Universidad Veracruzana

Health Sciences Institute

Letter of Informed Consent to participate in the; Comparative study of response to weight loss and metabolic conditions using two non-pharmacological nutritional programs Zelé 2021-001

Authorization Folio of the Ethics and Research Committee: 19CI 30 087 041

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Letter of Informed Consent to participate in the;

Comparative study of response to weight loss and metabolic conditions using two non-pharmacological nutritional programs Zelé 2021-001

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Informed Consent:

Introduction

If you have obesity, you are probably interested in participating in this clinical trial. This clinical trial is a treatment option for 90 patients with obesity. This document explains what clinical trials for the treatment of obesity are about and gives you the tools you need to decide to take part in it.

Please take as much time as necessary to read this document and ask the investigator about any questions you may have.

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

To decide whether or not to participate in this study, you should have sufficient knowledge about the risks and benefits in order to make an informed decision. This informed consent form will give you detailed information about the research study that you can discuss with your treating physician or a member of the research team. At the end you will be asked to be part of the project and if so, under no pressure or intimidation, you will be invited to sign this informed consent.

In obesity research, clinical trials are designed to answer questions about new ways of:

Treat obesity.
- Find and diagnose obesity and associated health problems.
- Prevent obesity and associated health problems.
- Program resources for the management of obesity and associated health problems.

The information in this paper will focus on studies aimed at treating obesity, specifically designed to answer questions about new treatments or new ways of using an old treatment and, how well it works. Specifically, this trial tests:

- The Very Low Calorie Ketogenic Protein Diet (VLCPD).
- The Hypocaloric Diet proposed by WHO.

INVITATION TO PARTICIPATE AND DESCRIPTION OF THE PROJECT

Sr.(a)_____

The Zélé Academy and the Institute of Health Sciences of the University of Veracruz, invite you to participate in this research study that aims to: Evaluate the differences in weight reduction between patients with obesity who follow the multidisciplinary Zélé method of weight loss and patients with obesity who follow a balanced hypocaloric diet according to the FAO/WHO/UN guidelines.

The justification for this study is centered on the fact that "Overweight and obesity have been associated with increased risk of multiple diseases, among which cardiovascular conditions and diabetes stand out, so the implementation of nutritional treatments that help reduce weight will favor the control and improve the quality of life of these patients, as it will reduce the risk of complications, while the direct benefits provided to the study population will be a close monitoring of their health condition, obtaining and applying knowledge in nutrition and how it impacts their health".

The duration of the study is: 3 to 4 months of treatment and two years of follow-up.
The approximate number of participants will be: 90 patients.
You were invited to the study because you have the following characteristics: _
You are a patient with obesity, according to the WHO definition, that is, you have a Body Mass Index greater than or equal to 30 kg/m2.
Has not received any type of treatment for obesity in the last 6 months.
And is between 18 and 65 years of age.

STUDY PROCEDURES

The treatment that will be evaluated is: Zélé® Method and will be compared against the treatment for obesity established by FAO/WHO/UN. Your probability to be assigned to one of the above-mentioned groups is: 2:1, and in the case of having been assigned to the control group, at the end of the 3 to 4 months of study you will be crossed to the study group, receiving the same benefits as the initially treated patients.

Your participation in the study consists of: If you are eligible for the study by completing a Medical History and your health conditions permit, you will be subject to a lottery to participate in either the study group or the control group.

Regardless of the group in which you participate, you will have to attend your evaluations every 7 days during the first 3 to 4 months of the study. At each visit to the VIME clinic you have chosen (namely VIME ROMA Valladolid 18 colonia Roma Norte, Cuauhtémoc 06700,

VIME Del Valle , Tlacoquemecatl 123, 3rd Floor, Benito Juárez 03200, VIME Coapa, Coapaplaza eje 1 Ote, Canal de Miramontes 3280 Local 22 Tlalpan 03280, VIME Satélite, Edificio Cristal Federico T de la Chica 17 Piso 4 Cd. Satélite 53100 Naucalpan Mex.) you will receive attention from a clinical nutritionist who will follow your progress in the nutritional program, a clinical psychologist who will provide psycho-emotional support during treatment and a physiotherapist who will provide guidance on appropriate physical activity for each patient. If necessary, the patient will also receive medical attention. Since the objectives of this study do not include the evaluation of psych emotional or physical progression, no instruments will be used to measure the psych emotional condition and physical activity. After the evaluation, each patient will be given a sheet with the evolution of his/her body composition condition and the result of the capillary ketone bodies measurement and will not be able to miss more than 2 consultations in a row. After this first stage, your check-ups will be every month during the first year and finally every 3 months until the end of the study. In these consultations, a social interview will be made with the patient. In these consultations, an interview about your health condition, your tolerance and acceptance to the treatment will be done. Your weight and body composition will be recorded and occasionally a micro blood sample will be taken from the tip of your finger to measure glucose levels and/or ketone bodies. During the study, fasting laboratory tests will be performed approximately every 2 months during the first 6 months, then every 6 months during the follow-up phase.

The proposed experimental interventions are the patients included in the experimental group will receive a package containing the functional foods (duly labeled with the information of its content and approved by COFEPRIS) necessary to cover the corresponding diet in 4 stages, in the first one a very low-calorie diet (600 to 800 Kcal/day) that covers the protein requirements (0. 8 to 1.2 gr. of proteins per Kg of ideal weight/day) provided through 5 intakes of functional foods (Proteins, Lipids and Carbohydrates) per day with an approximate cost and covered by Zélé of $3,000.00 per week per participant, which will be progressively substituted by conventional foods (Meat, Chicken, fish and eggs, fruits, vegetables, and cereals). In the second stage a low-calorie diet will be administered (1000 to 1500 Kcal/day), simple carbohydrates, complex carbohydrates, starches and finally fats will be progressively

incorporated. In the third stage, a balanced diet adapted to the energetic requirements of each patient will be given in which 50% of the caloric load will be provided by carbohydrates, 25% by lipids and 25% by proteins. The basic basket of conventional foods complementary to functional foods calculated according to the stage of nutritional treatment varies between $100 and $200 per day).

The control group will be provided with a balanced hypocaloric diet (caloric intake 25% below metabolic expenditure measured by multifrequency bioelectrical impedance). The usual caloric intake of a balanced hypocaloric diet is between 1,200 and 1,400 kcal per day. The intake of total fats (25%), carbohydrates (50%) and proteins (25%) will be reduced in a balanced way. Functional foods will be provided to guarantee the protein requirements (0.8 to 1.2 gr. of protein per kg of ideal weight/day), and a balanced diet of between 1100 and 1400 kCal per day. After 3 or 4 months, when the evaluation cut-off of this first treatment is made, the patient will be migrated to the study group, thus eliminating the placebo effect in the initial evaluation, and ensuring all the benefits of the Zélé program.

Both groups will receive vitamin and mineral supplementation provided by Zélé (at an approximate cost of $800.00 per week per participant), these supplements are properly labeled with the information of their content and authorized by COFEPRIS within their nutritional program, to avoid deficiencies during the protocol. They will also receive nutritional consultation, psycho-emotional support and guidance and personalized physical activity.

Your responsibility as a participant includes Complying 100% with the doctor's instructions, going to your doctor's appointments, and reporting any change in your state of health or condition that modifies your physical or emotional state. Also, to notify any change of address or telephone or e-mail contact.

RISKS AND INCONVENIENCES

The risks of participating in this study are the same as those of undergoing any weight reduction program and include fatigue, headache, nausea, constipation, cramps, dizziness when changing position rapidly, muscle weakness, hair loss.
In relation to the procedures related to the taking of samples, it is established in the Regulations of the General Health Law on Health Research, that obtaining biological samples represents a minimal risk in research. The risks of blood sampling are possibility of slight bleeding or bruising at the puncture site, dizziness or fainting sensation, and rarely arterial puncture may occur. The personnel who will draw the blood sample are trained to do so, which will minimize the risks of complications.

There is no risk of any kind in the collection of body measurement parameters or multifrequency bioimpedance or in the collection of the urine sample.

Data about your identity and 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 encryption of the samples and your information.

POTENTIAL BENEFITS

This study is designed to evaluate the response of patients to weight loss through two different methods that have proven to be effective, therefore the benefits for you as a patient are: Reduce the risk of early death associated with overweight or obesity, delay the onset of diabetes, or lower glucose levels and facilitate glucose control, lower blood pressure levels, and reduce the risk of cardiovascular and non-cardiovascular diseases associated with obesity, as well as improve your physical condition and self-esteem.

ECONOMIC CONSIDERATIONS

Since there is scientific evidence that affirms that when a patient with obesity receives his treatment for free, he does not take it as a real commitment, and the rate of abandonment of the same is increased, for such reason, Zélé, will cover 100% of the cost of the treatment during the 4 stages of the treatment, in addition, of the expenses of consultations, remaining only to the responsibility of the patient the expenses generated by the laboratory studies* that will be approximately $ 3,000. 3,000.00 spent 3 times during the whole treatment, the expenses derived from the rest of the food, transportation and/or mobilization expenses to go to their consultations or analysis will be the responsibility of each patient.

*Zelé will contact prestigious laboratories in the CDMX to obtain better prices for laboratory analysis.

COMPENSATION

As a patient you will not receive any financial compensation for participating in the study, and in the extreme case that you suffer any injury or complication resulting from your participation in the study, we will provide immediate treatment and refer you, if necessary, to the medical specialist you require, for which we have a fund established by Zélé for this purpose, as well as a liability insurance purchased with Zura (policy 100002177/2). We do not have a budget to finance compensation for injuries or to cover medical treatment for illnesses NOT resulting from the study, such as biliary or renal colic etc.

ALTERNATIVES TO YOUR PARTICIPATION:

Your participation is voluntary. However, you may choose not to participate in the study and attend to your overweight problem through any alternative supervised by health personnel or simply by modifying your lifestyle and diet since you are a healthy subject, you do not require immediate studies or therapeutic actions.

POSSIBLE COMMERCIAL PRODUCTS DERIVED FROM THE STUDY:

Zelé® Products are commercially registered products for such reason any modification or new product developed because of this study will be property of Zélé (DIET LINE LATIN AMERICA SAPI de CV) and you will not receive any financial benefit.

ACTIONS TO BE TAKEN AFTER COMPLETION OF THE STUDY:

Upon completion of the study, you may continue under physician surveillance or treatment now at your own expense.

PARTICIPATION AND WITHDRAWAL FROM THE STUDY:

Your participation is VOLUNTARY. If you decide not to participate, your relationship with Zelé or the principal investigator will not be affected, and you will retain your right to receive medical care or any services. If you choose to participate, you are free to withdraw your consent and discontinue your participation at any time without prejudice to your care. You will be informed in a timely manner if new information arises that may affect your decision to continue in the study.

The investigator or the study sponsor may exclude you from the study if you do not comply with the medical, nutritional, psychological or physical activity indications, if your behavior or treatment with the health personnel is inappropriate, if you miss two consecutive or three visits during the entire study, in the presence of a serious event that makes it necessary to suspend treatment, such as food intolerance, changes or worsening of hypertension or diabetes, which theoretically should improve with this treatment, or by suspension from the study.

Reasons for withdrawal from the study should be clearly documented in the registration notes. And any adverse reactions will be reported immediately to the Pharmaco-Surveillance system in charge of Dr. Francisco J Nachón García Principal Investigator.

The study may be terminated prematurely if adverse events are detected that put patients at risk or if the sponsor for any justifiable reason decides to stop funding the study.

CONFIDENTIALITY AND HANDLING OF YOUR INFORMATION

Your name will not be used in any of the studies. The biological samples obtained will not contain any personal information and will be coded with a serial number to avoid any possibility of identification. By law, biological samples, including blood, are classified as biohazardous waste and for this reason during the research your sample cannot be returned to you. It is possible that your biological samples, as well as your medical and/or genetic information may be used for other analogous research projects related to the disease under study. They may not be used for research studies unrelated to conditions other than those studied in this project. Your samples may be stored by researchers for up to two years.

The codes that identify your sample will be available only to the incumbent researchers, who are required by law not to disclose your identity. These codes will be kept in a locked file cabinet. Only the researchers will have access. There is a possibility that your privacy may be affected because of your participation in the study:

- If it is necessary to protect your rights and welfare (for example, if you have suffered an injury and require emergency treatment); or It is required by law.
- Study monitors or auditors may have access to participant information.
- If you decide to withdraw from the study, you may request the removal and destruction of your biological material and information. All data collection sheets will be kept with

the same confidentiality measures, and only the principal investigators will have access to the data that have your name on them.

