Hyperbaric Oxygen Therapy for Cognition in Diabetic Elderly at High Dementia Risk
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I the undersigned[1]:

First name:	Last name:
I.D number:	
Adress:	Zip code:

1) Hereby declare that I agree to participate in a clinical trial, as described herein.
2) Hereby declare that during the signing of this document, I am not participating in another clinical trial using any investigational product, and I pledge not to participate in any other clinical trial research involving the use of an investigational product throughout the duration of this trial.
3) Hereby declare that it was explained to me by:

Investigator:

3.1) That the principal inveatigator (doctor's name): **Prof. Ramit Revona-Springer** received from the medical institution the rights to perform the trial within the guidelines of the Public Health Regulations (Clinical Trials on humans 1980), the clinical trial is as follows:

3.2) That the principal investigator and the subinvestigators have **conflict of interest**[2] to the trial sponsor[3]. If there is, describe: The principle investigator and the trial sponsor are working in a collaborative research. **Trial protocol writing and concept**.

3.3) That the clinical trial is conducted on the subject: **The efficacy of hyperbaric oxygen therapy (HBOT) in improving cognition in mild cognitively impaired people with type 2 diabetes (T2D) in the age of 65+.**

3.4) That I am free to choose not to participate in the clinical trial, and that I am free to discontinue my participation at any time in the experiment, all without compromising my right to receive the common treatment.

3.5) That in the case of a questionnaire – I can decide not to answer all of the questions on the questionnaire or part thereof.

3.6) That it is guaranteed to me that my personal identity will be kept confidential by all those involved in the trial and will not be published in any publication, including scientific publications.

3.7) That the medical institution arranged proper insurance coverage for the researchers, doctors and the medical staff engaged in the clinical trial from claims submitted by participants in the clinical trial and / or third party claims associated with the clinical trial during the period of the trial and after it. The foregoing does not affect my rights according to the law.

[1] The form is written in the masculine form for convenience only and is intended for both sexes.
[2] Relation of wage employment, or commercial or business, or a personal or family relationship, and any other relationship, including the relationship of subordination at work, that could raise concern for conflict of interest or dependency.
[3] If the principal investigator is also initiatiating the trial, it should be noted explicitly and specify the nature of the interest.

3.8) That the sponsor of the trial will provide the investigational product free of charge for the duration of the trial and shall bear the additional costs arising from performing the trial, provided that these costs do not arise from the standard medical treatment of the disease.

3.9) That I am guaranteed willingness to answer questions I may have and the possibility of consulting with others (such as a family physician, relatives, etc.) in making the decision to take part and/or to continue in the clinical trial.

3.10) That I may contact **Prof. Ramit Revona-Springer** at Phone / Mobile: **03-5307261 ; 052-6666562** with any problem related to the clinical trial, at any time of the day. I must report immediately to the doctor noted above all medical problems, injury or other health events that may be related to the trial.
If I am injured as a result of my participation in the trial, I must contact the trial doctor to receive appropriate medical treatment and more information about my rights in this regard. Signing this form does not diminish my rights under the law.

4) Hereby declare that I have been given detailed information about the clinical trail, as outlined by the following topics:

4.1) **General background and the importance of the trial.** This trial is based on a pilot trial which deals with the implementation of a clinical treatment method using a pressure chamber. It examines the efficacy of hyperbaric oxygen therapy (HBOT) in improving cognition in mild cognitively impaired (MCI) elderly with type 2 diabetes (T2D), who have high dementia risk.

In order to carry out the research properly and as planned, there is a collaboration between four institutions: the Sheba Medical Center, Asaf Harofeh Medical Center (one of the largest hyperbaric units worldwide) Icahn School of Medicine at Mount Sinai, NY and the University of Wisconsin, USA.

The trial will be a randomized controlled trial (RCT), hence, the trial's participants will be divided into two groups randomly – one group will experience conditions in the hyperbaric chamber where the rate of oxygen is higher than in the normal environment, and the second group will serve as a placebo (control) in which the conditions in the hyperbaric chamber will be the condition which is found in the normal environment. There is a 1:1 chance of being in each of the two groups. This is a double blind study, meaning that neither you subject nor the investigator will know to which group you were assigned. At the end of the participant's 12 months participation in the trial, the participant can choose to receive HBOT treatment for which the costs will be covered by the study team. Anyone who chooses to receive the HBOT treatment, will receive full treatment (no sham). Participant who chooses to take part in the HBOT treatment that will be covered by the study team, will undergo an additional neuropsychological assessment at the end of the second treatments session. In the case of an emergency, if the type of treatment you will need because of the side effects will require unblinding, the blind will be broken.

Type 2 diabetes (T2D) isa vascular disease culminating in a deficiency of oxygen in the tissues, and which effects the blood vessels in the brain (increasing risk for cerebrovascular disease, which is an important factor in the risk of developing Alzheimer's disease). Impairment of cerebrovascular integrity may lead to reduced cerebral blood flow (CBF) on the vessel level, and reduction in the glucose utilization and metabolism on the neuronal level. The HBOT (hyperbaric oxygen therapy) treatment is a treatment that combines a high concentration of oxygen and high atmospheric pressure leading to significant improvements in the process of oxidation and renovation tissues which leads to improvement in blood vessels and improvement in blood flow to the brain efficiency (CBF- cerebral blood flow).

In the hyperbaric chamber high oxygen concentration is pumped into the chamber where the participant will be. In the chamber, the air pressure will be higher than the pressure in the normal environment which is one atmosphere – ATM 1.0 and there will be a high concentration of oxygen.
Recently, our research group has published findings from clinical studies indicating the beneficial effect of the HBOT for stroke and cognitive function improvement as well as an increase in brain activity.

Based on the understanding that diabetes is caused by damage to the blood vessels of the body in general and in the brain in particular, and that damage to the blood vessels in the brain is associated with a decline in mental function (cognitive) and Alzheimer's disease on the basis of preliminary studies, that treatment with HBOT is associated with a beneficial effect on other conditions where there is damage to the tool blood (for example, situations in the event of blocking blood vessel in the brain), we offer the current trail which addresses the impact of treatments in a hyperbaric chamber on cognition; hoping that there will be improvement in the cognitive function of participants or stop in the deterioration. The treatment's sessions in the hyperbaric chamber will take place at Asaf Harofeh Medical Center; the treatment's sessions will spread over three months (12 weeks) in which every week the participant will come in 5 times for a 90 minute session duration. Meaning, the total number of visits will be 60 sessions of hyperbaric chamber.

We will ask you to provide us with your general blood test results (sugar, hemoglobin A1c, creatinine, etc.) from your health maintenance organization, so we will be able to test whether certain factors such as blood sugar and blood pressure levels can be linked to the high efficiency of the treatment in the hyperbaric chamber.

4.2) **The goal of the trial.** To test the hypothesis – Will hyperbaric chamber treatment with high concentration of oxygen and high atmospheric pressure improve cognitive function, increase cerebral blood flow (CBF) and glucose utilization efficiency in the short term and / or the long term.

4.3) **Number of participants in the trial**. Approximately 250 people.

4.4) **Anticipated duration of participation in the trial.** Each participant will be aware that the duration of their

participation in the trial will take approximately one year (includes the treatment sessions and the follow-up sessions). Participant who chooses to take part in the second HBOT treatment at the end of his year of participantion, that will be covered by the study team, will be considered as participant until the end of the second HBOT treatment and the additional neuropsychological assessment that will performed at the end of the second treatment sessions. The entire study will take about four years, starting from recruitment of the subjects until the last visit of the last subject.

4.5) **Methods – Description of investigational product, a brief description of the various procedures for the experimental period (treatment and follow-up) with a clear distinction between research processes and common procedures in medicine, participant's chances of getting any of the treatments offered in the trial (including placebo).**

Investigational product description:

The hyperbaric chamber serves as a medical treatment that provides oxygen as a drug at higher doses to the blood and tissues. Under these conditions, the dose of the oxygen reaches values even 20 times higher than normal. A healthy person does not benefit from this, but for patients with a decrease in tissue oxidation, for example because of damage to small blood vessels in diabetic patients with wound healing problems, this is the only method to provide oxygen to the cells.

The hyperbaric chamber is a common medical technology to treat a wide range of pathologies: wounds, healing difficulties because of circulation disorders, damage to the central nervous system caused by lack of oxygen resulting from embolic gas or something else which causes a significant reduction in blood flow to the brain and disruption oxidation tissue, necrosis of bone, etc.

Trial period:

During your 1 year participation in the trial, which includes the treatment sessions in the hyperbaric chamber for three months (which will take place in Asaf Harofeh Medical Center), there will be 11 major visits – the screening visit, evaluation meeting 6 months after the base line visits and 3 visits that are each divided into three sessions, which will be evaluation meetings that will take place at the Sheba Medical Center. At the end of the first 12 months period, participants can choose to receive HBOT treatment, for which the costs will be covered by the study team, and will undergo additional neuropsychological assessment to evaluate their cognition state.

Location	Frequency	Visits
The Neuroscience Center in Sheba Medical Center	One time – visit that lasts four hours, includes signing the informed consent and the subject will be checked to see whether he is suitable for inclusion in the trial (physician exam and psychologist evaluation)	Screening
The 3 visits will be preformed in Sheba Medical Center in various departments The Neuroscience Center Nuclear Medicine Radiology	Divided into 3 sessions: 1. cognitive assessment, blood draw, and physician exam – visit that lasts about two to three hours 2. FDG-PET exam – takes about an hour and a half from arrival untill the end of the scan 3. MRI test – takes about two hours from arrival untill the end of the scan	BASE LINE
Asaf Harofeh Medical Center	5 times a week for 3 months (60 sessions), the duration of every treatment is 90 minutes	Treatment sessions in the hyperbaric chamber
The 3 visits will be preformed in Sheba Medical Center in various departments The Neuroscience Center Nuclear Medicine Radiology	Preformed after completion of the treatment session in the hyperbaric chamber (meaning after 12 weeks). Divided into 3 sessions: 1. cognitive assessment, blood draw, and physician exam – visit that lasts about two to three hours 2. FDG-PET exam – takes about an hour and a half from arrival untill the end of the scan 3. MRI test – takes about two hours from arrival untill the end of the scan	VISIT SESSION 2

Will be preformed in Sheba Medical Center in the Neuroscience Center	Preformed 6 months after the base line: cognitive assessment and physician exam – visit that lasts about two to three hours	VISIT 3
The 3 visits will be preformed in Sheba Medical Center in various departments The Neuroscience Center Nuclear Medicine Radiology	Preformed 12 months after the base line. Divided into 3 sessions: 1. cognitive assessment, blood draw, and physician exam – visit that lasts about two to three hours 2. FDG-PET exam – takes about an hour and a half from arrival untill the end of the scan 3. MRI test – takes about two hours from arrival untill the end of the scan	VISIT SESSION 4

It is important to note that the participant needs to bring, if he does have one, an updated lung X-ray from no longer than six month back. If he does not have an X-ray, we will schedule one to be conducted for him at one of the visits before the treatment session.

The participant needs to bring his last blood test results and the results of an eye examination from the last year that indicate a lack of proliferative retinopathy.

Description ot the tests:

- Cognitive assessment – we will use cognitive assessment that will examine many cognitive functions such as: memory, calculation, attention etc. and also questionnaires related to cognitive function such as depression questionnaire and activities of daily living. This part of the evaluation will take about an hour and a half. This assessment will be conducted at the base line visit, visit session 2, visit 3 and visit session 4.
- Medical history and physical and neurological examination – the trial's doctor will go over with the participant and ask him questions about his medical history and relevant questions about participation in

the study. This will take place at the screening visit. In addition, the participant will have to pass a physical exam.

- Blood draw to assess inflammatory markers tha may be correlated with Alzheimer's and Diabetes. 30 ml will be drawen
- blood draw to assess advanced glycation end products (AGEs) levels. AGEs are modifications of proteins or lipids that indicate blood sugar levels
- Informant interview- we require that you ask a family member or a close friend to attend the cognitive assessement and examination, to provide supplementary information (including, for example, reporting on their impressions of your cognitive status and day-to-day functioning.
- Hyperbaric chamber treatment – the investigational group will be in conditions of 100% oxygen concentration and atmospheric pressure up to 2 atm, while for the control group there will be normal conditions that are similar to our outer environment (the control participant will not feel the difference inside the hyperbaric chamber). This treatment will be provided for 3 months. In the hyperbaric chamber at the Asaf Harofeh Medical Center there is space for 11 people, seated on upholstered chairs. Nurses and experienced staff will be on site to supervise. As mentioned, the treatments will take place at a frequency of 5 times per week for three months (60 sessions), duration of treatment is 90 minutes. **In case of a situation where the participant is not coming to about 20% of the treatment's sessions he will not be able to continue in the trial**. If the participant is absent for two weeks, the reason for his absence will be checked and if its not medically critical, he will continue in the trial with the approval of the trial doctor.

  When the participant arrives on a treatment day – before entering the machine, the nurse will examine his glucose level, blood pressure and fever. Participants with glucose <75mg/dl, systolic blood pressure >170mmHg or <90mmHg or fever >38°C will not enter to the hyperbaric chamber until their condition will be improved. The physician that is present will determine whether the participant can be treated by local treatment (for example, if the participant is in hypoglycemia, the physician will give him candy and glucose levels will be measured again) or, if necessary, they will be sent home and won't carry out the treatment. Inside the hyperbaric area the paticipants will be able to drink and eat, sleep, listen to music, read, watch the television, etc. but the use of electronic devices is forbidden. Each participant will have his own mask. The sessions will start after random assignment of the participant to a group, ie. after the baseline visit.
- MRI – MRI test is a standard test used routinely in medicine for receiving anatomical images of the tested organs. The image is based on magnetic signals detection from water in the brain tissue. In order to perform the test, the subject is lays inside a magnetic field and is asked to avoid movement. There is no known danger of lying inside a magnetic field at the intensity of the MRI devices that are generally

accepted in the clinical service (such as the existing device here). Through which we can see structures and functions of different brain areas. The test is based on a powerful magnet and radio waves. During the test, the radio waves are broadcasted and received. Each tissue has a different way of returning the radio waves, and on this basis it is able to differentiate between the various tissues. The great advantage of MRI – is that the test does not include radiation. The test duration is about one hour. The test will take place after 4 hours of avoiding caffeine and nicotine. Trial participants will be asked to avoid using over the counter medication the night before the exam and the morning of the exam,. The subject needs an ID number in order to proform the test, his ID will be visible to the MRI's research team operators. Also, the test will be preserved in the MRI's test databases of Tel Hashomer hospital in order to use it for future clinical needs if the subject will need it. This is part of the Sheba Medical Center's work policy. This evaluation will be preformed in the base line visit, visit session 2 and visit session 4.

- PET CT – the mapping will be performed 60 minutes after intravenous injection of 18F-fluorodeoxyglucose FDG up to MBq (7mCi) 250. After receiving the injection, the subject needs to lay down for about an hour and then the test will be conducted. During the test the subject lays on his spine and the head is scanned. First, the CT scan is conducted (a low radiation dose in order to repair attenuation) and immediately afterwards the PET scan is performed, total of 10 minutes. The subject needs to fast 6 hours before the test (drinking water is permitted). This evaluation will be preformed in the baseline visit, visit session 2 and visit session 4.

4.6) **The expected benefits to the participant or others as a result of the experiment**

Participants can not be guaranteed advantage and direct benefit as a result of their participation in the trial.

Motor and cognitive function diagnosis is made and in addition, receiving the MRI scan results. Therefore, there is a possibility of early diagnosis of a problem in case there is one. If a problem will come up, we will notify the subject and we will recommned that they visit a doctor.

4.7) **Known risks and / or foreseeable discomfort to the participant in the trial. Incase there is a risk in the clinical trial to the participant - explanation of the medical treatment to be received in case of damage to his health and the responsibility of giving it.**

Blood draw may cause uneasyness, pain and bruising.

MRI test – participant may feel discomfort as a result of extended stays in the test device. During the test, the participant lays on a narrow table which enters into the tunnel. There is no danger of radiation resulting from the test.. The MRI may provoke claustrophobia, dizziness, and/or discomfort, because your head will be in a relatively narrow tube and the MRI makes loud sounds and may be cold. These side effects are transient and treatable.

PET scan – participation in the trial involves mild discomfort at the intravenous injection of the substance and while waiting after the injection. Side effects of the injected substance are extremely rare and include flushing, increase in blood pressure, headache, nausea and dizziness (1-2% of participants), but, the test is performed under full medical supervision. These side effects are transient and treatable.The injected substance is a radioactive substance in small amount, therefore there is exposure to radiation during the test (about 5.9 millisievert, about 2.5 times the average annual background radiation each person is exposed to). At the beginning of the PET scan, a CT scan is performed where there is low-dose radiation exposure (for repair attenuation).

This research study includes exposure to radiation from x-rays or gamma rays. This radiation exposure is for research purposes only and is in addition to any radiation needed for your medical care. X-rays and gamma rays from natural or medical sources can damage the genetic material (DNA) in your cells. At low radiation exposures, the body is usually able to repair the damage. Radiation risk is believed to be related to the total lifetime exposure. You should think about your own history of radiation exposure from tests (like x-rays or CT scans) in deciding about the radiation in this study. The estimated radiation exposure that you will get for this research study will be 17.7 mSv (an mSv is the scientific unit of measurement for whole body radiation dose, “effective dose”). The greatest annual exposure (17.7 mSv) is projected to be in year(s) 1. This exceeds the 2.4 mSv that the average person in the Israel gets each year from both natural sources like the sun, outer space, air, food and soil, as well as from medical procedures. It is less than the 50 mSv of radiation that is allowed each year for people who are exposed to radiation in their jobs. If you have done imaging scans in the past year, please inform us.

Hyperberic chamber –

- During the treatment in the hyperbaric chamber the air pressure is raised above 1 atm and this pressure is felt mainly in the ears. The high pressure can lead to problems in a number of organs: ears, sinuses and lungs. Ears - injury can result in pain, redness, edema, and in severe cases, rupture of the eardrum. These side effects are reversible.
- Sinus - injury can result in pain and bleeding from the nose. In order to prevent this damage it is necessary to equalize the pressure by "pumping" or execution of the swallowing operation while raising the pressure. Accordingly, while raising the pressure you will be asked to compare pressures by "pumping" - closing the nose and creating pressure in the mouth. Other options which enable pressure comparing include drinking water or execution of the swallowing operation. If this is not done, damage to the eardrum of the ear may develop in varying degrees – local edema and redness up to rupture of the eardrum. These side effects are reversible.
- Lungs – the increased pressure can cause damage to the lung tissue and lead to the development of "Pneumothorax"- the air that is coming out from the lungs is trapped between the lung tissue and the

chest wall. Therefore, before starting the treatment in the hyperbaric chamber, all the participants will undergo a chest X-ray and if there is a pathology which increases the risk of exposure to pressure, the treatment will not be given and the participant will not be permitted to enter the hyperbaric chamber. These side effects are reversible and/or treatable.

- Toxicity of high concentration of oxygen – High concentrations of oxygen can cause brain poisoning that can result in seizures. Therefore, the exposure to oxygen in the hyperbaric chamber is limited in time based on the pressure the patient is exposed to in order to minimize the likelihood of a seizure. In most cases the seizure is transient and can be treated by removing the oxygen mask and does not cause long-term brain damage. These side effects are transient and treatable.
- Sugar drop – During the treatment, levels of blood sugar can drop, mainly in patients with diagnosed diabetes. A drop in blood sugar levels can result in dizziness, headache, sweating, rapid heartbeat, faintness and loss of consciousness. Therefore, every time before entering the hyperbaric chamber, levels of glucose will be measured. If you will feel one of the symptoms, levels of sugar blood will be measured again while in chamber. If there are low blood sugar levels, you will be treated with sugar units. These side effects are transient and treatable.
- Decrease in visual acuity- as a result of the exposure to high pressure, in very rare cases, there is a small change (0.5 diopeter) in vision. This may feel like slightly better close-up vision, and slightly blurry distance vision. In the vast majority of cases this is reversible. Therefore vision assessments will be made during the study if you will feel changes in your vision. There have been anecdotal cases in which severe cataract may have exacerbated faster than expected with HBOT. Therefore, if you have been diagnosed with severe cataract, it is recommended to surgically remove the cataract prior performing the HBOT.
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Therefore, in cases where the review of the medical history in the baseline 1 visit reveals medical findings such as eye problems, abnormal chest radiograph, ear problems etc., admittance into the hyperbaric chamber therapy will depend on the approval of the trial doctor.

4.8) **Circumstances in which the participation in the clinical trial may be stopped by the investigator or the trial sponsor.**

I might leave the trial without my consent if I will need another treatment, if I do not follow the trial plan, if I will have a research related injury or any other reason including stopping the trial by the sponsor. For example removal from the trial because criterions don't match the inclusion criteria- such as misdiagnoses of MCI.

4.9) **If applicable, the trial doctor will give the participant information about medical consequences if the participant will decide to leave the trial before its end.**

In addition, if abnormal results will be received, the participant will be notified.

4.10) **Explanation to the participant about alternative treatments and their advantages and disadvantages, if there is any.**

If you decide not to participate or to quit the trial, the trial doctor can advise you about follow up treatment. Physical activity and good diabetes control are both alternative options that may help to maintain or improve cognitive functioning.

4.11) **Other relevant information (as provided by the sponsor of the trial).**

MRI scan – this scan is for research purposes only, and is not diagdonstic. Artifacts mat or may not presented in this scan, and will be reviewed by a radiologist, which will summarize the interpretation to Sheba's system. I agree to receive the interptetation vis Sheba connect, even if artifacts will be found.

Travel- reasonable expenses related to the trial for travel to Sheba and Asaf Harofe, and food, will be returned to you upon presentation of receipts. These expenses should be discussed with your trial doctor.

Withdrawal from the trial- the decision to participate in this trial is made by your own free will. You can decide to stop participation in the trial at any time by providing a notice to the trial doctor, without losing any benefits you are entitled to or any punitive measures taken against you. If at any time you consider to withdrawing from the trial, you will decide to provide or not provide the related outcome information. Providing the information will help the trial. To help you decide, the trial doctor can provide you with the information about the trial procedures and what data will be collected if you will choose to stay in the trial but leave the trial treatments.

Participant privacy- with the exception of the trial team in Sheba Medical Center and Asaf Harofe hospital, your identifying information will not be exposed. Your information will be treated in compliance with ethical rules and laws in effect. The medical and personal information about you that will be collected during this trial will remain confidential and secure as the applicable laws will enable.

Conflict of interest: Prof. Shai Efrati, the PI at Asaf Harofeh, is the chair of a consulting committee to Aviv Scientific LTD. Aviv Scientific focuses on cognitive and physilogical improvement in older adults, using HBOT as a treatment, in the USA and the UAE. Prof. Efrati holds shares in Aviv Scientific, and thus will not take part in the data analysis and reports. Other than that, Prof. Efrati will fulfil the PI position, including participants screening and assessments.

Your trial doctor will be responsible for maintaining a list of codes that identify the patients at the clinic. Using this list you can be identified by your patient number; however your name will not be provided to anyone besides the clinical trial staff that are responsible of your trial treatment.

Your data and the list of name codes will be stored for at least 15 years, or as required by the state; whichever is the more stringent of the two.

Data from this study may be shared with other researchers in the future, with your permission:

1) Do you agree that we share the information we collected about you with other investigators in the field of dementia and memory impairment research? The data will be shared with no identifiable information about you.

_____Yes _____No

2) Do you agree that we share the information we collected about you with other investigators who are not in the field of dementia and memory impairment but who might be interested in further understanding the role of hyperbaric oxygen therapy on health? The data will be shared with no identifiable information about you.

_____Yes _____No

5) Hereby declare that the above consent was given voluntarily and that I understood all of the above. Also, I received a copy of this informed consent form, dated and duly signed.
6) With my signature on this consent form, I authorize the sponsor of the clinical trial, the institutional Ethics Committee, the inspectional body of the hospital and the ministry of health direct access to my medical file, for verification of trial methods and clinical data. The access to my medical information will be made while maintaining confidentiality, in accordance with the laws and regulations of confidentiality.
7) The description of this clinical trial will appear on the website: www.clinicaltrials.gov, as required by US law and by the Israeli Ministry of Health. This site will not include any information that can identify you. At most, the Web site will include a summary of the results. You can visit this site at any time.
8) In cases where the clinical trial involves providing services: preforming medical tests or supply of devices, preparations or implants, I declare that I know and agree that the information of my participation in the clinical trial will be provided to my family doctor in the health care services where I am insured. I know that the NHS will not make any use of this information, other than for for treatment and medical monitoring.

Name of the participant in the clinical trial	Signature of the participant	Date

If needed[4]

Name of the independent witness	ID number	Witness signature	Date

Investigator / subinvestigator statement:

The consent above was accepted by me, after I explained to the participant in the clinical trial all of the above and I made sure that all my explanations were understood by him.

Name of the investigator	Signature, stamp and license number	Date

[4] in case the participant in the trial, or his legal representative, is not able to read the informed consent, independent witness must be present during the explanation about the nature of the clinical trial. After the participant or his legal representative, expressed his oral consent to participate in the trial, the witness will sign on the informed consent, while mentioning the date of signature.
