Australasian Research Institute

SYDNEY ADVENTIST HOSPITAL

PARTICIPANT INFORMATION STATEMENT & CONSENT FORM

Project Title
Assessment of the effect of a novel curcumin formulation on markers of inflammation and oxidative damage in middle age

Invitation
You are invited to take part in a study investigating the effectiveness of a new formulation of curcumin to reduce inflammation and damage caused to cells by free radicals; processes involved in the development and progression of disease.

This study is being conducted by:
Chief Investigator, Dr Ross Grant - Australasian Research Institute

Before you decide whether to participate in this study, 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 family and friends.

1. What is the purpose of the study?
Long-lasting low-grade inflammation and free radical damage are associated with the development and progression of a number of diseases. While positive lifestyle choices have been shown to positively influence inflammatory and free radical processes, for many people in the community, the busyness of life makes it difficult to consistently make healthy choices. In this instance, taking a supplement may help.
Curcumin, a naturally occurring yellow compound found in turmeric, is a widely used supplement. Previous studies have demonstrated its capacity to reduce markers of inflammation and associated physical symptoms (e.g. pain, stiffness, and erythema). A large amount of evidence has also confirmed that ingestion can reduce the production and damage caused by free radicals.

However, the absorption of naturally occurring curcumin by the body is poor. Fortunately advances in curcumin formulation have been shown to be more readily absorbed by the body. Among these, a new form of curcumin has been demonstrated to increase blood curcumin levels three times compared to natural curcumin. However, the effectiveness of this new curcumin formulation to reduce markers of inflammation and free radical damage has not yet been investigated. Therefore, the purpose of this study is to investigate the effectiveness of a new curcumin formulation to reduce markers of inflammation and free radical damaged compared to both the natural curcumin industry standard and a placebo.

2. Why have you been invited to participate in this study?
This study seeks to determine the effectiveness of a new curcumin formulation to reduce inflammation and free radical damage in middle-aged males and females; a group in which long lasting, low levels of inflammation and free radical damage is common. We are therefore asking men and women aged between 40 – 60 years, and who meet the criteria outlined in point 3 below, if they would like to take part.

3. Who can participate?
We are looking for individuals who:

- are aged between 40 – 60 years,
- are <u>not currently taking any medication</u> for inflammatory disorders including, rheumatoid arthritis and other autoimmune conditions including, Lupus, MS, Guillian-Barre syndrome, psoriasis etc.,
- do not have reduce/poor renal function (i.e. kidney problems),
- are not regularly taking aspirin, ibuprofen (e.g. Nurofen) or other anti-inflammatory medications,
- are willing to stop taking supplements (e.g. antioxidants, flavonoids, omega-3 etc.) for at least 7 days before the start of this study, and refrain from taking additional supplements for the duration of the study,
- have no known sensitivity to either turmeric, curcumin or related products or red/yellow food colouring
- are not known to be pregnant
- have no known current active infection, or an infection within the last two weeks.

Note: *If you are currently taking supplements based on medical/nutritionist/dietician advice, we ask that you please first seek medical advice before deciding to stop their ingestion in order to participate in this study*.

4. What does this study involve?

Once we have confirmed that you meet the criteria outlined in point 3 above and if, after reading this Participant Information Statement, you would like to take part, you will be asked to sign the Consent Form.
After signing the Consent Form, you will then be 'screened' to determine if you are eligible to take part in the entire study.

Screening

So that we can determine if the new curcumin formulation can reduce inflammation and free radical damage, we need to recruit participants who have a baseline inflammatory score (hsCRP) between 2.5 – 10.00 µg/mL.

To determine your inflammatory score, we will ask you to provide an overnight fasting blood sample. The amount of blood that we will collect is 25 mL. This equates to just over 5 teaspoons.
Blood samples will be collected using routine techniques by a trained phlebotomist.

If your baseline inflammatory score is within the required range, you will be invited to take part in the entire study (i.e. from Baseline Assessment onwards).
If you have been invited to take part in the entire study, we will store a portion of the blood sample you provided during Screening, at the Australasian Research Institute. This samples will be further analysed for additional markers of inflammation as well as free radical damage. The remainder of the screening sample will be stored at SAN Pathology until testing of standard pathology parameters is complete. After this initial analysis any remaining sample will be transported to, or remain at the Australasian Research Institute where it will be stored until the completion of the study when it will be discarded.

Blood samples provided by participants whose inflammatory score is not within the required range will be discarded.

Baseline Assessment *(eligible participants only)*

If eligible, before you start ingesting your allocated study supplement, we will ask you to complete a questionnaire to assess your pain, fatigue, itch and stiffness levels. We will also measure your blood pressure using an automated blood pressure cuff.

Randomisation to the Study Supplemental Arms

Once your Baseline data has been gathered you will be randomised to one of three study arms:

1) Placebo – Red/yellow food colouring plus silicon dioxide (a natural chemical mix of silicon and oxygen that is used in many food products). This is to be taken twice daily, morning & evening, before meals.
2) New curcumin formulation – two capsules daily, morning & evening, before meals. This equates to 752 mg of active curcumin per day (i.e. 2 x 376 mg tablets).
3) Natural curcumin – two capsules daily, morning & evening, before meals. This equates to 752 mg of active curcumin per day (i.e. 2 x 376 mg tablets).

You will be asked to consume your allocated supplement for 8 weeks.
Both you and the research personnel will not know what supplement you are taking.

Note: *You have a one in three chance of being randomly allocated to the Placebo, New curcumin formulation or Natural curcumin study arm.*

Study Duration - Assessments

In addition to the blood sample provided at screening, another four overnight fasting blood samples will be collected. Each of these will be about ~ 25 mL (i.e. 5 teaspoons) and will be collected at: Day 14, Day 28, Day 42 and Day 56 (8 weeks). The markers analysed at baseline will again be assessed at each of these time points. Blood pressure will also be measured at each time point and you will be asked to complete the questionnaire to assess pain, fatigue, itch and stiffness (see Study Flow Chart, next page).

5. How safe are the curcumin supplements?
All of the supplements used in this study are commercially available for purchase and are generally considered safe for consumption by healthy individuals at the levels prescribed in this study.

Greater than 100 products containing curcumin are listed on the Australian Register of Therapeutic Goods (ARTG) (including the curcumin tested in this study). ARTG listed medicines are considered relatively safe, and only contain well-known low-risk ingredients. These are assessed by the Therapeutic Goods Administration for quality and safety.

6. Are there any other risks/discomforts?
The majority of measures collected as part of this study are non-invasive and pose no risk.

We will however ask you to provide a total of 5 blood samples (the screening sample + 4 additional samples) over the 8 weeks of the study.

Blood will be collected by an accredited practitioner using best practice venepuncture techniques.
As with any object that punctures the skin, the insertion of a needle poses a slight risk of infection. You will also likely experience a small degree of pain and may develop a small bruise around the needle prick site.

As part of this study we may detect an adverse finding of clinical relevance. If this occurs, you will be advised to consult a General Practitioner and will be supplied with a copy of relevant results for your records.

7. What happens if I suffer injury, complications or side-effects as a result of the study?
It is highly unlikely that you would suffer any injuries or complications as a result of this study.
However despite the well-established safety of curcumin some minor negative side effects have been reported. These include diarrhoea, headache, rash, nausea and yellow stool.

If you feel unwell during the course of the study and believe this to be related to the test supplements, we ask you contact the Chief Investigator, Dr Ross Grant on 02 9487 9601 as soon as possible.
You will be asked to document any potential side-effects in the Adverse Event Record. However, for your safety it is important that you first contact the Chief Investigator, Dr Ross Grant on the phone number indicated above.

<u>If you feel unwell after hours, we recommend you call the NSW Government after hours GP helpline on 1800 022 222.</u>

<u>If the side-effect is severe, we recommend that you call 000 or present to your nearest emergency department for medical advice.</u> After you have received medical advice, we ask that you contact the Chief Investigator, Dr Ross Grant, on the phone number indicated above so that the side-effect can be documented.

Depending on the side-effect experienced, you may be withdrawn from the study to ensure your safety.

