STUDY TITLE: OPEN LABEL POSTMARKET EVALUATION OF ORALLY DOSED ALMEGA PL® ON CHOLESTEROL AND CARDIO-METABOLIC PARAMETERS.

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PARTICIPANT INFORMATION SHEET

1. Study Title: Open label post-market evaluation of orally dosed Almega PL on cholesterol and cardio-metabolic parameters.

2. Investigators: Dr Eneko Ganuza (iwi/Qualitas Health)

3. Sponsors: Qualitas Health (Texas, USA)

4. Study site: 2800 Post Oak Blvd, Suite 5858 Houston, TX 77056.

5. Introduction:

Cholesterol/iwi new customers are invited to take part in a study to test the effect of a new non-fish, algae-derived product that contains Almega®PL as its main ingredient. Participation in this study is purely voluntary and participants can withdraw at any point without prejudice. The following information describes the study and their role as a participant.

The Principal Investigator, Dr. Eneko Ganuza, will answer questions about the study. The information contained in this Information Sheet will help participants understand what participation in the study involves, and the possible risks and benefits that may result from participating in the study. Participants' rights and responsibilities will also be outlined. Dr. Ganuza is not a medical doctor and any advice related to a health condition will be directly provided by the participant's personal doctor.

6. Purpose of the Study:

The investigational product iwi/Cholesterol is a commercially available capsule-form herbal (algae) supplement containing Almega®PL, a *Nannochloropsis* algae-derived extract rich in eicosapentaenoic acid (EPA). A New EPA is a type of omega-3 essential fatty acid known to play a beneficial role in protection against cardiovascular disease. Iwi/Cholesterol is the only source of long chain omega-3 that does not contain the DHA that is present in other omega-3 sources (fish oil, krill oil, other algal oils). A previous, double-blind, placebo-controlled, randomized three-month clinical trial (Rao et al., 2020 *Nutrients*, 12, 1869), showed that this product decreases total cholesterol and VLDL-cholesterol. Almega®PL was registered at the Food and Drug Administration (FDA) as a New Dietary Ingredient (NDIN) in 2014.

The aim of this study is to assess the effectiveness of Almega PL on improving blood markers associated with heart health of iwi customers. Additionally, we would like to offer our customers the capacity to monitor their blood lipids to track their health progress and seek medical advice if required. This program will also increase consumer awareness and engagement towards iwi products and their health benefits. The impact of AlmegaPL in blood markets was demonstrated in a double-blind placebo-controlled randomized clinical trial (Rao et al., 2020 *Nutrients*, **12**, 1869). It is expected that the results observed in our previous clinical trial will translate to the general public and specifically to new iwi Cholesterol customers.

The study will involve over 200 male and female new consumers of this product. As part of the screening procedure, participants will complete a short questionnaire to make sure they are new iwi users. Any participant who is already using iwi will not be considered in the study. Any participant that has a serious condition (including but not limited to kidney, neurological, immunological, liver and gastrointestinal disease, any heart condition or diabetes) will also be disqualified for the program and directed to their doctor. Any participant attempting conception, pregnant or breastfeeding will also be disqualified. All other participants will be accepted into the limited study based on their time of application until the quota is completed.

The study will monitor blood lipid levels across a supplementation period (baseline, month 3 and month 6). The age, height, weight, gender, fasting total cholesterol, LDL-cholesterol, HDL-cholesterol, calculated VLDL-cholesterol, triglycerides, as well as hs-CRP inflammatory marker, and glucose and HbA1c as diabetes indicator of each participant will be recorded over the study period. **iwi** will receive the aggregated data of the participants only for statistical analyses. The data will be used by iwi as educational and marketing material.

Participants will be asked to take the allocated product according to the dose prescribed (2 capsules iwi/cholesterol per day) and adherence to the protocol will be evaluated with a follow up email. Participants will be asked to maintain their usual level of physical activity and diet for the duration of the study. The dose used in this trial is in agreement with the commercial dose communicated to the FDA and comparable to doses previously used in our clinical trials. There will be no cost incurred for this analytical assessment to the participant.

7. Study Procedures:

7.1 Treatment Schedule

Study Stage	**Specific Timing**	**Activity**
Planning 2 Months	N/A	● Approval of protocol ● Independent peer-review ● Logistical arrangements ● Recruitment
Pre-Study 1 Month	Upon approval and completion of recruitment	● Preliminary screening against inclusion and exclusion criteria ● Pre-study interview: o Information email and gain informed consent from the participant o Enrolled participants purchase the product and receive the testing kits along with instruction regarding the study requirements.
Study Week 0-24	Baseline data collection	First test kit will be shipped to Imaware
	Trial Period	● Participant takes product as instructed ● Participant will receive and send the test kits on month 3 and 6
Trial Months 0-6 (period begins at trial week 2)	Trial end interview	● Participant completes end-trial blood test. ● Participants exit email or phone interview to address adherence.

End-Study Month 3		
Post-Study	N/A	● Data verification and statistical analysis ● Report drafting and approval ● Study debrief and review

***** Please note that enrolment in the trial to receive product will only occur after all inclusion criteria have been met.

7.2 Length of Treatment Time
In total, participants will be required to send the test kits 3 times throughout the total trial time of 6 months.

At the completion of month 6, participants will repeat the baseline measures including a final blood test and a required exit interview.

Clinical interviews will be undertaken by email or phone.

8. Risks and Discomforts

As in the case of taking any treatment, we cannot guarantee that participants will not experience any uncomfortable effects during this study. The treatment includes the following ingredients: Almega PL.

There are 4 reported causes of adverse effects of orally dosed supplements containing EPA reported on the TGA database. Specifically, diarrhoea, dry skin, enteritis infection (inflammation of the small intestine) and nephrolithiasis (kidney stones). These events are 4 out of several thousands of participants. A 2011 study using a similar EPA based product and involving 229 participants found the product to be well tolerated.

There is also a risk of discomfort that may be experienced as a result of the blood draws with finger prick. Blood sampling can cause pain, bleeding, bruising, and/or swelling at the site of needle penetration (risk less than 1 in 50). Fainting may occur (risk less than 1 in 100) and infection rarely occurs (risk less than 1 in 1000).

Should participants experience any of these or other mild adverse effects or have other concerns about the treatment, blood collection, or data collection please contact the investigators (24 hours a day). Our contact details are found in the Contacts section of this document and the 24-hour contact mobile number is also on the product label.

9. Possible Benefits

Research is designed to benefit society by gaining new knowledge and improving our understanding of effective treatments for improved health and wellbeing. However, there may be no direct benefit to the individual participant for their involvement in the study.

10. Voluntary Participation/Right to Refuse or Withdraw

There is no obligation for participants to be involved in this study. If participants decide to participate in the study and later feel they no longer wish to be part of it, participants may withdraw from the study at any time without prejudice to any current or future involvement in clinical studies held by the study investigators or sponsor. If participants withdraw their consent, all data collected up until that time will be used in the analysis of the data.

All communications will be performed by a trained iwi Qualitas employee or Principal Investigator Dr. Ganuza. In the event that Dr. Ganuza does not screen the participant, Dr Ganuza will review case files before

participants are enrolled. Any participant that presents a response or result (e.g. blood test) that is outside of normal range will be directed by Imaware™ to medically trained professionals with their results.

11. Confidentiality

The study investigator will gather certain personal information about participants. This information will be held by Qualitas/iwi as aggregated data. Data will be identifiable via study number allocated at enrollment but not by participant name. All publicly shared data or data used in publications will be in a non-identifiable form.

Consent is sought for extended use of the data, which means it may be used in future research—for example, an extension of the current study and/or related studies conducted by Qualitas/iwi. Furthermore, data may be used for subsequent statistical analysis, which may be published in peer-reviewed journals; however, no identifiable personal details will be published or used.

Participant data will be stored in locked filing cabinets at the head office of Qualitas Health for a period of 15 years and will be accessed by Trial Co-Investigator and trial contact. At the end of this storage period participant data will be disposed of in a confidential manner, for example via shredding through a professional agency.

Participant data will also be stored on secure trial management software called 'Realtime' and data may be entered into spreadsheets for analysis. Spreadsheets are stored on password protected computers and no identifying information is contained within the spreadsheet.

Unless required by law, only the participants and their authorised representatives, will have access to data which identifies participants by name or from which participant identity is otherwise apparent or can be reasonably ascertained.

All personal information will be used only for the purpose of administering participation in this study and in accordance with the laws governing the protection and privacy of personal information under USA privacy legislation.

By signing the attached consent form, participants authorize the release of/or access to this confidential information in an aggregated non-identifiable form to the relevant study personnel and regulatory authorities as noted above.

Participants have the right to access personal information collected from them in connection with the study and request corrections of any such personal information that is incorrect.

12. Costs

All costs associated with the collection of data (i.e. blood samples) will be covered by Qualitas Health and Imaware. At no point during the study will a participant be required to pay any cost for any test.

13. Illness or Injury

If, as a result of being in this study, participants become ill or are injured, please immediately contact your doctor and then the principal investigator of the study. She or he will then provide all necessary information and treatment and will inform the trial sponsor.

If an adverse reaction to the allocated product including allergic reaction occurs at any time during the study please don't hesitate to first contact your doctor and then trial co-coordinator listed below. In the case of an emergency please dial 911.

14. Termination of the Study

This research project may be stopped for a variety of reasons.

During the trial, any participant that records out-of-range analytical levels will be referred to their GP for assessment of suitability/safety for continuation in the trial.

At the discretion of the GP the participant will either be placed on standard care of cholesterol-lowering medication (and removed from the trial) or continue in the trial on the supplementation.

The participant also has the option to stop supplementation at any point.

15. Investigator Benefits

The investigators are being remunerated to conduct this study. They will not allow a conflict of interest to compromise their position or this research study.

16. Consent

The Principal Investigator, Dr Eneko Ganuza, is required to provide participants with all information regarding the nature and purpose of the research study, risks/benefits and the possibility of alternative treatment; participants should be given the opportunity to discuss these. It must be stated that participants are free to withdraw anytime and that if participants do not participate, they will not suffer any prejudice.

19. Advice and Information – Contact Details

If participants have any further questions regarding this study, please do not hesitate to contact:

Eneko Ganzua –Trial Contact
Ph: +1 832 850 2022
24hr mobile: +1 480 519 5342

If unwarranted side effects occur please don't hesitate to contact a doctor and the study representative.
In the case of an emergency please dial 911.

Consent Form

Protocol Title: ***Almega for hypercholesterolemia & Inflammation***

I, _____, the undersigned hereby voluntarily consent to my involvement in the research project titled: Open label post-market evaluation of orally-dosed Almega PL on cholesterol and cardio-metabolic parameters.

OFFICE USE ONLY
Name:
Sign:
Date:

I acknowledge that the nature, purpose and risks of the research project and alternatives to participation have been fully explained to my satisfaction. Specifically, the details of the procedure(s) proposed and the anticipated length of time it will take, the frequency with which the procedure(s) will be performed and an indication of any discomfort that may be expected have been explained to me.

- I understand my participation in the trial is dependent on meeting all inclusion criteria, including the blood test results.
- I freely agree to participate in this research project according to the conditions in the Participant Information Sheet, which I confirm has been provided to me.
- I understand that my involvement in this study may not be of any direct benefit to me.
- I have been given the opportunity to have a member of my family or another person present while the study is explained to me.
- I have been told that no information regarding my medical history will be divulged to unauthorized third parties and the results of any tests involving me will not be published so as to reveal my identity.
- I understand that access may be required to my medical records for the purpose of this study as well as for quality assurance, auditing and in the event of a serious adverse event.
- I understand that I am free to withdraw from the study at any stage without prejudice to future treatment. If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.
- I am 18 years of age or over.
- I consent to my usual doctor/s being notified of my participation in this study and of any clinically relevant information noted by the study doctor in the conduct of the trial.
- I declare that all my questions have been answered to my satisfaction.
- I have read or have had read to me in a language in which I am fluent, and I understand the Participant Information Sheet, version 6, 5th February 2019.
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NAME OF STUDY PARTICIPANT: _____

SIGNATURE OF STUDY PARTICIPANT: _____ **DATE:** _____

Declaration by senior researcher:
A written explanation of the research project, its procedures and risks has been given to the participant and I believe that the participant has understood that explanation.

NAME OF SENIOR RESEARCHER: Eneko Ganuza

SIGNATURE OF SENIOR RESEARCHER: **DATE:** 2/07/2022