Informed Consent Form · Information Sheet

(Version Number: V1.0 Version Date: 2024.1.8)

Dear Participant,

We invite you to participate in a clinical study titled "Clinical Experimental Study on the Impact of PEG Laxatives for Bowel Preparation on the Gut Microbiota of Appendectomized Patients." The principal investigator for this study is Professor Xie Huaping from Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology. The research protocol has been reviewed and approved by the Medical Ethics Committee of Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology.

Before you decide whether to participate in this study, please read the following information carefully. It will help you understand the purpose of the study, why it is being conducted, the procedures and duration involved, as well as the potential benefits, risks, and discomforts. If you wish, you may discuss it with your family, friends, or your doctor to help you make an informed decision.

If you are currently participating in another clinical study, please inform your study doctor or research staff. Thank you for your consideration of this research.

I. Why is this study being done?

Colonoscopy is a mandatory component of colorectal cancer screening. For high-risk populations, annual screening is the most effective method for early prevention. Currently, large volumes of polyethylene glycol (PEG2000-4000) are used as a laxative and lubricant during colonoscopy. The extensive use of PEG can lead to long-term and potentially irreversible damage to the gut microbiota, posing significant health risks (Tropini, Lin Moss et al., 2018).

The appendix, a slender tube protruding from the posteromedial wall of the cecum, was once considered a redundant part of human evolution. Historically, acute appendicitis has been the most common cause of acute abdominal surgical conditions,

with appendectomy being the traditional treatment. However, recent research has revealed associations between appendectomy and various conditions, including psychiatric disorders, colorectal cancer, and cardiovascular disease. Beyond its role as an important immune organ, the appendix also serves as a reservoir and protector of gut microbiota. When the intestinal microbiota is disrupted, microbes stored in the appendix can be released into the gut to help mitigate the disturbance. Previous metagenomic sequencing by researchers has shown that the gut microbiota of appendectomized patients is significantly altered compared to healthy individuals. This alteration can affect central nervous system function via the microbiota-gut-brain axis, potentially impacting host health and behavior, with links to diseases like Parkinson's. Therefore, appendectomy may potentially have adverse effects, such as significantly altering the composition of the gut microbiota, reducing the resilience of gut homeostasis, and decreasing the production of short-chain fatty acids (SCFAs).

This study aims to observe the impact of PEG laxatives on the gut microbiota. By analyzing changes in the intestinal microecology before and after colonoscopy, we hope to provide a basis for designing better bowel-cleansing agents and restorative probiotics, thereby mitigating the adverse effects of colonoscopy on patients. Additionally, we will investigate the interaction between the appendix and the gut microbiota, and its significance.

II. Who will be invited to participate?

Patients who have undergone an appendectomy or a colectomy involving removal of the appendix within the past two years.

III. Study Sites and Number of Participants

The study will be conducted at Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology, and the College of Life Science and Technology, Huazhong University of Science and Technology. Approximately 10 participants will be enrolled in this study.

IV. What will happen if you take part?

1. Before enrollment: The doctor will ask about and record your medical history and conduct a routine inquiry regarding your colonoscopy preparation and appendectomy status. If you are eligible, you may voluntarily choose to participate by signing the informed consent form. If you prefer not to participate, your treatment preference will be respected.

2. If you voluntarily agree to participate, the following steps will occur:

(1) On the day you sign the informed consent form, you will receive 6 stool sample collection kits.

(2) On the same day, you will be asked to complete a questionnaire and return it to the clinic doctor.

(3) At the specified sampling time (before using the auricular acupoint stimulator), collect one stool sample, preferably from the middle portion of the stool, avoiding urine contamination. After collection, please contact the researcher, He Junqing (Tel: 13177628984), for sample delivery. The mailing address is: Mr. He Junqing, Building G, Wuhan National Laboratory for Optoelectronics, Huazhong University of Science and Technology (East Campus), No. 1037 Luoyu Road, Hongshan District, Wuhan City, Hubei Province. Please select "freight collect" for shipping costs.

(4) During the study, we will need to collect your stool samples (approximately 10g each) at five specific time points: (1) before colonoscopy, (2) first non-watery stool after colonoscopy, (3) one month after colonoscopy, (4) three months after colonoscopy, and (5) six months after colonoscopy. Your samples will be used solely for this research.

3. Your other responsibilities:

Please collect stool samples at the designated times. Refrain from taking antibiotics, probiotics, prebiotics, or similar products during the study period.

V. Potential Benefits of Participating

Analysis of your samples will help characterize your intestinal microecology and its changes before and after colonoscopy. This knowledge can contribute to the development of better bowel-cleansing drugs and restorative probiotics, ultimately

benefiting society. The study will also explore the interaction and significance of the appendix concerning the gut microbiota.

VI. Potential Adverse Reactions, Risks, Discomforts, and Inconveniences

Potential discomforts related to this study primarily involve psychological and sensory discomfort associated with collecting stool samples at home, such as feelings of nausea.

VII. Related Costs

The stool sample collection kits used in this experiment are provided free of charge. Postage for mailing stool samples will be covered by this project. The costs associated with high-throughput sequencing of the stool samples will also be covered by this project. Any discomfort arising from other causes during the trial period, and related medical expenses incurred, will not be covered by this project.

VIII. Confidentiality of Personal Information

Your medical records (including study case report forms, laboratory reports, etc.) will be kept securely at the hospital where you receive care. Your doctor will record laboratory and other test results in your medical file. Authorized representatives of the sponsor, the Ethics Committee, and regulatory authorities may be granted access to your medical records to verify the data and study procedures. Any public reports or publications resulting from this study will not disclose your personal identity. We will make every effort, within legal limits, to protect the privacy of your personal medical information.

In accordance with medical research ethics, study data (excluding personal privacy information) may be made available for public query and sharing. This sharing will be limited to web-based electronic databases and will be conducted in a manner that ensures no personal privacy information is disclosed.

IX. How to Obtain More Information

You may ask questions about any aspect of this study at any time, and they will be answered appropriately.

If important new information becomes available during the study that may affect your willingness to continue participating, your doctor will inform you promptly.

X. Voluntary Participation and Withdrawal

Participation in this study is entirely voluntary. You may refuse to participate or withdraw from the study at any time without penalty or loss of benefits to which you are entitled. Your decision will not affect your relationship with your doctor or your medical care in any way.

For your best interests, the doctor or researcher may terminate your participation in this study at any time.

If you withdraw from the study, for your health and safety, you may be asked about your use of the study drug. If deemed necessary by the doctor, you may also be asked to undergo physical and laboratory examinations, which would be beneficial for your health.

If your condition changes and you require alternative treatments, you are free to pursue them at any time. Please inform your doctor afterwards.

XI. What to Do Now

Your participation in this study is your decision (and that of your family). Before deciding to participate, please ask your doctor any questions you may have.

Thank you for reading this material. If you decide to participate, please inform your doctor. They will make all the necessary arrangements for the study. Please keep this information sheet for your records.

Informed Consent Form · Signature Page

Project Title: Clinical Experimental Study on the Impact of PEG Laxatives for Bowel Preparation on the Gut Microbiota of Appendectomized Patients

Responsible Institution: Tongji Hospital, Tongji Medical College, Huazhong University of Science and Technology

Statement of Consent

I have read the foregoing information about this study. I have had the opportunity to discuss it with the doctor and ask questions. All my questions have been answered to my satisfaction.

I understand the potential risks and benefits of participating in this study. I acknowledge that my participation is voluntary, and I confirm that I have had sufficient time to consider it. I understand that:

- I can freely consult the doctor for more information at any time.
- I can freely withdraw from the study at any time without discrimination or reprisal, and my medical care and rights will not be affected.

I agree that the Ethics Committee or regulatory authorities may review my study-related data.

I will receive a signed and dated copy of this informed consent form.

Finally, I decide to voluntarily participate in this study and agree to follow the study instructions to the best of my ability.

Participant's Signature:_____**Date:**____ Year ____ Month ____ Day

Contact Number:_____

I confirm that I have thoroughly explained the details of this study, including the rights, potential benefits, and risks, to the patient named above, and have provided them with a signed copy of this informed consent form.

Researcher's Signature:_____**Date:**____ Year ____ Month ____ Day

Contact Number: _____