Waipapa Taumata Rau University of Auckland

PARTICIPANT INFORMATION SHEET

OAK Study

Can complex breastmilk sugars protect the gut microbiome during antibiotic therapy in young children, reducing rapid weight gain and allergic diseases?

Formal Study Title:	**O**ligosaccharides during **A**ntibiotic treatment in **K**ids
Protocol Number:	WHO UTN: U1111-1324-5170
Study Site:	Liggins Institute Waipapa Taumata Rau | University of Auckland
Sponsor:	Waipapa Taumata Rau | University of Auckland
Lead Investigator:	Professor Wayne Cutfield
Contact Phone Number:	0800 OAK KIDS (0800 625 5437)
Contact Email:	OAK@auckland.ac.nz
Ethics Committee Ref.:	2025 FULL 23241

Taking part in this research is your choice.

You and your child do not have to take part.

If you choose not to take part or withdraw from the study, your normal care will not be affected.

This document is 11 pages long. Please make sure you have read and understood all the pages.

- You will be given time to decide whether you want to take part in this study.
- The study team will discuss the study with you and answer any questions you have before you decide.
- You may talk to family, whānau, friends, or healthcare providers before you decide.
- If you have private medical insurance, you may wish to check whether this study will impact your cover.
- If you decide to take part, you will be asked to sign the Consent Form on behalf of you and your child. You will also be given a copy of this information sheet and the signed consent.
- If you change your mind about taking part, you can withdraw from the study at any time by telling the study team.
- There may be no direct benefit to your child from taking part in this study, and there may be risks of injury or illness.

Introduction

You and your child are invited to take part in a study of Human Milk Oligosaccharides (HMOs) given during antibiotic treatment. It has been designed to investigate whether unhealthy weight gain and the development of allergic diseases in children can be prevented. Allergic diseases in this instance include eczema (a skin disorder) and wheezing illnesses which can sometimes develop into asthma.

Although antibiotics are necessary to treat bacterial infections, their use in young children can put them at an increased risk for gaining weight too rapidly as well as at an increased risk of developing allergic diseases. This might be linked to antibiotics disrupting the balance of healthy bacteria that normally live in the gut (the gut microbiome).

Human Milk Oligosaccharides (HMOs) are complex sugars naturally found in breastmilk. They are important for the development of a healthy gut microbiome. This study explores the benefits of giving a mix of HMOs as a supplement while children are receiving antibiotics to see if they can help the recovery of a healthy gut microbiome. This may help promote healthy weight gain and prevent allergic diseases.

There will be no differences in your child's normal healthcare if you decide not to participate in this study: the antibiotic prescription given by their doctor and any other treatment or follow up will not be affected.

What is the aim of this study?

This study looks at HMO supplementation in children aged 12 to 24 months prescribed antibiotics to see:

- How effective HMO supplementation is at promoting healthy weight gain and preventing allergic diseases.
- How HMO supplementation can help protect the gut microbiome or help it recover after antibiotics.

What type of study is this?

This is a blinded, randomised, placebo-controlled study.

Blinded	This means that you and the study team don't know which product your child is getting, but the study doctor can find out if needed in an emergency. You can find out which product your child received after the study has ended.
Randomised	This means your child will be assigned to receive either HMO supplementation or the placebo randomly (by chance). Your child has a 1 in 2 chance of getting the HMO supplementation. Your child has a 1 in 2 chance of getting the placebo. You will not be able to choose which group your child is in.
Placebo-controlled	This means the study uses a placebo to compare against the active HMO supplementation. The placebo looks the same but does not contain HMOs. The placebo for this study is Dextrose.

How is the study designed?

Study Sites	This study is being run in New Zealand only.
212 Participants	212 children will take part.
18 months in Study	You and your child will be in this study for 18 months.
4 Study Visits	You will have 4 scheduled study visits. You may be asked to come for extra visits if needed.

How will I give my child the HMO supplement or Placebo (Study Product)?

Study Product Ingredients:

HMO Supplement:	**Placebo**
• Dextrose	• Dextrose only
• And five HMOs: ○ 2'-fucosyllactose (2'-FL) ○ Lacto-N-tetraose (LNT) ○ Lacto-N-neotetraose (LNnT) ○ 6'-sialyllactose (6'-SL) ○ 3'-sialyllactose (3'-SL)	

The HMO supplement is a commercially available product that has been designed for children's use. Dextrose is a simple sugar; the daily amount we will give to children is the amount found in one to two small grapes, or a tablespoon of yoghurt.

Your child will be given a course of either the HMO supplement or the placebo to be started at the first study visit. This course will be a minimum of ten days, designed to be longer than the average course of antibiotics. This will be extended to two days longer than the duration of your child's antibiotics if their antibiotic prescription is nine days or longer.

You will receive each day's total dose as a dry powder in a bottle and add 15 mL (1 tablespoon) of water to make up a clear liquid. You will give your child 5 mL (1 teaspoon) of this study product orally, three times a day, preferably just after giving your child's antibiotic dose. We suggest the dose is given using the syringe we provide to ensure your child takes the full dose.

We expect the study products to taste the same (like slightly sweet water).

If your child is prescribed further courses of antibiotics during the follow up period, you will be asked to contact the research team for a repeat course of the Study Product. Your child will remain in the same group (receiving either the HMO supplement or the placebo) as at the beginning of the study.

Who can take part in the study?

To take part in this study your child must:	
✓	Be 12 to 24 months old
✓	Have started a course of oral antibiotics within the last 48 hours
✓	Are regularly eating at least three solid meals a day

Your child cannot take part in this study if they:	
X	Were born premature or had a low birth weight
X	Have a significant medical disorder that affects growth or immune function
X	Have frequent watery stools
X	Have had another course of antibiotics within the last week

There are other criteria your child must meet to be eligible for the study. The study team will discuss all of them with you to make sure you are able to take part.

What will taking part in the study involve?

1. Screening (In Person)	If you decide to take part, you will be asked to sign the consent section at the end of this form. The study team will then check whether your child meets all the criteria to take part. This is called Screening.

If your child can take part, you will continue directly to the First Visit.

2. First Visit (In Person)	Day 1 of participation in the study. Study questionnaires, measurements and stool collection. Starting the 10-day course of the Study Product.

Daily text message reminders during the course of the Study Product.

3. During the course of the Study Product (Phone Call)	Halfway through and at the end of the Study Product course. Phone review by the study team for any concerns or possible side effects while on the Study Product.
4. Sub-group Review (In Person)	Day 11 and Day 28 of participation. Almost half the children in the study will be chosen to have two very brief extra reviews for stool collection.
5. Follow Up Reviews: Second, Third and Fourth Visits (In Person)	Every 6 months until 18 months in the study. Study questionnaires, measurements and stool collection.

At each visit you and your child will have some of the assessments listed below. The table on page 5 gives a summary of what will happen at each visit. In person visits can be held either at your home or at our clinic.

You and your child may be asked to come for extra visits if the study team thinks this is needed for safety or other reasons. If we identify any significant abnormal results during the study, we will tell your GP.

Optional Follow Up

You and your child will be involved in this study for 18 months. We would appreciate being able to contact you when your child is 4 – 5 years old for further assessments of their growth, stool and health conditions. You do not have to agree to this now.

Study Assessments

Informed consent	You will read and sign an informed consent form on behalf of you and your child before you take part.
Eligibility check	We will check that your child qualifies for the study.
History and demographics	We will review your child's medical history, medications and lifestyle choices relevant to the study and record your and your child's age, gender, ethnicity and other background information.
Questionnaires	You will fill in some questionnaires about whether your child may have eczema, wheezing illnesses or other infections and any treatments needed for these.
Health and medication check	We will ask you about any changes in your child's health and any changes to their medications. This includes prescription and over-the-counter medications, herbal or homeopathic remedies, nutritional supplements and infant/ toddler formulas.
Weight and height	We will check your and your child's weight and height. We will ask you to report the weight and height of your child's other parent and ask them if we can directly measure their weight and height.
Physical examination	A study nurse or doctor will examine your child. This will include a check of their skin.
Stool sample	We will collect a stool sample from your child to identify the different bacteria present (the gut microbiome).
Adherence check	We will check how many doses of the Study Product your child has taken.
Adverse effect check	We will ask you if your child has had any problems with taking the Study Product.

Study Visit

Study Visit	Screening / First Visit	Days 5 and 11 And Days 2-10: daily text message	Day 11 Visit (Subgroup only)	Day 28 Visit (Subgroup only)	6 month (Second) Visit	12 month (Third) Visit	18 month (Fourth) Visit
Method	In person	Phone call	In person	In person	In person	In person	In person
Visit Length	90 minutes	10 minutes	15 minutes	15 minutes	30 - 45 minutes	30 - 45 minutes	30 - 45 minutes
Informed Consent	✓						
Eligibility Check	✓						
History and Demographics	✓						
Health and Medication Check	✓				✓	✓	✓
Questionnaires	✓				✓	✓	✓
Weight and length / height	✓			✓ Weight only	✓	✓	✓
Physical Exam	✓				✓	✓	✓
Stool Sample	✓		✓	✓	✓	✓	✓
Administration of Study Product	✓	✓					
Adherence Check		✓					
Adverse Effect Check		✓			✓	✓	✓

What are my responsibilities during the study?

Please let us know if:	
✓	Your child has difficulty taking the Study Product
✓	Your child is prescribed further courses of antibiotics (on the same day as the prescription)
✓	Your child develops a significant medical condition or is prescribed other medication

Please discuss with the research team before:	
X	Starting your child on toddler formula, probiotics or similar supplements
X	Considering your child's participation in another study involving an intervention

Can my child participate in other studies?

Due to the nature of this study, your child will not be able to participate in most other studies which involve an intervention (taking something or doing something). Studies that only ask you questions about your child might be alright, but please talk to the study team before agreeing to take part in **any** other studies.

What are the possible benefits of the study?

We hope this study will benefit children's gut microbiome, weight and reduce allergic diseases. We will share the results of this study with you. There may be no direct benefits to you or your child from being in the study.

What are the possible risks of the study?

Each oligosaccharide in the HMO supplement has been approved by Food Standards Australia New Zealand (FSANZ) for use in infant formulas and as stand-alone supplements by the Therapeutic Goods Administration (TGA Australia). They have been administered to newborns and infants in previous studies published in medical journals without evidence of harm.

The risk involved in you and your child taking part in this study is very small. The manufactured oligosaccharides are identical to those found naturally in breastmilk and therefore are safe for infant consumption. Other studies comparing HMO supplements to placebos have not shown an increased risk of side effects in babies and young children. The placebo is dextrose and therefore is not expected to cause harm.

It is possible that your child may experience some side effects from the Study Product. These could include abdominal discomfort, development of frequent loose stools or vomiting (less common). There may be risks of HMO Supplements that are not yet known but this is unlikely.

Your child will be monitored for risks and side effects while they are in the study. You should contact us if your child experiences any changes in their health. Your GP or other healthcare professionals may be contacted if we have concerns about your child's health. We will discuss this with you prior to contacting other parties, unless believed to be contrary to your best interests.

Allergic Reactions

If your child is allergic to anything, tell us before you join the study.

Children are unlikely to develop an allergy to the HMO supplement as it contains natural sugar molecules. Most allergic reactions occur in response to protein molecules; however an allergic reaction to HMOs is still possible.

Some symptoms of allergic reactions are listed below. If not treated promptly, an allergic reaction could become life-threatening:

- Rash
- Wheezing and difficulty breathing
- Dizziness, fainting, floppiness
- Swelling around the mouth, throat, or eyes
- A fast pulse
- Sweating

Life-threatening or fatal allergic reactions can occur. However, severe reactions are very rare. If your child has a severe allergic reaction, seek treatment immediately by dialing 111 or going to an Emergency Department.

Assessment risks

None of the study assessments have known risks.

New Information

If new information becomes available about HMO Supplements, the study team will let you know.

Will any costs be reimbursed?

There are no costs to you associated with taking part in this study, nor will you be paid. You will still have to pay for your non-study related medical care.

You will be reimbursed for any transport or study-related costs. This will be in the form of petrol vouchers and/or supermarket vouchers. Reimbursement is not subject to tax.

What if something goes wrong?

In the unlikely event that your child was injured in this study, you would be eligible to apply for compensation from ACC just as you would be if they were injured in an accident at work or at home. This does not mean that your claim will automatically be accepted. You will have to lodge a claim with ACC, which may take some time to assess. If your claim is accepted, you will receive funding to assist in your child's recovery.

If you have private health or life insurance, you may wish to check with your insurer that taking part in this study won't affect your cover.

What will happen to my child's samples?

Stool samples will be collected from your child during the study. You will be asked to scoop a pea-sized amount of stool from your child's nappy using the scooper and container we provide. These samples will be identified with their unique study code and initials for transportation by research staff to the university laboratory for processing. For longer term storage until formal analysis, they will be identified using your child's study code only.

The stool samples will be further processed to obtain information on what bacteria are present. This process separates out the genetic material (DNA) of the bacteria from the rest of the sample. The bacterial DNA sample will be sent to a laboratory in China for analysis. We can give you the name and address of the laboratory if you wish. Your child's genetic information (DNA) is NOT being assessed.

The samples will be kept for up to five years. They will then be destroyed using standard practices. The University of Auckland is responsible for looking after samples in New Zealand.

If you withdraw from the study, samples previously collected will still be used, unless you ask for the samples to be destroyed. Results from samples that have already been tested will be used for the study.

You may hold beliefs about a sacred and shared value of any tissue samples taken. The cultural issues associated with storing your tissue should be discussed with your whānau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage of samples citing whakapapa and advise their people to consult before participating in research where this occurs. However, it is acknowledged that individuals have the right to choose.

Should you have any concerns regarding appropriate practice/tikanga to address cultural issues arising from your participation in the study it is recommended that you consult with a kaumātua. We respect the importance of these values and beliefs so please inform us if there is any tikanga you would wish us to follow in the collection of any biological samples. You may also contact Dr Marcia Walker (Ngāti Porou and Whakatōhea) for cultural advice (details on Page 9).

What will happen to our information?

We will collect information ('data') about you, your child and your child's study participation. If needed, information from your and your child's hospital records and from your GPs may also be collected. We only collect information needed for the study, to contact you or identify your medical records. You cannot take part in the study if you do not want us to collect any of this information.

Identifiable information – *this information traces directly to you.*	
Examples?	e.g. information carrying your/ your child's name, initials, birthdate, contact details or NHI number
How is it stored?	• Paper: under restricted access at the Liggins Institute until the end of the study, then scanned and stored electronically on secure Waipapa Taumata Rau | University of Auckland servers. Scanned papers will be destroyed in a manner protecting confidentiality. • Electronic: on secure Waipapa Taumata Rau, University of Auckland servers.
Who has access?	• Local study staff that do your study assessments • Your GP / usual doctor if needed • Study auditors (see below) • Representatives from the Sponsor if you make a compensation claim for study-related injury. Identifiable information is required to assess your claim.
How long is it kept?	For at least 10 years after your child turns 16 years old

Coded information – *this information is labeled only with your unique study ID*	
Examples?	All your information that is loaded into the study database.
How is it stored?	• On a secure electronic server that complies with New Zealand data security guidelines.
Who has access?	• The research team and Sponsor (Waipapa Taumata Rau | University of Auckland) • Regulatory or other governmental agencies worldwide.
How long is it kept?	For at least 10 years after your child turns 16 years old

Extra information about our data

The lead investigator may need to share your identifiable information in the rare event of a serious threat to public health or safety, or to the life or health of you, your child or another person, OR if the information is required in certain legal situations.

Audits:

The study may be audited. Audits make sure studies are being carried out properly. Auditors need access to your identifiable study data and relevant health records to do this. Audits may be done by the Sponsor (Waipapa Taumata Rau | University of Auckland), NZ regulatory agencies or the approving Ethics Committee.

Data Access:

You have the right to request access to information about you and your child held by the research team, including the results of tests and procedures. You also have the right to request that any information you disagree with is corrected.

Study Withdrawal:

You can ask the study team to stop collecting information about you and your child at any time. This will end your participation in the study. Information collected up until this point will continue to be used, to protect the quality of the study.

Data Storage:

After the study, identifiable data will be stored electronically for at least 10 years after your child turns 16 years old on secure Waipapa Taumata Rau | University of Auckland servers. Your child's coded data will be stored indefinitely on secure electronic servers. All storage will comply with local data security guidelines.

Data Risks

Although efforts will be made to protect your child's privacy, absolute confidentiality cannot be guaranteed. There is a risk that people may access or use your child's information in ways that may not be acceptable to you.

Data sent overseas will be governed by overseas laws. These may not give as much protection as New Zealand laws. Only coded (not labelled with your child's personal information) stool samples are being sent overseas.

Māori Data

Māori data is a potential taonga. Māori data sovereignty permits Māori organisations to access coded Māori data, to support Māori development aspirations.

We would obtain your approval along with the Ethics Committee's before sharing your coded data.

Could the study end earlier than planned for me and my child?

If you wish to withdraw from the study, please let us know. We may ask if you could complete some end-of-study assessments if you withdraw early.

We may withdraw your child from the study if we believe it is not in your child's best interests to continue. We will discuss any withdrawal decisions with you and provide health care advice where appropriate.

Other reasons that your child may be withdrawn from the study are:

- Your child needs treatment that is not allowed in this study.
- You/ your child did not follow the instructions for the study.
- The study is stopped.
- Your child has a serious reaction or illness or injury that is not related to the study.

The HMO Supplement will not be provided to you after the study.

Can I find out the results of the study?

Information relating to this study, such as a summary of results, will be available at the Australian New Zealand Clinical Trials Registry (ANZCTR) at https://anzctr.org.au/
We also expect to publish study results in medical journals. You and your child will not be identified in any of these publications.

Who is funding the study?

We are not receiving funding from the company manufacturing the HMO supplement or any pharmaceutical companies for this study.

Waipapa Taumata Rau | University of Auckland has received a philanthropic donation from Rank Group Limited to complete this study. Apart from providing funds, the donor has had no involvement in the study design or implementation.
The study team members will only receive their ordinary wages for conducting this research.

Data and samples that lead to discoveries and inventions, or the development of a commercial product, will be owned by Waipapa Taumata Rau | University of Auckland. You will not have rights to ownership or benefit financially.

Who has approved this study?

This study has been approved by an independent group of people called a Health and Disability Ethics Committee (HDEC), who check that studies meet established ethical standards. The Northern B HDEC has approved this study.

Who do I contact for more information?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Prof Wayne Cutfield, Lead Investigator and Paediatrician
Katy Young, Trial Coordinator
Phone: 0800 OAK KIDS (0800 625 5437)
Email: OAK@auckland.ac.nz

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@advocacy.org.nz
Website: https://www.advocacy.org.nz/

For Māori cultural advice please contact:

Dr Marcia Walker, Investigator and GP
Email: dr.marciawalker@gmail.com

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 400 569 (Ministry of Health general inquiries)
Email: hdecs@health.govt.nz

CONSENT FORM

OAK Study

Formal Study Title:	Oligosaccharides during Antibiotic treatment in Kids
Sponsor:	Waipapa Taumata Rau | University of Auckland
Lead Investigator:	Prof Wayne Cutfield
Study Site:	Liggins Institute, Waipapa Taumata Rau | University of Auckland
Contact Phone:	0800 OAK KIDS (0800 625 5437)
Ethics Committee Ref.:	2025 FULL 23241

Please read through each statement:

I have read, or have had read to me, and I understand the Participant Information Sheet.
I have been given sufficient time to consider whether or not to take part in this study.
I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.
I am satisfied with the answers I have been given regarding the study and I will be given a copy of this consent form and information sheet.
I understand that taking part in this study is voluntary (my choice) and that I may withdraw from the study at any time without this affecting my or my child's usual care.
I consent to the research staff collecting and processing my and my child's information, including information about our health.
I consent to my child's samples being sent overseas.
If I decide to withdraw from the study, I understand that the information collected about me and my child and samples collected from my child up to the point when I withdraw will continue to be processed.
I consent to my child's GP or current provider being informed about their participation in the study.
I consent to my child's GP or current provider being informed of any significant abnormal results obtained during the study.
I consent to my child's GP or current provider being contacted, or Te Whatu Ora Regional Clinical Portals being accessed by the researchers to obtain my new contact details should they change during the course of the study.
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethics Committees, or any relevant regulatory authority or their approved representative reviewing my and my child's relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.
I understand that my and my child's participation in this study is confidential and that no material which could identify us personally will be used in any reports on this study.
I understand the compensation provisions in case of injury during the study.
I know who to contact if I have any questions about the study in general.
I understand my responsibilities as a parent/caregiver of the study participant (my child).

Optional Consent

I wish to receive a summary of the results from the study.	Yes □	No □
I agree to be contacted by the research team about taking part in future research and that Te Whatu Ora and my GP may pass on my new contact details to the researchers if I move home.	Yes □	No □

Declaration by Parent/ Legal Guardian:

I hereby consent to me and my child taking part in this study.

Child's name:

Parent/ Legal Guardian's name:

Signature: Date:

Declaration by member of the research team:

I have given a verbal explanation of the research project to the parent/ legal guardian of the child participant and have answered their questions about it.

I believe that the parent/ legal guardian of the child participant understands the study and has given informed consent for them and their child to participate.

Researcher's name:

Signature: Date: