The ORIP Trial

Participant Information Sheet and Informed Consent Form

Scientific Title: Omega-3 fats to Reduce the Incidence of Prematurity – the ORIP Trial

You are invited to participate in a study to determine whether increasing the amount of a special fat called DHA in the diet of pregnant women lowers the risk of preterm birth. This study is being conducted by Dr Jo Zhou and her colleagues from the Women's and Children's Health Research Institute and the University of Adelaide.

Why are we doing this study?

Most infants are born at term (around 40 weeks of pregnancy) but unfortunately some infants are born prematurely (before 37 weeks of pregnancy). Although we have made tremendous improvements in the care of premature infants there are still many health risks of being born early including developmental delay, chronic lung disease and even death in rare cases. These risks are greater the earlier the baby is born, particularly in those born very premature (less than 34 weeks). This study will investigate whether taking a natural dietary supplement, a fish oil extract rich in the omega 3 fat called DHA, will help prevent very premature delivery.

DHA is found in fish and fish oils and is thought to have a number of health benefits including helping to maintain a pregnancy to full term. We have found evidence to support this when we conducted a study of DHA supplementation in over 2,000 pregnant women to see if DHA supplementation in pregnancy benefits the development of children (the DOMInO trial). We observed that women who took DHA-rich fish oil supplements from 20 weeks until birth had pregnancies that were 1-2 days longer than women in the control group. We also saw that fewer women in the DHA-rich fish oil group gave birth to very premature babies. However, this was offset to some extent by an increase in the number of women who had gone over their due date and were induced or had Caesarean-sections.

In the ORIP trial, we will examine the effects of taking DHA supplements in pregnancy more carefully and focus on the rate of preterm birth. We will use the same treatment as in the DOMInO trial, but we will start the supplementation earlier and stop the supplements at 34 weeks. We hope that this can prevent very premature birth without increasing the need for inducing birth or Caesarean section.

What is involved?

You will be randomly assigned (like tossing a coin) to one of two groups. One group will be asked to take capsules with DHA-rich fish oil and the other group will take capsules containing a blend of vegetable oils (canola, sunflower and palm oils) with a small amount of fish oil with DHA to best match what is typical in the Australian diet and to aid masking. Neither you, nor the research team, will be able to choose which group you are in or know which type of capsules you have been assigned to take. You will be asked to take 3 capsules per day that are easy to swallow from enrolment until 34 weeks pregnancy or the birth of your baby, whichever comes first. The total amount of fat from the 3 capsules is tiny – only 1.5 gms per day which is negligible in terms of energy.

The dose of DHA in the DHA-rich fish oil capsules is the same as that used in DOMInO and has been shown to be safe. The only side effect was some women reporting fishy burps. The other

capsules will contain DHA at a level that approximates many DHA fortified foods, for example, 2 slices of DHA fortified bread.

You can be part of this study if you are under 20 weeks of pregnancy. If you are on multivitamin supplements containing fish oil you can still take part in the study if you are willing to stop taking those supplements or change to ones that do not contain fish oil.

What will happen during the study?

1. At enrolment, we will collect some information about you, including contact details, age, weight, height, education, occupation, smoking status and pregnancy related information.
2. A tiny blood sample by finger prick will be taken at enrolment and again at 34 weeks of pregnancy to assess fatty acid levels.
3. We will also contact you 2 weeks after enrolment and at 28 weeks of pregnancy to monitor your progress, ask a few questions about compliance and answer any questions you may have.
4. Following the birth of your baby, details about your pregnancy and birth as well as your infant will be collected from your medical records and your baby's medical records.

Optional blood and urine collection for an additional study related to the ORIP trial

The following samples are optional; if you decide not to have these samples taken you can still participate in the study. For those who choose to have these samples taken they will be used to measure inflammatory and metabolic markers. The collection and analysis of these optional additional samples will help to understand how DHA may improve immune function and lower the risk of preterm birth.

These samples include:

- An extra 20mL of blood collected via venepuncture once at the start and at mid-pregnancy between 22-26 weeks.
- A urine sample collected at mid-pregnancy between 22-26 weeks
- A cord blood and placenta sample collected at birth. The cord blood collected for this study will preclude families from using it for other purposes in the future.

We will reimburse you with $15 for your travel costs should your enrolment and / or 34 week appointments at the hospital fall outside your regular antenatal visits.

Possible benefits

You may or may not directly benefit by your participation in this study. However, participants taking the capsules containing the higher dose of DHA may be at less risk of giving birth to a very premature baby.

Possible risks

We have already shown in the DOMInO trial that DHA at the dose to be used in the study is safe. At extremely high doses (12 times higher than the dose in this study) DHA rich fish oil may result in an approximately 10% increase in blood clotting time and a 10% decrease in blood pressure, neither of which is considered dangerous. Taking blood may cause brief discomfort or pain. All blood samples will be taken by trained, experienced staff to minimise any discomfort.

Future follow-up studies

DHA has a number of potential health benefits. We may conduct follow-up studies to determine the potential benefits. If you consent to participate in this trial it does not mean you have agreed to any future studies. We may contact you in the future by phone, letter, email or social media using information that you have provided to us, to see if you are willing to take part as each study begins.

Alternate Contacts

We recognise that people often change their telephone number and address, and therefore cannot be contacted by researchers. To help keep in contact with you we are asking you to provide us with the names and contact details of persons who would be able to let us know your new contact details. These people are usually friends or relatives and are called alternate contacts. If we needed to use one of the alternate contacts we would call them, explain who we are and that you were involved in a study and have given us their contact details so that they can put us in touch with you.

Your rights

Participation in any research project is voluntary and you are free to withdraw from the study at any time without affecting yours or your child's care in any way. If you decide to withdraw, please let any member of the research team know. All information gathered will be treated with confidence and no information that could identify you or your baby will be released to any person not associated directly with the study. These results may eventually be published in medical journals or at professional meetings, but you or your child will not be identified in any way.

Your information will remain confidential except in the case of a legal requirement to pass on personal information to authorised third parties. This requirement is standard and applies to information collected both in research and non-research situations. Such requests to access information are rare; however we have an obligation to inform you of this possibility.

Any questions?

If at any time during the study you have any problems regarding appointments or have any other queries, please ring our office on **8161 7512** and leave a message on our answering machine. One of our staff will return your call as soon as possible. If you have a problem and would like to talk to us immediately please ring **0474 333 001** and one of our research team members will answer your call.

Study Updates

Detailed information about the ORIP study and other Child Nutrition Research Centre studies and trials can be found on the SAHMRI Healthy Mothers, Babies and Children web page: www.sahmri.com/our-research/themes/healthy-mothers-babies-children/theme/theme-overview. More information about the Child Nutrition Research Centre and the work we do can be found on Facebook at www.facebook.com/CNRCAdelaide.

Study approval

This study has been reviewed and approved by the Human Research Ethics Committee at the Women's & Children's Health Network. If you wish to discuss the approval process with someone not directly involved, or have any concern or complaint, you may contact the Research Secretariat, Ms Brenda Penny on: (08) 8161 6521.

WOMEN'S & CHILDREN'S HEALTH NETWORK (WCHN)
HUMAN RESEARCH ETHICS COMMITTEE (HREC)

CONSENT FORM

The ORIP trial

SCIENTIFIC TITLE: Omega-3 Fats to Reduce the Incidence of Prematurity - the ORIP trial

I _____

hereby consent to my involvement in the research project entitled:

"Omega-3 Fats to Reduce the Incidence of Prematurity"

1. The nature and purpose of the research project described on the attached Information Sheet has been explained to me. I understand it and agree to taking part.
2. I understand that I may not directly benefit by taking part in this study.
3. I acknowledge that the possible risks and/or side effects, discomforts and inconveniences, as outlined in the Information Sheet, have been explained to me.
4. I understand that I can withdraw from the study at any stage and that this will not affect medical care or any aspects of my own or my child's relationship with this healthcare service.
5. I understand that there will be no payment to me for taking part in this study but that I will be reimbursed for travel costs should my enrolment and / or 34 week appointments at the hospital fall outside my regular antenatal visits.
6. I have had the opportunity to discuss taking part in this research project with a family member or friend, and/or have had the opportunity to have a family member or friend present whilst the research project was being explained by the researcher.
7. I am aware that I should retain a copy of the Consent Form, when completed, and the Information Sheet.
8. I consent to the following:

   1) To take the assigned capsules from trial entry until 34 weeks of pregnancy or the birth of my baby, whichever comes first.

   2) At trial entry and at 34 weeks pregnancy or at birth whichever comes first, have a finger prick blood sample taken from me.

   3) To be contacted 2 weeks after enrolment and at 28 weeks of pregnancy to monitor my progress, ask a few questions about compliance.

9. I additionally consent to: (please circle)

   1) Have my blood collected from me at the start of the study and in mid-pregnancy (between 22-26 weeks) Yes / No

   2) Provide a urine sample in mid-pregnancy (between 22-26 weeks) Yes / No

   3) Have a cord blood sample collected at birth Yes / No

   4) Have a placenta sample collected at birth Yes/ No

10. I do / do not consent to the samples being used in any other research project, provided the project has the approval of the Women's & Children's Health Network Human Research Ethics Committee.

11. I agree to the accessing of my and my child's medical records at the Women's and Children's Health Network and any other hospitals my baby and I may be transferred to and from, for the purpose of this study.

12. I understand that the alternate contacts provided by me may be used to contact me as explained in the information sheet for study related purposes.

13. I am aware that I may be contacted regarding future follow-up studies.

14. I understand that my and my child's information will be kept confidential as explained in the information sheet except where there is a requirement by law for it to be divulged.

Signed: .....

Relationship to Patient: .....

Full name of patient: .....

Dated:.....

I certify that I have explained the study to the parent mother and consider that she understands what is involved.

Signed: ..... Title: .....

Dated: .....