Participant Information Sheet

Dear Parents of children,

We invite your child to participate in a prospective, multicenter, randomized, blinded, placebo-controlled clinical study of effects of Lactobacillus rhamnosus LRa05 intervention on growth and development, allergic disease and immune function of infants and young children approved by the Ethics committee of Baoxing County Center for Disease Control and Prevention. This study will be carried out in Baoxing County Center for Disease Control and Prevention, and it is expected to recruit 440 subjects to participate voluntarily. This study has been reviewed and approved by the Ethics Committee of Baoxing County Center for Disease Control and Prevention.

Some of the content covered in this article is governed by regulatory requirements and has been reviewed and approved by the ethics committee in order to protect the rights and interests of patients participating in this study.

Why was the study conducted?

The intestinal microecology of infants and young children undergoes rapid development during the first 3 years of life, and the early colonization of bacteria mainly comes from the birth canal and breast milk. At this stage, the stability of intestinal flora is insufficient and it is highly susceptible to changes in feeding patterns and environment. Bifidobacterium and Lactobacillus play a crucial role in maintaining intestinal homeostasis, defending against infection, and promoting growth and development. Rhamnose cheese coli LRa05 baby stool samples from health, has been preserved in microbial preservation management committee (CGMCC No. 24377) and the typical culture preservation center (ATCC No. PAT - 126815). LRa05 exhibits good gastric acid and bile salt tolerance in vitro, and has inhibitory and co-aggregation effects on common pathogens such as Escherichia coli, Salmonella and Staphylococcus aureus. At the same time, LRA05 has strong intestinal epithelial cell adhesion and colonization potential. Animal experiments have shown that LRa05 can improve the incidence of diarrhea, enhance intestinal immunity, regulate the composition of intestinal

flora, increase the abundance of Bifidobacterium and Lactobacillus, and improve intestinal function in mice.

It is worth highlighting that LRa05 has received a Generally Recognized As Safe (GRAS) no objection letter from the US FDA for its use as a regular food ingredient. Its safety assessment covers genomic analysis, in vitro toxicological testing, animal toxicological experiments and human studies. Whole genome sequencing showed that LRa05 had high genomic homology (ANI ≥ 98%, AAI ≥ 97%) with several strains of L. rhamnosus that had been approved by FDA, such as LGG, HN001, IDCC 3201, and had no antibiotic resistance, virulence factors, or pathogenicity related genes. In addition, a 24-month stability test confirmed that LRa05 maintained high activity at -18℃, which supported the feasibility of LRA05 as a long-term edible product for infants.

However, despite the LRa05 has in adults and sure to good security and live animal models, are still lack of systemic clinical evidence for infant and young child population. Given the central role of gut microbiota in growth and development, immune maturation and allergy development in infants, this study aims to evaluate the efficacy of LRa05 in promoting growth and development, reducing the incidence of allergy and improving immune function in infants and young children, and to verify its safety in infants and young children. To provide evidence for the application of LRA05 in healthy food for infants and clinical nutrition intervention.

How was the study conducted?

If you consent to your child's participation in the study, your child will be numbered and a medical record will be created. During the course of the study, we will need to collect some samples of your child's stool, which will be taken by a professional for your child. 5 grams of stool will be taken for a total of 3 times. Your child's sample will only be used for this clinical study.

Disposal of biological samples and information after the end of the study: The samples will be destroyed after use, no identifiable personal information will be used, and all specimens from this study will not be used for commercial purposes other than the study.

As a parent or guardian of a research subject, you have the following responsibilities: provide a truthful account of your child's medical history and current medical condition; Tell

the study doctor about any discomfort your child has experienced during the study; Your child must not take restricted prepackaged foods, etc. (other prepackaged probiotic products that contain the same strain); Tell the research doctor if your child has been involved in other recent studies or is currently involved in other studies. For infants and young children who are unable to answer questions independently and rationally, ask their parents or legal guardians.

What should I and my child do in the study?

The study will last for 24 weeks with 5 visits, during which time you will need to accompany your child to the hospital for some tests, return visits as scheduled, and let us know of any changes in your child.

Are there any other treatment options for my child?

Participation in this study may or may not improve your child's health. Your child may choose to:

- Do not participate in this study.
- Participate in another study.
- No intervention.

