Health Research Ethics Committee FKUI-RSCM

FK UI Central General Hospital

INFORMATION SHEET TO PROSPECTIVE SUBJECTS

The **DIVINE** Research Team led by **Dr. dr. Rina Agustina, M.Gizi** from the **Department of Nutrition, Faculty of Medicine, Universitas Indonesia** will conduct a study entitled **Dietary ModulatIon of Gut Microbiota on Nutritional Status and COVID-19 InfectioN in AdolEscents: Gut-Lung-Axis (DIVINE)** (***Modulasi Diet Mikrobiota Usus terhadap Status Gizi dan Infeksi COVID-19 pada Remaja: Gut-Lung-Axis***). This research is sponsored by the **Indonesia Endowment Fund for Education Agency of the Ministry of Finance of the Republic of Indonesia.**

We will provide you with information about this study and invite your son/daughter to be part of the study.

Your son/daughter can participate in this study by signing this form. If you agree for your son/daughter to participate in this study, your son/daughter can freely withdraw from the study at any time. You also have the right to receive updates from us regarding the ongoing research, and if you have any further questions regarding this study, please feel free to contact us as the research team. If you refuse your son/daughter to participate or withdraw from the study, your decision will not affect your relationship with us and will not impact their assessment at this school.

If you do not understand any of the statements in this form, you can ask us.

1. **Research objectives**

   The aim of this study was to determine the effect of probiotic supplementation **and health education** on nutritional status, immune response to COVID-19 vaccination, gut **bacteria**, diet quality, and cognitive function in **overweight** adolescents. In addition, this study also aims to analyse the factors that determine adolescent health.

2. **Participation in research**

   Overall, the study will run for 6 months with 5 months or 20 weeks for intervention procedures. If you decide to have your son/daughter participate in this study, your son/daughter will be asked to follow our schedule and ensure that your son/daughter can adhere to the schedule. The study will involve your son/daughter in several interview sessions. Each interview session will be approximately 1 to 2 hours long. In addition, your son/daughter will be measured for nutritional status, cognitive ability, and a sample of

their blood, saliva and faeces will be taken. This measurement and sampling session will last approximately 3 hours.

3. Reasons for choosing your son/daughter

Your son/daughter was selected to participate in this study because he/she fulfils the following criteria:

a. Male or female aged 12-17 years old;
b. Healthy;
c. Reside in Jakarta, Surabaya, Yogyakarta for at least 6 months;
d. Have received a complete dose of COVID-19 vaccine (2 doses) with CoronaVac® (Sinovac) vaccine at least 6 months prior to the intervention;
e. Have an active BPJS (national health insurance) or other health insurance;
f. You as a parent / guardian give permission by signing the *Informed Consent* Sheet and your son / daughter is willing to participate in the study by signing the *Informed Assent* Sheet.

4. Research procedure

The following is the research procedure that your son/daughter will undergo:

Stage 1

a. Your son/daughter will be interviewed by an enumerator to ask: Name, age, sociodemographic information (parents' education, occupation, and income, family size, place of residence and ethnic origin), history of illness, history of drug use, history of allergies, history of COVID- 19 vaccine, history of dietary intake and eating habits, physical activity and exercise habits, stage of puberty, behavioural and mental disorders and self-confidence, parental and peer support for nutritional behaviour, psychosocial conditions, sleep quality, and quality of life.
b. Undergoing a physical examination by a medical doctor to check health status.
c. Undergoing nutritional status measurement by a nutritionist, which includes body weight weighing, height measurement, upper arm circumference, waist circumference, hip circumference, waist-to-height ratio (WHtR).
d. Approximately one night before the study, you will be asked to fast, but allowed to drink water as needed.
e. On the day of the study, participants were asked to arrive at 6.45am for blood collection.
f. Blood is drawn by inserting a butterfly needle into a vein in the forearm. Blood is drawn through the butterfly needle that has been placed. Blood is taken in the amount of approximately two tablespoons. This blood collection is the initial data for laboratory examinations regarding the state of the blood, the body's immunity to COVID-19, inflammatory factors, cognitive function, and gastrointestinal function. Blood draws are done by nurses who are familiar with drawing blood.
g. Your son/daughter will also be asked to provide a stool sample. Self-contained stool collection

equipment will be provided by the researcher. The purpose of stool collection is to assess the condition of the gut microbiota, inflammation and GI tract integrity.

Stage 2

a. After conducting interviews, physical examinations, and nutritional status measurements, subjects were screened for inclusion criteria and excluded.
b. Furthermore, if your son/daughter meets the criteria, saliva samples will be collected by the officer. This saliva sample will be used to assess immune function against COVID-19.
c. Your son/daughter who meets the criteria will also be asked to provide a stool sample. Self-contained faecal collection equipment will be provided by the researcher. The purpose of stool collection is to assess gut microbiota, inflammation, GI tract integrity, SCFA, and untargeted fecal metabolomics.
d. Your son/daughter will undergo a cognitive ability measurement test which will be conducted by a psychologist. The preparation for the cognitive ability test is as follows: Your son/daughter will be asked to enter a controlled test room suitable for effective assessment of cognitive function. Your son/daughter will be asked to follow test instructions from one of the examiners (psychologist) and the overall administration of the test will be assisted by several testing assistants. Furthermore, test instructions, questionnaire and answer sheets will be distributed to all participants. The cognitive ability test is conducted using paper and pencil. At the assessment stage, your son/daughter will be asked to open the question booklet and begin writing his/her answers on the answer sheet. The questionnaire will present the participant with a diverse and complex visual pattern with one part omitted. The participant is then asked to find the missing part to complete the pattern from the given answer alternatives. There were five sections (A, B, C, D, and E) to be completed and each section consisted of twelve patterns to be completed. The average time given to complete the whole test is 1 hour. After the test is completed, the examiner will withdraw all the answer sheets and then participants will be asked to leave the examination room.
e. The study then proceeded to phase 2 where your overweight and obese son/daughter would be randomised into two groups where one group would receive probiotic supplementation while the other group would receive a blank supplement. Neither your son/daughter, you, nor the research team know who is getting the probiotic supplement and who is getting the blank supplement. Both groups will receive counselling on healthy eating, physical activity, and psychosocial stimulation which will be explained by the research team as supplementation.

f. Your son/daughter will be asked to take the supplement every day for 20 weeks, which will be delivered and deposited by the staff every month to the school and will be distributed by the teachers every morning. In addition, supplements taken on holidays will be delivered by our team of enumerators every month to the home.
g. Your son/daughter will also be asked to access educational modules on healthy eating, physical activity and psychosocial stimulation and complete a questionnaire on their understanding of these modules.
h. During the supplementation period (20 weeks), your son/daughter will be visited by our enumerators every 5 weeks for interviews on dietary intake, physical activity, medical history, and supplement compliance. In addition, nutritional status, body composition, and waist-to-height ratio measurements will also be taken.
i. At the end of weeks 10 and 20, blood and saliva samples will be collected according to the procedures described above to assess changes in blood status, immunity to COVID-19, inflammatory factors, cognitive function, and gastrointestinal function during the research process.
j. At the end of week 20, faecal samples will be collected according to the procedures described above to assess changes in the state of the gut microbiota, SCFA, inflammation, digestive tract integrity, and untargeted fecal metabolomic at the end of the study.
k. At the end of week 20, a cognitive ability measurement test will also be conducted again to assess changes at the end of the study.
l. At the end of week 20, your son/daughter will also be interviewed again regarding dietary intake history and eating habits, physical activity and exercise habits, disease history, behavioural and mental disorders and self-confidence, psychosocial conditions, sleep quality and quality of life to assess changes at the end of the study.

A summary of the research procedure is presented in tabular form in the appendix of this briefing paper.

5. Risks, side effects, and their management

Risks in this study may arise due to the blood collection process. Your son/daughter may experience pain and infection at the blood collection site. To prevent this from happening, the blood collection staff will carry out the blood collection process according to standard procedures. They will clean the forearm area, use disposable equipment and maintain sterile principles, use personal protective equipment (gloves and mask), cover the needle wound with sterile gauze, apply pressure on the wound area to prevent bleeding, and apply personal hygiene (wash hands before and after the blood collection procedure).

Probiotic supplements have been widely used for various health benefits such as maintaining gastrointestinal function, boosting immunity, and weight loss. The use of probiotic supplements has not been reported to have any adverse effects in healthy children and adolescents (Van den Nieuwboer *et al*., 2012),

2015). However, if your son/daughter has a complaint, please report it to us immediately. **If there are any side effects from the probiotic supplement, your son/daughter will be facilitated with treatment and we suggest that he/she** be immediately examined at the nearest health centre/clinic that works with **BPJS/other** health insurance **used by your son/daughter.**

6. Benefits

The benefits that your son/daughter can get are the results of measuring nutritional status, improving nutritional status, and laboratory tests to determine blood conditions, immunity to COVID-19, inflammatory factors, cognitive function, and gastrointestinal function for free. In addition, your son/daughter will also gain knowledge about healthy food, measurable physical activity, and useful psychosocial stimulation.

7. Compensation

Your son/daughter will receive a stipend for participating in this study in the amount of **IDR 50,000 per visit to the data collection site (**at the beginning, middle and end of the study).

8. Funding

The funding of this research was fully covered by the sponsor.

9. Confidentiality

All data collected in this study will be kept confidential. Presentation of research results at scientific meetings/conferences and publication in scientific journals will not include the name of your son/daughter. However, representatives from the sponsor and ethics committee will have access to the research data for verification.

10. Obligations of research subjects

As a research subject, your son/daughter is obliged to follow the research rules or instructions as written above. If there is anything that is not clear, you can ask further questions to the research team.

11. Right to refuse and withdraw

Your son/daughter does not have to participate in this study if you do not wish to. You should understand that even if you agree for your son/daughter to participate, your son/daughter has the right to withdraw from the study. If you refuse your son/daughter to participate in the study, your son/daughter has the right to withdraw from the study, such decision will not affect your relationship with me and will not impact their assessment at this school.

I will give you the opportunity at the end of this explanation to consider your decision.

12. Additional Information

You are given the opportunity to ask anything that is unclear in relation to this study. If at any time side effects occur or you need further explanation, you can contact the research team members at each research location, namely: dr. Karina Rahmadia E, M.Gizi/08989890246 (Jakarta), Dr. dr. Lilik Djuari, M.Kes/0811349350 (Surabaya), and dr. Wahyu Damayanti, MSc, SpA (K)/08121554106 (Yogyakarta).

13. Bibliography

Van den Nieuwboer M, Brummer RJ, Guarner F, Morelli L, Cabana M, Claassen E. Safety of probiotics and synbiotics in children under 18 years of age. Beneficial microbes. 2015 Oct 15;6(5):615-30.

CONSENT SHEET

For research subjects ..... ***(Subject's name)*** who participated in the study:

Dietary ModulatIon of Gut Microbiota on Nutritional Status and COVID-19 InfectioN in AdolEscents: Gut-Lung-Axis (DIVINE) (Dietary Modulation of Gut Microbiota on Nutritional Status and COVID-19 Infection in Adolescents: Gut-Lung-Axis)**,**

I have read and understood the information contained in the information sheet and have been given the opportunity to discuss and inquire about it. I agree to allow my child to be treated ***according to the research protocol***. I understand that I can refuse to participate in the study. I am aware that I can withdraw from this study at any time.

I, as the **PARENT/Guardian** of .....

AGREE to participate in this study.

Date **: .....**

Parent/Guardian signature **: .....**

Parent/Guardian Name : **.....**

Witness signature **: .....**

Witness Name **: .....**

If the subject is illiterate*:*
A witness who is not illiterate should sign it (if possible, this person should be chosen by the research subject/participant, not his/her parents, and should not have any relationship with the research team). Illiterate research subjects/participants must also have their fingerprints stamped.

I have witnessed the reading of the *consent* form to the subject/participant accurately, and have been given the opportunity to ask questions. I confirm that the subject/participant has given his/her consent freely.

Name of witness _____ **AND Fingerprints of research subjects**

Signature of witness _____

Date _____
date/month/year

Appendix 1 Research Procedure

Table 1 Research procedure

Activities	Stage/Week 1						
	Screening (0)	Initial (0)	1	5	Middle (10)	15	End (20)
Screening							
Tracking schools and research subject	x						
Explanation of the study and Informed consent	x						
Stage 1							
Subject interview		x					
Physical examination		x					
Measurements of nutritional status (BW, TB, upper arm circumference, waist circumference, and hip circumference)		x		x	x	x	x
Food consumption interview (1×24 hour *food recall* and FFQ)		x		x	x	x	x
Physical activity interview		x		x	x	x	x
Blood draw		x			x		x
Stage 2							
Explanation of the 2nd phase of research		x					
Physical examination		x					
Measurement of cognitive ability		x					x
Measurements of nutritional status (body weight, height, upper arm circumference, waist circumference, and hip circumference), waist-to-height ratio		x		x	x	x	x
Interview on food consumption (*food recall* 1×24 hours)		x		x	x	x	x
Physical activity interview		x		x	x	x	x
Saliva sampling		x			x		x
Collection of faecal samples		x					x
Supplementation			x	x	x	x	x
Access to educational modules (diet, physical activity, and psychosocial stimulation)			x	x	x	x	x