- The inclusion data of each patient will be duly safeguarded according to what is described in the ARCO rights: "every person has the right to the safeguarding of his/her personal information and also to access, rectification, cancellation and opposition on the treatment of his/her data, before the obliged subject that is in possession of the same in the terms established by law. Contemplated in article 16, second paragraph of the Mexican Constitution in force, independently of the above, to safeguard the identity of each patient in the project will be assigned an identification code that will be integrated by a 6-digit number in which the numbering of the clinic, the consecutive number of participation in the study and the sequence number of the randomization will be identified, in such a way that none of the participants can be identifiable or identified in the database of the study. The data will be entered in an electronic file stored in each of the VIME clinics in accordance with the privacy notice attached to this document.

The Research Ethics Committee of the Centro de Alta Especialidad del Estado de Veracruz (CONBIOETICA-30-CEI-001-20170221) evaluated and approved the ethical aspects of this study. This committee is the one who reviews, approves and supervises the research studies in human beings in the Institution. In the future, if we identify information that we think is important to your health, we will consult with the Ethics Committee overseeing this study to decide how best to give this information to you and your doctor. In addition, we ask that you give us permission to recontact you, if necessary, to request information that may be relevant to the development of this project.

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 prior to use of the data. At your request, your primary care physician will be informed of your participation in the study.

IDENTIFICATION OF THE INVESTIGATORS:

If you suffer harm related to the study, please contact El Dr. Francisco J Nachón Garcia. If you have questions about the study, you may contact Principal Investigator Dr. Francisco J. Nachon Garcia at fnachon@uv.mx or fnachon@zele.mx or tel +52 228 979 0016.

INFORMED CONSENT STATEMENT

I have carefully read this informed consent, asked any questions I have had, and all have been answered satisfactorily. To participate in the study, I agree to all the following:
I agree to participate in the study described above. The general and objectives of the recruitment and the possible harms and drawbacks have been explained to my satisfaction.
I agree to voluntarily donate my blood and urine biological 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 needs to collect additional information or if they find information relevant to my health.
My signature also indicates that I have received a duplicate copy of this informed consent.

Please answer the following questions	Yes	No
a) Have you read and understood the informed consent form, in your native language?		
b) Have you had 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 you had enough time to make a decision?		
e) Do you understand that your participation is voluntary and that you are free to discontinue 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) If applicable: Do you authorize access to your medical records for this research study and for regulatory purposes to _____, its representatives, auditors, study regulatory offices, other governmental health agencies in Mexico and possibly other governmental health agencies in other countries where the study drug may be considered for marketing approval?		
g) Do you understand the potential risks, some of which are not yet known, of participating in this study?		
h) Do you understand that you may not receive any direct benefit from participating in this study?		
i) Have you discussed other treatment options with the physician participating in the study and do you understand that other treatment options are available to you?		
j) Do you understand that you are not giving up any of your legal rights to which you are entitled?		
k) Do you understand that the study doctor can withdraw you from the study without your consent, either because you did not follow the study requirements or if the study doctor feels that it is medically in your best interest to withdraw?		
l) If applicable. Do you understand that the study can be stopped by the study sponsor at any time?		
m) Do you understand that you will receive a signed and dated original of this Consent Form for your personal records?		

Patient's declaration:

I, _____ declare that it is my decision to participate in the study. My participation is voluntary. I have been informed that I may refuse to participate or terminate my participation at any time during the study without penalty or loss of benefits. If I discontinue my participation, I will receive the usual

medical treatment to which I am entitled and will not be harmed in my medical care or in future research studies. I may request additional information about the potential risks or benefits of my participation in the study. I may obtain the results of my clinical tests upon request. I have been informed that if I have questions about the study, I can contact Dr. Francisco J. Nachon Garcia (228) 840 0602 or 228 979 0016. I must inform the investigators of any changes in my health status (e.g., use of new medications, changes in tobacco use) or in the city where I reside 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 form.

_____	_____	_____
Participant's Name Participant's fingerprint if unable to write	Signature	Date

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

_____	_____	_____
Name of Investigator who explained the document	Signature of Investigator	Date

_____	_____	_____
Witness 1 Name	Witness 1 Signature	Date

Relationship with the participant:_____

Address:_____

_____

_____

_____ _____ _____

Name of Witness 2 Signature of Witness 2 Date

Relationship with the participant:_____

Address:_____

_____

_____

(This document is an original and consists of 15 pages.)