INSTITUTO NACIONAL DE CIENCIAS MEDICAS Y NUTRICION SALVADOR ZUBIRAN

INFORMED CONSENT TO PARTICIPATE IN THE PROJECT:

"EFFECT ON GLUCEMICAL VARIABILITY, WEIGHT, OXIDATIVE STRESS MARKERS FGF21 OF A THREE-FOOD HYPOCALORIC FOOD TIME REGIME COMPARED TO A CONVENTIONAL HYPOCALORIC PLAN OF SIX TIMES WITH DENBITED DIABETTE DIABETY

VERSION 6 (APRIL 3, 2019)

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Researcher's contact phone number (including one for 24-hour emergencies): 54870900 (2405). Cell: 044 5527614851
Participating researchers: MAE María Guadalupe López Carrasco, LN Iliana Manjarrez Martínez, Valerie Vargas Abonce, Mariana Romero Ortiz, LIc Verónica Rubio Franco Héctor Donaldo Espinosa Salazar, L.N. Mariana Galindo Guzmán, Dr. Daniel Cuevas Ramos, Dr. Francisco J. Gómez Pérez, Dr. Alfonso Gulias Herrero, Lucía Palacios Báez, Issa Lill Santiago Falfán, Francisco Javier Álvarez Sánchez.
Name of study sponsor: None
Sponsor Address:
Informed consent version and date of preparation: Version 6, april 3, 2019.

INTRODUCTION:

This document is an invitation to participate in a research study of the Institute. Please take as much time as necessary to read this document; Ask the investigator about any questions you have.
Procedure to give your consent. You have the right to decide whether or not you want to participate as a research subject in this project. The researcher must explain to you the benefits and risks of the project without any pressure and you will have all the time you need to think, alone or with whom you decide to consult, before deciding if you agree to participate. Whatever your decision will have no effect on your medical care at the Institute.
In order to make a truly informed decision about whether or not you agree to participate in this study, you must have sufficient knowledge about the possible risks and benefits to your health when participating. This document will give you detailed information about the research study, which you can comment on whoever you want, for example a family member, your treating physician, the principal investigator of this study or with a member of the research team. In the end, once this information is read and understood, you will be invited to be part of the project and if you accept, without any pressure or intimidation, you will be invited to sign this informed consent.
This informed consent complies with the guidelines established in the Regulations of the General Health Law on Research for Health, the Declaration of Helsinki, and Good Clinical Practices issued by the National Bioethics Commission.

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

I. The justification and the objectives of the investigation.

II. The procedures to be used and their purpose, including the identification of what are experimental procedures.
III. The expected 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 the questions and clarify any doubts about the procedures, risks, benefits and other matters related to the investigation and treatment of the matter.
VII. The freedom you have to withdraw your consent at any time and stop participating in the study, without affecting your attention and treatment at the Institute.
VIII. The assurance that you will not be identified in a particular way and that the confidentiality of information regarding your privacy will be maintained.
IX. The researcher's commitment to provide you with the updated information that can be obtained during the study, although this could 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 request more time or take this form home before making a final decision on future days.

INVITATION TO PARTICIPATE AS A SUBJECT OF RESEARCH AND DESCRIPTION OF THE PROJECT.

