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| **HREC Number:** | HREC/19/WCHN/18 | | |
| **Short Name of Study:** | The Folic Acid Study | | |
| **Full Name of Study:** | Folic acid Supplementation and Maternal Late-gestation Folate Status – the Folic Acid Study | | |
| **Principal Researcher:** | Dr Karen Best, Research Fellow | | |
| **Version Number:** | Version 2.2 | **Version Date:** | 09/05/2019 |

Thank you for taking the time to read this **Participant Information Statement and Consent Form**. We would like to invite you to take part in a research study that is explained in this form.

This form is 7 pages long. Please make sure you have all the pages.

**What is an Information Statement and Consent Form?**

An Information Statement and Consent Form tells you about the research study and explains exactly what the research study will involve. This information is to help you decide whether or not you would like to take part in the research. Please read it carefully.

Before you decide if you want to take part or not, you can ask us any questions you may have about the study. You may want to talk about the study with your family, friends or a health care worker.

**Taking part in this research study is up to you.**

It is your choice whether or not you take part in the research study. You do not have to agree if you do not want to. If you decide you do not want to take part, it will not affect the treatment and care you get at The Women's and Children's Hospital.

**Signing the form.**

If you would like to take part in this research study, please sign the consent form at the end of this document. By signing the form, you are telling us that you:

- understand what you have read
- had a chance to ask questions and received satisfactory answers
- consent to taking part in the study.

We will give you a copy of this form to keep.

## 1. What is the research study about?

You are invited to take part in a study to measure folic acid levels in pregnant women (at 36 weeks gestation) who are taking a multivitamin with or without folic acid.

## 2. Who is running the study?

This study will be conducted by Dr Karen Best and her colleagues from the Healthy Mothers, Babies and Children theme at the South Australian Health and Medical Research Institute. This study is supported by a combination of funds received from the Royal Australian and New Zealand College of Obstetricians and Gynaecologists and the 'Nutrition for Mother and Child' Centre for Research Excellence.

## 3. Why am I being asked to take part?

Folate is a B-group vitamin found in food that essential for the healthy development of the fetus in *early* pregnancy, in particular their neural tube from which the brain and spinal cord develop. The synthetic version of folate is called 'folic acid', and this is what is added to food or taken as a supplement.

Folic acid taken before conception and during the first few weeks of pregnancy can prevent seven out of ten cases of neural tube defects. Since approximately half of all pregnancies are unplanned, many women do not begin taking vitamins and minerals until several weeks into their pregnancy - after the neural tube has developed.

To help reduce the number of babies born with neural tube defects, the Australian Government now requires that folic acid be added to all wheat flour used for bread. This means that most of the bread in Australia has been fortified (added) with folic acid. As well as adding folic acid to bread flour, a number of pregnancy guidelines recommend that women should take a folic acid supplement (0.4mg-0.5mg daily) for one month before conception and for the first 12 weeks of pregnancy. [1,2,3] The development of a baby's neural tube is complete at around 28 days of pregnancy, following this, there are no proven benefits of continuing to a take a folic acid supplement. However, many women continue to take prenatal supplements which often contain large amounts of folic acid. Too much folic acid can circulate in the blood unused by the cells, as 'unmetabolised folic acid'.

In this study, we would like to find out the level of folic acid in the blood of pregnant women at 36 weeks gestation who have either continued taking a multivitamin containing folic acid after 12 weeks gestation, or taken a multivitamin without folic acid. We would also like to see what the levels of unmetabolised folic acid are.

## 4. What is involved in this research study?

You may be able to take part in this study if you are more than 12 weeks but less than 16 weeks pregnant, currently taking a multivitamin containing folic acid and plan to continue. We will ask you to stop taking your current multivitamin and take the ones that we will supply to you free of charge until you are 36 weeks pregnant. The minerals and vitamins in the

*1 SA Health, 'Vitamin and Mineral Supplementation in Pregnancy Clinical Guidelines'*
*2 National Health and Medical Research Council (NHMRC), Pregnancy Care Guidelines*
*3 Royal Australian and New Zealand College of Obstetricians and Gynaecologists, Vitamin and Mineral Supplementation and Pregnancy*

multivitamin that we will provide to you have been formulated to match one of the leading brands of prenatal multivitamins available in Australia.

You will be randomly assigned (like tossing a coin) to one of two groups of multivitamins. One group will be asked to take a multivitamin capsule containing folic acid (control group) and the other group will be asked to take an identical multivitamin capsule without folic acid (intervention group). Neither you, nor the research team, will be able to choose which group you are in or know which type of supplements you have been assigned to take. You will be asked to take one, easy to swallow capsule per day, from the stat of the study until you deliver your baby. The total amount of folic acid contained in the capsules in the control group is 0.8 mg.

## 5. What will happen during the study?

5.1 At the start of the study (enrolment), we will collect some information about you, including your contact details, age, weight, height, education, occupation, smoking status, vitamin and medication use, and pregnancy related information from your medical records. We will take a small blood sample ~10mL to measure your folate and unmetabolised folic acid levels. We will try to coordinate the collection of this blood sample at the same time as your First Trimester Screening blood sample that is taken in the Hospital, however this may not be always be possible.

5.2 We will contact you one week after you enrol in the study and then at approximately 4-weekly intervals (up to six times) by phone call, SMS or email, (whichever is your preference). This contact will be brief, and we will ask about any health problems and how you are going with taking the daily capsule.

5.3 When you are 36 weeks pregnant, we will ask that you attend our SAHMRI clinic at the Women's and Children's Hospital. We will ask again about how you went with taking the capsules, whether you have had any problems during pregnancy, and we will take a small blood sample ~10mL to measure your folate and unmetabolised folic acid levels. We will ask that you bring any unused capsules with you at this visit and we will make sure you have enough to last the remainder of your pregnancy. We will collect information about your delivery by reviewing your medical records once you have had your baby.

5.4 We will reimburse you $25 for study visits that fall outside of your regular hospital visits.

5.5 Your blood samples (without any way to identify you) may be sent overseas where there are laboratory specialists who analyse blood for unmetabolised folic acid.

5.6 Your data (without any way to identify you) may be used in pooled results from different studies so we can gain a more complete understanding of folic acid use in pregnancy. Following analysis for the Folic Acid Study, remaining samples may be stored for use in future research studies that may or may not be related to the original research project following Human Research Ethics approval.

## 6. Can I withdraw from the study?

Taking part in any research study is voluntary and you are free to withdraw at any time. 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 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 will not be identified in any way.

Your information will remain private and 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.

**7. What are the possible benefits for me and other people in the future?**

You may not directly benefit by taking part in this study. However, data generated from this study may help to inform pregnant women and the community about multivitamin use in pregnancy.

**8. What are the possible risks, side-effects, discomforts and/or inconveniences?**

We don't expect any safety concerns as a result of being in this study. Removing folic acid from prenatal multivitamins after 12 weeks gestation, is the same as following the current pregnancy guidelines for taking folic acid in pregnancy. Taking a blood sample may cause brief discomfort or pain. In rare cases, blood collection may lead to minor infection; if this happens, it can be easily treated. All blood samples will be taken by trained, experienced staff to minimise any discomfort.

**9.**

**10. What will be done to make sure my information is confidential?**

In this study we will collect and use personal and health information about you and your baby for research purposes. Any identifying information will be treated as confidential. It will be used only in this project, unless we say otherwise. We can disclose the information only with your permission, except as required by law.

All information will be stored securely in the locked offices of SAHMRI Women and Kids Theme at the Women's and Children's Hospital. Electronic forms of data are stored on secure servers at SAHMRI.

The following people may access information collected as part of this research project:

the research team involved with this project
The Women's and Children's Health Network Human Research Ethics Committee

The stored information will be re-identifiable. This means that we will remove identifying information such as your name and give the information a special code number. Only the research team can match your name to your code number, if it is necessary to do so.

As participants in this project are pregnant, we will keep your information at least until the youngest baby turns 25 years old.

**11. Will I be informed of the results when the research study is finished?**

Detailed information about the Folic Acid Study and our other studies can be found on the SAHMRI Healthy Mothers, Babies and Children web page: https://www.sahmriresearch.org/our-research/themes/healthy-mothers-babies-children/theme-overview. More information about the work we do can be also found on Facebook at www.facebook.com/CNRCAdelaide.

## 12. Will there be future follow up studies?

If you consent to participate in this study, it does not mean you have agreed to participate in any future follow up studies. We would contact you again to see if you are willing to take part.

## 13. Further information and who to contact for more information?

We will collect your contact details so that we can communicate with you throughout the study. 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.

If you would like to contact us, the person you may need to contact will depend on the nature of your query. If you want any further information concerning this study or if you have any problems which may be related to your involvement in the study, please call our office at:

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| **Name:** | SAHMRI Healthy Mothers, Babies and Children |
| **Contact telephone:** | (08) 8128 4436 |
| **Email:** | hmbc@sahmri.com |

You can contact the Research Information Officer at the Women's and Children's Health Network if you:

- have any concerns or complaints about the study
- are worried about your rights as a research participant
- would like to speak to someone independent of the study.

The Research Information Officer can be contacted by telephone on (08) 8161 6521 or email at luke.fraser2@sa.gov.au.

## CONSENT FORM

**HREC Number:** HREC/19WCHN/18
**Short Name of Study:** The Folic Acid Study
**Version Number:** Version 2.2 **Version Date:** 09/05/2019

I

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**Participant full name**

hereby consent to my involvement in the research project entitled:

***"Folic acid Supplementation and Maternal Late-gestation Folate Status"***
***The Folic Acid Study***

1. The nature and purpose of the research study described on the attached Participant 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 my medical care or any aspects of my relationship with this healthcare service.

5. I understand that I will be provided with multivitamins until delivery of my baby at no cost to me and that I will be reimbursed $25.00 for any study related visits that fall outside of my regular hospital 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 with me while the study is explained to me.

7. I am aware that I should keep a copy of the Participant Information Sheet and Consent Form, when completed.

8. I consent to the following:

   1) To take the multivitamin capsules from the start of the study until 36 weeks of pregnancy or the birth of my baby, whichever comes first.

   2) To have a blood sample taken from me at the start of the study and at 36 weeks of pregnancy or at birth whichever comes first.

   3) To be contacted one week after enrolment and at approximately every 4 weeks until 36 weeks of pregnancy to monitor my progress.

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

10. I understand that the alternate contacts provided by me may be used to contact me as explained in the information sheet.

11. I am aware that I may be contacted to let me know about follow up studies.

12. I understand that my 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: .....**

**Full name of participant: …….....**

**Date: .....**

**I certify that I have explained the study participant and consider that she understands what is involved.**

**Signed: .....**

**Name: …… Title: .....**

**Date: .....**