Participant Information Sheet

THE UNIVERSITY OF SYDNEY
Faculty of Medicine and Health
The University of Sydney
NSW 2006
AUSTRALIA

Study title: The FIDGIT Study
Locality: Auckland / New Zealand
Ethics committee ref.: **20/CEN/197**
Sponsor (if applicable): *The University of Sydney*
Lead investigator: Sharon Erdrich
Contact phone number: 09 846 5566
Supervisor: Dr Joanna Harnett

You are invited to take part in a study looking at relationships between the digestive system, gut bacteria and symptoms of fibromyalgia. Whether or not you take part is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. If you do want to take part now, but change your mind later, you can pull out of the study at any time.
This Participant Information Sheet will help you decide if you'd like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and a copy of the Consent Form to keep.

This document is 13 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

The purpose of this study is to gather detailed information about digestive function, gut bacteria and their by-products as well as a range of symptoms affecting women with fibromyalgia and compare then to women without fibromyalgia.

- Fibromyalgia is a poorly understood, chronic pain condition. Results from other studies suggest that the digestive system and the bacteria that inhabit it may have a role in the symptoms experienced by people with fibromyalgia. We want to explore this thoroughly. To do this we will collect a range of samples of body tissues (blood, urine, faeces, breath and mouth swabs) so we can investigate the bacteria of the digestive system, and the things they produce, which may be related to symptoms in people with fibromyalgia. If you want more details about this, please ask the study team.
- This study does not involve any treatments.
- The study is being done by PhD candidate Mrs Sharon Erdrich under the supervision of Dr Joanna Harnett at the University of Sydney, Dr Jason Hawrelak at the University of Tasmania, and Professor Stephen Myers at Southern Cross University, Australia. Professor Richard Day is a Rheumatologist (in Sydney) advising the study.
- If you have any questions about the study, you can contact either Sharon Erdrich or Dr Harnett. Their contact details are on page 10

— Some of the tests and test equipment are being donated by QuinTron (USA) and House of Health. Viome Research Institute is collaborating to process the microbiome and related samples. A fundraising campaign is underway to help pay for some of the other tests. The researchers are donating their time to the study.

— This study has been approved by the NZ Health and Disability Ethics Committee, (HDEC), Ref no 20/CEN/197.

WHAT WILL MY PARTICIPATION IN THE STUDY INVOLVE?

You have been invited to take part in this study because you either have fibromyalgia or have volunteered as a "healthy control" without fibromyalgia.

If you decide to participate in the study, you will be asked to:

1. Complete a consent form and fill in an online questionnaire.
2. Do some tests and collect some specimens for testing.
3. Do a mouthwash during the breath test.
4. Complete a dietary survey

If you choose not to participate in this study, you will not be required to do any tests or complete any questionnaires. Nothing will happen if you do not take part.

Being involved in the study means we need you to:

1. Collect some saliva, urine, and stool (faeces) samples at home. You will need to be at home for the 4 hours of the urine collection (see the next page for more information)
2. Have a blood test.
3. Complete an online questionnaire. You can do this while you are doing the breath test. This questionnaire will collect health information from you.
4. Visit the research centre at recruitment and on 3 further occasions for breath testing. The first visit will take about ½ an hour and the other 3 will take about 3 hours for breath testing. Two of these three breath tests can also be collected at home if getting to the research center is difficult for you. Each breath test will require you to:
   - Follow a special diet the day before testing. This means you won't be able to eat some of the things you would normally eat. A list of allowed food is on page 5.
   - Stop eating the night before each test. You can drink water-only for the 12 hours (overnight) before each test. You will be able to eat & drink normally when each test is finished
   - Have a special drink, with a specific type of sugar, before and after which we will collect samples of your breath. We may also ask you to do mouth washing during the breath tests.

The mouthwash is using SalviaThymol® - the ingredients are listed below:

SalviaThymol® N, ingredients	
Essential oils of	**Other Ingredients**
Sage	L-menthol
Eucalyptus	Thymol
Peppermint	Ethanol 96% (V/V)
Cinnamon	Propylene glycol
Clove	Sodium dodecyl sulphate (surfactant)
Bitter fennel	Polysorbate 80 (solubiliser),
Star anise	Sodium saccharin (sweetener)
	Chlorophyll-copper complex (natural colouring)

IMPORTANT: Please notify the study team if you are allergic to any of the ingredients of the mouthwash.

At your first visit to the research center, we will:

- Measure your height and weight
- Take your temperature, measure your heart rate, blood pressure and oxygen levels, plus ask you some questions to screen you for the likelihood of infectious illness
- Collect blood samples.
- Explain procedures for collecting the urine, saliva, stool, and environmental samples with you. These are outlined below with a guideline for timing these tests. A checklist is also included.

5. Collect swabs from specific surfaces in your home and workplace (if applicable). This is to test for the presence of mould.

NOTE: Blood samples will be sent overseas to the same company that is analysing the faecal and saliva samples. This blood sample will be analysed for an immune marker (called IgG), and gene expression to identify patterns related to human metabolism and chronic diseases which will enhance understanding of this condition. DNA and genetically inherited diseases are not able to be analysed.

You may hold beliefs about a sacred and shared value of all or any tissue samples obtained. The cultural issues associated with sending your samples overseas and/or storing your tissue should be discussed with your family/ whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.

If you wish, you, or supporting whanau can perform a karakia prior to submitting tissue samples for this study. Please let the study team know.

Note that once your samples have been sent overseas, we will not be able to get them back. Results from microbiome and blood samples may be included in an international databank. If this happens, the information will not be identifiable as yours. If you do not agree to providing these samples, having them sent overseas, or these results being included in a databank, please let us know. In this case, you will not be included on our study.

THE URINE COLLECTIONS

There are 3 urine samples to be collected over a single 4-hour period. You need to wait at least 48 hours after doing this test before starting breath testing. Plan to do the urine test so you can bring it with you to your breath test appointment.

Do not plan to do the urine collections while you are menstruating, have a urinary tract infection or vaginal discharge. Please contact the study team if this applies to you.

It is important to follow the instructions carefully. Please contact us if you are not sure about any of these instructions.

A Four-Hour Urine Collection with Lactulose-Mannitol Challenge

Preparing for the Urine Collection.

A. The day before the test

1. *Avoid the following foods: Strawberries, celery, onions, pumpkin, mushrooms, jams/jelly, cough crops, sweets, chewing gum, probiotics (including yoghurt)*
2. *Please check the contents of the box. You should have 1x bottle with a solution of Lactulose & Mannitol, 1 collection cups, 3 test tubes, a pipette to draw the samples, a biohazard bag, and a gel-pack for transporting your samples.*
3. *Put the gel-pack in the freezer.*

IMPORTANT: Do not have anything to eat after 10pm the evening before the test (you can drink plain water during this time).

B. The day of the test

1. *Do not eat anything, nor drink anything except water as per the instructions for the first 4 hours of the test.*
2. *Do not take any medicines or supplements during the urine collection as these may interfere with the results. If you take <u>essential medication</u>, please inform the study team before starting the test.*

(Continued on next page)

COLLECTING THE URINE SAMPLES

STEP 1

a. *Completely empty your bladder, catching some of the urine in the collection cup provided.*
b. *Use the pipette to fill the white-top tube labelled #1 to 1cm below the top of the tube with urine. Screw the cap tightly on the tube and invert several times.*
c. *Write the time, and date of collection on the tube label. Note the time on the form provided. THIS IS SAMPLE #1*
d. *Place the tube in the Biohazard bag and refrigerate.*
e. *Discard the remaining urine. Rinse the collection cup and pipette with water and let air-dry.*
f. *Wash your hands.*
g. *Mix the lactulose & mannitol solution with a whole (250mL) glass of water and drink it all. Do not have anything else to drink until instructed (see Step 2, f)*

STEP 2

a. *About 2 hours after you started, please urinate, catching all the urine passed.*
b. *Take a 10mL sample with the pipette and fill one of the other tubes as in Step 1. Label the tube with the date and time. THIS IS SAMPLE #2*
c. *Put the rest of the urine into the large collection container provided. Write down the total volume in the collection container on the form.*
d. ***Note: If you need to urinate before the two-hour time point, collect your urine and put it in the container.***
e. *Wash your hands then drink one (1) glass of water (250mL).*

STEP 3

a. *4 hours after you started, urinate again, add it to the large collection container, mix it then extract the third 10mL urine sample*

- ***Note: If you need to urinate between Step 2 and Step 3, collect your urine and add it to the collection container.***

b. *Read the total volume of urine off the side of the container, write this on the test form. Then take a 10mL sample of this urine with the pipette provided and fill one of the tubes as in step one. Label the tube with the date and the time. Add to the Biohazard bag and refrigerate. THIS IS SAMPLE #3*

   NOTE: if it will be more than 48 hours until your clinic appointment, please ***freeze*** *these samples.*

c. *Discard the urine (in the large collection container), rinse, then put the bottle, collection cup and pipette in the trash.*
d. *Wash your hands.*

COLLECTING THE STOOL SPECIMENS

It is important that you collect this sample the morning you start (or the day before you start) your urine collection.

1. *First, check you have all the equipment: Container to catch your stool sample, collection vials (one with preservative fluid inside), a disposable glove, a zip-lock bag for putting the sample into.*
2. *Attach the collection paper to the toilet as per instructions. Pass a bowel motion, catching it on the paper. Put on your glove.*
   - *Use the scooper in the collection vial to transfer a pea-sized scoop of stool into the brown-capped tube. More is not better!*
   - *Add the preservative as per the instructions with the collection kit.*

3. ***Remove the glove and wash your hands thoroughly.***

Place all samples in the small carton with the frozen gel-pack provided. Keep cold until your visit to the research centre (within 48 hours) or drop it off to us.

Bring all your samples to the breath testing appointment. We don't require anything further from you once all the samples are collected and the questionnaires are complete.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

Preparing for breath testing involves a special diet for a day and an overnight fast. For some people being hungry is uncomfortable.

As part of the breath testing procedure, you may be asked to do a mouthwash using SalviaThymol® N, a product (licence number 6430752.00.00) made with essential oils. Please see the list of ingredients above. If you are allergic to any of the ingredients, your mouthwash will be with chlorhexidine (such as Savacol) or plain water.

Taking part in this study includes providing blood samples. This involves a needle and can hurt.

- We don't expect there to be any other risks associated with being involved in this study

We cannot promise that there will be any direct benefits of this being involved in this study.

We will take care of you while you are at the research centre. If you need help related to the study while you are at home, please call us on 09 8465566

WHO PAYS FOR THE STUDY?

Being involved in this study will not cost you anything, except costs associated with getting to the research centre. All the testing is free.

Participants will not receive any financial benefits for taking part in this study.

WHAT IF SOMETHING GOES WRONG?

If you were injured in this study, you would be eligible **to apply** for compensation from ACC just as you would be if you were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

WHAT ARE MY RIGHTS?

Taking part in the study is completely your choice and you do not have to take part. You are free to decline to participate, or to withdraw from the research at any practicable time, without experiencing any disadvantage. Not taking part or withdrawing from the study will not affect your relationship with anyone at House of Health or the study team, or with your health practitioner.

You have the right to access information about you that we collect as part of the study. If any of the information is incorrect, we will correct it.

If we learn any information from the study that may have an impact on your health, we will let your health practitioner know.

Your information will be kept confidential. We will only use your age and sex in our results. Your other personal information will be removed and replaced with a code so that no-one will know that it is your information.

WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?

The purpose of this study is investigating possible contribution of the gut microbiome to the condition and symptoms of fibromyalgia. We are not investigating a treatment.
After the study is completed:

- Paper documentation and test results will be retained for 10 years.
- The file containing the identification code will be destroyed at the end of the study by deletion from the server.
- Other data (including microbiome data) from the study may be stored indefinitely for possible future use.
- Biological specimens collected during the research will be destroyed at the conclusion of the study.

We expect to publish the results of our study in medical journals. You can request a letter telling you about the study results. The letter will be sent to you once the final study report is available (this can take 1 – 2 years).

WHAT WILL HAPPEN TO MY INFORMATION?

During this study the researchers and other staff at the research centre (House of Health) will record information about you and your study participation. This includes the results of any study assessments, such as breath testing. You cannot take part in this study if you do not consent to the collection of this information.

IDENTIFIABLE INFORMATION

Identifiable information is any data that could identify you (e.g. your name, date of birth, or address). In addition to Sharon Erdrich and Dr Harnett, the following groups may have access to your identifiable information:

- House of Health staff (to complete study assessments)
- Ethics committees, approved auditors from HDEC and other regulatory bodies or government agencies from New Zealand or the University of Sydney, if the study or site is audited. Audits are done to make sure that participants are protected, the study is run properly, and the data collected is correct.
- Your usual doctor, if a study test gives an unexpected result that could be important for your health. This allows appropriate follow-up to be arranged.

Rarely, it may be necessary for the study team or your doctor to share your information with other people – for example, if there is a serious threat to public health or safety, or to the life or health of you or another person OR if the information is required in certain legal situations.

DE-IDENTIFIED (CODED) INFORMATION

To make sure your personal information is kept confidential, the study co-ordinator will keep a list linking your code with your name, so that you can be identified by your coded data if needed. This list will be encrypted before saving on a password-protected computer. All analysis files

use these codes only. No identifying information about you will be included in any report generated by the research project.

The following people may have access to your coded information:

- Sharon Erdrich and Dr Joanna Harnett, for the purposes of this study.
- House of Health staff, for the purposes of this study (this may include up to 3 additional people).

ANONYMISED INFORMATION

Prior to any microbiome data being included in larger databanks, it will be anonymised. This means that the code linking the data to you will be removed from your de-identified information. This makes it very difficult (but not impossible) to identify the information that belongs to you.

FUTURE RESEARCH USING YOUR INFORMATION

If you agree to inclusion in this study, your de-identified information may be also used for future research related to fibromyalgia. This future research may be conducted overseas. You will not be told when future research is undertaken using your de-identified information. This information may be shared widely with other researchers or companies. Your de-identified information may also be added to information from other studies, to form much larger sets of data.

You will not get reports or other information about research that is done using your information in other studies.

By consenting to participating in this study, you are also agreeing that your de-identified and anonymised information may be used indefinitely for future research. If you change your mind, it may be extremely difficult or impossible to access your information, or withdraw consent for its use, once your information has been shared for future research.

SECURITY AND STORAGE OF YOUR INFORMATION

Your consent form contains identifiable information and is held in a locked filing cabinet at House of Health (Auckland, NZ) during the study. A file containing the code that links your information to test results will be stored as outlined on page 8. Samples sent for processing will be identified only with the assigned code. After the study your consent form and any other paper documents associated with the study are transferred to a secure archiving site at the University of Sydney and stored for at least ten (10) years, then destroyed. All data storage will comply with local and/or international data security guidelines.

All data and health information being transmitted will be encrypted and stored on secure servers.

None of the overseas laboratories will have access to your identifying information, nor to the file that allows matching of your information to your samples. All human sequence data is filtered out of microbiome samples by blasting against a reference database and removing all data that matches the reference from the sequence data. No human genes (e.g., ancestry or inheritable disease-related) are analysed – all human DNA is degraded from samples before analysis.

Before uploading to a large microbiome databank, all the data are anonymised.

RISKS

Although efforts will be made to protect your privacy, absolute confidentiality of your information cannot be guaranteed. Even with coded and anonymised information, there is no guarantee

that you cannot be identified. The risk of people accessing and misusing your information (e.g. making it harder for you to get or keep a job or health insurance) is currently very small but may increase in the future as people find new ways of tracing information.

Your coded samples may be sent overseas. Other countries may have lower levels of data protection than New Zealand. There may be no New Zealand representation on overseas organisations which make decisions about the use of your information. There is a risk that overseas researchers may work with information in a way that is not culturally appropriate for New Zealanders.

This research includes basic information such as your ethnic group, age, sex and level of education. It is possible that this research could one day help people in the same groups as you. However, it is also possible that research findings could be used inappropriately to support negative stereotypes, stigmatise, or discriminate against members of the same groups as you.

RIGHTS TO ACCESS YOUR INFORMATION AND RESULTS

The results of the study may be published or presented, but not in a form in which you would be identifiable.

You can request a letter telling you about the study results. The letter will be sent to you once the final study report is available (this can take 1 – 2 years). A description of this trial will also be available on the ANZCTR trial registry website. This website will not include information that can identify you. At most, it will include a summary of study results

You have the right to request access to your information held by the research team. You also have the right to request that any information you disagree with is corrected.

If you have any questions about the collection and use of information about you, you should contact Sharon Erdrich, the coordinating investigator of this study.

RIGHTS TO WITHDRAW INFORMATION

You may withdraw your consent for the collection and use of your information at any time, by informing the study coordinator (Sharon Erdrich).

If you withdraw your consent, your study participation will end, and the study team will stop collecting information from you.

Information collected up until your withdrawal from the study may continue to be used and included in the study. This is to protect the quality of the study. Once the results of the study are published, you will not be able to access, correct or withdraw your information, even if you change your mind about it being used

DATABANK/REGISTRY

As part of this study, we may be required to submit your anonymised information into a microbiome databank. Submitting this information into the databank is mandatory.

The purpose of the databank is to gather information about the gut microbiome to enable researchers to understand how gastrointestinal bacteria may contribute to fibromyalgia and other health conditions.

The study team and researchers may access the information in the microbiome databank for cross-analysis of large data sets obtained from other, similar studies and data obtained in citizen science projects.

Data obtained from human RNA will be included in a larger databank, and the information will no longer be identifiable as yours, therefore you will be unable to seek access to that information, nor will you be able to withdraw your data from the databank.

You may have access to the larger databank's website where any results of these larger projects will be published.

The information in the databank is kept on a secure server with software firewalls, that no-one without security clearance can access. Your privacy will be protected by anonymisation of your data.

Your information stored in the databank/ registry may be stored indefinitely.

If you have any questions about the databank, you may contact Sharon Erdrich, study coordinator or Momo Vuyisich, Chief Science Officer, Viome Research Institute, by emailing studies@viome.com

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

- Sharon Erdrich PhD Researcher/ Study co-ordinator
  - Phone 09 846 5566
  - sharon.erdrich@sydney.edu.au

- Dr Joanna Harnett (Supervisor)
  - + 61 2 9351 7009
  - Joanna.harnett@sydney.edu.au or

If you want to talk to someone who isn't involved with the study, you can contact an independent Health and Disability (HDC) advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

For Maori health support please contact :

Donna Kerridge. Ngāti Tahinga, Ngāti Mahuta, Ngāti Maniapoto.
Rongoā Māori Practitioner
Phone: 027 255 9534
Email: donna@oranewzealand.com

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHIC (0800 4 38442) or +64 4 819 6877
Email: hdecs@health.govt.nz

THE UNIVERSITY OF SYDNEY

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CONSENT FORM

Please tick to indicate you consent to the following

I have read or have had read to me in my first language, and I understand the Participant Information Sheet.	☐	
I have been given enough time to consider whether or not to participate in this study.	☐	
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	☐	
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	☐	
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my medical care.	☐	
I consent to the research staff collecting and processing my information, including information about my health.	☐	
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.	Yes ☐	No ☐
I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I agree to my oral, urine, blood, stool samples being sent overseas, and I am aware that I will not be able to have them returned to me. These samples will be disposed of using established guidelines for discarding biohazard waste.	☐	
I understand that data from my samples may be retained in a large databank for future research and I will not be able to have it removed.	☐	
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committees, or any relevant regulatory authority or their approved representative reviewing my relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	☐	
I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.	☐	
I understand the compensation provisions in case of injury during the study.	☐	

I know who to contact if I have any questions about the study in general.	☐	
I understand my responsibilities as a study participant.	☐	
I agree to my coded information being used for any future, related studies.	☐	
I wish to receive a summary of the results from the study.	Yes ☐	No ☐

Declaration by participant:
I hereby consent to take part in this study.

Participant's name:

Signature: Date:

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name:

Signature: Date: