Informed Consent for Participation in Research

Participant's Name: _____ **Subject ID Number:** _____

TITLE:	A Prospective, Randomized, Multi-center, Double-Blinded, Clinical Study to Assess the Efficacy and Safety of Vibrant Capsule vs. Placebo, for the Treatment of Chronic Idiopathic Constipation
PROTOCOL NO.:	280CLD IRB Protocol #20212571
SPONSOR:	Vibrant Ltd.
INVESTIGATOR:	Dr. Stanley Hui, MD SF Research Institute 2435 Ocean, Ave, San Francisco, CA 94127
STUDY-RELATED PHONE NUMBER(S):	Phone Number Phone Number (24 hours) 415-745-4340

Before consenting to participate in this research study, you should have enough time to read the information in this form, or have it read to you. A member of the research team will discuss it with you. Be sure to ask questions about anything that is not clear before giving consent.

Your participation in this study is voluntary. You can choose not to participate at any time, even after starting the study, without any penalty or loss of benefits to which you are otherwise entitled.

Why me: You are being asked to participate in a research study because you suffer from Chronic Idiopathic Constipation (CIC). Constipation is a common intestinal disorder that is often chronic, negatively affects patients' daily lives, and is associated with high healthcare costs. Constipation occurs when bowel movements become difficult or less frequent. The normal length of time between bowel movements ranges widely from person to person.

Study Purpose: This study aims to evaluate the performance and safety of a new experimental medical device – the Vibrant Capsule. The purpose of studying this new experimental medical device is to evaluate the Vibrant capsule performance for patients like you, who did not experience satisfactory improvement of their chronic constipation symptoms with other available treatment(s). The Vibrant Capsule is designed to mechanically induce a normal peristaltic wave in the large intestine, thus aiding in relieving constipated patients.

This study involves research and there are certain outcomes that are unknown. This is a randomized (the likelihood of getting an active capsule or placebo capsule will be by chance), double- blind (nor you or site's staff responsible for study assessments won't know which capsule you get), placebo-controlled study. The expected time you will be in the study is 10-12 weeks. Up to 25 study participants will be enrolled at SF Research Institute, and about 100 throughout the study. You will have procedures done that are considered research and may or may not be a part of the usual care for your condition. There are other alternatives than participating in this research. If you decide to participate, your private health information will be collected; however the researchers in this study will take appropriate measures to protect the confidentiality of your information. In the case you are injured as a result of the study, medical treatment is available.

If you go to SF Research Institute or another healthcare facility or provider for any reason while participating in this study, you should inform them that you are involved in this research study, as it may impact the type(s) of care provided and protect your safety.

What is the usual approach to my condition?

In some cases dietary and lifestyle changes will help relieve symptoms of Chronic Constipation. Also recommended: increased fluid and fibers consumption (such as Psyllium or Bran). A treatment with laxatives or enemas may be recommended for a limited time.

The study doctor will discuss study alternatives with you and their risks and benefits.

What is the Vibrant capsule?

The Vibrant study capsule is medication-free, does not interact with any other body system and does not deliver medication of any kind. The study capsule will be excreted from your body in its entirety during a normal bowel movement (through the stool).

The study capsules are activated by using a base unit which is simple and easy to use. Each capsule should be placed in the base unit before ingesting it. You will be instructed accordingly by the study team.

What risks will I face by taking part in the study and how will researchers protect me from these risks?

Undergoing an MRI while on the study: Undergoing an MRI while the capsule is inside your body may result in serious damage to your intestinal tract or abdominal cavity. If you require an MRI, please tell the study physician. The study capsule will be stopped for a few days, to allow for evacuation of all capsules from your body. Capsule excretion will be verified via abdominal X-ray before undergoing the MRI examination. The X-ray will expose you to radiation.

You will be asked to stop use of any medications or supplements you normally use to induce bowel movements throughout the 10-12 week study period, including the 2-4 week run-in period prior to use of the Vibrant study capsule or the inactive placebo capsule. This may result in severe

constipation with abdominal pain and cramping. Still, you will be allowed to use rescue medications (as explained below) in case of 3 consecutive days without a bowel movement.