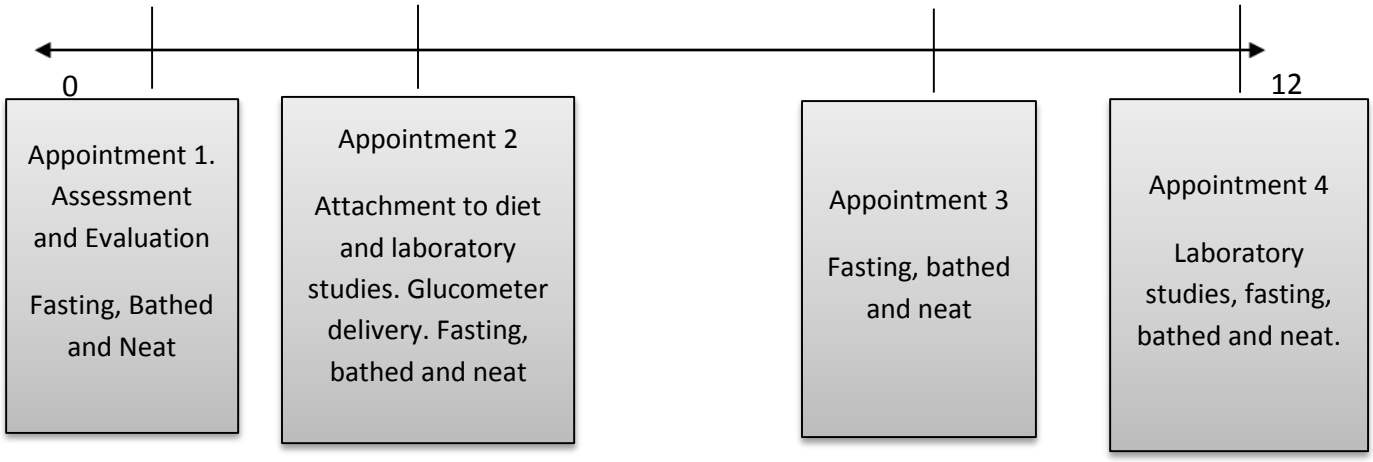
Dear Mr. _____

Instituto Nacional de Ciencias Mèdicas y Nutriciòn Salvador Zubiràn (INCMNSZ), through the research group, invites you to participate as a research subject in this study that aims to: Compare the impact on glycemic variability and weight loss of a three-stroke hypocaloric diet (TC3) and a conventional six-stroke hypocaloric plan (TC6) in patients with DM2 and overweight or obesity.
The total duration of the study is: One Year.
Your participation in the study will last: 12 weeks.
The approximate number of participants will be: 50 patients.
You were invited to the study because it has the following characteristics: Type 2 Diabetes Mellitus, Overweight or Obesity, between 40 and 70 years of age, oral hypoglycemic treatment, HbA1c less than 9% and less than 10 years of disease progression.
STUDY PROCEDURES
50 patients with DM2 will be recruited from the Institute's Diabetes clinic who are overweight or obese and who are between 40 and 70 years old and who are with oral hypoglycemic agents, with an HbA1c less than 9% and who are less than 10 years old of evolution
Clinical evaluation
A complete medical history and physical examination will be performed in order to confirm the presence of the inclusion criteria and rule out the presence of exclusion criteria. An anthropometric evaluation and body composition (waist and hip circumference, height, weight and percentage of fat) will be made, as well as blood pressure measurement. An interrogation will be conducted to document a history of

coronary heart disease, menopausal status and use of hormonal therapy, smoking, alcohol consumption and physical activity (through a validated physical activity questionnaire in the Mexican population).
The procedures performed during your participation in the study will be:
You will be subjected to a regime with calorie restriction of 15% of your usual daily intake. It will be raffled if a regime with only 3 meal times or a 6 meal schedule will be played. The period during which you must follow the diet is 12 weeks.
During the study, several blood studies will be done, which are: Lipid Profile, Glucose, Insulin, FGF-21. Also measured: Weight, Size, Waist, Hip, Blood Pressure.

The procedure will be as follows:
You will be summoned to a first evaluation consultation where you will develop a medical history with complete physical examination in which vital signs, neck and head examination, chest and abdomen examination, upper and lower limb examination will be measured. As well as a complete nutritional evaluation that includes, anthropometric evaluation by segments using dry-label tape measure, plicometer and dry-label anthropoment; Body composition assessment using OMRON brand 512 impedance, 72hrs food consumption reminder to collect information about your diet. Based on the information collected, the individualized meal plan will be prescribed and a food reminder format will be delivered in 24 hours for 7 days to be filled out by you for a week, in addition to giving you the indication to perform a blood glucose measurement at home. once a day in random scheme. To this appointment you must go on a fast, bathed and neat.

To assess the adherence to the nutritional plan, you will be summoned 15 days later to make a daily consumption assessment using the 24/7 reminder format filled out by you and a 72hrs reminder made through an interview. Likewise, their levels of Hunger-Satiety will be measured with some tables of the Joslin Institute validated for the Mexican population. If you adhere to the diet you will proceed to perform blood samples for the measurement of Glycosylated Hemoglobin, Glucose, Lipid Profile, Insulin, FGF-21 and after this you will be asked to perform a constant capillary glucose monitoring, 3 times per day for 7 days and you will be given the form for the registration of glucoses. At the end of 7 days, the patient will be summoned to review their monitoring and re-evaluate the diet.
The meal plan will continue for 6 weeks, and at the end of this period you will be summoned to re-perform blood samples to measure HbA1C, Glucose, Lipid Profile, Insulin, FGF-21, Weight, Blood Pressure and Hunger levels. Satiety. To this appointment you must go on a fast, bathed and neat.



The study procedures include: Laboratory and cabinet studies (HbA1c, Fasting blood glucose, Lipid profile, FGF21), through blood samples, Anthropometric measurement (weight, height, BMI, Hip Circumference, Waist Circumference and body composition) using a Seca brand measuring tape, a Seca brand plyometer and an OMRON 512 impedance.
The interventions included in the study that are part of your usual (standard) treatment required for your condition are: Fasting Blood Glucose and Continuous Glucose Monitoring.
Participants' responsibilities include: Sticking as much as possible to the diet. Attend punctual appointments. Take care of the material used to carry out the protocol. Report any change in your health status in a timely manner. Report any changes in contact information. Give correct, concrete and accurate information.

RISKS AND DISADVANTAGES

The Regulation of the General Law of Health in Research Matters for Health, states that obtaining biological samples represents a minimum risk within the investigation. The risks of blood sampling are: possibility of slight bleeding or bruising at the puncture site, dizziness or fainting, and rarely arterial puncture can occur. The personnel that will extract the blood sample is trained for this, which will minimize the risks of complications.

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

POTENTIAL BENEFITS

-Weight reduction.
-Improvement in glycemic control reflected by fasting glucose and glycosylated hemoglobin.
-Better lipid control.
-Best quality of life.
-Continuous monitoring of your condition.

ECONOMIC CONSIDERATIONS

No fee will be charged for participating in the study and no payment will be made.
Being part of the medical care required for your condition, outside of this study, the costs caused by the following items will be covered by you: Medications, Test strips for glucose measurement, glucometer, medical consultations and analysis or studies not required by the study.

COMPENSATION

If a complication arises as a direct result of your participation in this study, we will provide you with the immediate treatment by the protocol and will refer you, if necessary, to the medical specialist you require.

ALTERNATIVES TO YOUR PARTICIPATION:
Your participation is voluntary. So you can choose not to participate in the study.

POSSIBLE COMMERCIAL PRODUCTS DERIVABLE FROM THE STUDY:
The results or materials obtained in the study will be property of INCMNSZ. If a commercial product is developed as a result of the study, such input will be the property of the Institute or who they designate. In that case, you will not receive a financial benefit for it.

ACTIONS TO FOLLOW AFTER THE TERM OF THE STUDY:
You can request the results of your clinical exams and the conclusions of the study from Dr. Miguel A. Gómez Sámano of INCMNSZ (tel. 54870900 (2405)). Research is a long and complex process. Obtaining the final results of the project can take several months.

PARTICIPATION AND WITHDRAWAL OF THE STUDY:
Remember that your participation is VOLUNTARY. If you decide not to participate, both your usual relationship with INCMNSZ and your right to receive medical care or any service to which you are entitled will not be affected. If you decide to participate, you have the freedom to withdraw your consent and interrupt your participation at any time without harming your attention at INCMNSZ. You will be informed in time if new information is obtained that may affect your decision to continue the study.
The researcher or the sponsor of the study can exclude it from the study if the guidelines set forth in the section “The responsibilities of the participants” are definitely not fulfilled. The procedures that will be necessary if the investigator or the sponsor withdraws it from the study are: Signature of protocol exclusion for non-compliance of the participant's responsibilities.

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 encoded with a serial number to avoid any possibility of identification. By legal provision, biological samples, including blood, are classified as bio-infectious hazardous waste and for this reason during the course of the investigation your sample cannot be returned. It is possible that their biological samples, as well as their medical and / or genetic information, may be used for other similar research projects related to the disease being studied. They may not be used for research studies that are related to conditions other than those studied in this project, and these studies must be submitted for approval by an Ethics Committee.

Your samples may be stored by researchers for up to 5 years.

The codes that identify your sample will only be available to the regular investigators, who are required by law not to disclose their identity. These codes will be stored in a locked file cabinet. Only researchers

will have access to them. The study staff (monitors or auditors) may have access to the information of the participants.

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 established by law, assigning codes to your information. The code is an identification number that does not include personal data. No information about your person will be shared with others without your authorization, except:

- If necessary to protect your rights and well-being (for example, if you have suffered an injury and require emergency treatment); or
- It is requested by law.

If you decide to withdraw from the study, you may request the removal and destruction of your biological material and your information. All data collection sheets will be kept with the same confidentiality measures, and only incumbent researchers will have access to the data that has their name. If you wish, you should contact Dr. Miguel Ángel Gómez Sámano and express your decision in writing.

The Research Ethics Committee of INCMNSZ approved the completion of this study. This committee is the one who reviews, approves and supervises human research studies at the Institute. In the future, if we identify information that we consider important for 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 that you 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 could be used in publications or medical presentations. Your name and other personal information will be deleted before using the data.

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

IDENTIFICATION OF RESEARCHERS:

In case you suffer damage related to the study, please contact Dr. Miguel Ángel Gómez Sámano at INCMNSZ (telephone: 54870900 (2405)). Cell 0445527614851

If you have questions about the study, you can contact Dr. Miguel Ángel Gómez Sámano at INCMNSZ (phone: 54870900 (2405)). Cell 0445527614851.

If you have questions about your rights as a participant in the study, you can speak with the president of the Research Ethics Committee of INCMNSZ (Dr. Arturo Galindo Fraga. Telephone: 54870900 ext. 6101).

DECLARATION OF INFORMED CONSENT

I have carefully read this informed consent, I have asked all the questions I have had and all have been answered satisfactorily. In order to participate in the study, I agree with all the following points:

• I agree to participate in the study described above. The general objectives, particular to recruitment and possible damages and inconveniences have been explained to my satisfaction.
• I agree to voluntarily donate my biological samples (blood and urine samples) 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**	**NO**
Have you read and understood the informed consent form, in your mother tongue?	☐	☐
Have you had the opportunity to ask questions and discuss this study?	☐	☐
Have you received satisfactory answers to all your questions?	☐	☐
Have you received enough information about the study and had enough time to make the decision?	☐	☐
Do you understand that your participation is voluntary and that you are free to suspend your participation in this study at any time without having to justify your decision and without this affecting your medical care or without losing the benefits to which you otherwise have law?	☐	☐
Do you authorize access to your medical records for this research study and for regulatory purposes to Miguel Ángel Gómez Sámano, his representatives, the auditors, regulatory offices of the study, other government health agencies in Mexico and possibly other government agencies of the health in other countries where the drug under study can be considered for approval of its commercialization?	☐	☐

	YES	NO
Do you understand the possible risks, some of which are still unknown, of participating in this study?	☐	☐
Do you understand that you may not receive any direct benefit from participating in this study?	☐	☐
Do you understand that you are not giving up any of your legal rights that you are otherwise entitled to as a subject in a research study?	☐	☐
Do you understand that the doctor participating in the study can withdraw it without your consent, either because you did not follow the study requirements or if the doctor participating in the study considers that your withdrawal is medically in your best interest?	☐	☐
Do you understand that the study can be suspended by the study sponsor at any time?	☐	☐
Do you understand that you will receive a signed and dated original of this Consent Form for your personal records?	☐	☐

Patient statement: I, _____ declare that it is my decision to participate as a subject of clinical research in the study. My participation is voluntary.

I have been informed that I can refuse to participate or terminate my participation at any time during the study without suffering any penalty or loss of benefits. If I suspend my participation, my medical care will not be affected even in future research studies. I may request additional information about the potential risks or benefits arising from my participation in this study. I can also get the results of my clinical exams if I request them.
If I have questions about the study, I can contact Dr. Miguel Ángel Gómez Sámano tel. 5527614851

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

I have read and understood all the information they have given 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 am clear that if I have questions about my rights as a subject of clinical research in this study, problems, concerns or doubts, and I wish to obtain additional information, or comment on the development of the study, I am free to speak with the Chairman of the Research Ethics Committee of INCMNSZ ([Arturo Galindo Fraga, telephone: 54870900 ext. 6101)

_____ _____

Name of Participant Signature of Participant

_____

Date

_____

Place the participant's fingerprint on this line if you cannot write

_____ _____

Name of legal representative (if applicable) Signature of legal representative

_____

Date

_____ _____

Researcher's Name who explained the document Researcher's Signature

_____

Date

_____ _____

Witness Name 1 Witness Signature 1

_____ _____

Date Relationship with the participant:

Address:_____

_____

_____ _____

Witness Name 2 Witness Signature 2

_____ _____

Date Relationship with the participant:

Address: _____

_____

Place and date: _____

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