Please read the following information carefully, do not hesitate to discuss any questions you may have with your Doctor/Investigator

1. Study Title:

Effect of High-Dose-Vitamin-B Multivitamin Supplement on Neural Connectivity and Oxidative Metabolism in Healthy Adults: A Randomised, Double-Blind, Placebo-Controlled, Phase I Clinical Trial

2. Introduction (Scientific basis of the study)

Multivitamin and multi-mineral supplementation has been shown to enhance brain cognitive functions (ability to process and analyze information). Previous study has reported reduction in fatigue and improved cognitive function following 9-week supplementation while another study reported improved cognitive function after 16-week supplementation. In addition, acute multivitamin supplementation has been reported in producing positive effect in contentment and cognitive task performance in adults, while multivitamin supplementation for 12-week in children has improved cognitive performance. These studies suggested that multivitamin and multi-mineral supplementation could improve mood and cognitive functions/brain performance.

3. What is the purpose of this study?

This study was taken to investigate the effects of a multivitamin and multi-mineral supplementation with high dose B-vitamins on brain activity and functions after a 6-month supplementation.

4. What do I need to do during the study?

Before enrollment, our medical doctors will explain to you about the risks and benefits of this study and you will be asked to sign a consent form upon agreement. The doctors or researchers will then do some basic surveys and physical examinations on you, for example, asking for your medical history, measuring your height and weight, blood pressure, heart rate and blood glucose. You will then be asked to complete the Scale of Intelligence. Once you fulfill all the inclusion and exclusion criteria, you will be enrolled to the study. You will be given a bottle of supplement. You need to take two oral supplement tablets daily – one tablet after breakfast and one tablet after lunch, for a period of 6 months. You will need to stop all other supplements during this period of time. Besides, you will have to provide 10 mL blood samples (about half table spoon each time) during visit 1 (Day 0), Visit 2 (Day 42) and Visit 4 (Day 168), and perform MRI brain scanning during Visit 1 (Day 0), Visit 2 (Day 42), Visit 3 (Day 84) and Visit 4 (Day 168) at the University of Malaya Medical Centre. You will need to inform the researchers if you forgot to take the supplement or have any abrupt change on your routine lifestyle. Participant who fails to follow the above instructions will be excluded from the study.
(Note: Day 1 indicates the first day when the supplement is started)

5. What are the compositions of the investigatory products? Are they safe?

The supplement contains multivitamin and multi-minerals such as Vitamin B1, B2, B3, B5, B6, B7, B8, B9, B12, Vitamin C, Vitamin E, Magnesium, Potassium, Choline, Zinc, Oats and Passion flower extract. All the ingredients are safe to consume and the amounts are within the recommended safe limit. There are no known side effects documented from these ingredients.

6. What is MRI scan? Is it safe and are there any risks from MRI Scan?

MRI stands for Magnetic Resonance Imaging. It uses magnetic field and radiofrequency wave to acquire 3D images of our internal organs. It is safe and does not produce any ionizing radiation. During the scanning, you will lie down on a couch inside the scanner for about 30 minutes. You may hear some noise during the scanning but it is completely safe. A pair of earplugs will be provided so that you will feel comfortable. No invasive procedure or injection will be carried out during the MRI scan.

Because MRI uses powerful magnets, the presence of metal in your body can be a safety hazard if attracted to the magnet. Before having a MRI scan, you will be requested to complete a questionnaire that asks if you have any metallic or electronic devices implanted in your body. You will not be eligible to undergo the MRI scan if you have any metallic or electronic implant in your body. Our researchers will explain to you if you have any doubts or worries regarding the MRI scan. In addition, some people may have fear to go inside the MRI tunnel due to a condition called claustrophobia (fear to stay inside a small space). Our researchers will guide you to overcome the fear by explaining to you the structure of the scanner and all the safety precautions that ensure your safety. You will be provided an emergency button (you can hold it with your hand throughout the scanning process). In case of emergency or when you feel uncomfortable, you can press the button and the scanning will stop immediately and the couch will automatically remove you from the scanner. For people who cannot overcome the fear, they will be excluded from the study.

7. How is the study going to be conducted?

This is a single-site, double-blind, randomized, and placebo-controlled clinical trial utilising active and placebo formulations to assess the effect of high-dose B-vitamins multivitamin supplement with and without Passion flower herbal extract on brain activity and functions in healthy adults. The study will be conducted between July, 2020 to June, 2021 at the Taylor's University Lakeside Campus, Subang Jaya, Malaysia and the 3T MRI Research Centre, University of Malaya, Kuala Lumpur, Malaysia. A total of 90 participants will be randomly divided into three groups, namely: active intervention A, active intervention B and placebo, with 30 subjects in each group. The formulation of each group are as follows:

Active intervention A:	with Passion flower herbal extract
Active intervention B:	without Passion flower herbal extract
Placebo:	contains only glucose and trace quantities of Riboflavin (Vitamin B2) to match the colour and taste of the active ingredients.

8. What is Placebo? Does it carry any risk?

Placebo is a formulation that looks and tastes identical as the active formulations but it does not contain any active ingredients. It is used to eliminate the psychological effects towards the efficacy of the active intervention, as expectations about efficacy can influence results. The placebo contains only glucose (sugar) and a tiny amount of Vitamin B2 that will not bring any risk or side effect to the consumer.

9. Can I choose the group/formulation that I want to participate in?

You cannot choose the group/formulation that you want to participate in. The study is double-blinded. A double-blind study is one in which neither the participants nor the researchers know who is receiving the actual supplement and who is receiving a placebo. This procedure is utilized to prevent bias in research results due to researchers' biases and placebo effects. Each formulation will be labeled with a unique code and only the authorized persons at the Sponsor site will have the information of the formulation. Randomization will be done by the Research Manager with 1:1:1 ratio. It means that you will be randomly assigned to a particular group/formulation with an equal chance of 33%.

10. How long will I be involved in this study?

You will need to take the supplement tablets for 6 months.

11. Who should not participate in this study (exclusion criteria)?

- Cigarette smoker.
- Regular alcohol drinker exceeding 14 standard drinks per week for women and 28 standard drinks per week for men).
- Gluten intolerance.
- Having claustrophobia (fear to be in a constraint space).
- Diagnosis of Type 1 or Type 2 diabetes.
- History of anxiety, depression, psychiatric disorders or epilepsy.
- History of / currently suffers from heart disease or high blood pressure.
- History of head injury/stroke.
- Evidence or history of any clinically significant (in the judgment of the investigator) renal, endocrine, pulmonary, gastrointestinal, cardiovascular, psychiatric, neurological, within the last 5 years.
- Currently taking Warfarin.
- Clinically relevant abnormalities in their medical history that would render them ineligible for MRI.
- Having metallic implants and other abnormalities in their medical history that would render them ineligible for MRI.

12. Who will have access to the participant's medical records or data?

Only authorized personnel directly involved in the research will have access to your medical records and data (less than 10 people). These include the principal investigator, co-investigators, representatives from the sponsor and site manager employed to manage the study.

13. Will the records/data be kept confidential?

The record and data will be kept strictly confidential. The record and data will be kept in a specific participant's folder and secured in a locked facility. Only authorized personnel will have the key access to the participant's folder. A unique three-digit identifier code will be assigned by the investigator to each trial subject to protect the subject's identity. The code (001 to 999) will be generated based on chorological sequence of recruitment and will be used throughout the study duration.

14. What will be the benefits of the study to the participant and community?

With the supplements, it is possible to improve your brain activity and functions. The product could help to reduce stress levels, improve brain functions and hence promoting a healthier living community.

15. What are the possible drawbacks (side effects, etc.) of taking the tablet?

The risk of any complications is minimal. In rare occasions, you may experience stomach discomfort if the tablets are taken before food and this can be prevented by taking the tablets after food. Other possible side effects including skin rashes/flushing, nausea, diarrhea and vomiting are rare conditions after taking the supplement tablet. Please inform our researchers immediately if you discover any other discomfort after taking the tablets.

16 Are there any risks from the blood draws?

The risks involved in drawing blood may include temporary discomfort at the site of the blood draw, possible bruising, redness, and swelling around the site, bleeding at the site, feeling of lightheadedness when the blood is drawn, and rarely, an infection at the site of the blood draw.

17. Is the investigatory product derived from a source that may be cultural sensitive, eg: bovine or porcine? (if applicable)

No.

18. What compensation or reimbursement will be given to the participant?

The participants will be receiving certain amount of travel compensation to the transportation cost for each scheduled visits as follow:

Study Visit	Amount of Travel Allowance (RM)
1	100
2	100
3	100
4	150

In the cases of study-related injuries or complications (proven by a certified medical doctor), the medical expenses or associated compensations will be covered by insurance acquired under this study.

19. Can I refuse to take part in the study and what are the consequences?

Your participation in this study is completely voluntarily and you can choose to leave the study anytime as you wish. Refuse to participate or withdrawing from the study will not affect your entitled medical services.

20. What treatment will I receive after the study? Will I continue to receive the investigatory product after completion of the study?

No treatment will be given to you after the study. You will not receive the investigatory product after completion of the study.

21. Will I be informed of the findings after completion of the study?

We will not inform you regarding the findings of the study. However, if you are interested to know the findings, you can contact the principle investigator listed below.

22. Will I be informed if there is any new information or amendment added to the consent?

Yes, we will inform you if there is any new information or amendment added to the consent.

23. Who will be paying the anticipated expenses in this study?

Taylor's University will be paying for all the anticipated expenses in this study, including the costs for MRI scanning and blood tests.

24. Who is sponsoring this study?

This study is sponsored by Blackmores Institute, Australia.

25. Who should I contact if I have additional questions during the course of the study?

Principal Investigator: Associate Professor Dr Yeong Chai Hong
School of Medicine,
Faculty of Health and Medical Sciences,
Taylor's University
Phone: +6016-7016879
E-mail: chaihong.yeong@taylors.edu.my

26. Who are the other researchers involved in this study?

- Professor Dr Rusli Nordin – Taylor's University
- Professor Dr Anjan Kumar Das – Taylor's University
- Dr Wong Yin How – Taylor's University
- Associate Professor Dr Karuthan Chinna – Taylor's University
- Mr. Selvaraja Seerangam – Taylor's University
- Professor Dr. Norlisah Ramli – University of Malaya
- Dr Azlan Che Ahmad – University of Malaya
- Dr Tan Li Kuo – University of Malaya

27. Who should I contact if I have additional questions about my right as a participant?

Medical Research Ethics Committee (MREC) – NIH Secretariat
Ministry of Health Malaysia
c/o Institute for Health Management,
Block A, Kompleks Institut Kesihatan Negara (NIH)
No 1 Jalan Setia Murni U13/52,
Seksyen U13 Bandar Setia Alam,
40170 Shah Alam
Phone: 03-3362 8888/8205
Email: nihsec@@moh.gov.my

I, …… Identity Card No……..……
[Name of Participant]

of ……...
[Address]

hereby agree to take part in the clinical research (clinical study/questionnaire study/drug trial) specified below:

Title of Study: **Effect of High–Dose–Vitamin–B Multivitamin Supplement on Neural Connectivity and Oxidative Metabolism in Healthy Adults: A Randomised, Double–Blind, Placebo–Controlled, Phase I Clinical Trial**

the nature and purpose of which has been explained to me by

..……..……..……..……..
[Name & Designation of Attending Personnel (IC Number)]

and interpreted by ……..……..……..…….... ……..……
[Name & Designation of Interpreter (IC Number)] *[Signature of Interpreter]*

to the best of his/her ability in ……..…… language/dialect on ……..……....
[Date]

I have been told about the nature of the clinical research in terms of methodology, possible adverse effects and complications (as per participant information sheet). After knowing and understanding all the possible advantages and disadvantages of this clinical research, I voluntarily consent of my own free will to participate in the clinical research specified above.

I understand that I can withdraw from this clinical research at any time without assigning any reason whatsoever and in such a situation shall not be denied the benefits of usual treatment by the attending doctors.

Date: ……...…….. Signature or Thumbprint ……..……
[Participant]

IN THE PRESENCE OF

Name ……..…..……..…)
)
Identity Card No. ……..……..……)

Designation ……..……) ……..
[Witness for Signature of Participant]

Date ……..)

I confirm that I have explained to the patient the nature and purpose of the above-mentioned clinical research.

Date …….. Signature ……
[Attending Personnel]