Consult with your child's doctor about your decision.

How will participating in the study affect my child's life?

Your child may find these visits and examinations inconvenient and will require special arrangements. In addition, some examinations may be uncomfortable for your child. If you and your child have any questions about the tests and procedures used in the study, talk to the study doctor.

During the study, your child will not be allowed to use other prepackaged probiotic products that contain the same strain. Your child's study doctor will inform you of which medications your child can and cannot take during the study. Consult with your child's study physician before taking any new prescribed medications.

If your child was taking another probiotic that was prohibited in the study prior to enrollment, your child will have to discontinue the medication for 4 weeks before participating in our study. If your child needs to discontinue the medication, you will need to consult your child's study physician on how to discontinue the medication for the safety of your child.

Your child may not participate in any other clinical study of the drug or medical device during the study period.

What are the risks and adverse effects of my child's participation in the study?

Your child may experience adverse reactions during the study. All patients in the study will be monitored for any adverse reactions. If your child experiences any adverse reactions between visits, please promptly call your child's study physician for a consultation.

Currently, the most common adverse reactions caused by L. rhamnosus may include: None reported.

You may want to tell your family or close friends that your child is participating in a clinical study and that they may be aware of the events described above. If they have questions about your child's participation in the study, you can tell them how to contact your child's study doctor.

Placebo Risks:

Some patients may be using a placebo (maltodextrin). Taking a placebo means your child is not taking any probiotics for intervention. If you have any questions about your child's placebo use, consult your child's study physician.

Other risks:

What benefits will my child get from this research?

Participation in this study may or may not promote growth and development, optimize the composition of gut microbiota, improve immune function, reduce the risk of common infectious diseases and allergic diseases, and improve the quality of life of children. The detection of your child's stool samples helps to understand the characteristics of your baby's intestinal flora, provide relevant evidence for future individualized nutritional intervention, and provide useful information for research in this field.

What will my child be paid for participating in this study?

Your child will not receive any remuneration for participating in this study. To compensate your child for any inconvenience your child may have caused by participating in the study, the study will pay for the examination of your child's stool while participating in the study and for the examination at the follow-up visit, and the study products will be provided free of charge.

What happens if my child is harmed while participating in the study?

There is an extensive safety profile for L. rhamnosus. If your child's health does suffer from study-related harm as a result of participating in this study, please notify the study physician immediately and they will be responsible for taking appropriate treatment measures for your child. Even if you have consented to your child's participation in the study and have signed this informed consent form, you still retain all of your child's legal rights.

Will my child's personal information be kept confidential?

Your child's medical records will be kept at the hospital, and the investigator, the research authority, the ethics committee will be allowed access to your child's medical records. Your child's personal identity will not be disclosed in any public report of the results of this study. We will make every effort to protect the privacy of your child's personal medical data to the extent permitted by law.

Personal and medical information about your child will be kept confidential and kept in a safe and secure place. At any time, you may request access to your child's personal information (such as your child's name and address) and modify this information if necessary.

When you consent to your child's participation in the study and sign this informed consent form, you consent to your child's personal and medical information being used for the purposes described above.

Does my child have to participate in the study?

Participation in the study is entirely voluntary, and you may refuse your child's participation or withdraw from the study at any time during the study without any reason. This decision will not affect your child's future treatment. If your child does not participate in this study, or drops out of the study, there are many alternative interventions available.

If you decide that your child will withdraw from this study, please notify your child's study physician in advance. For the safety of your child, your child may be required to undergo relevant examinations, which are in the interest of protecting your child's health.

Subject Consent Statement:

I have read the above introduction about this study and am fully aware of the risks and

benefits that may arise from participating in this study. I have voluntarily agreed to participate in the clinical study described in this article.

I agree □ Do not agree □ Use of my medical records and pathological examination specimens for research other than this study.

Signature of the Child's Guardian:

Date:

Name in block letters:

Subject contact number:

Signature of legal representative (if any) :

Date:

Name in block letters:

Statement by the investigator:

I confirm that the details of this study, particularly the risks and benefits that may arise from participating in this study, have been explained to the child's guardian.

Investigator Signature:

Date:

Investigator's name in block letters:

Investigator contact number: