Participant Information Sheet

This information sheet is for those participants who will provide a blood sample for the study.

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Project Title

The validation of measures of female sex hormones in saliva and the relationship between salivary sex hormone profiles and symptoms across the menstrual cycle in healthy eumenorrheic females: A feasibility study.

An Invitation

My name is Natalie Hardaker, I am a PhD candidate based at the Sports Performance Research Institute New Zealand (SPRINZ) at Auckland University of Technology (AUT) Millennium. My PhD supervisor and co-investigator in this study is Professor Patria Hume. You are invited to take part in the above-mentioned research project. Your participation in this research is voluntary. If you don't want to take part, you do not have to give a reason, and it won't influence any present and/or future involvement with the Auckland University of Technology. If you do want to take part now, but change your mind later, you can stop at any time. This Participant Information Sheet will help you decide if you'd like to take part in the study. It explains why we are doing the study, what your participation will involve, what the benefits and risks to you might be, and what will happen after the study has finished. 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, coaches or healthcare providers. If you agree to take part in this study, you will be asked to sign a Consent Form. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep. This document is 4 pages long, excluding the Consent Form. Please make sure you have read and understood all the pages.

What is the purpose of this research?

The purpose of this study is to investigate the relationship between salivary hormone profiles and symptoms across the menstrual cycle as monitored by a menstrual cycle tracking app (WILD AI) in healthy eumenorrheic (naturally regularly menstruating) females. The hormones included in the salivary measures will be Estrogen, Progesterone and Cortisol. The second part of this study is to confirm salivary measures of Estrogen and Progesterone against blood serum.

Estrogen and Progesterone, the primary female sex hormones are typically associated with reproduction and are linked to brain health. Cortisol is the primary stress hormone and levels of cortisol can influence female sex hormones.

Knowledge gained from this study about how salivary hormone profiles change in relation to symptoms throughout the menstrual cycle will be used to inform a related study that will investigate symptoms in females recovering from sports-related concussion.

The findings of this research may be used for academic publications and presentations and may inform future research grant applications.

How was I identified and why am I being invited to participate in this research?

If you are currently studying with Professor Patria Hume as your supervisor, you will not be eligible to participate in this study. You have been invited to take part in this study because you are a healthy female with a natural regular menstrual cycle. You will be able to start the study if you meet the inclusion criteria outlined below:

Inclusion criteria:

- Female aged 16yrs or older (and had a menstrual cycle for a minimum of 2 years)
- Natural regular menstrual cycle ~28-40 days long

Exclusion criteria are:

- Current student of Prof Patria Hume
- Unable or unwilling to store saliva samples in your home freezer
- Started taking medication in the last 3 months that could alter reproductive hormone concentrations (glucocorticoids – eg prednisone. Antidepressant or antipsychotic medication).
- Current or Previous brain injury
- Current musculoskeletal injury
- Current clinical diagnosis of an eating disorder
- Currently taking the Oral Contraceptive Pill (OCP)
- Currently have an IUD

- Currently have Amenorrhea (no periods)
- Pregnant, lactating or planning a pregnancy during the length of the study (3 full menstrual cycles)
- Post-menopause

How do I agree to participate in this research?

Your participation in this research is voluntary (i.e. it is your choice) and whether or not you choose to participate will not advantage nor disadvantage you. If you do choose to participate, you can withdraw from the study at any time and you do not need to provide a reason. If you choose to withdraw from the study you will have the choice to have your blood and saliva samples/information used in the study, returned to you or destroyed. Once analysis has been conducted on the blood and saliva samples, it will not be possible to return them to you. But if you choose to withdraw from the study after the blood and saliva analysis you have the option to have your data included or removed from the study. However, once the findings have been produced, removal of your data may not be possible.

What will happen in this research?

If you want to take part in this study, you will be asked to complete a Low Energy in Females Questionnaire (LEAF-Q). The LEAF-Q will evaluate the symptoms of insufficient energy intake (e.g., fatigue, irritability) and also contains questions regarding injuries, gastrointestinal (digestive/gut) and reproductive function and information to further identify any females that may need to be excluded from the study.

The LEAF-Q information will be recorded in a database only accessible to the investigators directly involved in the study. You may be excluded from the study if you report any significant health problems or injuries.

During this study you will be asked to download and use the 'WILD AI' app free of charge. 'WILD AI' is a menstrual cycle tracking app with artificial intelligence (AI), you will be required to log symptoms/metrics each day for the duration of the study. WILD AI can also be linked to a research platform. In this study the research platform will be used to allow you as participant to share your profile data with Natalie Hardaker as the primary investigator. You will be given a unique identifier number and digitally consent to link your profile to the research platform. Your data will not be seen by or shared with any other participants in this study. If you are an existing user of WILD AI, you will just need to use the unique identifier number assigned you as a participant in this study to link to the research platform.

You will also be asked to provide up to a total of 120 daily (3 full menstrual cycles - one full menstrual cycle is from menstruation/bleeding phase to menstruation/bleeding phase) saliva samples every morning upon waking and before breakfast (ideally between the hours of 06:00 and 09:00). Approximately 2ml of saliva (approx. ½ a teaspoon) will be collected in each sample by passively drooling into a small tube. Before providing each saliva sample you will need to take a small sip of water, you will swish the water around in your mouth for a few seconds, and then swallow the water. This will stimulate saliva release and clear any food debris that may be in your mouth. The collection of each sample should take 1-3 minutes. These samples can all be collected at home. You will need to store your saliva samples at home in your freezer and drop them off at an agreed location or send them.

You will be asked to collect this data for three consecutive menstrual cycles to look for patterns.

You will also be asked to attend the Otago Medical School, Wellington Regional Hospital, 23A Mein Street, Newtown, Wellington 6242 or the AUT Millennium research lab, 17 Antares Place, Rosedale, Auckland 0632 to give a blood sample on 3 separate visits. The research team will provide you with the information of the days which you will need to go in for the blood draw. Blood samples will need to be collected in the morning before breakfast (ideally between the hours of 06:00 and 09:00). Approximately 2.5 ml of blood (approx. ½ a teaspoon) will be collected in each sample via standard venepuncture procedure. The collection of each sample should take up to 10 minutes. Each visit to the lab will be approximately 30 minutes. Natalie Hardaker has been certified to take blood via venepuncture.

As a participant in this study you will have to adhere to several instructions to ensure sample collection is standardised, this includes:

- Taking the saliva sample before you brush your teeth and before you eat or drink anything every morning.
- Daily input into WILD AI menstrual tracking app.
- Attend the lab to provide a blood sample at 3 separate time points during your third menstrual cycle.
- Providing the blood sample in a fasted state (i.e. before you eat or drink anything other than water) on the morning of your scheduled lab day visit.
- You will be provided with a free standardised saliva collection kit including everything you need to collect your data for this study.
- You will need to store your saliva samples at home in your freezer and drop them off at an agreed location.

		Menstrual Cycle		
Task	**Frequency/time**	**1**	**2**	**3**
Take saliva sample	Daily	X	X	X
Input app data	Daily	X	X	X
Blood sample #1	Low Hormone Phase – Day 1-2			X
Blood sample #2	Ovulation			X
Blood sample #3	Highest hormone phase			X

Your blood samples and saliva samples will be processed at the AUT Roche lab (AUT Roche Lab Department of Sciences Building WS level 5 Auckland 1010).

All samples will be processed and stored at -80C until the end of the study. Once all samples have been collected from all participants, the samples will be thawed and collectively analysed to measure levels of sex hormones (estrogen and progesterone) and cortisol.

Data logged in WILD AI will be accessible to Natalie Hardaker if you link your registration to the research view which has been set up for this study. Your data will not be seen by or shared with any other participants in this study. You will be able to continue using WILD AI free of charge after this study has finished and you profile will not continue to be linked to the research platform.

Data will be extracted from the app platform and exported to a Microsoft Excel master spreadsheet.

As a participant in this study you will be assigned a unique identifier number. Your identifier number will be used to label all of your samples and corresponding data to protect your identity and confidentiality as a participant in this study. You will use this number to link to the research platform in the WILD AI app. The consent form and the LEAF-Q will be the only documents in this study that include your name and contact information. All consent forms will be securely stored by Professor Patria Hume. Your identity and your individual data will not be reported in any analysis or publications that are produced from this study, only group results will be reported.

What are the discomforts and risks?

There is no more risk in participating in this study than what is already voluntarily accepted in day to day activities. There may be some discomfort during the blood draw; this would be similar to a routine blood test procedure. You may experience mild personal discomfort (embarrassment) in talking about your menstrual cycle.

There is a time cost to you as the participant in this study as outlined in the sections above.

How will these discomforts and risks be alleviated?

Any discussion about the normal menstrual cycle in an open forum will be with a positive and supportive approach. Individual information will not be shared or discussed. If you have experienced discomfort with blood draws previously you are encouraged to let the Lab staff know.

What are the benefits?

As a participant you personally may benefit from this study by learning more about your hormones and tracking of your menstrual cycle.

Information gained from this research will advance our current understanding of how hormone profiles measured in saliva relate to symptoms across the menstrual cycle in healthy eumenorrheic females. This current study tests the ideas and data collection methods that may be used in a future study investigating females recovering from concussion. Saliva sampling offers a non-invasive methodology and understanding how salivary sex hormones relate to symptoms in healthy females will inform the interpretation and analysis of samples collected in a clinical setting from females recovering from concussion.

These studies form part of Natalie's PhD research.

How will my privacy be protected?

All of your personal information will be kept in secure storage under the responsibility of the principal investigator of the study in accordance with the requirements of the New Zealand Privacy Act (1993). Only named members of the research team will have access to this information. You will be assigned a unique code so that your data can be de-

identified. Analysis and reporting of data will be de-identified and at the group level. All data included in reports and publications will be de-identified and at the group level.

In the case of you recording a potential medical issue it will be discussed with the appropriate healthcare professional or guardian. As a researcher I do have a legal duty of care to report any significant concerns to the relevant parties. All data will be stored in accordance with AUTEC policy, the data will be stored securely for a period of 10 years.

What are the costs of participating in this research?

There are no direct financial costs to you as a participant in this study; this PhD research is part funded by Injury Prevention at the Accident Compensation Corporation.

There will be a small daily time cost for the duration of the study; approximately 6 minutes per day for up to 120 days. On three days of this study you will also need to spend the time attending the lab to provide a blood sample.

Where additional travel is required to deliver saliva samples and give a blood sample you will receive koha in the form of petrol vouchers.

What opportunity do I have to consider this invitation?

Please take your time to consider the invitation to participate in this research. It is reiterated that your participation in this research is completely voluntary. The latest date to enter the study is June 2022.

If you require further information about the research topic, please feel free to contact Natalie Hardaker (details are at the bottom of this information sheet).

You may withdraw from the study at any time without needing to give a reason.

Will I receive feedback on the results of this research?

If you would like to receive a summary of your own individual results, please check the box on the consent form and include your email address in the space provided. When the study is complete, a 1-2 page fact sheet summarising the main findings of the study will be available within 90 days of the end of the study (including data analysis). The fact sheet will not include your personal information, it will include the information collected from the whole group. If you are interested and would like to receive this fact sheet please check the box on the consent form and include your email address in the space provided.

What do I do if I have concerns about this research?

Any concerns regarding the nature of this project should be notified in the first instance to the Project Supervisor, Patria Hume, patria.hume@aut.ac.nz +64 9 921 9999 ext. 7306.

Concerns regarding the conduct of the research should be notified to the Executive Secretary of AUTEC, *ethics@aut.ac.nz* , (+649) 921 9999 ext 6038.

Whom do I contact for further information about this research?

Please keep this Information Sheet and a copy of the Consent Form for your future reference. You are also able to contact the research team as follows:

Lead investigator – Natalie Hardaker, PhD candidate
Phone: 027 898 9023
Email: Natalie.hardaker@aut.ac.nz

Project supervisor – Professor Patria Hume
Phone: +64 9 921 9999 ext. 7306.
Email: patria.hume@aut.ac.nz

Approved by the Auckland University of Technology Ethics Committee on *09 July 2022*, AUTEC Reference number *21/167*.