FIT test			X		
Follow up phone calls[2]			X		
Capsule Excretion				X	
Abdominal x-ray[3]				X	
Subject Satisfaction Survey				X	X
Boston Bowel Preparation Scale (BBPS)					X
Colonoscopy Report	X[4]				X
Follow up visit call				X	X
Adverse Events		X	X	X	
Study Exit					X

[1]Urine pregnancy test for women of childbearing potential
[2]Minimum of two phone calls per day until capsule excretion
[3]Abdominal x-ray ONLY if suspected that capsule has not been excreted (subject will come to office/unscheduled visit)
[4]Collection of a previous colonoscopy report, if available

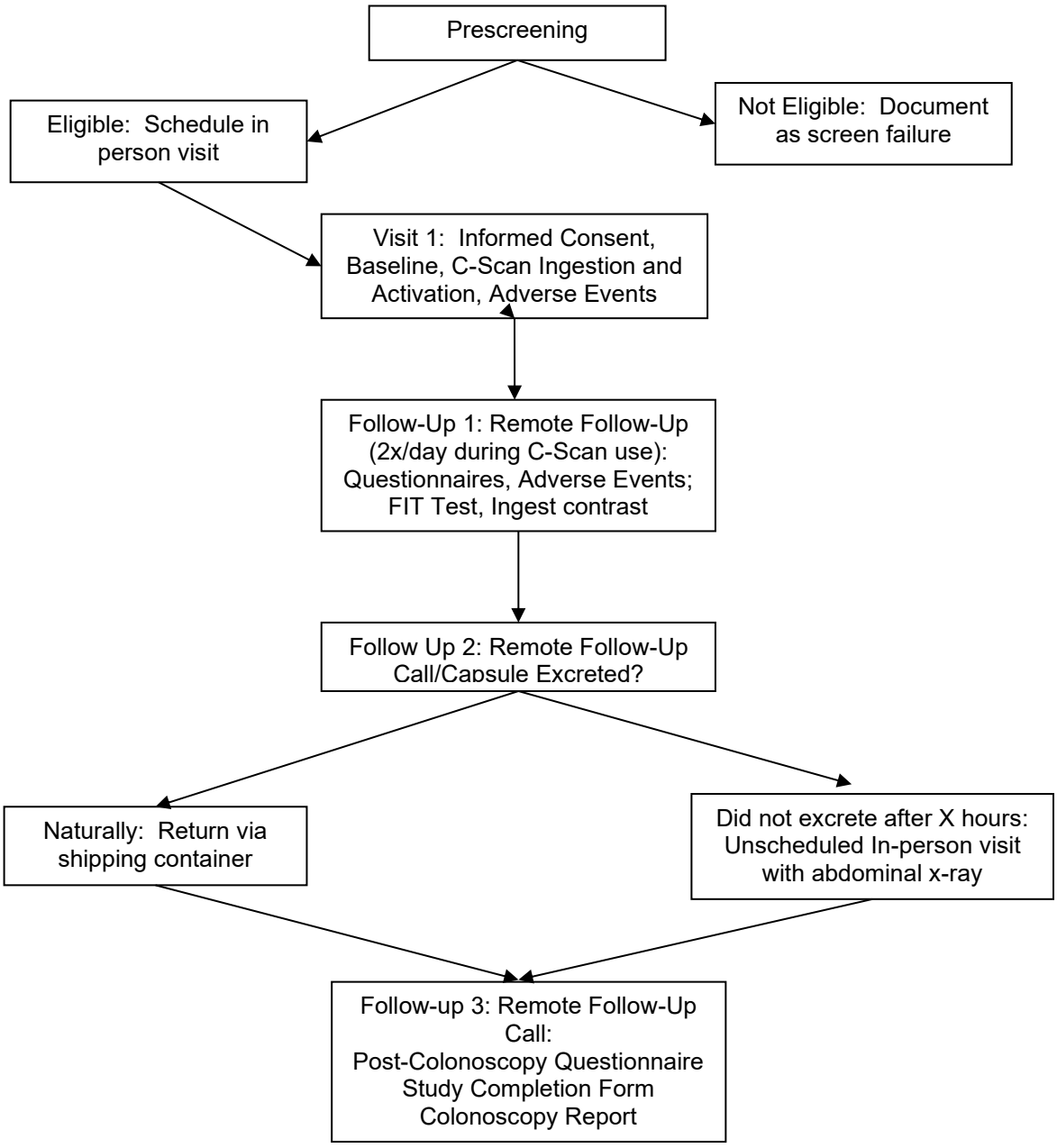

Figure 3: Study Procedure Flow Chart

13.2 Study Documentation

The following documents and information will be collected:

- Completed Visit and Follow-up Case Report Forms (CRFs)
- Referring procedure report (optical colonoscopy or virtual colonoscopy), if applicable
- FIT Results (+ photo)
- Subject's diary with all daily activities during home procedure
- Subject's usability questionnaire
- Subject Satisfaction Questionnaire
- C-Scan procedure raw data
- C-Scan report
- Optical Colonoscopy report
- Video recording of Optical Colonoscopy
- Pictures of Optical Colonoscopy, if taken
- Copy of pathology report, if conducted

13.3 Prescreening

Potential eligible patients scheduling an optical colonoscopy may be approached regarding participation in this study. Patients will be prescreened may be completed in person or via phone and logged on the Prescreening Log with outcomes regarding potential eligibility.

13.4 Informed Consent Process

An explanation of the study device, the study and participation requirements will be provided to each eligible prescreened patient. The informed consent document will be reviewed with each patient and they will be provided time to ask questions. Consent to participate in this study must be given in writing. The signed informed consent will remain in subject's file. A signed copy will be given to the subject.

Informed consent will be obtained prior to any study procedures being conducted. Site will maintain a log with all subjects who signed an informed consent to participate in the trial. The log will include the subject's full name, subject's study code and date of enrollment. Enrollment log will be kept in the site's Regulatory Binder which is maintained in a secure location. The subject is considered enrolled at the completion of the informed consent process

13.5 Visit 1: Baseline

Upon completion of the informed consent process, subject's eligibility will be assessed against the Inclusion and Exclusion criteria. Previous reports of optical or virtual colonoscopy should be collected and kept with the subject's file.

If the subject does not meet the inclusion/exclusion criteria, they will be considered a screen failure and excluded from the analysis.

The following information will be collected at this visit:

- General medical history and concomitant medication will also be assessed and documented.
- Subject's demographic and baseline information will be assessed and documented, including: date of birth, gender, height, weight, belly circumference, prior abdominal surgery, GI symptoms, and reason for referral.
- If applicable, documentation of previous GI procedures, such as optical colonoscopy

13.5.1 C-Scan Procedure

Subjects will be instructed to skip breakfast or lunch on the day of C-Scan Capsule ingestion to expedite gastric passage. Liquids are allowed.

The subjects will be connected to the C-Scan Track and after successful system's activation (BIT – built in test), the subject will be asked to ingest the C-Scan Capsule with some water, contrast media (GE Omnipaque 350) and non-soluble fiber, in the presence of a physician investigator or designee. The subject will also be provided with an RF watch. A representative of the sponsor will attend the ingestion procedure, as needed to assure proper activation.

Post ingestion, the subject will receive detailed instructions about the daily routine and activities as well as use of the RF watch and then will be discharged home with written instructions on the procedure Instructions for use (IFU), daily diary, FIT kit and capsule return kit.

13.6 Follow-Up 1

13.6.1 FIT Procedure

All subjects will be required to perform FIT procedure using [OC-Light] FIT Kit prior or during the capsule procedure.

The subjects can perform the test at their home, per their convenience, as per package insert instructions, and report the results to study team (photo of the strip with 1-2 lines). Additional guidance will be provided by the site clinical team as required. Alternatively, FIT procedure may be conducted at the clinic, on the day of C-Scan Capsule ingestion. In case of unclear results, the FIT test will be repeated. One positive result in any of the tests will be considered as positive. FIT procedure date and results will be recorded and documented.

13.6.2 Capsule Progress Days: Contrast Ingestion, Laxatives and Non-Soluble Fiber

One the days in which the capsule is progressing within the subject, the subject is required to ingest contrast media (GE Omnipaque 350, FDA approved under NDA 018956) as well as non-soluble fiber supplements. The subject will be required to ingest daily dose (3 X 15 ml) of contrast media, to be consumed three times per day as well a non-soluble fiber 3x/day with normal diet.
The subject will be provided with Laxadin (5 mg tablets) to be ingested according to the doctor recommendation, on an as needed basis. In routine procedures, subjects might be instructed to take 2 X 5 mg tablets 48-72 hours after ingestions (unless the capsule was already excreted).

13.6.3 Subject Diary

All subjects will be required to keep a log ('Subject's Diary') during procedure documenting general activities, contrast media intake, fibers intake, and food consumption, bowel movement, and system visual/auditory indicators.

13.6.4 Follow-Up Phone Calls

During capsule procedure/progress days, the subjects will be contacted by phone several times daily by the site clinical study team or by dedicated external trained personnel to assess the subjects well-being and to monitor for any change or discomfort, subject satisfaction adverse events and procedure progress.

During the call, if a complaint related to the technical functioning of the device is received, subjects may be also monitored by the technical team (either at home or at the clinic), who may need to examine the

system or inquire the subjects about the system visual/auditory indicators in order to assure optimal operation of the C-Scan system. If an adverse vent is reported, the caller will notify the site study team and determine the appropriate course of action.

13.7 Follow Up 2: Capsule excretion and collection

13.7.1 Capsule Return

Capsule procedure is completed upon capsule excretion or system auditory indication of 'End of Procedure'. Subjects will be instructed to inform the study coordinator or designee upon capsule excretion.

The subjects will be provided with a dedicated capsule collection kit, to assist the subjects in collecting the capsule. Subjects will be instructed to retrieve the capsule upon excretion. Return packaging and instructions will be provided. The subject will return with the Kit the diary, the questionnaire and all unused materials.

In case of doubt regarding capsule excretion, and per physician discretion, subjects may be referred to abdominal X-Ray to confirm capsule excretion.

13.7.2 Usability Questionnaire

Usability questionnaire will be provided with each Kit and the subjects are instructed to answer these questions once the procedure is completed. A question regarding whether the subject has experienced any adverse events will be included.

13.8 Follow-Up 3: Post-Colonoscopy Procedure

Subject will be telephoned by study site to assess subject satisfaction with the colonoscopy procedure as compared to the C-Scan. Follow up window is 1-3 days post-colonoscopy. Additionally, the BBPS and colonoscopy report will be collected from the test site for comparative analysis with the C-Scan procedure. The subject will be exited from the study upon completion of this follow-up

13.9 Unscheduled Visit(s)

After 100 hours following Capsule ingestion, if the subject is unaware of the excretion of the capsule, or if it suspected that the capsule has not been excreted naturally, the subject will call the site to determine options for excretion. They may be asked to return to the investigative site for an abdominal x-ray to see if the capsule remains in the body. If so, measures will be taken by site personnel to ensure capsule excretion. See Capsule Retention section below.

13.10 C-Scan Analysis

Upon return of the capsule to the investigational site, the capsule data will be downloaded from the "Track" and validated for completeness by the technical team. Next, the raw data will be transformed to 3D format ('reconstruction') by the View workstation and optionally, selected bookmarks will be prepared for the Viewers.

The files will be transferred to designated centralized reading center (may be located outside the United States) and reviewed by three trained medical reviewers for clinical analysis and preparation of procedure subject report. Each reviewer will generate a final report including 'per patient' recommendations.

Decision on presence/absence of polyps will be determined by majority.

C-Scan findings will be compared to the FIT results and to the study Optical Colonoscopy procedure.

14 STATISTICAL ANALYSIS

14.1.1 Sample Size Considerations

This is a pilot safety study; therefore, sample size is not determined by power analysis.
Up to 45 subjects will be recruited to the study.

14.1.2 Primary Analysis Set

The primary objective of the study is to establish the safety of the Check-Cap C-Scan system.
The primary analysis set for establishing the safety of the Check-Cap C-Scan system will include all subjects who underwent C-Scan procedure per protocol.

14.1.3 Operational Analysis Set

Technical or operational failures that will be discarded from the trial statistical analysis will include all cases where the system did not function as expected:

- Capsule operational failure.
- Track operational failure.
- Subject's noncompliance with procedure requirements

14.1.4 Data analysis

Descriptive statistics for all parameters will be calculated. For continuous parameters descriptive statistics including mean, standard error, median, minimum, and maximum values will be reported overall and at each time-point. For ordinal parameters, counts and percentages may be reported in addition to the mean, standard error, median, minimum, and maximum values. Categorical parameters will have counts and percentages reported overall and at each time-point.

14.1.5 Interim Review of Data

An interim report may be generated depending on rate of enrollment and completeness of study data generated from patients enrolled. It is anticipated that enrollment will be conducted quickly and the potential timing for an interim analysis may not be feasible.

15 SAFETY CONSIDERATIONS

15.1 Safety Parameters

15.1.1 Risks Associated with Participation In The Clinical Investigation

The risks associated with the C-Scan system are similar to those risks associated with regular Capsule Endoscopy. Risks associated with both Capsule Endoscopy and the Colon Capsule include but not limited to the following: constipation or diarrhea, capsule delay or retention throughout the GI tract, erosion of the colon mucosa, allergic reaction to the ingested contrast material, pain and discomfort.

15.1.2 Potential Risk From The Capsule Procedure

- Delayed excretion or retention of the capsule in the GI tract
- Exposure to low dose X-ray radiation during the capsule passage and from the abdominal X-ray (if required, post questionable excretion)
- Exposure to low level electromagnetic radiation
- Change in bowel habits or abdominal discomfort during the passage of the capsule
- Unexpected capsule related Adverse Events

15.1.3 Capsule Retention

There is a low risk of capsule retention, *i.e.*, no excretion of the capsule after more than 300 hours (defined as SAE). Delayed capsule excretion is defined as no excretion of the capsule after 100 hours (approximately 4 days). In some instances, intervention is required to remove the capsule. Intervention, based on the physician's decision and imaging of the capsules location may include: use of laxatives, non-soluble fiber supplements, removal by colonoscopy or surgery.

15.1.3.1 Possible Scenarios and Recommended Physician's Action:

In all cases the physician may opt to use local protocols for patients administered with gastrointestinal capsules; medical intervention or lack of, which remains at physician's discretion.

- **Capsule is Not Found After C-Scan® Track indicates it was expelled**
  - Advise the subject to look in the toilet. If it is found, the subject should notify the clinic which will arrange for the collection of the C-Scan system.
  - If the capsule is not found, the subject should speak with a physician at the clinic as there is a chance it was not expelled despite the positive indication. The physician might recommend using a laxative at home to try to expel the capsule. Make sure that the subject knows to use the collection kit during any bowel movements. Or, the physician investigator may recommend the subject to come to the clinic for a physical exam, and depending on findings, consider abdominal X-Ray imaging.

- **Capsule Not Expelled After 4 Days (~100 hours)**
  - If 4 days have passed and the capsule was not expelled, the subject should speak with a physician at the clinic (if needed, be sure to initiate a contact with the patient). The physician might recommend using a laxative at home to try to expel the capsule. Make sure that the subject knows to use the collection kit during any bowel movements. Or, the physician investigator may recommend the subject to come to the clinic for a physical exam, and depending on

findings, consider abdominal X-Ray imaging.
- Intervention, based on the physician's decision and imaging of the capsule's location, may include: use of laxatives, fibers, removal by colonoscopy, or by surgery.
- In case that the capsule is retained in the small bowel, as suspected according to the X-Ray imaging, the recommended Intervention, based on the physician's decision, may include: use of laxatives, prokinetic drugs, removal by SB enteroscopy (with double balloon if available) or by surgery.

- **Capsule lost communication (no flashing lights on Track) at any time between ingestion and 100 hours**:
  - Advise the subject to verify that the batteries in the Track are in position and the compartment is well secured
  - Verify that the patient is still wearing the Track on his/her back
  - If communication is still interrupted or missing, contact the technical support to consult about potential malfunctions and interventions.
  - If the problem is not resolved and the communication is missing - have the patient come to the clinic
  - There is no reason to assume there is a safety malfunction, but since the procedure is not yielding any additional valuable clinical data, it is recommended to take steps to expel the capsule out.
  - The clinic team (technician and/or physician) should perform, in case the capsule has not been excreted and collected already, abdominal X-Ray to assure the capsule location within the GI tract.
  - Intervention, based on the physician's decision and imaging of the capsule's location, may include: use of laxatives, fibers, removal by colonoscopy, or by surgery.

- **Technical Malfunction – C-Scan® Track Sent a Fault Indication**
  - Verify that the auditory indication was from the C-Scan® Track and not a background noise. A C-Scan® Track safety fault indication is identified by a series of repeated beeps.
  - Ask the subject if a single indication was received, or was it repeated at regular intervals.
  - Ask if the subject feels any discomfort.
  - If it is a Safety malfunction (risk of higher than usual body radiation exposure), have the subject come to the clinic ASAP and no later than 48 hours post call.
  - If the capsule has not already been excreted and collected, the clinic team (technician and/or physician) should perform abdominal X-Ray to assure the capsule location within the GI tract.
  - In the case of Safety Malfunction, intervention is required to remove the capsule without delay (recommended within 24 hours). Intervention, based on the physician's decision and imaging of the capsule's location, may include: use of laxatives, fiber supplements, removal by colonoscopy, or by surgery.

- Efforts should be made to minimize the subject's exposure by removing the capsule out of the body.

15.1.4 Low X-Ray Body dose

In addition, the capsule emits low level X-Ray radiation for a few seconds each time it scans the colon. The major source of radiation dose is from Ta182, a byproduct contaminant.

The radiation may potentially cause damage to the colon or nearby organs. Based on calculations the radiation dose level is rather low: 100 times lower than CT Colonography or similar to the radiation your body absorbs while flying from Europe to New York (8 hour flight = 0.06 mSv).

Once the capsule is excreted, the risk of radiation is eliminated.

16 ADVERSE EVENTS

Subjects will be carefully monitored for adverse events. Subjects will be guided to report if they feel any pain or discomfort during the trial. At each visit or phone contact, subjects will be asked if they experienced any adverse reaction since the last visit.

Any adverse events with an onset following beginning of bowel preparation to colonoscopy procedure will not be collected. Colonoscopy related adverse events are not part of the study, are considered standard of care and will not be reported.

16.1 Adverse Event Definitions

16.1.1 Adverse Event

An Adverse Event is any unwanted medical occurrence in a subject (e.g. sign, symptom, illness, abnormal laboratory value, or other medical event) occurring to a subject that appears or worsens during a clinical study, whether or not considered related to the device.

16.1.2 Serious Adverse Event

An SAE is any adverse event that:

- Led to death
- Led to a serious deterioration in the health of the subject
- Resulted in permanent impairment of a body structure or body function. Required in subject hospitalization or prolongation of existing hospitalization
- Resulted in medical or surgical intervention to prevent life threatening illness or permanent impairment to body structure or body function
- Led to fetal distress, fetal death, or congenital anomaly/birth defect

16.1.3 Unanticipated Adverse Device Effect (UADE)

An unanticipated adverse event is any serious, device related adverse event, if that event was not previously identified in the risk analysis and consent form in

- Nature
- Severity or frequency
- Unreasonable risk is not defined. It shall be determined by the management on a case-by-case basis through evaluation of serious and unanticipated adverse events

16.1.4 Device Malfunction/Failure

Malfunction means the failure for device to meet its performance specifications or otherwise perform as intended. In general, this is related to a component of the system not functioning as intended to provide the required outputs. Examples of a device malfunction include:

- C-Scan capsule does not traverse through the colon – the scanning of the colon is aborted prior to reaching the rectum or the image scan density throughout the colon is inadequate for clinical interpretation
- C-Scan shield does not retract – temporarily excessive radiation from the capsule
- C-Scan does not record tracking through colon- temporarily or continuous loss of tracking of the capsule by the recorder, causing inadequate or partial activation of the scanning function
- Corrupted data – the stored data in the recorder is corrupted and cannot be interpreted by the C=Scan View for clinical data analysis
- External interference – External electromagnetic interference (Hybrid cars, generators or other sources) cause interference to the communication with the capsule or to the tracking circuitry, thus causing periods of lost data during the procedure

- Physiological causes – subjects who fail to ingest the capsule, or subjects in which the capsule dwells in the caecum for a period of ~100 h or more, thus exceeding the operation time of the C-Scan system

16.2 Anticipated Adverse Events

The following events are known potential adverse events from the C-Scan procedure. They will be reported as adverse events for the purposes of the study:

- Delayed C-Scan Capsule excretion
- Capsule retention
- Change in bowel habits
- A small amount of fresh blood in the stool
- Potential difficulty swallowing the capsule
- Abdominal discomfort during the passage of the capsule
- Abdominal pain, cramps
- Back pain
- Nausea
- Loss of appetite
- Soft/runny stool
- More than 2/day bowel movements
- Diarrhea
- Constipation
- Allergic reaction to the ingested contrast material
- Skin irritation caused by the stickers on back
- Impaired night sleep caused by the C-Scan track (recorder on the back)
- Excessive radiation exposure (> 200 [uSv] microSivert) Note: This threshold was calculated as 2X the max body dose in a long, but normal, procedure: total transit time of 100 hours and with 4000 scanning pages, which is the maximum ever reached during a normal procedure.

16.3 Recording and Documentation of Adverse Events

All adverse events should be evaluated by the Investigator, and should be medically handled per investigator discretion. All adverse events shall be recorded in the subject's Adverse Event Case Report Form. The following data should be carefully documented:

- Subject's study ID/code
- Type of event
- Time of occurrence (i.e. date & time)
- Time of resolution (i.e. date & time)
- Severity degree (mild/moderate/severe/unknown)
- Relationship to study device (definitely/probably/possibly/probably-not/not-related)
- Measures taken (e.g. concomitant medication, hospitalization, etc.)
- Event outcome (unchanged/worsened/improved/resolved/unknown/death)

Adverse events will be assessed in terms of seriousness, duration, intensity and relationship to the study device and/or procedure. All anticipated and unanticipated adverse events will be collected and reported.

16.3.1 Severity

The outcome of each adverse event will be observed and documented. Adverse events will be graded as follows:

- Mild: Sign or symptom, usually transient, requiring no special treatment and generally not interfering with usual activities.
- Moderate: Sign or symptom, which may be improve by simple therapeutic measures, may interfere with usual activities.
- Severe: Sign or symptom that is intense or debilitating and that interferes with usual activities. Recovery is usually aided by therapeutic measures and the discontinuation of the study device may be required.

16.3.2 Relationship

The relationship of the adverse event to the study is defined as follows:

- Definitely: An adverse event was shown to be related to the study device.
- Probably: An adverse event has a strong temporal relationship to study device, and another etiology is unlikely or significantly less likely.
- Possibly: An adverse event has a strong temporal relationship to the study device, and an alternative etiology is equally or less likely compared to the potential relationship to the study.
- Probably not: An adverse event has little or no temporal relationship to the study device and/or a more likely alternative etiology exists.
- Unrelated: An adverse event has no temporal relationship to study device or has a much more likely alternative etiology.

16.4 Safety Reporting Procedures

16.4.1 Adverse Events Reporting

Subjects are encouraged to report any event to the study team and consult the PI for any change in their well-being. Subjects will be asked for any change in their medical condition during each study visit or phone call with the exception of Visit 2 for the standard of care Colonoscopy and the associated preparation procedure.

16.4.2 Serious Adverse Events Reporting

Serious adverse events shall be reported to Check-Cap/Clinical Research Organization (CRO) in writing (using the Serious Adverse Events Form taken from the CRF) within 24 hours of the investigator's awareness of the event, and should be reported to the local Ethical Committee per their requirements.

16.4.3 Unanticipated Adverse Device Effect Reporting

Unanticipated adverse device effects shall be reported to Check-Cap/CRO in writing (using the Serious Adverse Events Form taken from the CRF) within 24 hours of the investigator's awareness of the event.

Check-Cap/CRO will request additional information if needed and Check-Cap will report the event to the FDA within 10 working days of first notification of the event. The Investigator must notify their IRB of the event no later than 10 working days after learning of the vent.

17 DATA COLLECTION AND QUALITY CONTROL

17.1 Data Collection

Each investigative site will complete CRFs during the study. Each subject participating in the study must have all applicable CRFs accurately and diligently completed. It is the investigator responsibility to ensure by signature the completeness and accuracy of the CRFs.

Procedures report (e.g. optical colonoscopy report) and forms completed by the subjects (e.g. Diary) will be considered as source documents and provided to the sponsor de-identified. Copies of the CRFs may also be print out and used as source documents per site team convenience, as long as these are marked as source documents.

CRFs and any other study documents will not include any identifying details of the subjects, and all identifying details will be decoded to include study specific numeric code and subject initials.

Completed CRFs shall be monitored and verified against source documents, and signed by the investigator as a confirmation of accuracy and adequacy.

17.2 Data Monitoring

Monitoring will be conducted by the sponsor or designees per the study monitoring plan. Informed Consent Forms will be monitored for 100% adequacy and accuracy and study data will be monitored via a risk based approach outlined in the monitoring plan.

17.3 Data Archiving

All study documentation will be kept for a period of 2 years from study completion or termination, or the date which the records are no longer needed to support a premarket approval or De Novo classification application. Prior to discarding records, the investigative site should contact Check-Cap to receive clearance for proceeding or obtain alternative instructions

18 LABELING

All equipment associated with the clinical study will be identified with visible markings stating: "CAUTION--Investigational device. Limited by Federal (or United States) law to investigational use"

19 DELIVERY, STORAGE AND DISPOSITION

The C-Scan capsule and accessory kit will be shipped to the investigative site in advance of the procedure. Based upon the cadence of scheduled procedures, the site may be provided several units at a time to have inventory on hand.

All device and accessories must be tracked within the device accountability log and stored in a secure location available to only authorized study personnel. C-Scan should be kept in a dry location at room temperature.

At the end of the C-Scan procedure, a representative of the sponsor will collect the Kit, document and all unused material directly from the subject. C-Scan units returned from the subject will be shipped back to the sponsor.

20 ETHICAL AND LEGAL ASPECTS

20.1 Ethical Committee Review and Approval

Study protocol and applicable documents must be submitted to the Ethics Committee/IRB for approval prior to study commence. Documented approval will be obtained for all participating sites. When needed, study extension, amendment or renewal of the Ethical Committee approval must be obtained.

20.2 Ethical Conduct of the Study

The procedures set for the in this study protocol are designed to ensure adherence with Good Clinical Practices. This study must also comply with the local regulatory requirements.

Both the Investigator and the Sponsor are required to maintain study records, including regulatory approvals, as required by the applicable regulatory requirements.

The investigator must agree to the inspection of study related records by a regulatory authority or Check-Cap representatives and must allow direct access to source documents and any other study related documents.

20.3 Subject Information and Consent

Prior to the beginning of the trial, the investigator is responsible to obtain the Institutional Review Board approval of the written informed consent and any other written information provided to the subjects. Institutional Review Board approvals must be filed in the study records.

The process of obtaining informed consent must be in accordance with IRB approval, Good Clinical Practice, and local regulatory requirements. Written informed consent must be obtained prior to any study specific procedure.

20.4 Confidentiality

All subjects identifying records will be kept confidential. Subjects names will be kept confidential and all study records will include only subject study code and initials. If any identifying details (e.g. name, address, etc.) appears on any study related document, it must be redacted.

The subjects will be informed in writing (i.e. Informed consent), that representatives of the sponsor, CRO, Institutional Review Board or other 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 strict confidence and in accordance with local laws. Subjects will be informed in writing that any future publication will not include identifying information.

20.5 Insurance

The sponsor is responsible to provide insurance coverage for the clinical trial.

21 DISCLOSURE AND PUBLICATION OF INFORMATION

All proprietary information including; Check-Cap Ltd's operations, patent application, formulas, manufacturing processes, basic scientific data, and formulation information provided to the investigator or the methodologies used in this study, as well as proprietary information obtained during the course of the study are confidential and will remain the sole property of Check-Cap Ltd.

The investigator agrees not to disclose any proprietary information supplied by Check-Cap Ltd. in any way without prior written permission.

Individual subject data obtained during this study are confidential and will not be disclosed to third parties with the following exceptions:

1. When the data is needed by the subject's personal physician or other medical personnel responsible for the subject's welfare.
2. For data inspection and verification by Check-Cap Ltd. or designee, United States Food and Drug Administration, European Union or Israeli regulatory authority auditors or by the IRB.

Any manuscript or abstract produced by the investigators must be provided to Check-Cap LTD for review and approval at least 60 days prior to submission. Individual subject identity cannot be divulged in any publication.

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23 APPENDICES:

- Subject's Satisfaction Questionnaire
- Subject's Satisfaction Questionnaire-Colonoscopy

23.1 ATTACHMENT 1: SUBJECT'S SATISFACTION QUESTIONNAIRE

Subject Satisfaction Questionnaire	
Please circle the most appropriate answer for each question according to the following scale: 1. Strongly disagree 2. Disagree 3. Neither agree or disagree 4. Agree 5. Strongly agree Space is provided for comments.	Scale
1. I have not experienced any inconvenience during the C-Scan procedure. If 1 or 2 are given, please explain:	1 2 3 4 5
2. I have not experienced any pain during the C-Scan procedure. If 1 or 2 are given, please explain:	1 2 3 4 5
3. I did not need any analgesic or other pain medication during the C-Scan procedure. If 1 or 2 are given, please explain:	1 2 3 4 5
4. I have not experienced any inconvenience while ingesting the contrast media 3 times a day If 1 or 2 are given, please explain:	1 2 3 4 5
5. I Would recommend the C-Scan procedure for colonic screening If 1 or 2 are given, please explain:	1 2 3 4 5
6. The C-Scan procedure didn't affect my daily routine If 1 or 2 are given, please explain:	1 2 3 4 5
7. I have not experienced any inconvenience during capsule excursion If 4 or 5 are given, please specify:	1 2 3 4 5
8. Do you have any additional comments regarding the C-Scan procedure?	

23.2 ATTACHMENT 3: SUBJECT'S SATISFACTION QUESTIONNAIRE-COLONOSCOPY

Subject Satisfaction Questionnaire	
Please circle the most appropriate answer for each question according to the following scale: 1. Strongly disagree 2. Disagree 3. Neither agree or disagree 4. Agree 5. Strongly agree Space is provided for comments.	Scale
1. I have not experienced any inconvenience during the Colonoscopy procedure. Please explain:	1 2 3 4 5
2. I have not experienced any pain during the Colonoscopy procedure. Please explain:	1 2 3 4 5
3. I did not need any analgesic or other pain medication during the Colonoscopy procedure. Please explain:	1 2 3 4 5
4. The C-scan procedure was easier for me compare to the Colonoscopy procedure Please explain:	1 2 3 4 5
5. For my next colonic screening I will prefer the C-Scan procedure Please explain:	1 2 3 4 5
6. Please specify the advantages of the C-Scan ver. Colonoscopy in your opinion:	
7. Do you have any additional comments regarding the C-Scan procedure?	