8. What will happen to the sample(s) I provide?
The sample(s) you provide will be stored at the Australasian Research Institute until biochemical analysis for inflammatory and free radical damage markers. These are research markers and have not been validated for clinical use.

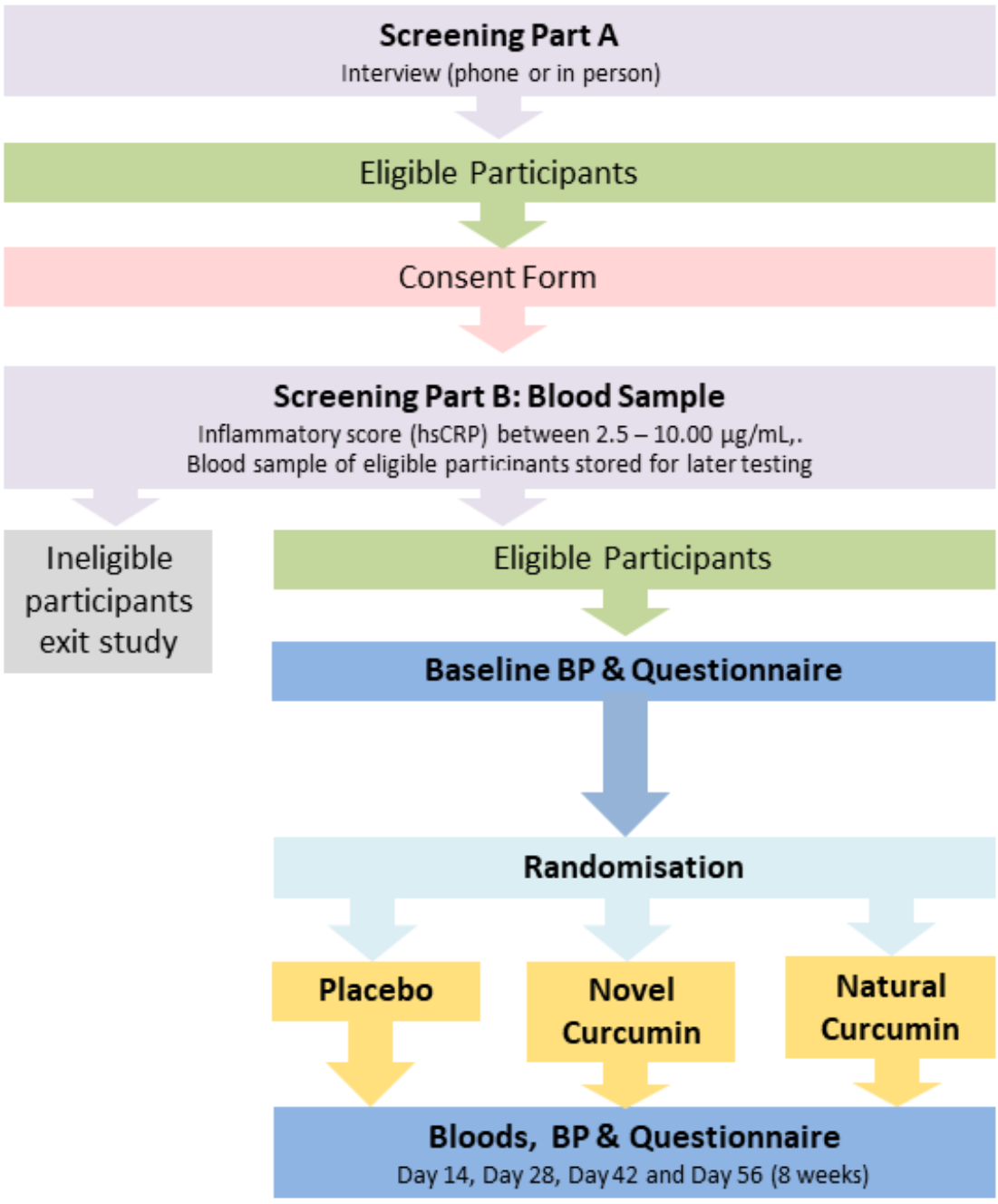
Only your participant identification number and initials will be recorded on blood samples analysed and stored by the ARI. Associated results will be in a re-identifiable format only.

You blood samples will also be transported to SAN Pathology where they will be analysed to monitor any changes in inflammation and how your liver, kidney and bone marrow are functioning. Specifically, the following blood tests will be conducted: Multiple biochemical analysis (MBA), Electrolytes urea, creatinine (EUC), Liver function tests (LFT), glycosylated hemoglobin (HbA1c) and high sensitivity C-reactive protein (hsCRP).

Your blood samples will be sent to SAN pathology in an identifiable format. This is to ensure that your results can be matched to you. SAN Pathology is committed to maintaining patient privacy and confidentiality and complies with all applicable Australian federal and state privacy laws. The Chief Investigator will de-identify blood analysis reports before distribution to research personnel.

At the completion of the project, blood samples will be disposed as clinical waste according to the standard processes and procedures of the Sydney Adventist Hospital.

Figure 1: Study Flowchart



9. Will analysis of my samples, or any of the assessments, reveal important information about my health?
The majority of biomarkers to be analysed in the blood samples you provide will not generate results that are clinically important.

The exception to this is the standard pathology markers tested by SAN Pathology. In addition, we may detect high blood pressure levels. If anything abnormal, that is clinically important, is detected, we will advise you to visit your GP. A copy of these results will be provided to you.

10. How will my confidentiality be protected?
The Australasian Research Institute is committed to maintaining your privacy and confidentiality and comply with all applicable Australian federal and state privacy laws.
Only research personnel will be aware of your participation. The research database will be compiled without the use of personal identifiers. The database will be held securely on the Sydney Adventist Hospital main frame server.
Any information that is obtained in connection with this study and that can be identified with you will remain confidential and will be disclosed only with your permission, except as required by law or in case of exceptional emergency.

11. Will I benefit from this study?
Participation in this study is voluntary and will not directly benefit you. If you would like to know your individual results, please contact the Chief Investigator who will happily discuss your Screening and Baseline inflammatory and oxidative damage markers with you.

12. Will taking part in this study cost me anything, and will I be paid?
Participation in this study will not cost you anything, nor will you be reimbursed for participating in the study.

13. How will the study findings be used?
We plan to publish the results in a relevant peer reviewed health journal so that others may benefit from our findings. We may also make a public statement in the popular media. In any publication, information will be presented in such a way that you will not be able to be identified.

Group data only, in the form of a report detailing the study findings, will be provided to the study sponsor.
Upon request, de-identified data (removal of Participant ID, DOB) may be made available. The study sponsor may also use group data in marketing/advertising campaigns.

You will be provided with a short summary of the overall study findings (group data) via email. If you have any questions about the overall study findings, please feel free to contact the Chief Investigator.

14. How is this study being paid for?
This study is funded by Pharmako Pty Ltd; the developer of the novel curcumin supplement to be tested.

15. What should I do if I want to discuss this study further before I decide?
If you have any other questions please contact the research project co-ordinator Dr Jade Berg, or the Chief Investigator Dr Ross Grant, on 02 9487 9601, who will be happy to answer them.

16. What happens if I do not take part or wish to withdraw from this study?
It is completely up to you whether you wish to participate. Your decision will not prejudice your future relations with Sydney Adventist Hospital or the Australasian Research Institute. If you decide to participate, you are free to withdraw your consent and to discontinue your participation at any time without prejudice or reason.

17. Who should I contact if I wish to withdraw from the study?
If you would like to withdraw your consent and discontinue your participation in this study or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact the study Chief Investigator Dr Ross Grant or the Project Coordinator, Dr Jade Berg on 02 9487 9601.

18. Who should I contact if I have concerns about the conduct of this study?
This study has been approved by the Adventist HealthCare Limited Human Research Ethics Committee. Complaints and concerns may be directed to;

Research Office - Adventist Healthcare Limited 185 Fox Valley Rd, Wahroonga NSW 2076 **AHCL project ID:** 2020-025	
Phone	02 9487 9604
Email	research@sah.org.au

Any complaint you make will be treated in confidence and investigated, and you will be informed of the outcome.