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Participant Information Statement

Lactoferrin and Immune Function: The 'LIFE' Clinical Trial

Invitation

You are invited to participate in a research trial examining whether a dietary supplement can improve immune function in older adults. Immune function can be described as a measure of how well your body's immune system can protect you against infection and foreign substances.

This trial is being conducted by Professor Lisa Wood from the Hunter Medical Research Institute (HMRI) and the University of Newcastle. Before you decide whether or not you wish to participate in this trial, it is important for you to understand why the research is being done and what it will involve. Please take the time to read the following information carefully and discuss it with others if you wish.

1. What is the purpose of this trial?'

We will investigate whether taking a lactoferrin supplement, daily for 4 weeks can improve immune function and protect against virus infection in older adults. We will do this by looking at changes in immune cells from blood samples taken before and after the 4-week trial.

Lactoferrin is a protein made in the human body, normally present in human breast milk and other bodily fluids, which is an important regulator of immune function. Lactoferrin can also be extracted from cows' milk and used as a dietary supplement to improve immune function. Clinical trials in adults and children have shown that lactoferrin can reduce respiratory tract infections, though little research has been done to help us understand how lactoferrin improves immune function to protect against respiratory tract infections.

2. 'Why have I been invited to participate in this trial?'

This trial may be suitable for you if you are aged 50 years or older.

3. 'Are there any reasons why this trial may not be suitable for me?"

This trial is not suitable for you, if you:

- Are under the age of 50 years
- Are a current smoker
- Are allergic to cow's milk
- Cannot speak, read or hear English
- Have a significant life-limiting illness or cancer
- Have used any product (e.g. dietary or nutritional supplements) containing lactoferrin within the previous 4 weeks.
- Irregularly use other dietary or nutritional supplements. *If appropriate to do so, participants who use supplements inconsistently or use lactoferrin supplements, which are not being taken for a health condition, could potentially become eligible if they cease using their supplements 2-4 weeks prior to commencing the study.*
- Are prescribed ongoing systemic corticosteroid, immunosuppressive or antibiotic drugs.

4. What is the supplement that I will be asked to take?

The supplement used in this trial is called Lactoferrin, which is a whey protein that has been extracted from cow's milk. It contains ingredients that are approved foods and considered safe and suitable for use in food in Australia. There are no known side effects, though it is not suitable for people with allergies to cow's milk. The trial supplement does not contain lactose, so it is safe to consume for people with

lactose intolerance. The placebo capsules contain beetroot powder and microcrystalline cellulose, which is made from fibrous plant material. Both lactoferrin and cellulose are also added to some food products as an ingredient. The lactoferrin supplement (and placebo) will be provided in capsules, packaged into a bottle. During the trial you will be asked to take two capsules every morning, before food. Depending on which group you are allocated to, the capsules you will take will be either:

Group 1: High dose lactoferrin or
Group 2: Low dose lactoferrin or
Group 3: Placebo (microcrystalline cellulose)

The placebo will look the same as the high and low doses of lactoferrin but does not contain any active ingredients. The group you are allocated to will be randomly decided (like tossing a coin). You will have an equal chance of allocation to each group, but we cannot place you in the group of your choice.

This trial is double blinded, which means that neither you, nor the research staff, will know which supplement you are taking. At the end of the trial, we will compare the results to work out whether lactoferrin improves immune function, and which dose of lactoferrin is required to see beneficial effects. Please note that you will be supplied with the trial supplements required for this trial.

5. What does this trial involve?

Telephone screening

To check whether the trial is suitable for you we will ask you some questions over the telephone. These questions will be about any diagnosed medical conditions, the medications you currently take, whether you smoke and if you have any allergies.

We will also ask you about any recent or planned vaccinations, such as influenza (Fluvax) or COVID-19 vaccinations or booster shots. You will still be suitable for the trial if you have recently received any vaccinations or plan to, and we will not ask you to postpone these. However, your first trial visit will be scheduled at least 4 weeks after recent vaccinations (including Fluvax and COVID-19 vaccines).

If the telephone screening indicates that the trial is suitable for you, and if you choose to participate, we will organise a mutually convenient time for you to attend the HMRI clinic for the first trial visit.