As with any research study, there may be additional risks that are unknown or unexpected. If these become known, the study team will notify you in a timely manner of any changes that may affect your willingness to participate. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

Side Effects of Use of the Vibrant Capsule:

Following are the possible side effects:

- Abdominal pain/discomfort/cramping
- Blood in the stool may develop or increase
- Bloating/Flatulence
- Diarrhea
- Nausea may develop or increase
- Rectal pain may develop or increase
- Sensation of vibration in the abdomen
- Uncontrolled leakage of stool may occur
- Vomiting may develop
- Bowel obstruction which may result in endoscopic or surgical procedure as intervention

There might be other side effects that researchers do not yet know about.

If important, new side effects are found, the study doctor will discuss these with you.

Pregnancy: You cannot be pregnant or breast feeding while you are in the study. The effect on an unborn or nursing child is unknown. You will receive at least two pregnancy tests during the study. If you are a female and can have children, a hormonal (i.e., oral, implantable, or injectable) and a single-barrier method, or a double-barrier method of birth control must be used throughout the study.

Blood Draw: Risks and discomforts associated with drawing blood samples may include pain, bruising, bleeding and on rare occasions, infection at the needle stick site. Other risks are feeling lightheaded and faint.

The researchers have taken steps to minimize the risks of this study. Please tell the researchers in the contact section on page one about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

How could I and others benefit if I take part in this study?

There is no guarantee that your condition will improve as a result of your participation in this study. It may stay the same or worsen. However, the information learned from this study may help other people with this condition in the future.

Are there any costs or payments?

The sponsor of the study will cover the cost of study capsules and all study related supplies as well as the office visits associated with this study.

Neither you nor your health care plan/insurance carrier will be billed for the collection of the information that will be used for this study.

You and/or your insurance company will be responsible for payment of items and services that you would receive if you were not participating in the research study. You will be responsible for your normal co-payments and co-insurance/deductibles not associated with your participation in this research study.

You will receive $75 for each completed study visit to reimburse you for your time and travel while taking part in this study.

Assuming electronic diary was completed properly and dosage regimen was kept throughout the study, you will receive an additional compensation of $100 at the end of the study (upon completion 8 weeks of treatment) after bringing back all remaining study capsules and the base unit.

Who could profit or financially benefit from the study results?

This study is paid for by the Sponsor (Vibrant Ltd) which owns the device being tested and thus has a financial interest in the outcome of the study. Payments are made to SF Research Institute and the funds are used to cover the expenses of the study and related academic and research activities of the institution.

What extra tests and procedures will I have if I take part in the study?

Most of the exams, tests, and procedures are part of the usual approach for your condition. However, there are some extra office visits that you will need to have if you take part in this study.

Before you begin the study

No study procedures are done without a signed informed consent form. If you agree to sign the informed consent form, you will be asked to come to the study clinic for at least 4 visits: Screening, baseline, after 4 weeks of treatment, and after 8 weeks of treatment.

Screening:

The screening visit (visit 1) tests and procedures are performed to confirm you are eligible to be in the study. This visit will take about 3 hours. The screening tests and procedures will include:

- A physical examination, including a digital rectal exam
- Record of your vital signs (blood pressure, pulse, heart rate)
- Record of your demographic information (age, gender, weight, height)
- A review of your medical history and what medications you are taking
- A review of your history of constipation and what medications you are taking or used to take for your constipation
- A blood sample [about 1 tablespoon] will be drawn for routine laboratory tests
- Women who can have children will take a blood pregnancy test. The test must be negative for you to be in this study. You must not be breastfeeding or pregnant during the study
- An interview for constipation evaluation
- Completing questionnaires relating to your health status

If the exams, tests, and procedures show that you can take part in the study, and you choose to take part, you will have the following information collected study clinic visits which are not part of the usual approach for your condition.

If you choose to participate in the study, you will be asked to refrain from using any medication or supplement that relieves constipation, during the entire time of the study.

This constraint is necessary and very important in order to evaluate the Vibrant Capsule treatment.

Rescue Medication:
In order to prevent suffering during the study, you will be permitted to take rescue medication, in case you need 'rescue', but according to specific rules which you must accept to follow during the entire study.

Prior to taking rescue medication, you must follow these three rules:

1) You must wait at least 3 consecutive days (72 hours) without a bowel movement before you are permitted to take a rescue medication
2) You must document all rescue intake in the daily electronic diary (eDiary)
3) The following treatment is recommended, but not mandatory

    a. Dulcolax® suppository/bisacodyl suppository
    b. Fleet Enema®
    c. Dulcolax®/bisacodyl tablet (1x5mg)

You are permitted to take another rescue medication if you wish – as long as you document it in the eDiary.

Prohibited medications: Certain medications are not allowed during this study.

Medications that may affect bowel mobility cannot be taken during this study, these medications include (but are not limited to):

- Narcotics (opiates/opioids)
- Chronic use of NSAIDs (Non-Steroidal Anti-inflammatory Drugs) – such as ibuprofen. Patients on daily cardiac doses of aspirin are allowed in the study
- Prokinetics (drugs which enhance gastrointestinal motility, i.e. Domperidone, Cisapride etc.)
- Anti-Parkinsonian medications,
- Verapamil
- Nifedipine
- Iron
- Magnesium supplements
- Tricyclic Antidepressants (TCAs)
- Heparin
- Warfarin
- Baclofen

The following medications are allowed ONLY if you are on a stable dose for at least 3 months:

- Antidepressants (other than TCAs)
- Thyroid or hormonal replacement therapy

During the first 2 to 4 weeks after the screening visit, you will be asked to complete (on a daily basis, at bedtime) an electronic diary regarding your bowel movements as well as related clinical assessments, change in your general health condition and any medication taken (if applicable). The study coordinator may call you from time to time to see how you are doing and if you have taken a rescue medication (a medication to help you have a bowel movement) which is allowed in certain situations as mentioned above.

You need to have a smartphone, a tablet or a computer connected to the internet in order to complete the electronic diary on a daily basis (at bedtime).

Baseline Visit (Day 0)

14 to 28 days after the screening visit and in case your participation in the study is confirmed by the Sponsor (based on the diaries completed up until this point) you will return to the study clinic for a meeting with your study doctor and study staff. Your compatibility to the study will be re-confirmed. This visit will take about 3 hours.

If you are a female and of child-bearing potential you will undergo a urine pregnancy test. The test must be negative for you to be in the study.

If the study doctor determines that you meet the inclusion criteria for this study, you will be randomized (like a flip of a coin) to one of the two study groups listed below:

- Vibrant Capsule
- Placebo Capsule

Randomization: You will be randomly assigned (by chance) into one of the two study groups in a 1:1 ratio. This means that you will have an equal chance of being placed in any group.

This is a double-blind study. This means that neither you nor the site's staff responsible for study assessments will know which capsule is administered to you. In the event of an emergency your study doctor can discover which group you are assigned to.

You will be instructed to swallow one (1) study capsule twice a week, every Monday and Thursday, preferably between 9-10 pm.

During this visit you will be trained by the site staff how to use the capsule and the base unit. Then, you will swallow the first capsule and complete a short questionnaire to confirm your understanding about key elements of the training.

All future capsules will be swallowed at home, following usage of the base unit **every Monday and Thursday between 9 to 10 pm**.

Important note: The base unit transmits information about capsule usage via Wi-Fi in real time. The data transmitted from the base unit is extremely reliable and will be used to monitor your compliance with the study capsule.

A Wi-Fi router will be provided to you during the baseline visit. You will be required to plug-in the router and the base unit at your home during the entire study, thereby ensuring that all data related to capsules' intake will be transmitted via Wi-Fi.

The study capsules will be dispensed to you during the baseline visit by the study nurse/coordinator. One base unit and one router will be dispensed as well. You will be required to continue completing the electronic diary on a daily basis regarding your capsule intake, your bowel movements as well as related clinical assessments and any medication taken (if applicable). Your compliance related to the electronic daily diary will be monitored throughout the entire study period.

4 weeks Visit (Day 28):

You will return to the study clinic on Day 28 (visit 3) for evaluation (this visit will take about 1 hour).

Please bring back to the study clinic all the remaining capsules in your possession (including the spare capsules given at the baseline visit). This is needed for accountability.

Before leaving the study clinic you will receive a new supply of study capsules, for the remaining 4 weeks of the treatment period.

8 weeks Visit (Day 56):

After 8 weeks of study capsule administration, you will return to the study clinic for evaluation of your clinical status and you will be asked to complete questionnaires regarding your constipation and trial participation. A thorough review of the electronic diary will be checked for completeness. This visit will take about 1 hour.

At this visit, you will be required to return the Wi-Fi router, the base unit and all remaining capsules still in your possession (including the spare capsules given at the 4 weeks visit).

During these 8 weeks, the study coordinator may call you to see how you are doing and if you have taken a rescue medication (a medication to help you have a bowel movement) which is allowed as described above.

Additionally, the study coordinator will call you if you do not complete your daily diary entries as this data is imperative for study success.

If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You cannot take part in more than one study without approval from the researchers involved in each study.

If I want to stop participating in the study, what should I do?

If you wish to stop your participation in this research study at any time and for any reason you should let the principal investigator/study coordinator know as soon as possible so that you can stop safely. You may be asked why you are leaving the study and your reasons for leaving may be kept as part of the study record.

Could the researchers take me out of the study even if I want to continue to participate?

The researchers could remove you from the study if:

- ✓ The researcher believes that it is not in your best interest to stay in the study.
- ✓ You become ineligible to participate.
- ✓ Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- ✓ You do not follow instructions from the researchers (e.g. non-compliance to the rescue medication rules or non-compliance to complete a daily diary).
- ✓ The study is suspended or canceled.

If you are taken out of active participation, ongoing follow-up may continue.

What happens if I get hurt, my condition worsens, or I have other problems as a result of this research?

If you are injured as a direct result of this study, contact the study doctor and medical care will be available at no cost to you or your insurance company. No long-term medical care or financial compensation for research-related injuries is planned to be provided by SF Research Institute. If you are injured as a result of this study, you do not waive (give up) your rights to pursue a claim through the legal system by signing this informed consent form.

What information about me could be seen by the researchers or by other people? Why? Who might see it? How will it be protected?

Release of Health Information – If you decide to participate in this study, information about your health may be used or disclosed (shared outside of the clinic) for the purposes of conducting this study. This information may include information from your medical record that is relevant to this study, such as your medical history, medications, test results, diagnoses, treatments, operative reports (reports from operations that you have undergone), and discharge summaries. It may also include information relating to: Human Immunodeficiency Virus ("HIV") infection or Acquired Immunodeficiency Syndrome ("AIDS"); treatment for or history of drug or alcohol abuse; or mental or behavioral health or psychiatric care. Information collected by the study doctor and/or research staff specifically for this study, such as test results, blood samples, physical examinations, information about possible side effects, and surveys you might be asked to complete could also be used or disclosed.

Individuals that may use or release this information include: physicians, physicians' office staff, hospital staff, the study doctor, and authorized members of the study doctor's research staff. These individuals may release this information to the study doctor, authorized members of the study doctor's staff, the Sponsor of the study *Vibrant Ltd* as well as its agents or contractors, other researchers, the Institutional Review Board (IRB), the United States Food and Drug Administration (FDA) and its representatives, and other government agencies.

In most cases, the information released to the above listed individuals or entities will not contain your name, social security number, or any other personal information. However, authorized representatives of your study doctor, IRB, FDA, or other government agencies may review records containing personal information to make sure that the study information is correct. Because of the need to provide information to these parties, absolute confidentiality cannot be guaranteed.

Use of Information – This information may be used to determine whether you meet all requirements for participation in the study, to monitor your healthcare during the study, to enable the sponsor to answer the scientific questions for which the study was designed, and to ensure that the study has been done properly. Examples of the use of this information are as follows: the sponsor may use the information in submissions to government agencies throughout the world, to request approval of the study device; the sponsor may use the information for reporting adverse events to government agencies, such as the FDA; the sponsor may also transfer the information to business partners or companies it hires to provide study-related services; the sponsor may also provide overall study results, including your information, to other study

doctors; and the sponsor may reanalyze the data from this study in the future or combine it with data from other studies for analysis. In addition, both the sponsor and the study doctor may use the information to prepare reports or publications of the study results. However, when results of the research study are reported in medical journals or at scientific meetings, the people who were in the study are not named and identified. Therefore, your name would not be disclosed in any presentation or publication.

Once your personal health information (PHI) has been released to someone other than Researchers, it may no longer be protected by US law relating to data privacy and could be used or re-disclosed in ways other than those listed in this section of the consent form.

You have the right to see and copy your medical records but information relating to this study may be withheld until the end of this study.

What happens to information about me after the study is over or if I cancel my permission?

If you stop participating in this study, you also have the right to revoke (withdraw) your authorization to disclose and use your information. Revoking your authorization means taking back the permission you gave the study doctor to send information about you to the sponsor and entities formally mentioned in this informed consent form. If you revoke your authorization, your study doctor will not use or release any further information about you after receiving your request, except to tell the sponsor that you have stopped early and have revoked your authorization. However, the sponsor and the study doctor can still keep and use any information that it has already been received to the extent necessary to preserve the integrity of the research study. To revoke this authorization, you must notify the study doctor in writing at the address listed on page 1 of this form.

When does my permission expire?

Your authorization to disclose and use this information will expire on December 31, 2069, unless revoked by you, in writing, as previously mentioned. Your study doctor may need to add to or correct information about you even after your study participation is over; including providing updates of your health status if that is important to the purpose of the study. The review of your medical records may also take place after the study is over. This authorization will remain in effect unless you revoke it.

Authorization – By signing this consent form, you authorize use and disclosure of personal information to, and review of your medical records by, the people and entities described above. You do not have to authorize this disclosure of information. However, if you do not, you will not be able to participate in this study.

What are my rights in this study?

Taking part in this study is your choice. No matter what decision you make, and even if your decision changes, there will be no penalty to you. You will not lose medical care or any legal rights.

For questions about your rights as a research participant, or if you have complaints, concerns, or questions about the research, please contact:

WCG IRB
1019 39th Avenue SE Suite 120
Puyallup, Washington 98374-2115
Telephone: 855-818-2289
E-mail: researchquestions@wcgirb.com

WCG IRB is a group of people who perform independent review of research.

WCG IRB will not be able to answer some study-specific questions, such as questions about appointment times. However, you may contact WCG IRB if the research staff cannot be reached or if you wish to talk to someone other than the research staff.

The research team will take proper precautions to ensure that any information regarding your identity obtained in connection with this research will remain confidential.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

Where can I get more information?

If you have any questions regarding your participation in this study, please ask us. If you have any additional questions, concerns, or complaints, or if at any time you feel you have had a research-related injury, please contact the researchers listed below:

Principal Investigator: Dr. Stanley Hui

Mailing Address: 2435 Ocean, Ave, San Francisco, CA 94127

Telephone: 415-745-4340 (24 hours)

Study Coordinator Office: SF Research Institute

Mailing Address: 2435 Ocean, Ave, San Francisco, CA 94127

Telephone: 415-745-4340tbs

Signatures

Study Participant

I have had ample time to read this consent form. I have discussed it with the study team and my questions have been answered to my satisfaction. I will be given a signed copy of this form for my records. I agree to take part in this study.

Signature: _____ **Date**:_____ **Time**:_____

Name (Print Legal Name): _____

Person Obtaining Consent:

I have given this research subject information about this study that I believe is accurate and complete. The subject has indicated that he or she understands the nature of the study and the risks and benefits of participating.

Name: _____ Title: _____

Signature: _____ Date:_____ Time:_____

AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR RESEARCH PURPOSES

What information may be used and given to others?
The study doctor will get your personal and medical information. For example:
- Past and present medical records
- Research records
- Records about phone calls made as part of this research
- Records about your study visits.

Who may use and give out information about you?
The study doctor and the study staff.

Who might get this information?
The sponsor of this research. "Sponsor" means any persons or companies that are:
- working for or with the sponsor, or
- owned by the sponsor.

Your information <u>may</u> be given to:
- The U.S. Food and Drug Administration (FDA),
- Department of Health and Human Services (DHHS) agencies,
- Governmental agencies in other countries,
- The institution where the research is being done,
- Governmental agencies to whom certain diseases (reportable diseases) must be reported, and
- Institutional Review Board (IRB).

Why will this information be used and/or given to others?
- To do the research,
- to study the results, and
- to make sure that the research was done right.

If the results of this study are made public, information that identifies you will not be used.

What if I decide not to give permission to use and give out my health information?
Then you will not be able to be in this research study.

May I review or copy my information?
Yes, but only after the research is over.

May I withdraw or revoke (cancel) my permission?
This permission will be good until December 31, 2070.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor. If you withdraw your permission, you will not be able to stay in this study.

When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

Is my health information protected after it has been given to others?
There is a risk that your information will be given to others without your permission.

Authorization:
I have been given the information about the use and disclosure of my health information for this research study. My questions have been answered.

I authorize the use and disclosure of my health information to the parties listed in the authorization section of this consent for the purposes described above.

AUTHORIZATION SIGNATURE:

Signature of Subject	**Date**