

## PARTICIPANT INFORMATION SHEET

### Gut Bugs in Autism

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<b>Study Site:</b>	Liggins Institute, University of Auckland
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<b>Ethics committee reference:</b>	21/CEN/211

You are invited to participate in the study **Gut Bugs in Autism: Gut microbiome transfer to improve gut health in autism**. This study is not testing a 'treatment' for autism but a treatment for gut issues in autistic people and to improve wellbeing. Whether you take part or not is your choice. If you don't want to take part, you don't have to give a reason, and it won't affect the care you receive. Also, if you do decide to take part now, but change your mind later, you can pull out of the study at any time.

This Participant Information Sheet will help you decide if you want to participate. It explains:

- Why we are doing the study
- What your participation would involve
- What the benefits and risks to you might be
- What happens after the study ends

You do not have to decide if you want to participate in this study immediately because you may want to talk about the study with other people, such as family/whānau, friends, support workers or healthcare providers.

If you agree to participate in this study, we will ask you to sign the Consent Form on the last page of this document. We will give you a copy of this Participant Information Sheet and the signed Consent Form to keep. This document is 13 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

#### What is the purpose of the study?

Autism, also known as autism spectrum disorders (ASD), are common in children and adults worldwide, with 1 in 50 people diagnosed autistic. In New Zealand, it has been estimated that more than 90,000 people are autistic, with nearly half of them experiencing long-standing gut problems which impact their quality of life. Unfortunately, the current treatments for gut problems in autistic people are limited.

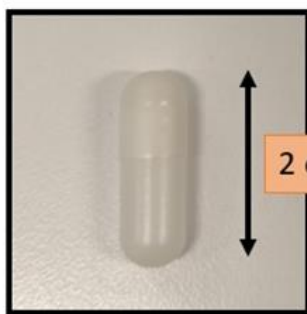
Gut microbiome transfer has been used regularly, safely, and effectively to treat and cure severe diarrhoea. This study will test whether a 'gut microbiome transfer' from physically healthy non-

autistic donors into autistic people with gut problems can improve their gut health and general well-being. If it works, it may become an important and effective treatment for gut problems in autistic people.

## Who can take part in the study?

We aim to recruit 100 participants, who must meet all the criteria listed below:

- Be aged 14-45 years
- Have a formal diagnosis of autism [including Autism Spectrum Disorder, Asperger syndrome, and Pervasive Developmental Disorder-Not Otherwise Specified (PDD-NOS)]<sup>1</sup>
- Have moderate or severe gut problems, such as:
  - Pain in your stomach
  - Burning sensation in the chest
  - Discomfort due to the sensation of regurgitating sour or bitter fluid from the stomach up to the throat
  - Discomfort due to feeling of sickness and/or vomiting
  - Discomfort due to swelling of your stomach
  - Discomfort due to reduced ability to empty your bowels
  - Discomfort due to frequent emptying of your bowels
  - Discomfort due to the urgent need to empty your bowels
- Are able to complete the clinical assessments described in this information sheet
- Are able to swallow capsules (smooth, large cylindrical-shaped pills approximately 2 cm in length, as shown below) with water or diluted juice.



The capsules are:

- smooth
- cylindrical-shaped
- approximately 2 cm in length
- tasteless & odourless

However, you will not be able to participate in the study if you:

- Are pregnant
- Took any antibiotics or probiotic supplements within the four weeks before beginning treatment
- Are on regular oral/inhaled steroid treatment

<sup>1</sup> We recognise that not all autistic people have a formal diagnosis. However, a formal diagnosis is required for this clinical trial because it will help encourage decisions about whether this treatment should become available to all autistic people if we find that it improves gut health and general well-being.

- Require the use of a tube for feeding
- Are currently experiencing moderate to severe depression
- Have serious medical problems that require specific treatment (e.g. inflammatory bowel disease, coeliac disease)
- Any known allergies to medication or foods
- Have a known allergy to macrogol (a type of laxative)

To ensure you meet the criteria to participate described above, we will talk with you over the phone/video call and ask you several questions, including about your gut health. We will also go through the Participant Information Sheet and answer any questions you have. If you are unsure whether you meet certain inclusion or exclusion criteria, please get in touch, and we can discuss.

If you meet all the criteria to be in the study and want to participate after our discussion, we will invite you to come to our clinic for further assessments.

### What will my participation in the study involve?

This study will be carried out at the Clinical Research Unit at the Liggins Institute, within the University of Auckland (Grafton Campus).

Participation includes:

- 1 baseline clinical assessment visit (2½ hours)
- 1 or 2 consecutive treatment visits based on your preference (scheduled on mornings before breakfast; 1½ to 2 hours each)
- 3 follow-up clinical assessment visits (6, 12 and 26 weeks after treatment; 2½ hours each)
- 3 phone calls to assess any possible side effects of treatment (10 minutes each)

### Treatment

This study is a double-blinded randomised controlled trial, which is a study that can test if a treatment works without the results being affected by participants thinking or hoping it might work or changing their habits. To do this, we will use a computer programme to randomly assign participants into a treatment or placebo group. The treatment group will receive the 'treatment' that is being tested. The control group will receive a 'placebo', which looks and feels the same as the 'treatment' but has no active ingredients.

The study team and participants will remain blinded to which of the two group participants are allocated to, meaning neither the study team nor you will be able to know if you have taken the treatment or the placebo before the end of the study.

You will receive a total of 20 identical capsules to swallow that contain either:

- The treatment (gut bacteria from healthy donors) or
- The placebo (diluted salt water).

You will have the choice to take all 20 capsules in one morning or 10 capsules per day over two consecutive mornings (you will receive 10 capsules on Day 1 and 10 capsules on Day 2). If you are in the treatment group, we will safely seal the gut bacteria inside two layers of capsules to ensure the bacteria will only be released in your gut (and not in your mouth or stomach).

If we find the treatment was effective at the end of the study, we will offer it to those who received the placebo at no cost to you.

### **What you need to do before Treatment Day 1**

On the evening before taking the capsules, you need to:

1. Take an oral solution containing Glycoprep-C.

Glycoprep-C is a medication that helps to clean out the bowel to try and help the new microbiome bacteria get established. To make up the oral solution, you need to mix 1 sachet of Glycoprep-C into a 1.5L labelled bottle of water we will provide.

After drinking this solution, you will pass some watery stools for a few hours, which is absolutely normal. You should plan to take the Glycoprep-C solution at home between 4 and 6 pm, where you have easy access to a toilet. If you do not pass any stool by the next morning after drinking this solution, please let the research team know as soon as possible.

2. Fast for at least 8 hours.

After taking the Glycoprep-C solution, please have dinner between 7 and 9 pm, as you need to start fasting from 10 pm. This means you can only drink water after 10 pm, cannot have anything else to eat or drink, and cannot have breakfast in the morning before taking the capsules.

### **What to expect on Treatment Day 1**

You will come into the Liggins Clinical Research Unit first thing in the morning, after fasting overnight and before breakfast. There you will swallow either 10 or 20 capsules, based on your choice, with water or diluted juice. Taking all capsules within 10 to 15 minutes would be best, but don't worry if you cannot do this because you will have plenty of time (1 hour) to swallow all the capsules. The capsules will be slightly cold because we will have only taken them out of a storage freezer on the morning of your treatment appointment.

Allergic reactions and adverse events are rare. However, to monitor for possible allergic reactions, you must stay in the clinic for at least 1 hour after swallowing the capsules. You are welcome to stay in the clinic for the 2 hours after treatment and we will provide breakfast for you. Please let us know if you have any dietary requirements. Alternatively, you may leave the clinic after 1 hour, but please wait at least another hour before having something to eat or drink (other than water).

## **What you need to do before Treatment Day 2 (only if you choose to take the treatment over 2 days)**

You **will not** need to take Glycoprep-C solution before the treatment on Day 2. However, you will still need to fast again for at least 8 hours before you take your second set of capsules. Please have nothing to eat after midnight the evening before your second treatment appointment in the Liggins Clinical Research Unit. This means you can only drink water after midnight, and cannot have breakfast in the morning before taking the capsules. As in day 1, you will be able to have breakfast 2 hours after swallowing the capsules.

## **What to expect on Treatment Day 2**

On Day 2, the number of capsules and the steps to taking the capsules are the same as Day 1. We will also ask you to complete a questionnaire so you can tell us your thoughts about the treatment. If you swallowed all 20 capsules on treatment day 1, we will ask you to complete the questionnaire after you swallow the capsules on day 1.

Symptoms/side effects that might be associated with the treatment include tummy pain, loose stools, fever, vomiting, or nausea. We will monitor these symptoms at regular intervals during the trial over the phone and during clinic visits.

## **Clinical assessment visits**

The following assessments will be performed during your clinic visits before your first treatment (baseline) and at 6, 12, and 26 weeks after treatment.

- Questionnaires  
At the start of the study, we will ask you to complete a questionnaire about your background information. We will also ask you to complete other questionnaires to evaluate your gut symptoms, well-being, sleep quality, and diet.
- Body measurements  
We will measure your height, weight, and waist and hip circumferences.
- Body Composition  
We will measure your body composition (amount of muscles, bones, and fat) using a dual energy X-ray absorptiometry (DXA) machine to scan your body. This scan is a quick, safe, and accurate measure of body composition. We can also provide a copy of these results to you at the end of the study.
- Hair sample collection<sup>2</sup>  
We will ask you to provide a small hair sample to measure stress hormone levels. We will cut some strands of your hair as close to the back of your scalp as possible. This will not leave behind any noticeable bald patches.
- Stool sample collection<sup>2</sup>

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<sup>2</sup> We will not use your hair, stool, urine and optional blood samples to look for drug targets for treating autism.

We will ask you to provide stool samples to monitor changes in your gut microbiome. We will provide you with a stool sample collection kit with easy-to-follow instructions, and you can choose to collect your stool samples at home on the day of your clinic visit or during your clinic visit.

- Urine sample collection<sup>2</sup>

We will ask you to provide urine samples to study biomarkers linked to gut issues and well-being in autistic people.

- Blood sample collection (optional)<sup>2</sup>

We will ask you to provide a blood sample to study the metabolites produced by your gut bacteria. If you do not feel comfortable having a blood sample taken, you are welcome to decline it, and this will not affect your participation in the trial.

**Table 1. Study schedule**

	Baseline clinical assessment	Treatment		1 week phone call	3 week phone call	6 week clinical assessment	12 week clinical assessment	26 week clinical assessment
		Day 1	Day 2					
Swallow capsules		✓	✓					
Symptom check-up		✓	✓	✓	✓	✓	✓	✓
Body measurements	✓					✓	✓	✓
Body composition (DXA)	✓							✓
<b>Questionnaires:</b>								
Treatment views			✓			✓		
Background	✓							
Gut symptoms	✓					✓	✓	✓
Well-being	✓					✓	✓	✓
Sleep quality	✓					✓	✓	✓
Diet	✓					✓	✓	✓
<b>Sample collection:</b>								
Hair	✓					✓	✓	✓
Stool	✓					✓	✓	✓
Urine	✓					✓	✓	✓
Blood (optional)	✓					✓	✓	✓

## What are the possible benefits and risks of participating?

### Benefits

Participating in this study will help researchers better understand the impact of the gut microbiome on gut health and well-being of autistic people. We hope this may lead to new treatments for gut problems in autistic people.

You will also receive valuable information on your health and gut bacteria as soon as they are available. The study results will be available after they have been peer-reviewed and published in scientific journals.

## Risks

Because the treatment involves the transfer of live gut bacteria, there is a risk of introducing an infection or allergen. However, we greatly minimise this risk by using very strict screening selection criteria for donors that are over and above those used for blood donation in New Zealand. We use extensive screening procedures to ensure donors do not have bacteria or viruses that could cause an infection. We have used this screening procedure in several other studies, and none of our participants experienced any serious infections or allergens related to this treatment.

The DXA machine (body composition scan) delivers an extremely low dose of radiation exposure; about the same as that of spending one day outside in the sun or during a 1 hour flight.

There is also the risk of localised infection, bleeding, and pain from the needle puncture to collect blood samples. However, all assessments will be done by an experienced medical doctor and research nurse to ensure that care is provided to you during the study.

## Protection against COVID-19

All our study donors are regularly tested for SARS-CoV-2 in our pathogen screening protocol.

## What will my participation cost?

Participation is free and will not cost you anything. We appreciate that participating in this study will take up some of your time and transport to and from the Liggins Institute. We will therefore provide all participants with a \$50 gift voucher at the end of each clinical assessment visit (\$200 in total). Free parking will also be made available to you during your clinic visits. If you live outside of Auckland or the cost of travelling to attend clinic appointments in Auckland would prevent you from taking part, please let us know. It may be possible to support additional travel costs in some cases or to conduct the assessment at a clinic closer to your home.

## What if something goes wrong?

If you get injured in this study, you would be eligible to apply for compensation from ACC just as you would be if you 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 recovery. If your ACC claim is rejected, you may apply for compensation from the University of Auckland Human Health Research Insurance. 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 health information and samples?

## Health information

The information we collect about you during this study will be kept strictly confidential and will only be accessible to members of the research team and approved regulatory agencies who wish to audit the study. Your information (not identifiable because we will assign you a unique study ID) will be entered and stored on a secure password-protected electronic database (REDCap) for 20 years after completing the study and then destroyed.

### **Samples**

All samples collected from you (i.e., hair, stool, urine, and blood) will be labelled with your de-identified study ID and safely stored at Te Ira Kāwai, the Auckland Regional Biobank for up to 10 years. On completion of our analyses, any remaining samples will be disposed of using established guidelines for discarding human samples. Please indicate on the Consent Form if you would like to have a Karakia performed on your samples before disposal or have your samples returned to you. Samples will only be accessible to the study investigators for the purposes of this study unless you consent to their use for future unspecified research (refer to section 'future research your information').

### **Cultural considerations**

You are encouraged to consult with your family/whānau, hapū, or iwi and/or a friend regarding your participation in this project. We acknowledge there are different views among Māori on the sacred value of body samples. Some iwi disagree with the storage of samples, citing whakapapa, and advise their people to consult prior to participation in research where this occurs. We have a Māori health advisor Mr Keri Opai who is available to speak with you about any cultural concerns (see page 10 for his contact details).

### **Study findings**

Analyses will be conducted using pooled participants' data and the results will be published in peer-reviewed journals. The study findings will also be presented to both scientific and public audiences. No information that could personally identify you will be used in any reports, publications, or presentations from this study.

You will receive a letter from us notifying you once the study's main findings are published in a peer-reviewed journal. Please note that there will be a delay between your study participation and the publication of the results. You will also be provided with information on your individual results. If our analyses of your health data uncover any risk factors, we will contact you and advise you to seek medical follow-up. We will be available to answer your questions about any of our study findings or individual test results.

### **Referral to mental health support services**

In this study, you will be assessed for symptoms of depression and anxiety using specialised questionnaires and discussions with a medical doctor. If the doctor is concerned about your mental health (e.g. if you are experiencing suicidal thoughts) we will ask your permission to discuss your case with the study psychiatrist. We will inform your GP and/or specialist to ensure you access additional mental health care. For this reason, we will be asking you for the contact details of your routine care provider (e.g. your doctor, psychiatrist, psychologist, or other therapist) when you enrol in the study. We will not contact your routine care provider without your knowledge and consent unless we consider you are a risk to yourself and/or others.



### **Future research using your information**

After the study is finished, you may consent for your anonymised health information data to be shared with other researchers for future studies upon request, pending approval from the Clinical Data Research Hub (CDRH) Data Access Committee at the Liggins Institute.

You have the option to consent for your anonymised gut microbiome data to be deposited in an international sequence database where it may be used for future microbiome research outside of this study. The purpose of this database is to help build the global catalogue of microbiome data to help with science reproducibility and new discoveries.

Please note that we are unable to inform you of future research undertaken using your anonymised data. But if you would like more information regarding data sharing, please contact the principal investigators of this study Professor Wayne Cutfield or Professor Justin O' Sullivan. Their contact details are provided on page 10.

## **What are my rights and what happens if I change my mind?**

### **Right to withdraw from the study**

Participation in this study is entirely voluntary. If you decide to participate but change your mind later, you are free to withdraw from the study at any time. Also, if we feel your participation is not in your best interest (e.g. due to strong adverse effects or we have serious concerns about your mental health), we will withdraw you from the study. In either case, your participation will end, and the research team will stop collecting information from you. However, we will retain and use all information and samples collected until your withdrawal from the study in the analyses and you will still receive koha for the sessions you have attended. Withdrawing from the study will not affect any future care or treatment you may receive.

### **Right to access your information**

You have the right to request access to your information held by the research team. Please note that access to other study-specific information will not be made available to you until after the study is over and the primary results have been published.

## **Who has approved the study?**

This study was approved by the Central Health and Disability Ethics Committee on 24 August 2021(reference 21/CEN/211). This committee is part of the Health and Disability Ethics Committees (HDEC), whose members are appointed by the Minister of Health. Their role is to ensure clinical studies in New Zealand meet established ethical standards and protect the best interests of study participants.

The trial is registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR), Registration Number ACTRN12622000015741.

## Who is funding the study?

This study is funded by a generous donation to the Liggins Institute from the Rockfield Trust.

## Who do I contact for more information or if I have any concerns?

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

### **The Gut Bugs Team**

[gutbugsautism@auckland.ac.nz](mailto:gutbugsautism@auckland.ac.nz)

### **Professor Wayne Cutfield**

*Co-Principal investigator*

*Professor of Paediatric Endocrinology, Liggins Institute, University of Auckland*

*09 923 4476*

*w.cutfield@auckland.ac.nz*

### **Professor Justin O'Sullivan**

*Co-Principal investigator*

*Professor of Microbiology and Genomics, Liggins Institute, University of Auckland*

*09 923 9868*

*justin.osullivan@auckland.ac.nz*

For Māori health support, please contact:

### **Mr Keri Opai**

*Tātāriki Cultural Lead at Wise Group*

[keri.opai@gmail.com](mailto:keri.opai@gmail.com)

If you would like to speak to an autistic advisor, please contact:

### **Dr Ruth Monk**

*Member of Autism NZ Community Advisory Group*

*r.monk@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:

*0800 555 050*

*0800 2 SUPPORT (0800 2787 7678)*

[advocacy@advocacy.org.nz](mailto:advocacy@advocacy.org.nz)

For help with depression and anxiety, please contact:

Need to Talk? Free text or call 1737

LifeLine 0800 543 354 (0800 LIFELINE) or free text 4357 (HELP).

You can also contact the Central Health and Disability Ethics Committee that approved this study on:



**LIGGINS**  
INSTITUTE

0800 4 ETHICS  
*hdecs@moh.govt.nz*

## CONSENT FORM

### Gut Bugs in Autism

Please read through each statement and tick to consent to the following:

- I have read the participant information sheet or have had it read to me in my first language, and I understand its content.
- 
- I have been given sufficient time to consider whether to participate 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 have a copy of this consent form and information sheet.
- 
- I understand taking part in this study is voluntary (my choice) and I may withdraw from the study at any time without this affecting my medical care.
- 
- If I decide to withdraw from the study, I agree the information and samples collected from me up to the point when I withdraw will continue to be processed.
- 
- I consent to the research staff collecting and processing my health information and samples.
- 
- I consent to having my relevant medical records reviewed by an approved regulatory agency/auditor for the sole purpose of checking the accuracy of study records.
- 
- I understand my participation in this study is confidential and no material that could identify me personally will be used in any reports on this study.
- 
- I understand the compensation provisions in case of injury during the study.
- 
- I understand my responsibilities as a study participant and know who to contact if I have any questions about the study in general.
- 
- I consent to my anonymised gut microbiome data being deposited in an international sequence database where it may be used for future research outside of this study.
- 
- I consent to my anonymised health information being shared with researchers outside of this study for future research deemed appropriate by the Clinical Data Research Hub (CDRH) Data Access Committee at the Liggins Institute.
-

**Optional:**

Would you like to have a support person accompany you during the study? Yes  No

Would you like to receive a summary of the results from the study? Yes  No

Would you like any of your unused samples returned to you at the end of the main study (5 years)? Yes  No

Would like a Karakia performed on your samples prior to disposal? Yes  No

Would you like to be contacted about future research Yes  No

**Declaration by participant:**

I hereby consent to take part in this study.

Participant's name: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_

**Declaration by member of research team:**

I have given a verbal explanation of the research project to the participant, and have answered the participant's questions about it.

I believe that the participant understands the study and has given informed consent to participate.

Researcher's name: \_\_\_\_\_

Signature: \_\_\_\_\_

Date: \_\_\_\_\_