INSTITUTO NACIONAL DE CIENCIAS MEDICAS Y NUTRICION SALVADOR ZUBIRAN

INFORMED CONSENT

INFORMED CONSENT LETTER TO PARTICIPATE IN THE PROJECT:

Validation of advanced colorectal neoplasm risk categories in screening colonoscopy and identification of biomarkers in a prospective cohort in Mexico.
Version 3, March 12, 2020.

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INTRODUCTION:

This document is an invitation to participate in an Institut's research study. Please take all the needed time to read this document; ask the investigator any doubt that you may have.

Procedure to give your consent: You have the right to decide whether you want to participate or not as a subject of investigation in this protocol. The investigator ought to fully explain the benefits and risks of the project without any type of pressure and **you will have all the needed time to think, alone or with whom you decide to consult, before deciding if you want to participate.** Whichever, your decision will not have any effect on your medical attention in the Institute.

In order to make a truly informed decision about whether or not you agree to participate in this study, you should have enough knowledge about the possible risks and health benefits of participating. This document will give you detailed information about the research study, which you may discuss with whoever you want, for example, a family member, your treating physician, the main investigator of this study, or a member of the investigators. Finally, once you have read and understood this information, you will be invited to take part in the project and if you accept, without any pressure or intimidation, will be invited to sign this informed consent.

This informed consent complies with the guidelines established in the Regulation of the General Health Law on Research for Health, the Helsinki Declaration, and to the Good Clinical Practices issued by the National Bioethics Commission.

At the end of the explanation, you must understand the following points:

I. The justification and objectives of the investigation.
II. The procedures to be used and their purpose, including the identification of the experimental procedures.
III. The anticipated risks or inconveniences.
IV. The benefits that can be observed.
V. Alternative procedures that may be advantageous to you
VI. Guarantee to receive answers to questions and clarify any doubts about the procedures, risks, benefits, and other matters related to research and treatment.
VII. The freedom you have to withdraw your consent at any time and stop participating in the study, without affecting the medical care and treatment at the Institute.
VIII. The certainty that you will not be identified in a particular way and that the confidentiality of information relating to your privacy will be kept.
IX. The investigator's commitment to provide updated information that may be obtained during the study, although this may affect your willingness to continue with your participation.
X. The availability of medical treatment and compensation to which you are legally entitled, in the event of damage caused directly by the investigation.

You can ask for more time or take this form home before making a final decision in future days.

INVITATION TO PARTICIPATE AS A SUBJECT OF RESEARCH AND PROJECT'S DESCRIPTION

Dear Mr(s) _____-

The Instituto Nacional de Ciencias Médicas y Nutrición Salvador Zubirán (INCMNSZ), through the research group in gastrointestinal tumors, invites you to participate as a research subject in this study which has as objective: "To prove that it is possible to identify people who have more or less risk of developing colorectal cancer through the application of a simple questionnaire. The ultimate goal of this study is to direct efforts for the early detection and prevention of colon and rectal cancer in this subgroup of patients. At the same time, the study will help to define which is the best way to perform timely detection of this cancer in our population: by colonoscopy or by detection of occult blood in feces (by the Fecal Inmunochemical Test known as FIT). Finally, blood and urine samples will be taken and stored to search at a later time for abnormalities in the genes or proteins in the blood or urine that allow the non-invasive identification of patients at risk of colon and rectal cancer. Blood and urine samples will be taken on a single occasion for each subject. These samples can be stored for up to a period of 15 years.

The total duration of this study is 36 months.

Your participation in the study will have a duration of approximately 1 month.

The approximate number of participants will be 2000.

You were invited to participate in this study because you are eligible for early detection and prevention of colorectal cancer based on the fulfillment of the following characteristics: man or woman between 50 and 75 years of age, WITHOUT symptoms suggestive of colon and rectal cancer such as blood in stools or unintentional weight loss, no personal history of colorectal cancer, or inflammatory bowel disease (Crohn's disease or UC) and have no previous studies of colon cancer screening in recent years.

STUDY PROCEDURES

Your participation in the study consists of two medical interviews, a screening colonoscopy and a fecal occult blood test (FIT). Optionally you can participate in the collection of tissue, blood, and urine samples for future biomedical research. In the first interview, you will be given a questionnaire to assess whether you can participate in the study. If you meet the requirements to participate, you will receive standardized information on colorectal cancer screening. If you agree to participate in the study, an informed consent will be given to you and a FIT will be scheduled. The day you attend to leave the stool test, a questionnaire about risk factors for colorectal cancer will be performed. During this interview, optionally, a 15 ml blood sample and a 5 ml urine sample will be taken and a screening colonoscopy will be programmed. The screening colonoscopy will be scheduled in the course of the following month after you deliver the stool test. In a second interview, you will be informed of the results of the tests carried out and recommendations will be provided based on the test findings.

The study procedures include:

1. A first interview in which a brief questionnaire will be performed in order to know if you accomplish the requirements to participate in this study. In case of requirements fulfillment, you will receive standardized information about the early detection (screening) of colorectal cancer. Afterward, if you accept to participate, an informed consent will be delivered and explained and a FIT will be programmed.
2. On the day the FIT is scheduled you will submit a stool sample to the Institute’s laboratory. In addition, during this visit you will answer a questionnaire that includes your name, telephone number, age, gender, family history of colorectal cancer, smoking, height, weight, presence or absence of diabetes, menopausal status, hormone intake, questions about your dietary and physical activity habits. The answering of this questionnaire takes approximately 20 minutes. During this visit, at the end of the interview, if you accept, a venous blood sample of 15 ml will be drawn and you will be given material to collect 20 ml of urine. The blood sample consists of the puncture and extraction of blood from a vein. A colonoscopy will be scheduled and you will be explained how to prepare for the test.
3. The screening colonoscopy consist of the insertion of a colonoscope (flexible tube) through the anal opening and advance it throughout the colon to visualize and,if necessary, take biopsies. To perform a colonoscopy, the intestine ought to be clean of fecal debris. This requires a preparation of the colon by the oral intake of laxatives. These substances are administered the previous day of performing the test and produce abundant diarrhea, which result in the cleansing of the colon. This study is

performed under sedation, i.e; the patient is asleep, NOT anesthetized, and does not feel any discomfort during the study. In case of identifying any lesions during the colonoscopy, a biopsy will be taken to establish a diagnosis.

4. Second interview: in which the results of the performed tests will be discussed and according recommendations will be given. In case of accepting the screening procedures and not having them done, a second interview will be made to complete a questionnaire on rejections reasons. You may be contacted by telephone to give follow-up of the performed tests.

Note: the collection of biological samples to use in future biomedical research is optional. At the end of this document, you will define whether you will participate or not in the collection of these samples. In case of acceptance, 15 mL of blood and 20 mL of urine will be obtained and stored.

The tissue samples to be used will be those that have been taken for diagnostic purposes during the colonoscopy. Additional biopsies not required for your medical care will not be taken. Your samples will be used as long as they are not already required to establish a diagnosis.

The biological samples obtained will be stored for up to 15 years after the end of this study.

The samples may be used to identify colorectal cancer risk biomarkers. Different scientific methodologies may be used for this purpose: genomics, transcriptomics, proteomics. This could involve collaboration with different investigators, institutions, sponsors and laboratories, both nationally and internationally. Each possible biomarker to be investigated in the future will be reported to the ethics committee and biological samples will only be used with prior approval by the ethics committee.

The biological samples obtained will not be used to develop permanent or immortal cell lines.

Experimental interventions do not exist.

The responsibilities of the participants include: performing the colonoscopy and fecal occult blood test, if not done, accepting to answer a questionnaire informing the reasons for this decision.

RISKS AND INCONVENIENTS

Both colonoscopy and FIT are tools recommended by different medical associations for the timely detection of colorectal cancer in adults over 50 years of age.

For blood samples, the blood draw may cause mild to moderate pain when the needle is inserted. Some people may experience dizziness or fainting. The staff that will take the sample is well trained to do it.

There are no risks in obtaining the stool and urine samples.

On the other hand, the risks associated with performing a colonoscopy include:

1. During the preparation with laxatives you may feel bothered by the diarrhea that will be triggered.
2. A venous catheter will be introduced for the administration of medications and fluids, this procedure can cause pain and a bruise at the puncture site.
3. During sedation, you may have an allergic reaction to it, and cardiac arrhythmias may also occur. Both complications are rare.
4. During the colonoscopy, you may feel abdominal discomfort or the need to defecate. There is a minimal risk of perforation from the colonoscope. Perforation has been reported in 1 in 1,000 or 1 in 10,000 colonoscopies. If a suspicious lesion such as a polyp or tumor is identified, a biopsy will be taken. After the biopsy, you can see traces of blood in the stool for a few days. In the hours after the procedure you will feel drowsy, you may not remember the procedure. You may feel swollen in the abdomen and increase gas expulsion.

The staff that will perform the colonoscopy is trained to do so, which will minimize the risks of complications.

The data about your identity and your medical information will not be revealed at any time as stipulated by law, therefore, in the collection of clinical data you do not face greater risks than those related to the protection of confidentiality, which will be protected by coding samples and their information.

POTENTIAL BENEFITS

Both colonoscopy and FIT are tools recommended by different medical associations for the timely detection of colorectal cancer in healthy adults over 50 years of age. People who do any of these strategies decrease their risk of death from colon and rectal cancer. You will receive the benefit of performing both studies for free, in addition, according to the results of the tests, you will receive the pertinent recommendations that you shall follow.

ECONOMICAL CONSIDERATIONS

No fee will be charged for participating in the study and no payment will be made to you. The investigator will cover the costs of the FIT, the colonoscopy and, if required, the biopsy.

COMPENSATION

If any complications arise as a direct result of your participation in this study, we will provide you with immediate treatment and refer you, if warranted, to the required medical specialist, as per the protocol. Hospitalization expenses will not be paid in case of any

complication since both tests (colonoscopy and FIT) are recommended as conventional screening.

ALTERNATIVES TO YOUR PARTICIPATION

Your participation is voluntary. You can choose not to participate in the study. If you decide not to participate, in case you are patient, you will continue to receive medical care at the institute. Usual recommendations for colorectal screening that consist of annual fecal occult blood test, or sigmoidoscopy every 5 years, or virtual colonography every 5 years, or colonoscopy every 10 years will be given to you.

POSSIBLE COMMERCIAL PRODUCTS DERIVED FROM THE STUDY:

The results or materials obtained from this study will be the property of the INCMNSZ. If a commercial product is developed as a result of the study, such input will be the property of the Institute or the laboratory that develops it. In such a case, you will not receive a financial benefit for it. The Institute and/or the sponsors do not plan to provide you, now or in the future, with any compensation, royalty, or any other financial benefit derived from any product, procedure, or other item that may be developed from studying your samples or from any information or data derived from said investigation.

ACTIONS TO FOLLOW AFTER THE TERM OF THE STUDY

You can request the results of your clinical tests and the conclusions of the study to Dr. Fidel David Huitzil Meléndez of INCMNSZ (tel. +52 54-87-09-00, Ext. 2254).

PARTICIPATION AND WITHDRAWAL FROM THE STUDY

Remember that your participation is VOLUNTARY. If you decide not to participate, both your regular relationship with the INCMNSZ (in case being patient) and your right to receive medical attention or any service to which you are entitled will not be affected. If you decide to participate, you are free to withdraw your consent and discontinue your participation at any time without jeopardizing your attendance at the INCMNSZ (if you are patient from this institution). You will be informed with time if new information becomes available that may affect your decision to continue in the study.

The study investigator may exclude you from the study if the colonoscopy is not performed. Procedures that will be necessary if the investigator or sponsor withdraws you from the study include completing a questionnaire about the reasons why the colonoscopy was not performed.

The study may be terminated prematurely if the study budget is exhausted.

You do not require any additional procedure at the end of your participation in the study.

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CONFIDENTIALITY AND MANAGEMENT OF YOUR INFORMATION

Your name will not be used in any of the public reports of the study. The biological samples obtained will not contain any personal information and will be coded with a serial number to avoid any possibility of identification. The codes that identify your sample will only be available to the main investigators, who are required by law not to disclose their identity. These codes will be kept in a locked file cabinet. Only investigators will have access to them. Study staff (monitors or auditors) may have access to participant information.

While there is a possibility that your privacy may be affected as a result of your participation in the study, your confidentiality will be protected as required by law by assigning codes to your information. The code is an identification number that does not include personal data.

No information about you will be shared with others without your permission, except:
- If necessary to protect your rights and welfare (for example, if you have been injured and require emergency treatment); or
- It is required by law.

If you decide to withdraw from the study, you may request the withdrawal and destruction of your information and biological samples. All the data collection sheets will be kept with the same confidentiality measures, and only the main investigators will have access to the data they collect which have your name. If you wish, you should contact Dr. Fidel David Huitzil Meléndez and express your written decision.

The Research Ethics Committee of the INCMNSZ approved the conduct of this study. This committee is the one who reviews, approves and supervises research studies in humans at the Institute. In the future, if we identify information that we believe is important to your health, we will consult with the Research Ethics Committee to decide the best way to give this information to you and your doctor. In addition, we ask you to authorize us to contact you, if necessary, to request information that could be relevant for the development of this project.

The scientific data obtained as part of this study may be used in medical publications or presentations. Your name and other personal information will be removed before the data is used.

If you request it, your general physician will be informed about your participation in the study.

IDENTIFICATION OF INVESTIGATORS:

In case you suffer an injury related to the study, please contact Dr. Fidel David Huitzil Meléndez at INCMNSZ (phone: +52 54-87-09-00, Ext. 2254).

If you have questions about the study, you can contact Dr. Fidel David Huitzil Meléndez at INCMNSZ (phone: +52 54-87-09-00, Ext. 2254).

If you have questions about your rights as a study participant, you can talk to the President of the Research Ethics Committee of the INCMNSZ ([Dr. Arturo Galindo Fraga], telephone: +52 54 87 09 00 ext. 6101).

DECLARATION OF INFORMED CONSENT

I have carefully read this informed consent, I have asked all the questions that I have had and all have been answered satisfactorily. In order to participate in the study, I agree with all of the following points:
I agree to participate in the study described above. The general objectives, particulars of recruitment and the possible damages and inconveniences have been explained to me to my entire satisfaction.
I agree to voluntarily donate my biological samples (blood, stool and urine) to be used in this study. Likewise, my medical and biological information may be used for the same purposes.
I agree, if necessary, to be contacted in the future if the project requires collecting additional information or if they find information relevant to my health.
My signature also indicates that I have received a duplicate of this informed consent.

Please answer the following questions:

		YES (please mark)	**NO (please mark)**
a.	Have you read and understood the informed consent form in your native language?	□	□
b.	Have you have the opportunity to ask questions and discuss this study?	□	□
c.	Have you received satisfactory answers to all your questions?	□	□
d.	Have you received enough information about the study and have enough time to make your decision?	□	□
e.	Do you understand that your participation is voluntary and that you are free to withdraw your participation in this study at any time without having to justify your decision and without affecting your medical care or loss of benefits to which you are otherwise entitled?	□	□
f.	Do you understand the possible risks of participating in this study?	□	□
g.	Do you understand that you may not receive any direct benefit from participating in this study?	□	□
h.	Do you understand that you are not giving up any of your otherwise entitled legal rights as a subject in a research study?	□	□

		YES (please mark)	NO (please mark)
i.	Do you understand that the study physician may withdraw you from the study without your consent, either because you did not follow the study requirements or if the physician participating in the study believes that your retirement is medically in your best interest?	□	□
j.	Do you understand that you will receive a signed and dated original of this Consent Form for your personal records?	□	□
K.	I wish to participate in the collection of blood and urine samples for future biomedical research	□	□

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Patient's declaration: I,

_____

declare that it is my own decision to participate as a clinical research subject in this study. My participation is voluntary.

I have been informed that I may refuse to participate or terminate my participation in the study at any time without penalty or loss of benefits. If I discontinue my participation, I will receive the usual medical care to which I am entitled at the Instituto Nacional de Ciencias Médicas y Nutrición: Salvador Zubirán (INCMNSZ) (in case being patient) and I will not suffer prejudice in my medical care or in future research studies. I may request additional information about the potential risks or benefits of my participation in this study.
I can also get the results of my clinical tests if I request them.
If I have questions about the study, I can contact Dr. Fidel David Huitzil Melendez, tel. +52 54-87-09-00, Ext. 2254.

I must inform the investigators of any changes in my health status (for example, use of new medications, changes in tobacco use) or in the city where I live, as soon as possible.

I have read and understand all the information given to me about my participation in the study.
I have had the opportunity to discuss it and ask questions. All questions have been answered to my satisfaction. I understand that I will receive a signed copy of this informed consent.
I understand that if I have questions about my rights as a clinical research subject in this study, problems, concerns, or worries, and would like additional information or comments

about the conduct of the study, I am free to speak with the President of the Research Ethics Committee of the INCMNSZ ([Dr. Arturo Galindo Fraga], tel: +52 54870900. ext. 6101).

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Name of the participant	Signature of the participant

Date

Place the participant's fingerprint on this line
if they do not know how to write

Name of the legal representant (if it applies)	Signature of the legal representant

Date

Name of the Investigator that explained the document	Signature of the Investigator

Date

Name of Witness 1	Signature of Witness 1

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Date	Relationship with the participant

Adress:

Name of Witness 2	Signature of Witness 2

Date	Relationship with the participant

Adress:

Place and date: _____

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