**Participant information sheet**

**HI-FIVE STUDY**

UREC 17/18 (10th April 2017)

Thank you for your interest in the study.

You have been invited to take part in a study investigating the effect of fish oil on platelets and on tiny particles called extracellular vesicles in the blood (HI-FIVE STUDY). Before you decide to participate please take time to read the following information carefully. Please ask us if there is anything that is not clear or if you would like more information.

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**Background of study**

It is now well established that the role of diet is significant in the prevention and treatment of cardiovascular diseases (CVDs). There are many risk factors which can affect the risks of developing CVD. Some are not modifiable, such as genetics and age, while others are modifiable, such as smoking and diet. Fish oil, containing omega-3 (or n-3) polyunsaturated fatty acids (n-3 PUFA), is suggested to have a favourable effect on several risk factors associated with CVDs, but there is still a great deal that is not understood. In this study, we wish to investigate the effects of fish oil on newly emerging risk factors for CVD, extracellular vesicles (EVs). EVs are tiny particles released from many types of cells and from platelets, particularly when they are stimulated, activated or damaged. High numbers of EVs in the blood have been associated with a higher risk of CVD, but it is not clear exactly what EVs do in the body.

A few studies, including our own, suggest that fish oil reduces numbers of EVs, but research is limited.

**What is the purpose of the study?**

This study aims to investigate whether fish oil supplements alter (i) the number and profile of EVs in the blood, (ii) the way the EVs in the blood behave, (iii) production of platelet-derived EVs (PEVs) by platelets taken from blood and (iv) the behaviour of the PEVs in the blood.

**Am I suitable to take part?**

We are aiming to recruit male and female participants between the ages of 40 and 70 years, non-smokers, who are generally healthy, but may be considered to have moderate risk for heart disease (risk will be evaluated by an online calculator called “QRISK2”).

Suitable volunteers should have a normal liver and kidney function and haematology and a weekly alcohol intake of <21 units (men) / <15 units (women). A unit of alcohol is half a pint of beer/lager, a single pub measure of spirits e.g. gin/vodka or a small glass of wine (125 ml).

You will not be able to take part if you:

* BMI: ＜18.5 kg/m2
* Have hyperlipidemia
* Have diabetes mellitus or other endocrine disorders.
* Have heart problems.
* Have renal, gastrointestinal, respiratory, liver or bowel disease
* Have inflammatory disease.
* Take drug treatment for hypertension, hyperlipidaemia, inflammatory conditions, depression or thyropathy.
* Take aspirin, ibuprofen or other nonsteroidal anti-inflammatory drugs (NSAIDs) > 4 times per month, or once in the week preceding the study.
* Take any other anti-platelet or anti-coagulant drugs, like triflusal, clopidogrel and warfarin.
* Have allergies.
* Smoking (including e-cigarettes and nicotine products)
* Have a history of alcohol misuse.
* Regularly consume oily fish and/or dietary supplements.
* Planning to start or on a weight reducing regimen.
* Participate in intense aerobic exercise (＞20 min, three times a week).
* Pregnant, lactating, or if of reproductive age and not using a reliable form of contraception (including abstinence).
* Have participated in another clinical trial within the last three months.

The medical and lifestyle questionnaire that you have already completed and some blood tests will be used to screen for the eligibility of study.

**Do I have to take part?**

It is up to you to decide whether to take part or not. If you decide to take part, you will be given this information sheet to keep and asked to sign a consent form. Your participation remains purely voluntary. You may withdraw at any stage and without giving a reason.

**What would happen to me if I take part?**

If you are willing to participate in the study after reading this information sheet, your initial eligibility will be determined via the medical and lifestyle questionnaire sent together with this sheet. If you meet the criteria, you will be invited to attend a screening visit at the Hugh Sinclair Unit of Human Nutrition at the University of Reading.

***Screening visit***

You will need to come in the morning in an unfed state (fasted, not eating or drinking anything but water from 8 pm the night before). All of the procedures of this study will be explained in detail to you and you will be offered the opportunity to ask questions. After your consent for participation being taken, we will measure your height, weight, and blood pressure. A small blood sample (~15 ml, volume equivalent to one tablespoon) will be collected as well. The screening visit should take approximately 30 minutes.

If you are found suitable for the study and are willing to proceed, we will confirm your participation in the study and inform your GP of your wish to take part. If your screening

results indicate any cause for concern, we will advise you to discuss this with your GP.

***Study visit***

If you agree to participate and are suitable for the study, you will need to consume capsules containing one oil per day (with breakfast, lunch and dinner) for a period of 12 weeks. This will be followed by a 12-week ‘washout’ period when you will have no treatment. The final phase will be a 12-week period when you will be asked to consume capsules containing similar dose of another oil per day again. During one of the periods, the capsules will contain fish oil at a dose of 1.8g n-3 PUFA per day, and during another, they will contain a ‘placebo’ or ‘dummy’ oil, which consists ofsafflower oil. Some individuals will receive the fish oil capsules first, while others will receive the placebo first, but all subjects will receive both types of capsule during the study. However, neither you nor researchers will know the order in which you are receiving the capsules.

During the study, there will be four ‘intervention’ visits, which will take place at the beginning and end of each 12-week intervention period (weeks 0, 12, 24 and 36). Before each study visit, you will be asked to abstain from alcohol and strenuous exercise during the 24 hours prior to the study day. On each visit day, you will be asked to come to the nutrition unit in an unfed state (fasted, not eating or drinking anything but water from 8 pm the night before). After detecting the weight and blood pressure, a blood sample of approximately 100 ml (volume equivalent to six tablespoons) will be collected from you. During each intervention visit, you will be given the opportunity to discuss any issues with the study or the capsules. Each visit will last approximately 30 minutes.

Following screening, if you are eligible for the study, you will be given a food frequency questionnaire, which will be used to assess your normal diet. We will need you to complete this questionnaire at home before your first visit and again during each arm of the intervention study (weeks 0, 12, 24 and 36). The questionnaire can take up to one hour to complete.

**What will be measured in the blood samples collected?**

The blood sample collected at screening visit will be used to measure levels of blood fats, glucose, markers of kidney and liver function and to perform a full blood count.

This is necessary to further determine your suitability for participation in the study.

The blood samples collected during study visits will be used to measure (i) the number and profile of EVs in the blood, (ii) the way the EVs in the blood affect blood clotting, (iii) production of platelet-derived EVs (PEVs) by platelets taken from blood, (iv) the way the PEVs in the blood affect blood clotting and (v) levels of n-3 PUFA in your blood.

Blood will be frozen for analysis and the Department of Food and Nutritional Sciences has a licence for storing such material for the purpose of research, which has been obtained from the Human Tissue Authority.

**Do I have to modify my diet or lifestyle in any way?**

During the study period, you will be asked to maintain your normal diet, exercise and carry out your usual activities. Volunteers are also advised not to drink alcohol and do strenuous exercise 24 hours before the study day. We do ask that you inform us if at any time during the study period you are prescribed any medication or if you are advised to stop any medication that you are taking at the start of the study period.

**What are the possible disadvantages of taking part?**

There are no reported severe adverse effects of the study treatment as fish oil and safflower oil are widely consumed and tested. However, some mild side effects like nausea, dizziness and stomach discomfort have been seldom reported. Therefore, during each intervention visit, you are encouraged to discuss any issues with the study or the capsules. Any adverse effect will be recorded and discussed with you and our nurses to estimate whether intervention should be terminated. Any dropout due to adverse effect will be followed up and your GPs will be informed as well.

Blood sampling is an invasive procedure, so there can be a small discomfort as any blood sampling which may affect some people more than others. You should not experience any pain during or after this procedure. You may develop a small bruise at the site of the blood sample, but this will fade like any bruise. This procedure will be performed by a fully trained researcher or nurse in accordance with the University of

Reading guidance on research involving blood samples collection and first aid. The volume of blood collected, approximately 100 ml, will cause no adverse consequences.

**What are the possible benefits of taking part?**

The knowledge gained from the study will help us to identify whether there are any new means by which fish oil could have a beneficial effect on the risk of developing heart disease.

**Would my taking part in this study be kept confidential?**

Confidential information will be stored securely and can only be accessed by the study investigators. All information collected during the study will be treated in strict confidence in accordance with the relevant data protection legislation. Your data will only be identifiable by a unique volunteer number, not by your name, so information will be disclosed in any way which will allow the identification of yourself. Information obtained from the study may be published in scientific journals but only in the form of average values for the group. No results for the individual subjects will be published or presented in scientific meetings.

**Will the results be available to me?**

You will be supplied with your screening results. Once the study is completed and analysed statistically, we can provide you with some feedback about what we have found in the study and what it may mean for future research.

**What would happen to the results of the research?**

The results of this study will contribute to the PhD thesis of a postgraduate student and will be published anonymously in scientific journals, oral presentations or other scientific contributions. The results of this study will also be provided to the Biotechnology and Biological Sciences Research Council Diet & Health Research Industry Club (BBSRC-DRINC), who are funding this study.

**What will happen if I don’t want to carry on with the study?**

If you do decide to take part, you will be asked to sign a consent form during the screening visit and you will be given a copy of this to keep. However, you will still be free to withdraw from the study at any time and without giving a reason. This will not

affect your participation in future studies. While you are participating in the study, it is important for you to attend all visits to the best of your ability. If the appointment is not

convenient on a particular date, please contact the study investigators as soon as possible so that an alternative date can be offered to you.

**What if there is a problem?**

***Complaints***

If you have a concern about any aspect of this study, you should ask to speak to the investigators who will do their best to answer your questions. If you remain unhappy and wish to complain formally, you can do this through Professor Richard Frazier (Head of Department) (see contact details at the end of this Participant Information Sheet).

***Harm***

In the event that something does go wrong and you are harmed during the study, the University of Reading has in place Professional Indemnity Insurances that provides cover against negligence, error or omission for the activities of its employers.

**Will I get paid for taking part?**

An honorarium will be paid as an inconvenience allowance of £200 upon completion of the study, which includes any travel costs you may incur.

**Who is organising and funding the research?**

This research is being organised by the University of Reading’s Hugh Sinclair Unit of Human Nutrition, and funded by BBSRC-DRINC.

**Who reviewed this study?**

This project has been reviewed by the University Research Ethics Committee and has been given a favourable ethical opinion for conduct.

**Contact Information**

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| *Main point of contact:*  **Ruihan Zhou (PhD student, Study Researcher)**  Email: hi-five@reading.ac.uk  Address: Department of Food and Nutritional Sciences, PO Box 266, University of Reading, Whiteknights Campus, Reading, RG6 6AP  Office: 2-01, Harry Nursten Building | *For formal complaints:*  **Professor Richard Frazier (Head of Department)**  Email: r.a.frazier@reading.ac.uk  Tel: 0118 378 8709  Address: Department of Food and Nutritional Sciences, PO Box 266, University of Reading, Whiteknights Campus, Reading, RG6 6AP  Office: 2-41, Harry Nursten Building |

**Thank you for reading this information sheet. If you decide to take part in this study you will be given a copy of the information sheet and a signed consent form to keep.**