Clinical Trial Informed Consent Form

Protocol Title: English: (not mandatory, fill in according to trial conditions)Screening for stomach diseases and colorectal neoplasms with the fecal testing：a population-based randomized study	
Trial Institution: National Taiwan University Hospital	Sponsor/Pharmaceutical Company: Health Promotion Administration, Ministry of Health and Welfare
Title: Chiu, Han-Mo Chief/Attending Physician Title: Wu, Ming-Shiang Chief/Attending Physician Title: Lee, Yi-Chia/Attending Physician Title: Liang, Jin-Tung/Attending Physician Title: Chen , Chieh-Chang/Attending Physician Title: Chen, Meng-Kan/Attending Physician Title: Lai, Ho-Hsien/Attending Physician	Title: Yang, Kuen-Cheh/Attending Physician Title: Hsu, Wen-Feng/Attending Physician Title: Chang, Chi-Yang/Attending Physician Title: Chen, Li-Sheng/Attending Physician Title: Yen, Ming-Fang/Attending Physician Title: Chiu, Yueh-Hsia/Attending Physician
24-hour emergency contact person:Ou Mei-Yue	Telephone No.: +886-2-33668 Title: Chief/Attending Physician 707

You are being invited to participate in this clinical trial. This form provides information related to this trial. The principal investigator or his/her authorized staff will explain the content of this trial to you and answer any questions you may have. Please do not sign this consent form until all of your questions have been answered satisfactorily. You do not have to decide whether you will take part in this trial right away. Please consider carefully before you sign your name. You must sign the consent form to participate in this trial. If you are willing to participate in this trial, this document will be considered as the record of your consent. You can withdraw from the trial at any time without any reason, even after you have given consent. If you wish to withdraw from this trial, you should inform the institution in any possible way.

(I). Trial objective:

This trial is a Taiwan single center clinical trial. The primary endpoint of this trial is the detection of CRC. The secondary endpoints include FIT participation rate, FIT positivity rate, colonoscopy rate after positive FIT, and detection rates for advanced adenoma.

All treatments bear risk, and this clinical trial is not an exception. Please consider carefully before deciding whether to participate in this trial.

(II). Inclusion and exclusion criteria of the trial:

The physicians or relevant researchers of National Taiwan University Hospital who perform this research study will discuss with you the necessary conditions for participation in this research. Please cooperate with us and be honest with us about your past health condition. If you do not meet the requirements of this research, you may not be allowed to participate in this research study.

Inclusion criteria:

1. 50 to 75 years average-risk subjects for FIT

Exclusion criteria:

1. Subjects who are unwilling to participate
2. Subjects ineligible for colonoscopy (for the one-day vs two day FIT screening).

(III).Methods and related procedures of this trial

Growing body of evidences have shown that fecal immunochemical test (FIT) outperform guaiac fecal occult blood test (gFOBT) in terms of sensitivity, neoplasm detection rate and public participation. Though direct outcome evidence is still lacking for FIT, it is anticipated to have higher colorectal cancer (CRC) mortality and incidence reduction compared with gFOBT. In Taiwan, nation-wide CRC screening program has been launched since the year of 2004, which provides biennial FIT screening for adults aged 50 to 69 years. Currently available data from the Bureau of Health Promotion has shown a significant stage-shift effect, an early indicator of screening effectiveness, by this screening program.

Nevertheless, the aforementioned advantages of FIT, missed neoplasms and interval cancer still exists under the current one-day stool sampling method with biennial screening interval, which might affect the effectiveness of overall screening program. Increase the number of stool samples or shortening of screening interval may be helpful for early detection of clinically significant neoplasms but it remains unclear whether such an approach may lower the screenee compliance or public participation. Moreover, its impact on the demand of confirmatory colonoscopy and cost-effectiveness of the whole screening program is still largely unknown and need to be further investigated.

In this study, we firstly aim to randomly allocate screening attendee to one of the following four arms: one-day sampling with annual screening, one-day sampling with biennial screening, two-day sampling with annual screening, and two-day sampling with biennial screening. Participation rate, positive rates of FIT, detection rate for neoplasms, positive predictive value, and long-term outcome including cancer incidence and mortality will be calculated and compared among four groups.

Secondly, in the Taiwanese population, which is a typical presentation of Asian populations, although the incidence of colorectal cancer is rapidly increasing, Helicobacter pylori-related upper gastrointestinal pathologies remain highly prevalent, which may imply that mass screening solely based on FIT could be insufficient as significant upper GI pathologies can be missed. Since the FIT does not predict upper GI pathologies, the adjunct of an 'Helicobacter pylori stool-antigen test (HpSA)' may be a potential candidate to realize a pan-detecting assay based on stool samples in a population in which both lower and upper GI lesions are equally prevalent. Therefore, in the present study, we will also evaluate the value of simultaneous FIT and HpSA test in the community-based mass screening. We invited subjects in a randomized study to receive the FIT or the FIT plus HPSA. Those who are tested positive for HPSA will receive upper endoscopic examination and anti-H. pylori treatment. For the short-term indicators, we will evaluate the participation rate and diagnostic yield when the HPSA is added. For the long-term indicators, we will compare the incidence and mortality of gastric cancer as well as complicated peptic ulcers.

To summary, this study includes two randomized trials:

1. To make a comparison between one-day sampling with annual screening, one-day sampling with biennial screening, two-day sampling with annual screening, and two-day sampling with biennial screening using FIT;
2. To make a comparison between FIT plus HpSA and FIT alone for screening.

(IV) Possible side effects and their incidence and countermeasures:

The bowel preparation before a colonoscopy can be unpleasant. The test itself may be uncomfortable, but the sedative usually helps with this, and most people feel normal once the effects of the sedative wear off. Some people may have gas pains or cramping for a while after the test.

In some cases, people may have low blood pressure or changes in heart rhythms due to the sedation during the test, although these are rarely serious.

If a polyp is removed or a biopsy is done during the colonoscopy, you may notice some blood in your stool for a day or 2 after the test. Significant bleeding is slightly more likely with colonoscopy than with sigmoidoscopy, but it is still uncommon. In rare cases, continued bleeding might require treatment.

Colonoscopy is a safe procedure, but on rare occasions the colonoscope can puncture the wall of the colon or rectum. This is called a perforation. It can be a serious complication and may require surgical repair. Talk to your doctor about the risk of this complication.

If you experience any of these serious or dangerous side effects, you should take the following actions as soon as possible:

1. Call the 24-hour emergency contact person as soon as possible.
2. Go to the nearest emergency room if necessary.

(V) Alternative treatments and explanations

Fecal immunochemical test (FIT) outperform guaiac fecal occult blood test (gFOBT) in terms of sensitivity. You are not obliged to participate. If you do not participate in this research, you can receive routine treatment or other possible treatments including drug treatments or / and surgery, and past experience of the study drug usage in humans indicates that .

(VI) Anticipated trial benefits:

1. Two-day sampling can significantly increase the detection rate for advanced neoplasms and cost-effectiveness
2. Helicobacter pylori Ag test (Feces) is a simple test, followed by esophagogastroduodenoscopy provides the opportunities for early detection of major diseases such as chronic gastritis, peptic ulcer, precancerous lesions of gastric cancer, early gastritis and duodenal ulcer, etc. In addition, clearance of Helicobacter pylori Infection may lower the risk of future gastric diseases.

Even with the above information, participating in this trial does not guarantee improvement of your disease or bring you any other direct benefits. However, the trial research results may be helpful to the Sponsor and/or Principal Investigator and may also benefit other patients with the same disease in the future

(VII) Contraindications, restrictions and rules that must be abided by during the trial:

During the trial period, for your safety, we need your cooperation in the following matters:

-Provide correct information on your past medical history, medical records, and current medical condition.
-Do not give the study drug to other people. Keep the study drug in (method of storage: room temperature, refrigerated, etc.) and make sure children do not have access to it.
-Return the unused study drug and empty packaging of the tablet to us. (according to the trial protocol)
-For your safety, please return to the hospital for scheduled visits. If you are not able to come as scheduled, please contact the trial staff.
-Please fill out the diary timely to record your condition. (according to the trial protocol)
-For your safety, please inform the trial physician of any discomfort that you may experience.
-Do not take other medications, including over-the-counter drugs, Chinese medicine and health supplements. If you need to use other medications, please discuss it with your trial physician. (according to the trial protocol)
-If you have any questions, feel free to ask your trial staff (physician or nurse) directly.

(VIII) Confidentiality of subject's personal information：

National Taiwan University Hospital will abide by the law to keep the confidentiality of any record containing your identification and your personal private information, and will not disclose it. The research staff will assign you with a research code, and this code will not show any identifiable information such as your name, identification number or address. In the event that trial results are published, your identification will continue to be kept confidential. You also understand that by signing this consent form, you are approving direct use of your original medical records by the monitors, auditors, (the name of the hospital IRB) and the competent authorities, in order to ensure that the clinical trial is conducted and data are collected in accordance with applicable laws and regulations. The aforementioned personnel guarantee the confidentiality of your identity will not be violated. Except the aforementioned authorities inspection as required by law, we will carefully protect your privacy.

(IX) Withdrawal and termination of the trial

You are free to decide whether to take part in this trial. During the trial, you can withdraw your consent and leave the trial at any time, without giving any reason, and no unpleasantness will be caused, nor will your medical care from your physician be affected. For your safety, you must withdraw from the trial in case of the following conditions:

(please list all conditions for withdrawal)

During the course of the trial, you will be informed of important new information (i.e. information relating to your rights/benefits or that will affect your willingness to continue taking part in this trial/research), and provided you with further explanation. Please consider whether to continue taking part in the trial. You are free to make a decision and this decision will not cause any unpleasantness or affect your future medical care.

It is also possible that the Principal Investigator or the Trial Sponsor will terminate the clinical trial or your participation in the trial whenever necessary.

If you decide to withdraw from the trial, or if the Principal Investigator decides to terminate your participation in this trial, the data collected before your withdrawal will be preserved, and will not be deleted. After withdrawal, you may decide the handling method of the samples you previously provided, and decide whether to give consent to allow the Principal Investigator or Trial Sponsor to continue collecting your data.

1. For the samples that I have previously provided,

☐ I give my consent to authorize the trial to continue using the samples for research related to the trial disease. Another consent from me should be obtained if the scope of use exceeds this original informed written consent.

☐ I do not give my consent to authorize the trial to continue using the samples. However, to ensure the accuracy of the completed tests, I agree to allow the laboratory to destroy the trial-related samples after re-verification.

☐ I do not give my consent to authorize the trial to continue using the samples. Please destroy my trial-related samples on the day of my withdrawal.

2. The Principal Investigator or Trial Sponsor is authorized to continue collecting my data, e.g. accessing my medical records to obtain the follow-up medical procedures and lab test results. During the period of continuous data collection, your privacy and personal information will remain confidential.

☐I consent to collection

☐I do not consent to continuous collection or inspection of my data.

(X) Compensation and insurance:

All clinical trials have risks. To ensure the protection you may receive for damages resulting from the adverse events of participating in this trial, please be sure to read the content of this section:

1. National Taiwan University Hospital will jointly bear liabilities for compensation of damages caused by the adverse events resulting from following the protocol designed for this clinical trial . However, no compensation will be made with respect to the expected adverse events described in this Informed Consent

Form.

2. The hospital will provide professional medical care and consultations for adverse events or damages resulting from following the protocol designed for this clinical trial. You will not be responsible for the necessary medical expenses with respect to the treatment for the adverse events or damages.
3. This trial does not provide compensation in any form other than the compensation and the medical care set forth in above 2 points. If you do not accept this level of risk, please do not participate in the trial.
4. You will not lose any legal rights pursuant to your signing of this Informed Consent Form.
5. This trial is (or is not) insured against human research liability. (Note: The sponsor and trial institution can decide whether to specify matters related to insurance.)

If the damages are caused by the adverse events resulting from your participation in the trial, the compensation mentioned above includes reasonable medical expenses. However, the following requirements must be met: you follow the instructions given by your trial physician on using the study drug; your damage is not caused intentionally; you obey the medical recommendations given by your trial physician.

(XI) Storage, use and reuse of subject's samples (including their derivatives) and personal information

1. Storage and Use of Samples and Residual Samples

(1) Storage and use of samples (including their derivatives)

For the research, your samples collected by us will be used as indicated in the trial protocol and be stored in National Taiwan University Hospital (unit or lab; if the sample will be delivered to a foreign laboratory, please describe in detail the country, city, place and name of the institution where the lab is located). We will store your samples until year _15_, and we will destroy the samples in accordance with laws and regulations when the expiration date is due. To protect your privacy, we will replace your name and relevant personal information with a trial code in order to ensure your samples and relevant information are completely confidential. If you have any concerns about the use of the samples or you have any need to destroy the samples, please contact us immediately (Contact person:Yiru Chen Tel: +886-2-23123456 #65689, Contact unit: Department of Internal Medicine Address: No. 7, Chung-Shan South Road, Taipei, Taiwan), and we will destroy your samples..

All new research studies need to be reviewed and approved by the Institutional Review Board. If the Institutional Review Board determines the new research is has exceeded the scope of your consent, we will be required to obtain your consent again.

Do you give consent to store residual samples? Do you agree to provide your residual samples for ____ research in the future, and authorize the ___ Institutional Review Board to determine whether your additional consent is required?

☐ I do not consent to having my residual samples preserved. Please destroy them after the trial is completed.
☐ I give consent to preserve my residual samples by not de-linking. Another consent from me is required before my samples can be used to conduct new research if the usage has exceeded the scope of use.

(XII) Rights of the subject:

1. During the trial, if you have any questions about the nature of the trial or any concerns about your rights as a patient, or suspect that you have suffered injury as a result of participating in this research, please contact the (National Taiwan University IRB) to request for consultation. The telephone number is +886-2-23123456 ext. 63155.
2. During the trial, any significant findings that are related to your health or the disease and may affect your willingness to continue participating in the clinical trial will be provided to you in a timely manner. If you decide to withdraw, the physician will make arrangements for you so that you will continue to receive medical care. If you decide to continue participating in the trial, you may need to sign an updated version of the Consent Form.
3. You will receive care by Dr. __Chiu__ during the course of the clinical trial. If you have any questions or conditions now, or during the clinical trial, please do not hesitate to contact Dr. _Chiu__ at Department of Internal Medicine (24-hr contact number: +886-2-33668707).
4. This consent form is made in duplicate. The Principal Investigator or authorized staff has given you a

copy of the consent form and has fully explained the nature and purpose of this research. The physician has answered all your questions about the research.

(XIV) Signature:

1. The Principal Investigator/Sub-investigator or his/her authorized personnel has explained in detail the nature and objectives of the above research method in this protocol, as well as the possible risks and benefits.

   Signature of Principal Investigator/Sub-investigator:_____

   Date: _____(Month) _____(Day), _____(Year)

   Other research staff participating in the consenting process, including discussion and explanation:

   Date: _____(Month) _____(Day), _____(Year)
2. I fully understand the research method mentioned above and the possible risks and benefits after the explanation, and my questions about the clinical trial have been answered in full detail. I agree to participate in this research voluntarily and will hold a duplicate of the Informed Consent Form.

   Signature of the Subject Date: ____(Month)_____(Day), _____ (Year)

   Date of Birth: ____(Month)_____(Day), _____ (Year) Telephone No.:

   National ID Number: Gender:

   Correspondence Address:

   Signature of the Legal Representative, Person who Has Right to Give Consent: Date: ____(Month)_____(Day), ____ (Year)

   Relationship with the Subject:

   Correspondence Address: Telephone No.:

* For those that the proviso of paragraph 1 of Article 79 of the Medical Care Act or the proviso of paragraph 1 of Article 12 of the Human Subjects Research Act applies to, exercising their right to give consent should be in accordance with paragraph 2 of Article 79 of the Medical Care Act, Article 5 of the Regulations on Human Trials, or paragraphs 3 and 4 of Article12 of the Human Subjects Research Act.

Signature of the Witness:_____ Date: ____(Month)_____(Day), ____ (Year)

* In the event that none of the subject, legal representative or the person who has right to give consent can read, a witness shall be present during every discussion of subject's consent. The witness shall confirm that the consent given by the subject, legal representative or person who has right to give consent is of voluntary nature before signing and dating the Informed Consent Form. The trial staff shall not be a witness.