UNIVERSITY OF CALIFORNIA, SAN FRANCISCO
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: Trial of Infant Probiotic Supplementation to Prevent Asthma

This is a medical research study. A member of the study team, led by Michael Cabana, MD, MPH from the UCSF Department of Pediatrics will explain this study to you.

Medical research studies include only people who choose to take part. Take your time to make your decision about your child's participation. You may discuss your decision with your family and friends and with your health care team. If you have any questions, you may ask your doctor or the study doctor.

We are asking your permission to include your child in this study because he/she has at least one parent with a history of asthma. Children of one or more parents with asthma are at increased risk for developing asthma later in life.

Why is this study being done?

The purpose of this study is to find out if newborn babies who eat of *Lactobacillus GG* supplements (*Lactobacillus GG* is a bacteria that is normally found in yogurt) once a day for the first 6-months of life have a decreased risk for developing early signs of asthma. Eczema is a skin condition often seen with asthma and is one of the early signs that researchers will be monitoring.

The study is being funded by the National Institutes of Health, via the National Heart, Lung and Blood Institute.

How many people will take part in this study?

Approximately 276 children will take part in this study.

Before your child begins the main part of the study...

Your baby will need to have the following "screening" exams, tests or procedures to find out if he or she can be in the main part of the study.

- **Medical chart review:** Your baby's medical chart will be reviewed by the study research team or doctors.

During the main part of the study...

If the screening exams, tests or procedures show that your baby can continue to be in the study, and you choose to allow your baby to take part, then your baby will have the following tests and procedures done.

- Your baby will have a 50/50 chance (like flipping a coin) of being placed in one of two groups. Neither your doctor nor you will make the choice, so that bias in the study is reduced. The two groups are (a) active Lactobacillus GG supplement or (b) placebo (inactive substance). Both the active supplement and the placebo are packaged in capsules and look the same. A small amount of breast milk, formula or water is added and the mixture is put into a dispensing syringe. This is the kind of

syringe used by parents to give medicine to an infant. The mixture is then given to the infant. This is done for six months.

If you decide not to breast feed your baby, we will ask that you use a standard baby formula (Nestle Carnation Good Start Supreme). Studies have shown that the type of formula can affect the risk of developing eczema (one of our outcomes of interest). As a result, we are encouraging all parents to use the same formula, if possible. We will provide the formula free of charge until your baby is one year of age.

We will obtain 8 stool samples: While your child is in the nursery, and during follow-up at 1, 3 and 6 months of age, we will obtain two stool samples. One is to test if your child has been exposed to Lactobacillus, either through the supplement or through his/her regular diet. The other is to look at the different types of bacteria present in your child's stool, and see if Lactobacillus feeding had any effect on the types of bacteria present. After all routine tests required for your care are finished, instead of discarding your leftover specimens we will save them in what is called a "tissue bank" for possible future research.

We will conduct 6 telephone surveys: During the first 6 months, we will conduct monthly telephone surveys to assess if your baby is tolerating the supplement well and to assess if your baby is developing any of the signs of asthma or eczema (a history of wheezing, eczema—dry itchy skin) or frequent infections. There will be questions about the mother's diet (if the mother is breastfeeding) and both parent's smoking history.

We will conduct 3 physical examinations: During follow-up at 1, 3, 6, months of age, we will physically examine your baby to assess the development of early signs of asthma, such as a history of wheezing, eczema and hay fever. The physical exams do not replace the standard care that your child will receive from your regular physician. They are being performed more often than usual as part of the study. During the physical exams we may photograph your child.

When your child is finished receiving the supplement at 6 months of age

The follow-up period for the study will be 3 years. The time required will be approximately a half an hour for each telephone follow-up call and between 1 to 2 hours for each follow-up visit.

We will conduct 8 more telephone surveys: During the first 12 months, we will conduct monthly telephone surveys to assess if your baby is tolerating the supplement well, and to assess if your baby is developing any of the signs of asthma or eczema (a history of wheezing, eczema—dry itchy skin) or frequent infections.

We will conduct 3 more physical examinations: During follow-up at 12, 24, and 36 months of age, we will physically examine your baby to assess the development of early signs of asthma or eczema, such as a history of wheezing or dry itchy skin.

Blood drawing (venipuncture): During follow-up at 12, 24 and 36 months of age, a blood sample will be drawn by inserting a needle into a vein in your child's arm. Each sample will be approximately *2* teaspoons; a total of about *6* teaspoons will be drawn for the whole study. After all routine tests required for your care are finished, instead of discarding your leftover specimens we will save them in what is called a "tissue bank" for possible future research.

We will do one skin test: At 36 months of age, we will do a 'skin-prick' test to determine if your child is allergic to certain substances.

We will obtain four more stool sample: We will collect two stool samples at 9 months and two stool samples at 12 months of age, to see if Lactobacillus feeding during the first six months of life

has an effect on the types of bacteria in your child's stool even after the supplement is stopped. We will provide you with a specimen kit and ask that you mail in the samples at 9 months.

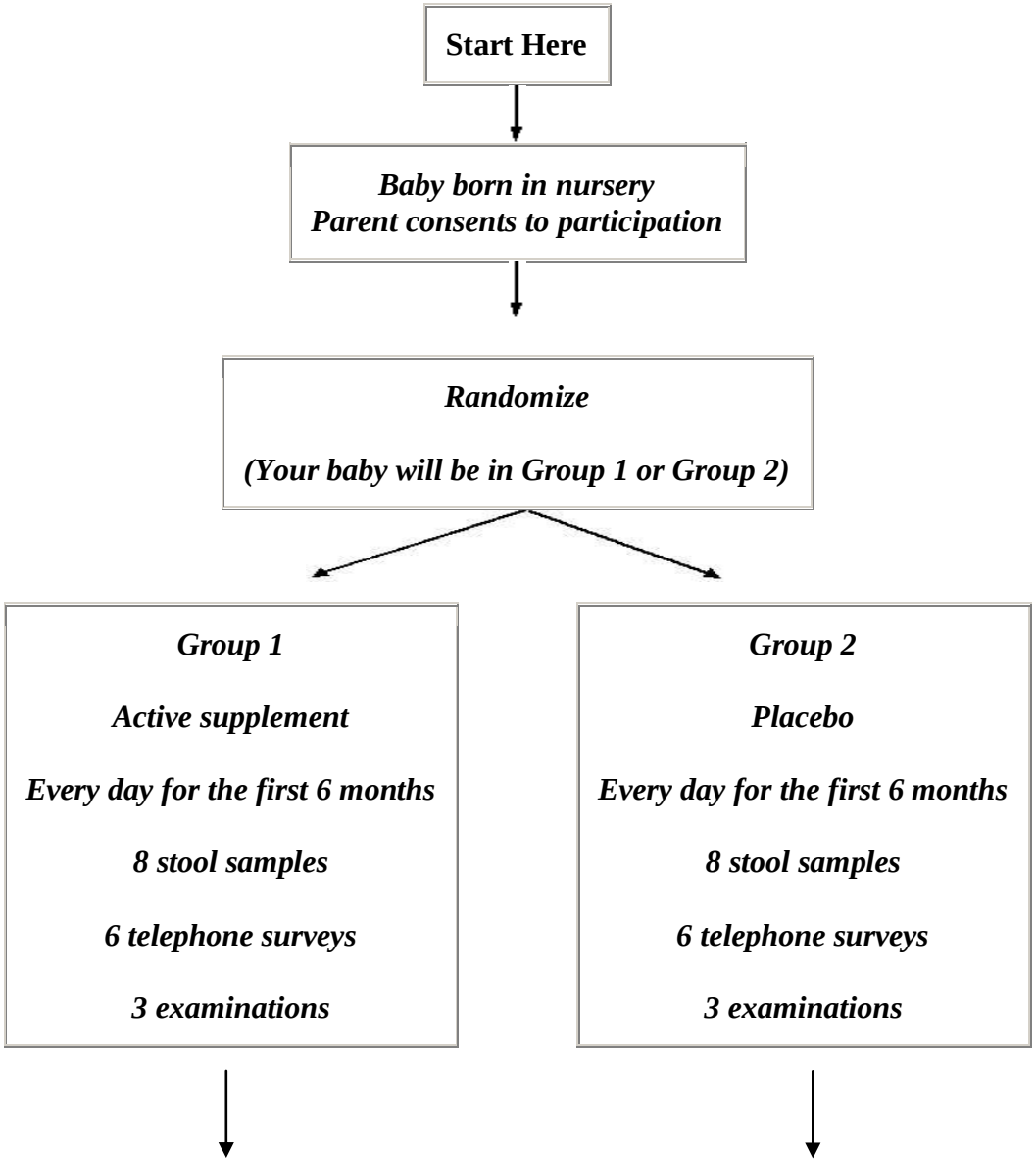
The physical exams do not replace the standard care that your child will receive from your regular physician. They are being performed more often than usual as part of the study.

The blood tests, stool studies and skin test are not part of standard pediatric care. They are being performed as part of the study.

- **Study location:** All study procedures will be done at an outpatient office, or the Pediatric Clinical Research Center (PCRC) at UCSF.

Study Plan

Another way to find out what will happen to your child during the study is to read the chart below. Start reading at the top and read down the list, following the lines and arrows.



Group 1 follow-up	***Group 2 follow-up***
(until baby is 3 years old)	*(until baby is 3 years old)*
8 more telephone surveys	***8 more telephone surveys***
3 more examinations	***3 more examinations***
3 blood tests	***3 blood tests***
1 skin prick test	***1 skin prick test***
4 stool sample	***4 stool sample***

How long will my child be in the study?

Your baby will receive the supplement for 6 months, however, the follow-up period will last until your child is 3 years old.

Can I stop my child's participation in the study?

Yes. You can decide to stop your child's participation at any time. Tell the study doctor if you are thinking about stopping or decide to stop. He or she will tell you how to stop your child's participation safely.

The study doctor may stop your child from taking part in this study at any time if he/she believes it is in your child's best interest, if you do not follow the study rules, or if the study is stopped.

What side effects or risks can I expect from my child being in the study?

Your baby may have side effects while on the study. Everyone taking part in the study will be watched carefully for any side effects. However, doctors don't know all the side effects that may happen. Side effects may be mild or very serious. Your health care team may give you medicines to help lessen side effects.

You should talk to your study doctor about any side effects you believe that your baby is experiencing while taking part in the study.

<u>Likely</u>

- Your baby may not like the taste of the supplement, as a result, there may be poor feeding or vomiting. We will ask about how your baby is feeding during the monthly telephone calls and discuss with you the best action to take.
- Your baby may not like the taste of the Good Start Supreme infant formula: We will ask you about feeding at each follow-up visit and we will allow you to change the formula and advise you of different options. We will still need to keep track of the name of the formula your baby drinks.

Less Likely

- Inability to obtain blood samples. Specially trained medical staff will only make 3 attempts to draw blood. If they are unsuccessful during those attempts, we will wait until the next visit 12 months later. You may always refuse permission for your child's blood draws.
- Inability to add supplement to the breast milk: If you are unable to pump breast milk and find that participation in the study is affecting the success of breastfeeding, we will recommend that your infant be removed from the study.

Rare but serious

- Infection from the supplement. Since 1966, according to the National Library of Medicine, there have been 3 cases of infection from the *Lactobacillus* supplement, however, they occurred in babies that were receiving antibiotics via an intravenous line. As a result, we will not include babies that require intravenous access (e.g., central lines) or have a serious infection requiring intravenous antibiotics.
- Although extremely unlikely, there is a theoretical risk with allergy to the formula or to the supplement—theoretically, an allergic reaction can occur with any processed formula or supplement and would most likely be due to the methods used to process the formula or supplement, as opposed to the actual ingredients of the supplement or formula.

- **Randomization risks:** Your child will be assigned to a group by chance, and the group you are in may prove to be less effective or to have more side effects than the other group.

- **Blood drawing (venipuncture) risks:** Drawing blood may cause temporary discomfort from the needle stick, bruising, and infection.

- **Unknown Risks:** The experimental supplements may have side effects that no one knows about yet. The researchers will let you know if they learn anything that might make you change your mind about your child's participation in the study.

- For more information about risks and side effects, ask your study doctor.

Are there benefits to taking part in the study?

Taking part in this study may or may not make your child's health better. While doctors hope the Lactobacillus supplement will decrease or delay the onset of asthma, there is no proof of this yet.

If your child is in the group that receives *Lactobacillus GG* and it proves to prevent the development of early markers of asthma, your child may benefit from participating in the study, but this cannot be guaranteed.

What other choices do I have if my child does not take part in this study?

Your other choices may include:

- Not participating. Participating or not participating will not affect the usual care that your child will receive.
- You may wish to administer over the counter probiotics to your infant without participating in the study.

Please talk to your doctor about your choices before deciding if you will take part in this study.

Will my child's medical information be kept private?

We will do our best to make sure that the personal information in your child's medical record is kept private. However, we cannot guarantee total privacy. Your child's personal information may be given out if required by law. If information from this study is published or presented at scientific meetings, your name, your child's name, and other personal information will not be used.

Organizations that may look at and/or copy your child's medical records for research, quality assurance, and data analysis include:

- The National Institutes of Health
- The UCSF Committee on Human Research

Participation in research may involve a loss of privacy, but information about your child will be handled as confidentially as possible. A medical record will be created because of your child's participation in this study. Your child's consent form and some of your child's research test results will be included in this record. Therefore, your child's other doctors may become aware of your child's participation. Hospital regulations require that all health care providers treat information in medical records confidentially.

If information is collected as part of this study that State or Federal law requires to be reported the researcher will complete the necessary reporting requirements.

What are the costs of taking part in this study?

You will not be charged for any of the study activities.

Will I be paid for taking part in this study?

In return for your time, effort and travel expenses, you will receive a $25 gift certificate for each of your child's outpatient visits. There are a total of 6 visits over the next 3 years. As a result, you can potentially receive $150.

What happens if my child is injured because I took part in this study?

It is important that you tell your study doctor, Dr. Michael Cabana, if you feel that your child has been injured because of taking part in this study. You can tell the doctor in person or call him/her at 415-514-2660.

Treatment and Compensation for Injury: If your child is injured as a result of being in this study, treatment will be available. The costs of the treatment may be covered by the University of California, depending on a number of factors. The University does not normally provide any other form of compensation for injury. For further information about this, you may call the office of the Committee on Human Research at 415- 476-1814.

What are my rights if I allow my child to take part in this study?

Allowing your child to take part in this study is your choice. You may choose for him/her either to take part or not to take part in the study. If you decide to allow your child to take part in this study, you may remove your child from the study at any time. No matter what decision you make, there will be no penalty to you or your child, and you will not lose any of your child's regular benefits. Leaving the study will not affect your child's medical care. Your child can still get medical care from our institution.

We will tell you about new information or changes in the study that may affect your child's health or your willingness to allow them to continue in the study.

In the case of injury resulting from this study, you do not lose any of your or your child's legal rights to seek payment by signing this form.

Who can answer my questions about the study?

You can talk to your study doctor about any questions or concerns you have about this study. Contact your study doctor, Michael D. Cabana at 415-514-2660.

For questions about your child's rights while taking part in this study, call the office of the **Committee on Human Research**, UCSF's Institutional Review Board (a group of people who review the research to protect your rights) at **415-476-1814**.

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CONSENT

You have been given copies of this consent form and the Experimental Subject's Bill of Rights to keep.

You will be asked to sign a separate form authorizing access, use, creation, or disclosure of health information about you and your child.

PARTICIPATION IN RESEARCH IS VOLUNTARY. You have the right to decline to participate or to withdraw your child's participation at any point in this study without penalty or loss of benefits to which you are otherwise entitled.

If you wish for your child to participate in this study, you should sign below.

_____ _____

Date Participant's Signature for Consent (Biological Mother)

_____ _____

Date Participant's Signature for Consent (Biological Father)

_____ _____

Date Person Obtaining Consent

UNIVERSITY OF CALIFORNIA, SAN FRANCISCO

EXPERIMENTAL SUBJECT'S BILL OF RIGHTS

The rights below are the rights of every person who is asked to be in a research study. As an experimental subject I have the following rights:

1) To be told what the study is trying to find out,

2) To be told what will happen to me and whether any of the procedures, drugs, or devices is different from what would be used in standard practice,

3) To be told about the frequent and/or important risks, side effects, or discomforts of the things that will happen to me for research purposes,

4) To be told if I can expect any benefit from participating, and, if so, what the benefit might be,

5) To be told of the other choices I have and how they may be better or worse than being in the study,

6) To be allowed to ask any questions concerning the study both before agreeing to be involved and during the course of the study,

7) To be told what sort of medical treatment is available if any complications arise,

8) To refuse to participate at all or to change my mind about participation after the study is started. This decision will not affect my right to receive the care I would receive if I were not in the study,

9) To receive a copy of the signed and dated consent form,

10) To be free of pressure when considering whether I wish to agree to be in the study.

If I have other questions I should ask the researcher or the research assistant. In addition, I may contact the Committee on Human Research, which is concerned with protection of volunteers in research projects. I may reach the committee office by calling: (415) 476-1814 from 8:00 AM to 5:00 PM, Monday to Friday, or by writing to the Committee on Human Research, Box 0962, University of California, San Francisco, CA 94143.