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PARTICIPANT INFORMATION AND CONSENT FORM

Title:	Examine the effect of CocoMCT® on clinical factors related to health, cognition, quality of life and Alzheimer's disease – Tolerance Study
Study Acronym:	Coconut Oil in Alzheimer's disease – Prevention.001 (COAD-P.001)
Protocol No.:	COAD-P.001
Sponsors:	Macquarie University, New South Wales, 2109 Chemrez Technologies Inc. (Philippines)
Principal Investigators:	**Professor Ralph Martins** Department of Biomedical Sciences Faculty of Medicine and Health Sciences (FMHS) phone: (02) 9850 4573 email: ralph.martins@mq.edu.au
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Associated Investigators:	Dr Cintia Dias, Dr Pratishtha Chatterjee, Dr Binosha Fernando, Dr Tejal Shah, Mitra Elmi, Associate Professor Dr Hamid Sohrabi, Associate Professor Kathryn Goozee
Study Centre:	MQ Health Cardiology Clinic Suite 203, Level 2, F10A Building 2 Technology Place Macquarie University, New South Wales, 2109

This document is 13 pages long – please ensure that you have all 13 pages

We would like to invite you to take part in a research study. You are being contacted for this study because you have either expressed an interest for this study or you are enrolled into or have completed participation in one of our on-going studies at Macquarie University or at KaRa Institute of Neurological Diseases, New South Wales (NSW).

This Participant Information and Consent Form has information to help you understand the study, the tests and treatments involved as well as the possible risks and benefits associated with taking part in this research study. This document may contain words that you do not understand. Take your time, read this document carefully, and ask the study staff to explain any word or information that you do not clearly understand. Feel free to ask as many questions as you wish and take as much time as you like to decide. We encourage you to discuss this study with friends, family and primary healthcare providers including your general practitioner (GP) prior to consenting to trial participation. We also encourage you to bring a close relative or friend to accompany you during your study visits. You should not sign this document until you understand all the information presented in the following pages and until all your questions about the research have been answered to your satisfaction.

Your participation in this research study is voluntary and if you choose not to participate, your medical care will not be affected in any way. You may also withdraw from the study at any time after you have commenced, and this will not affect your current or future medical care.

If you decide to take part in this study, you will be asked to sign the Participant Consent Form at the back of this document, with the study doctor or one of the suitably qualified study investigators. You will be given a copy of the signed Participant Information and Consent Form to keep. No study specific procedures can be conducted without you first signing this form.

WHY IS THIS RESEARCH BEING DONE?

Memory loss is common among the general adult population. It may not be of clinical significance, or it may be a symptom of another condition, as depression and anxiety, or an early sign of dementia. The most common form of dementia (i.e. loss of memory, language skills, ability to make decisions and other mental abilities) is Alzheimer's disease. Unfortunately, there is no cure for this type of dementia. Current medications treat the symptoms of dementia but are not capable of halting its progression or preventing it. Thus, primary prevention measures appear to be more beneficial than treatment. By primary prevention, we mean any activity or intervention that may decrease the risk of future dementia. Researchers worldwide are working toward the development of medications that may prevent, stop or delay the progressive decline of individuals with dementia. To facilitate drug discoveries, research is needed to better understand the biochemical nature of memory loss and dementia.

Based on previous research, we believe that coconut oil has nutritional properties that may prove useful in preventing or delaying the process of neurodegeneration, a process in which our brain cells gradually lose their ability to function or to survive. Coconut oil is mostly comprised of medium-chain fatty acids that are easily absorbed by our body. Our body can then convert the medium chain fatty acids into ketone bodies. Ketone bodies are considered an

alternative source of energy for the brain, and therefore, may improve our cognitive function and other mental abilities. Therefore, the aim of this study is to investigate the effect of Coconut oil on your memory and other mental abilities.

WHO CAN PARTICIPATE?

To take part on this study you must be:

- ✓ Males or females aged 50 to 80 years
- ✓ Able and willing to complete the study protocol
- ✓ Able to provide written consent in English

You are NOT eligible to participate if you have:

- ✓ History of dementia including Alzheimer's disease
- ✓ Significant gastrointestinal disorders including history of reflux, diarrhoea, constipation, irritable bowel syndrome, diverticular disease, chronic gastritis.
- ✓ Renal disease or insufficiency
- ✓ Liver disease or insufficiency
- ✓ History of high blood fat (LDL cholesterol > 5.0 mmol/L)
- ✓ Cardiovascular disease
- ✓ Multiple sclerosis
- ✓ Myocardial infarction within the last two years
- ✓ Uncontrolled hypertension
- ✓ Diabetes Mellitus
- ✓ Allergy to coconut, coconut oil
- ✓ Participated in another clinical drug or device intervention trial within the past 30 days.

WHAT WILL YOU BE ASKED TO DO?

A staff member will speak to you over the phone. After obtaining your consent, he/she will ask you some questions to see if you meet the study eligibility criteria described above. The staff member will also do a very quick memory and thinking test and ask some medical history related questions over the phone, before you are requested to come in for your first appointment.

Before your first appointment and each subsequent appointment you will be asked to complete a 3-day food record, you will write everything you eat and drink for 3 days (1 weekend day and 2 week days). Instructions will be given on how to complete this task. You will also be asked to fast overnight (10 hours), and to refrain from alcohol and physical activity 24 hours prior to your appointment. At each appointment, the study team will confirm with you the next appointment's date, time, location and instructions.

You will attend 9 appointments over 2 months at the MQ Health Cardiology Clinic Suite 203, level 2, located at 2 Technology Place, Macquarie University. Each appointment will take about 5 hours:

- ✓ **Appointment 1**: You will sign the Participant Consent Form and will answer to a screening memory assessment to confirm you are eligible. If you are on any medications, even if it is

herbal or a complementary medication or any supplement, you must tell the study doctor. Please note that if you are not completely truthful with the study doctor regarding your health history, you may possibly harm yourself by participating in the study. If found eligible, you will then be asked to answer to some questionnaires, donate fasting blood samples and have your anthropometric measurements and blood pressure taken. You will then be served breakfast and will go through some memory tests. After the memory tests, you will be served a snack and the test food product, and you will have a finger prick blood sample collected before and 1 and 2 hours (1 drop each time) after having the study product. During this appointment you will also have an electrocardiogram (ECG) done. You will also receive enough study product for 1 week and instructions on how to consume it.

- ✓ **Appointments 2 to 8**: You will be asked to return your unused and empty bottles. You will be asked to answer to some questionnaires, donate fasting blood samples and have your anthropometric measurements and blood pressure taken. You will then be served breakfast and will go through some memory tests. After the memory tests, you will be served a snack and the test food product, and you will have a finger prick blood sample collected before and 1 and 2 hours (1 drop each time) after having the study product. You will also receive enough study product for 1 week and instructions on how to consume it.
- ✓ **Appointment 9**: You will be asked to return your unused and empty bottles. You will be asked to answer to some questionnaires, donate fasting blood samples and have your anthropometric measurements and blood pressure taken. You will then be served breakfast and will go through some memory tests.

It should be noted that coconut oil is largely used in food preparation at home and in the food industry. However, you must only use the product given to you in the way it has been instructed for the purposes of this study.

During the study, you will be required to complete a daily dosing diary. You will also be asked to report any condition that you may develop during the study, no matter whether you think it is related to the study medication or not, so that if necessary, we can refer you to medical practitioner for proper examination and follow up.

You will be requested to remain in the study for its entire duration (2 months) unless you are unable to tolerate the study interventional product; the study doctor or investigator thinks that you should not continue for medical reasons; you begin another treatment that may interfere with the study outcomes; or you decide to withdraw your consent from participating any further in the study; and if the study is terminated.

STUDY INVESTIGATIONAL PRODUCT

The purpose of this research study is to investigate the effects of Laurin MCT Coconut Oil (CocoMCT®). CocoMCT oil is a non-prescription, pure (100%) coconut oil that contains only medium chain triglycerides plus Lauric oil extracted from coconut. CocoMCT oil is manufactured by Chemrez Technologies Inc. (Philippines) as a food supplement. This product is not currently available for purchase in Australian supermarkets or health shops.

Previous clinical studies have shown that coconut oil (from which CocoMCT is derived) may improve cognitive function (e.g. memory, problem solving ability) and increase body and brain energy uptake as well as high-density lipoprotein cholesterol (also known as good cholesterol) in the blood. In addition, it has been shown that coconut oil may decrease the accumulation of specific proteins which are thought to be risk factors for Alzheimer's disease. Therefore, it is proposed that taking coconut oil may provide a potential preventative treatment for Alzheimer's disease.

This is an experimental research study as CocoMCT oil has not been approved for the treatment of memory impairment or any other health condition in Australia. However, CocoMCT oil has been registered by the Philippines Food and Drug Administration, as an oil-food supplement. For this study, the use of CocoMCT oil has been approved by the Therapeutic Goods Administration - TGA (TGA is a regulatory body in Australia that give approval for use of drugs and medical devices).

This study will investigate the effects of CocoMCT oil on your cognitive function and thinking abilities as well as health and quality of life. We will also examine the effect of taking CocoMCT oil on blood-biomarkers associated with Alzheimer's disease (blood-biomarkers are components found in the blood that can be used to assess differences between healthy ageing individuals and those who may develop Alzheimer's disease). The circulating levels of these biomarkers may change with the development of symptoms of Alzheimer's disease. From this information, we will investigate if the study treatment (coconut oil) has benefits in preventing Alzheimer's disease. A positive result would provide grounds for further evaluation in a larger clinical study in the future.

STUDY PROCEDURES

Blood collection and analysis

A qualified phlebotomist will collect a sample of your blood using a sterile, disposable needle. The amount of blood to be collected will be 80 ml (approximately 5-7 tablespoons). A small amount is sent to a local pathology centre and the rest is stored by us for further analysis. The phlebotomist will also perform 3 finger prick tests (fasting, 1 and 2 hours after consuming the investigational product). Overall, any abnormal results will be communicated to you and your local GP.

Researchers will analyse and review several blood markers that may offer insights into the cause of Alzheimer's disease. Blood samples may be sent to other research institutions within Australia or overseas for further testing if necessary (i.e. any new blood marker identified that we are unable to test). All samples will be labelled with a unique code, to maintain your anonymity. This code protects your identity from technicians at the laboratory where the samples are analysed but allows your study doctor and members of the research team to identify your results, should they require to (e.g. to communicate you and your GP of any abnormal results). If any blood assessments are carried out overseas, this work will meet all appropriate Australian ethical and privacy standards. Your identity will not be disclosed to individuals working in these other institutions. Blood samples will be stored at Macquarie University until

used (at least 2 years) and then destroyed. Samples of whole blood and blood fractions will also be retained for future research and any use will be approved by a HREC.

One of the blood samples collected at your first appointment will be used for determining APOE-ε4, a gene that is a risk factor for Alzheimer's disease. If you do not want to consent to the storage of your DNA and RNA, anything that remains of this sample will be destroyed after your APOE-ε4 status has been determined. This sample will be labelled with a unique code for confidentiality reasons.

After your fasting blood sample is collected, you will be provided with breakfast by the study centre before further testing is done.

Memory testing assessments

The memory testing will comprise of a few tests (pen and paper, and computer based) which are widely used for the assessment of brain function and behavioural observations, including tasks sensitive to memory loss. Experienced and trained study staff will administer the assessments which relate to the mental processes of memory, judgment and reasoning. The study staff will be supervised by a neuropsychologist who specializes in brain and behaviour relationships. These tests will take approximately 1 hour and 30 minutes to administer. You will not be required to persist with any task you find too difficult to complete.

Questionnaires

Questions will ask about your current and past health conditions, any medications you take (including prescription and over-the-counter medications or vitamins and dietary supplements), physical activity and food consumption.

Electrocardiogram

An electrocardiogram is a test that registers the electrical activity of the heart, it allows the doctor to determine the heart's rhythm and some heart conditions.

Measurement of Cardiovascular Assessment (Optional):

You will have the option to undergo a 2D-Echocardiography, also called an echo test or heart ultrasound, if you feel comfortable with the test. Echocardiography is a test that takes moving pictures of the heart with sound waves; it is a very precise method to detect the hearts movement and shape. The findings of this test will be used for your baseline cardiovascular assessments. The test will be done by a trained sonographer at Macquarie Health Cardiology, Macquarie University Hospital, NSW 2019, or the Macquarie Heart Clinic, South Tower, Railway Street, Chatswood 2067. This echo test may require an additional visit due to the limited availability of resources. The echo test is completed within an hour, is painless and has no side effects. In a lying down position on a bed, the sonographer will apply a special gel on a probe and move it over your chest area. The ultra-high-frequency sound waves pick up images of the heart and valves and the heart's movements can be displayed on a video screen. A video recording and photographs will be made of the images. The test will be used to determine the size and shape of your heart, its overall function and its valves; the test can also determine the

presence or absence of a blood clot. All test results will be used for research purposes only and stored under strict secure conditions for the purposes of the study. Any coincidental abnormal findings may be released to your general practitioner. All assessments completed are available free of cost to you.

This test is entirely optional and will not affect a person's participation in the ongoing study should you decide not to participate. The test can be done in any person. It is a routinely and commercially available test applied in clinical assessment of cardiovascular patients.

RISKS OF PARTICIPATING

Blood collection

During blood collection there is a small risk of discomfort, bruising, dizziness and in extremely rare cases, infection at the site of the needle puncture. Some people may faint after donating blood. Please advise the phlebotomist, if you have previously experienced these conditions or if you have any concerns.

Questionnaires and memory tests

You may experience some level of anxiety or psychological discomfort while completing the memory and thinking assessments and other questionnaires.

Interventional products

The study investigational products may cause complications or undesirable side-effects that are unknown at this time. You may have none, some or all the side-effects listed below, and they may be mild, moderate or severe. If you have any of these side-effects, or are worried about them, seek medical care, including emergency care if required and advise the study staff as soon as possible. The study staff will also be looking out for side-effects. Many side-effects go away shortly after the treatment ends. However, sometimes side-effects can be serious, long lasting or permanent. If a severe side-effect or reaction occurs, the study doctor may need you to stop your study medication. Tell the study doctor if you have any problems. The study doctor will discuss the best way of managing any side-effects with you.

Although CocoMCT oil is 100% coconut oil and is considered a safe food-supplement, side-effects may occur in some people. Remember if you have new symptoms after starting to use coconut oil, you should advise the study staff as soon as possible and follow their recommendation. You may experience the following symptoms, specially at the higher doses:

- Diarrhoea
- Increase in weight
- Acid reflux, burning sensation in the stomach
- Bloating
- Loose bowel movements
- Increase in cholesterol levels (your cholesterol levels will be closely monitored in the study)

- Chest pain
- Nausea with/without feeling light headed and dizzy
- Skin dry, flaky or itchy, redness on the skin, similar to a sunburn
- Headaches
- Palpitations
- Allergic reactions that may result in anaphylaxis reactions

If you have allergy to coconut or coconut oil you should not participate in this study. In acute cases of allergic reaction, you may develop anaphylaxis. This may happen if you have been allergic to coconut or its derivate or other nuts. It may also happen if you have not previously used coconut or its oil in anyway. However, it may also occur without any previous reaction. Anaphylaxis reaction is a life-threatening condition in which the entire body becomes severely affected suddenly. Some medicines may interact with CocoMCT oil. However, no specific interactions with CocoMCT are known at this time.

If you feel unwell or experience any side-effects, physical or mental, even if they are not listed here, please contact the study doctor.

Risks associated Electrocardiogram

An ECG is safe, non-invasive and does not hurt. There may be some discomfort when the electrodes are being applied or removed.

Risks associated with 2D Echocardiography

Echocardiograms are considered very safe. Unlike other imaging techniques, such as X-rays, echocardiograms don’t use radiation. A transthoracic echocardiogram carries no risk. There’s a chance for slight discomfort when the electrodes are removed from your skin. This may feel like pulling off a Band-Aid.

Risks Associated with Providing Personal Information

As with the collection of any personal (private) information, there is a very slight risk of accidental disclosure of information or breach of computer security. Extensive safeguards are in place to minimise this potential risk, with hard copies of your information stored in a locked facility and electronic data stored on personal computers with password restricted access.

Unknown Risks

In addition to the risks listed above, the study medication and study procedures may have unknown risks. There is always the possibility that you will have a side-effect that is currently unknown or not expected. It is important that you report any symptoms and all health problems to the study doctor, whether you think these problems are related to the study medication or study procedures or not. You will be monitored for side-effects, and the study doctor may decide that you should be withdrawn from the study for your safety.

BENEFITS OF PARTICIPATING

It is possible that you will not gain any therapeutic benefits from the study. However, society may benefit from this research study, this study may help develop a new preventive therapy or may help to delay the onset for people who are at risk of developing Alzheimer's disease.

Investigations undertaken may reveal previously undetected health conditions which may enable earlier treatment. Any abnormal findings or pathology will be reported to your general practitioner for follow-up.

MEDICAL CARE AND COMPENSATION

The study does not provide any renumeration or in-kind contributions should you decide to take part in the study. Your participation in this study does not prejudice any right to compensation, which you may have under statute or common law. If any adverse event or injury occurs due to participation in this study, the research team will ensure you receive appropriate medical care. There is provision for compensation under Indemnity and Public Liability coverage held by the Macquarie University.

WITHDRAWAL AND TERMINATION

If at any time you wish to withdraw from this study, you are free to do so without prejudice or without affecting your current or future medical care. You will be requested to return empty and unused bottles containing study products. If you leave the study, all the information you gave us before you left the study will still be used for the study unless you give us explicit instructions otherwise.

The doctor in charge of this study may also decide to withdraw you from the study without your consent for the following reasons:

- Based on his/her judgment to improve your medical care or for your safety;
- If you do not take the study products as instructed or if you do not follow the study schedule;
- If the study is terminated;
- For any administrative reason which is at the discretion of the study investigators.

NEW FINDINGS

During the study, you will be informed of any significant new findings that may develop which might affect your willingness to continue participation in the study.

RESULTS OF THE RESEARCH STUDY

Data describing the outcome of this study will be available to participants either at public lectures, in press releases and in research articles published in peer reviewed journals. If you would like to receive the scientific papers published about this study, please let us know. Your identity will not be disclosed in any publication or report regarding the study results.

This study's interventional product will not be made available to participants after the completion of the study.

COSTS, REIMBURSEMENTS AND PAYMENTS

You will not be paid for your participation in this research. The study medication, study-related procedures and tests, and study visits will be free of charge. Based on available funding, you may be offered a cab voucher for one or more of your study-related visits. However, this is not guaranteed. Breakfast will be provided at all visits.

PRIVACY AND CONFIDENTIALITY

If you decide to take part in the study, by signing the Participant Consent Form, you give us permission to use unidentifiable information about you and to share it with the sponsor, health authorities and other study personnel representing the sponsor, or ethics committee to verify the study procedures or the accuracy of the data. This permission continues until the study is over, and up to 15 years thereafter if required.

Confidentiality of your records will be maintained. Your personal contact details and your key-coded medical data ("key-coded" means that at the time of your enrolment you will be assigned a code that will be used instead of your name to identify you in any study-related documentation) will be stored in a secure database and will not be made available to the public.

Other research centres within Australia and overseas may assist us with our research in exchange for our study findings and data. If this is the case, neither your name nor any other information that may identify you personally will be given to these other research centres. Instead they will only be given data or blood biospecimen with your identification code. Therefore, please be assured that all personal information collected about you as part of this study will remain strictly confidential throughout the conduct of this study.

Throughout the study, you have the right to ask what kind of data is recorded about you, who keeps your data, and who has access to it. You also have the right to review or ask that your data be corrected if necessary.

The collected data will be combined with data from other participants in the study and the results will be used for scientific reasons including research, publications or presentations at scientific meetings.

As part of your consent for this study you will be asked to agree to the exchange of information between your GP or medical specialists and the study doctor. This is to ensure that your doctors are aware of the treatment you are receiving and that information regarding your health history can be confirmed by your doctors if required. Your GP may be notified of your involvement in this study and may be sent details of some of your results if medically indicated.

FUNDING

This project is sponsored by Macquarie University and by Chemrez Technologies Inc. (Philippines). Macquarie University will provide funds and in-kind contributions, and Chemrez will provide funds and supply the study interventional product (CocoMCT®).

ETHICAL APPROVAL AND CONTACT DETAILS

The ethical aspects of this research study have been approved by the Macquarie University Human Research Ethics Committee (Medical Sciences). If you have any questions regarding

your rights as a research participant, you may contact the Macquarie University Human Research Ethics Committee (Medical Sciences) ethics secretariat on +61 2 98504459 or by email: ethics.secretariat@mq.edu.au.

If you have additional questions or in the event of a research-related illness or injury, please contact one of the study doctors or study investigators via the contact information below:

Name of Principal Investigator: Dr Edward Barin, contact number (02) 98123000, email: edward.barin@mqhealth.org.au.

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PARTICIPANT CONSENT FORM

Study Title: Examine the effect of CocoMCT® on clinical factors related to health, cognition, quality of life and Alzheimer's disease – Tolerance Study

Protocol Number: COAD-P.001

Principal Investigators: Professor Ralph Martins, Dr. Ann Bacsi, Dr Edward Barin

Associate Investigators: Dr Cintia Dias, Dr Pratishtha Chatterjee, Dr Binosha Fernando, Dr Tejal Shah, Mrs Mitra Elmi, Associate Professor Hamid Sohrabi, Associate Professor Kathryn Goozee

By signing this consent form, you agree to take part in this study and confirm that you have:

- Read this study's information sheet
- Had an opportunity to ask questions and discuss the study
- Received satisfactory answers to all your questions
- Received enough information about this study
- Understood that you are free to withdraw from this study at any time without giving a reason and without affecting your current or future medical care
- Understand that blood samples will be stored for analysis (including DNA and RNA)

I (the participant) **have read** / **have had read to me** (where appropriate) and understand the information above, and any questions I have asked, have been answered to my satisfaction. I agree to participate in this research, knowing that I can withdraw at any time without consequence. I have been given a copy of this form to keep.

I **consent / do not consent** the storage of DNA and RNA, after my APOE-ε4 status has been determined.

Participant's Name: _____ (Block letters)

Participant's Signature: _____ Date: _____

Investigator's Name: _____ (Block letters)

Investigator's Signature: _____ Date: _____
(INVESTIGATOR's [OR PARTICIPANT'S] COPY)