

National Taiwan University Hospital

Informed Consent Form for Clinical Trial/Research

Participants

Project Title: To evaluate the influence of LUA probiotics on uric acid

NCT Number: NCT06969469

Date: 2021/09/10

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Informed Consent Form for Clinical Trial/Research Participants

IRB Approval Number: 202012224RSD

Please read this form carefully. Sign only after the principal investigator or an authorized person has explained it to you.

Project Title

To evaluate the influence of "LUA probiotics" on uric acid.

Trial Institution: Department of Internal Medicine, National Taiwan University Hospital

Sponsor / CRO: Super Laboratory Co., Ltd.

Funding Source: Grape King Bio Ltd., Longtan Branch

Principal Investigator: Dr. Jyh-Ming Liou

Co-Investigators: Dr. Chien-Chuan Chen, Dr. Chieh-Chang Chen, Dr. Mei-Chih Chen

24-Hour Emergency Contact: Yu-Chun Huang

Phone: 0934-173838

(If unavailable, please leave a text or voicemail. The study team will contact you as soon as possible.)

Participant Name:

Medical Record Number:

You are invited to participate in this clinical observational study. This form provides you with relevant information about the study. The principal investigator or an authorized person will explain the study to you and answer your questions. Please do not sign the consent form until all your questions are satisfactorily answered. You are not required to make an immediate decision. You may take your time to consider it. You must sign this form to participate in the study. Even after signing, you may withdraw at any time without needing to provide a reason.

1. Study Purpose

Hyperuricemia is a condition characterized by abnormally high levels of uric acid in the blood. It is a major risk factor for gout and is also associated with various diseases. Therefore, its prevention and treatment have gained attention. Recent research in cell and animal models suggests that lactic acid bacteria (LAB) may help lower uric acid levels, but rigorous clinical studies are lacking.

This study aims to evaluate whether taking “LUA probiotics” can reduce serum uric acid levels and help prevent gout before symptoms occur, thereby reducing the need for long-term medication. A total of 20 participants will be recruited for this clinical observational study.

2. Study Background and Product Information

(1) Product Information:

“LUA Probiotics” is developed by Grape King Bio Ltd., Longtan Branch. Its main ingredients include *Lactobacillus reuteri*, beta-carotene, silicon dioxide, and magnesium stearate.

In cell studies, *L. reuteri* has been shown to enhance purine metabolism; in animal models, LAB helped reduce uric acid levels, possibly by promoting purine breakdown.

The placebo used in this study is also manufactured by Grape King Bio Ltd., and is identical to the test product except it contains no *Lactobacillus reuteri*.

This study does **not** involve drugs, medical devices, or medical technology.

(2) Market Status:

The product has not yet been marketed.

3. Inclusion and Exclusion Criteria

Inclusion Criteria:

- 20 male or female participants aged ≥ 20
- Mentally competent, voluntarily participating, and signed informed consent
- Diagnosed with hyperuricemia (uric acid ≥ 7.5 mg/dL) or gout but not on uric acid-lowering medication

Exclusion Criteria:

- Diagnosed with catastrophic illness per NHI regulations
- Pregnant or planning pregnancy within 6 months
- Abnormal liver function (AST/ALT > 2X upper limit)
- Renal impairment (serum creatinine > 1.5 mg/dL)
- Gastrointestinal disorders (e.g., surgery, frequent diarrhea)
- Continuous use of antibiotics, H2-blockers, PPIs, antioxidants, probiotics, or laxatives
- Severe complications (e.g., stroke, MI, trauma, or surgery) within the past 6 months
- Allergic to *Lactobacillus*
- Unable to provide informed consent
- Irregular eating habits or unable to comply with study protocol
- Poor medication compliance

4. Study Method and Procedures

- Confirm eligibility per inclusion/exclusion criteria
- Enroll 20 qualified participants
- Participants fill out a consent form and a GI questionnaire (includes personal data, medical history, lifestyle, GI symptoms; ~20 min)
- Two study phases over 6 weeks:
 - **Phase 1 (2 weeks):** 2 capsules of Test Product A (500 mg each) after dinner daily
 - **Phase 2 (4 weeks):** 2 capsules of Test Product B (500 mg each) after dinner daily
- Blood samples (20 c.c., fasting) at Week 0, 2, and 6 to measure:
 - Uric acid, CBC, fasting glucose, TG, TC, HDL, LDL
 - Cytokines: IL-1 β , IL-6, IL-10, IL-13, IL-17, IL-18, TNF- α , IFN- γ
- Data analysis using SPSS 16.0; results as Mean $\pm$ SD; $p < 0.05$ is significant

5. Risks and Side Effects

- Blood draws may cause minor discomfort, bruising, swelling, or bleeding
- If gout occurs during the trial, seek medical attention immediately
- *Lactobacillus reuteri* is a probiotic and not pathogenic; may help GI health

and reduce *H. pylori*

- Side effects are rare (< 5%) and may include diarrhea, nausea, abdominal pain, or constipation
- Discontinue if any serious adverse events occur

6. Alternative Treatment

You are not obligated to join the study. Standard treatments include uric acid-lowering drugs such as allopurinol, benzbromarone, and febuxostat.

7. Expected Benefits

This study investigates whether LUA probiotics may help lower uric acid without medication. It does not provide treatment. If you feel unwell, seek medical care.

8. Participant Responsibilities and Restrictions

Maintain regular dietary habits. Avoid binge eating or special foods. Avoid medications such as antibiotics, PPIs, antioxidants, probiotics, or laxatives. Inform the study team if using any of these.

9. Confidentiality

All personal information and identifiable records will be treated confidentially per regulations. Study results may be published, but your identity will be protected. You authorize the study sponsor, auditors, IRB, and regulatory bodies to review your records for compliance checks.

10. Withdrawal from the Study

You may withdraw at any time without penalty or loss of medical care. Data and samples collected up to the point of withdrawal will be retained unless otherwise requested. You may choose how to handle your previously provided samples and data.

11. Compensation and Insurance

- The sponsor, Super Laboratory Co., Ltd., will be responsible for compensation due to unexpected adverse effects, but not for known side effects.
- No separate liability insurance is provided, but the company holds product liability insurance.
- NTUH will provide appropriate medical care and consultation.
- No financial compensation beyond medical care will be provided.
- Signing this form does not waive any of your legal rights.

12. Sample and Data Use and Retention

- Samples stored for 5 years at NTUH; anonymized using a research ID.
- If reused for future hyperuricemia or probiotic research, IRB approval is required.
- Participants can choose to allow or deny future use of leftover samples and data.
- Data stored in locked cabinets or password-protected computers for 5 years.
- International data sharing will follow confidentiality and legal standards.

13. Participant Rights

- The study has been reviewed and approved by the NTUH Research Ethics Committee (REC).
- The REC includes professionals from medicine, law, social work, and public representatives.
- If you have concerns or feel harmed, contact the REC at (02)2312-3456 ext. 63155.
- If major new findings arise during the study that may affect your participation decision, you will be informed.
- If you have any questions, contact the PI: Dr. Jyh-Ming Liou (24-hour contact: 0972-651883).
- You will receive a copy of the signed consent form.
- Transportation allowance of NT\$1,000 will be provided at Week 0, 2, and 6.
- You will be notified if unexpected safety issues arise within 2 years post-

trial.

14. Commercial Benefits

Any commercial benefits from discoveries or products developed from this study will belong to the sponsor. You and your family will not receive financial compensation or rights.

15. Signatures

- (1) The principal investigator, co-investigator, or authorized personnel has thoroughly explained the nature and purpose of the research methods described above, as well as the potential risks and benefits.

Signature of Principal Investigator / Co-Investigator: _____

Date: _____ Year ____ Month ____ Day

Signature of Other Research Staff Involved in the Explanation and Consent Process: _____

Date: _____ Year ____ Month ____ Day

- (2) After the explanation, I fully understand the research methods and the possible risks and benefits described above. Any questions I had regarding this clinical trial/research have been clearly answered. I voluntarily agree to participate in this study and will retain a signed copy of the consent form.

Participant Signature: _____

Date: _____ Year ____ Month ____ Day

Date of Birth: _____ Year ____ Month ____ Day

Phone: _____

National ID Number: _____

Gender: _____

Mailing Address: _____

Signature of Legal Representative / Authorized Consenter:

Date: _____ Year ____ Month ____ Day

Relationship to Participant (please circle): Spouse / Father / Mother / Son / Daughter / Other: _____

Date of Birth: _____ Year ____ Month ____ Day

Phone: _____

National ID Number: _____

Mailing Address: _____

If the situation falls under Article 79 Paragraph 1 proviso of the Medical Care Act or Article 12 Paragraph 1 proviso of the Human Research Act, the exercise of consent rights shall follow Article 79 Paragraph 2 of the Medical Care Act, Article 5 of the Regulations on Human Trials, or Paragraphs 3 and 4 of Article 12 of the Human Research Act:

- If the subject has no legal capacity (e.g., under 7 years of age or under guardianship), consent must be given by the legal representative. For those under guardianship, the guardian serves as legal representative.
- If the subject has limited legal capacity (e.g., minors over 7 years old, or those under assistance due to mental or intellectual disabilities), both the subject and the legal representative or assistant must provide consent.
- If the subject is not legally incapacitated or limited but is unable to effectively communicate or make decisions due to confusion, mental, or intellectual impairments, consent must be provided by an authorized person.

Order of Authorized Consent Providers:

1. For clinical trials involving new drugs, devices, or techniques (per Article 5 of the Human Trials Regulations):
(1) Spouse (2) Parents (3) Co-residing adult children (4) Co-residing grandparents (5) Co-residing siblings (6) Other relatives who have cohabited within the past year
2. For human research (per Article 12 of the Human Research Act):
(1) Spouse (2) Adult children (3) Parents (4) Siblings (5) Grandparents

If multiple people qualify, the priority follows the above order. Among people of the same level, those with closer kinship take precedence; if kinship is equal, co-

residing relatives take precedence; if not co-residing, the elder takes precedence.

Witness Signature: _____

Date: _____ Year ____ Month ____ Day

If the participant, legal representative, or authorized person cannot read, a witness must be present during the entire consent discussion. The witness must ensure consent is given voluntarily and confirm this by signing and dating the form. Study personnel cannot serve as witnesses.

If the participant is conscious but unable to sign personally, a fingerprint may be used in place of a signature, but a witness must be present.