WESTERN SYDNEY
UNIVERSITY

Participant Information Sheet

Project Title: ***Investigation on the Safety and Effectiveness of Chinese Herbal Medicine for the Treatment of Insomnia.***

Project Summary:

You are invited to take part in this research project. The aim is to test an herbal treatment for insomnia. This treatment is called Zao Ren An Shen (ZRAS) capsule.

This project is conducted by Yoann Birling, PhD candidate at NICM Health Research Institute (NICM). He is supervised by Associate Professor Xiaoshu Zhu (School of Science and Health, NICM), Professor Alan Bensoussan (NICM), and Professor Jerome Sarris (NICM).

Insomnia disorder is a common disease. It may severely affect people's body, mind and daytime performance. Current advised treatments include drugs and psychotherapy. Drugs such as sleeping pills can improve insomnia symptoms. However, they may also bring about side effects and dependency. Psychotherapy can benefit people with insomnia, but it requires a lot of time, energy and involvement. It is also largely not available. Thus, there is a need for other treatments.

Zao Ren An Shen (ZRAS) capsule is an herbal medicine. It has been used in China for insomnia for more than 30 years. It is composed of Suan zao ren (Ziziphi Spinosae Semen), Wu wei zi (Schisandrae Chinensis Fructus), and Dan shen (Salviae Miltiorrhizae Radix et Rhizoma). Previous studies have shown that this drug is efficient. Its effect is better or similar to that of sleeping pills. Its side-effects are mild and relatively rare.

This aim of the project is to assess the benefits and limitations of ZRAS capsule for insomnia.

How is the study being paid for?

This research is funded by Western Sydney University.

ZRAS capsules and placebos were provided by Global Therapeutics Pty Ltd.

The principal investigator (Yoann Birling) is a recipient of a Blackmores-NICM Scholarship.

What will I be asked to do?

Participation in any research is voluntary. If you agree to participate in this study, you may be asked to sign a Participant Consent Form; one copy retained by the researcher/s and copy given to keep.

In this study, you may receive either the treatment or a placebo. You cannot choose or change group. The look, taste and smell of the placebo are similar with the tested medicine. However, it has no medical effect. Neither you nor your investigator will know which treatment you are receiving. We aim at including 90 people in this study.

For this study, participants will be contacted twice over the phone and will be required to attend a Western Sydney University campus (Westmead, Campbelltown, Parramatta or Bankstown) three times. At these clinic visits, you will be asked questions about your health, including current diseases, medication, and substance use. You will also be asked to complete questionnaires about your sleep, mood and health. Additionally, your blood pressure will be measured and the investigator will examine your tongue and pulse.

Participants will need to complete a sleep diary every morning for seven weeks. You will need to complete a survey on your beliefs about different medicines and your opinion about the treatment as well as electronic questionnaires about your sleep, mood and overall feeling. You will need to take three blood tests (at no cost); if you have done these tests in the past six months, you should give the results to the investigator.

Participants will be provided with a five-week treatment, and will be required to take three capsules of ZRAS (or a placebo) once a day, one hour before bedtime. During five weeks, you will not be allowed to start any other treatment for insomnia. These treatments include drugs and psychotherapy. You can take your regular medication if not used to treat insomnia. A treatment for insomnia can only be used occasionally as a rescue.

Participants will be required to wear an actigraph, a device used to detect movement, for 24-hour every day and may also be required to wear an oximeter, a device used to measure oxygen levels, every night for one week. You will be asked to take good care of these devices during the study and to recharge the actigraph when necessary. For the duration of the study, you will also be asked to control your caffeine, alcohol and nicotine consumption to your usual levels. You may still donate blood and if you are fertile, you will be asked to use birth-control methods and to not donate sperm for the duration of the study.

If you fall under one or more of the following situations, you **will not be eligible** to take part in this study:

- Are aged under 18.
- Do not have an insomnia disorder.
- Unwilling or unable to stop other treatments for insomnia for the duration of the trial.
- Are fertile and unwilling to use birth control methods for the duration of the trial.
- Unable to read and understand English.
- Imminent need of mental or medical care.
- Abnormal blood test results within the last six months, if not approved by a general practitioner.
- The symptoms can be explained by another disease or the use of a substance.
- Have undergone a treatment for insomnia less than 14 days prior to the second visit.
- Have any psychotic or bipolar disorder, if not treated or unstable.
- Have alcohol or drug addiction.
- Other mental disorders such as depression or anxiety, if the disease is not treated or stable for less than one month.
- Cognitive problems that prevent you from following the trial instructions or giving informed consent.
- Taking a Warfarin-type drug.
- Allergy history to any of the ingredient of the ZRAS capsule or the placebo.
- Are pregnant or breastfeeding.
- Considered not suitable for the trial by the investigator.

How much of my time will I need to give?

- About 1 to 1.5 hours for each of the three visit of the study. During the visits, you will be asked questions about your characteristics and your health.
- About 40 to 50 minutes for each of the two phone interviews. During these phone calls, questions about your symptoms and health status will be asked.
- About 3 to 10 minutes per day to complete the sleep diary.
- About 30 minutes for the survey.
  30-60 minutes to take the blood tests, if needed (only once).

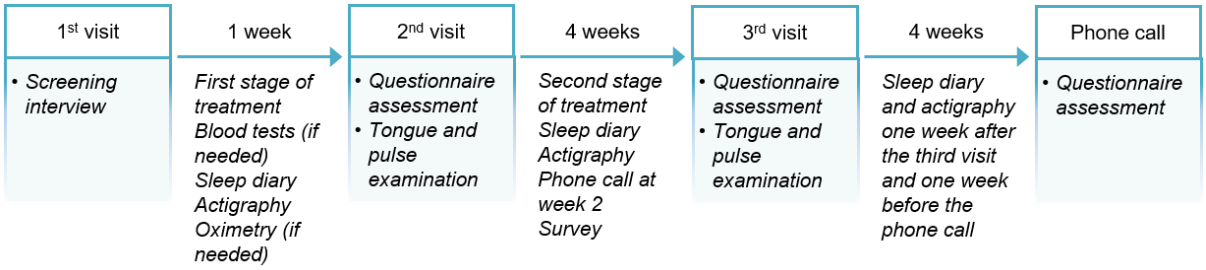

Figure 1 Flowchart of the trial procedure.

What benefits will I, and/or the broader community, receive for participating?

There is the potential that you may experience improvement in your insomnia symptoms and overall health. The study may also help you to understand your condition better, and may also help other insomnia patients, health practitioners and policy makers better understand the benefits and limitations of ZRAS as an alternative treatment for insomnia.

You will be given reimbursement for your travel costs (up to $20 per visit) for participating in this study.

Will the study involve any risk or discomfort for me? If so, what will be done to rectify it?

Medical treatments often cause side effects. You may have none, some or all of the effects listed below. They may be mild, moderate, or severe. If you have any of these side effects, or are worried about them, talk to your investigator. Your investigator will also be looking out for side effects. Previous studies have identified the following side effects for this treatment. The incidence rate is about 0 to 10.67%.

- Fatigue
- Stomach discomfort
- Acid reflux
- Diarrhoea
- Lip numbness

There may be side effects that the investigator does not expect or does not know about. It could be serious. Tell your study investigator immediately about any new or unusual symptom/s that you get.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, your investigator may need to stop your treatment. You may be referred to a general practitioner or a hospital.

The effects of ZRAS capsule on the unborn child and on the newborn baby are not known. Because of this, it is important that participants are not pregnant or breastfeeding and do not become pregnant during the course of the research project.

How do you intend to publish or disseminate the results?

The results of this study will be published and/or presented as part of the investigator PhD thesis, journal articles, and conference presentations. In any publication and/or presentation, it will be impossible to identify you, except with your permission.

Identified data allow someone to be identified, such as a name or an address. These data will be kept confidential. Electronic identified data will be stored in a computer. The computer is protected by a password. Hardware identified data will be stored in a locked cabinet. Both type of data can only be reached by the investigator.

The monitor(s), the auditor(s), the Human Research Ethics Committee, and the regulatory authority(ies) will be granted access to your original medical records. They will verify the clinical trial procedures and/or data. They will not violate the confidentiality of the participants, to the extent permitted by the applicable law and regulations. By signing this form, you authorise such access.

The raw data collected from the actigraph will be stored and managed in Amazon servers. They are in the USA. This data cannot reveal your identity.

Will the data and information that I have provided be disposed of?

No. Your data will be used as per Western Sydney University's Open Access Policy. The non-identified data from this study can be made available online and worldwide. Identified data will be kept for 15 years in a shared drive with restricted access, however please be assured that only the researchers will have access to the raw data you provide.

Can I withdraw from the study?

Participation in the research is voluntary. You are not obliged to be involved. If you do participate you can withdraw at any time. You will be asked to come to the visit site to return all equipment. You will be asked to detail the reasons for wishing to withdraw. If provided, these will be recorded. If willing, you will complete the questionnaires of the study. If willing, you may be contacted to provide the information of the other assessments as well. If you do choose to withdraw and specify, any information that you have supplied can be destroyed and not included in the analysis.

Whatever your decision, it will not affect your future care or your relationship with the research staff.

Under the following circumstances, you may be withdrawn from the study:

- If you start a new treatment for insomnia;
- If your insomnia condition gets worse and additional treatment is required;
- If a serious medical condition occurs,
- If you fall pregnant.

Can I tell other people about the study?

Yes, you can tell other people about the study. You can provide them with the investigator's contact details. They can contact the investigator to discuss their participation in the research project and obtain a copy of the information sheet.

What if I require further information?

If you wish to discuss the research further before deciding whether or not to take part in, please contact the investigator.

If there is any information relevant to your willingness to continue the study, you will be informed in time.

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What if I have a complaint?

If you have any complaints or reservations about the ethical conduct of this research, you may contact the Ethics Committee through Research Engagement, Development and Innovation (REDI) on Tel +61 2 4736 0229 or email humanethics@westernsydney.edu.au.

Any issues you raise will be treated in confidence and investigated fully, and you will be informed of the outcome.

This study has been approved by the Western Sydney University Human Research Ethics Committee. The Approval number is H12990.