If you agree to participate in this trial, you will be asked to:

- Sign the Participant Consent Form, at your first study visit.
- Attend two visits, 4 weeks apart, at the Hunter Medical Research Institute Clinical Trials Unit (details to follow).
- Take two capsules, once each day for 4 weeks. At your first visit to HMRI you will be provided with the trial supplement capsules.

Trial Visits: 'What happens at each visit?'

Timepoint:	**Visit 1 - Week 0**	**Phone Call - Week 2**	**Visit 2 - Week 4**
Duration:	• 1 hour	• 15 minutes	• 1 hour
Assessments:	• Blood collection • Height, weight and blood pressure • Questionnaires	• The researcher will ask about unusual symptoms or illness	• Blood collection • Weight and blood pressure • Questionnaires

There are two (2) trial visits, which will be scheduled in the morning. These visits will take approximately 1 hour. At each visit we will also ask you to undergo some tests and assessments. These include:

- A brief medical examination including measurement of your height and weight, and blood pressure using an automatic blood pressure monitor.

- Blood Test: We ask your permission to collect a blood sample at each study visit (about 1.5 tablespoons or 36mL). Before you attend these visits, we would like you to fast for 12 hours, however you may drink plain water during this time. Blood will be collected at the beginning of the study visit, from a vein in your forearm. After your blood sample is collected you will be offered a light breakfast. We will test your blood sample for signs of inflammation and measure immune function.
- Questionnaires**:** We will ask you about your medical history, smoking history and medication usage. You will also be asked to complete questionnaires related to your quality of life and dietary intake. These questionnaires will take between 10-15 minutes to complete.

Phone Call - Week 2

We will telephone you two weeks after your first visit to check how you are going with the trial. We will arrange to call you at a time convenient to you, this should only take 15 minutes of your time.

Trial Diary

You will be supplied with a trial diary, to record when you take the trial supplement, and if you experience any unusual symptoms or become unwell. This will take about 1 minute of your time each day, for 4 weeks.

Home visits

In the event that NSW Health issues "Stay at Home" orders which prevent you from attending HMRI for your scheduled trial visits we would like to visit you at your home instead. The home visit will include blood collection only, all questionnaires will be completed via telephone. You do not have agree to participating in a home visit if you do not feel comfortable doing so. If you do consent to participating in a home visit, a member of the research team will contact you via telephone to schedule a time that is convenient to you, and ask you questions about where you live, and who you live with to complete a risk assessment. Home visits will be conducted according to strict safety protocols to ensure you are not placed at any additional risk.

6. 'What if I don't want to take part in this trial, or if I want to withdraw later?'

Participation in this trial is voluntary. It is completely up to you whether you participate. If you decide not to participate, it will not affect the treatment you receive now or in the future. Whatever your decision, it will not affect your relationship with the staff caring for you.

If you decide to withdraw from the trial, you have the option of withdrawing all data relating to you and have any blood samples that have been taken destroyed. An exception to this is in the case of an adverse event, or a serious adverse event, where the data needs to be retained for regulatory reporting.

If you wish to withdraw from the trial once it has started, you can do so at any time without having to give a reason.

7. 'Are there risks to me in taking part in this trial?'

All medical procedures involve some risk. The side effects of having blood collected may include bleeding or bruising at the injection site and possible dizziness and/or fainting. Please advise the research team if you normally feel dizzy or faint when you have blood collected.

8. 'What happens if I suffer injury or complications as a result of the trial?'

If you suffer any injuries or complications because of this trial, you should contact the trial coordinator as soon as possible, who will assist you in arranging appropriate medical treatment.

9. 'Will I benefit from the trial?'

You may not personally benefit from being in this trial. Involvement in the trial is purely voluntary and you may withdraw at any time.

10. 'How will my confidentiality be protected?'

Only the researchers named below, and other clinical staff involved in your care will know whether or not you are participating in this trial. Any identifiable information that is collected about you in connection with this trial will remain confidential and will be disclosed only with your permission, or except as required by law. Only the researchers named below will have access to your details and results that will be held securely at the Hunter Medical Research Institute.

11. 'What happens with my blood samples?'

By consenting to take part in this study, you also consent to the collection, storage and use of the blood samples collected during the study period. Blood samples will be tested in the Hunter Medical Research Respiratory Research Laboratory and stored for additional analysis at the Kirby Institute, Sydney.

Stored samples will be de-identified and kept in freezers at -80°C in a restricted-access laboratory. This means that any identifying information will be replaced with a code so that you will not be identifiable. If you give us permission, we would like to store unused blood samples for up to 15 years. The de-identified blood samples may be used for future research that is closely related to this research project, if you give your consent for this to occur. During and after the study, you retain the right to have your samples destroyed at any time by contacting the chief investigator.

12. 'What happens with the results?'

Your participation in the trial will benefit our understanding of how lactoferrin affects the immune system. A participant summary of the results will be available to you at the completion of the trial, if you wish to receive it. However, you should be aware that the trial may take over a year to complete.

We plan to discuss/publish the results of the trial. In any publication, information will be provided in such a way that you cannot be identified. Results will be presented to researchers and clinicians via seminars at local universities, presentations at national and international conferences, and publication in peer reviewed journal articles. It may also be shared on social media and other media/events for researchers, clinicians, and the public.

If you are enrolled in another study within the Priority Research Centre for Healthy Lungs and both studies need the same data/information from you, you can give us permission to share the data collected during our study with these other researchers to reduce the need for you to have further testing.

13. Costs

Participation in this trial will not cost you anything. Parking will not cost you anything and a parking space will be reserved for you prior to each visit.

14. 'How is this trial being paid for?'

This trial is funded by the Commonwealth of Australia Department of Industry, Innovation and Science in partnership with Noumi Limited and the University of Newcastle. The researchers will receive no direct payment from the industry partner for conducting this trial and are free to publish the study results.

15. 'What should I do if I want to discuss this trial further before I decide?'

When you have read this information, one of the researchers will discuss it and any queries you may have with you. If you would like to know more at any stage, please do not hesitate to contact him/her or any of the other investigators on the numbers listed.

Chief Investigator: Professor Lisa Wood
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Trial Coordinator: Dr Bronwyn Berthon
Immune Health Research Program
University of Newcastle. T: 02 4042 0116
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16. 'Who should I contact if I have concerns about the conduct of this trial?'

This trial has been **approved** by the Hunter New England Human Research Ethics Committee, reference number 2021/ETH1098. Should you have concerns about your rights as a participant in this research, or you have a complaint about the way the research is conducted, it may be given to the researcher, or, if an independent person is preferred, please contact the HNE Research Office, Hunter New England Local Health District, Level 3, POD, HMRI, Lot 1 Kookaburra Circuit, New Lambton Heights NSW 2305. Telephone: 02 4921 4140. Email: HNELHD-ResearchOffice@health.nsw.gov.au and quote the reference number: 2021/ETH1098.

Thank you for taking the time to consider this trial.
If you wish to take part in it, please contact the trial coordinator above.
This information sheet is for you to keep.

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Participant Consent Form

- I agree to participate in the above research project and give my consent freely.
- I understand that the project will be conducted as described in the information statement, a copy of which I have retained.
- I understand I can withdraw from the project at any time and do not have to give any reason for withdrawing.
- **I consent to-**
  - **1)** Completing the tests involved in the trial
  - **2)** Completing questionnaires to obtain research data
  - **3)** A copy of my results being sent to my General Practitioner, if indicated
  - **4)** Allowing other studies that I am enrolled in within the Priority Research Centre for Healthy Lungs to access data that is duplicate to the data collected in this study: *(please circle response)* **Yes / No**
  - **5)** Storage of my blood samples for future research: *(please circle response)* **Yes / No**
  - **6)** Participating in home visits for blood collection, only if necessary: *(please circle response)* **Yes / No**

- I would like to receive a participant summary of the trial results:

  (please circle response) **Yes - via Email / Yes – via Post / No**

I understand that my personal information will remain confidential to the researchers.

I have had the opportunity to have questions answered to my satisfaction.

Name _____

Signature _____ **Date** _____

I have informed the above person about this research and am sure that they understand both the content of the Information statement and the additional information I have provided.

_____

Investigator/Delegate Name (printed) Signature Date