You are invited to participate in a research study designed to help improve treatment of type 2 diabetes by learning how individuals respond to different blood sugar lowering medications.

This Participant Information Sheet will help you decide if you would like to take part. It sets out why we are doing the study, what your participation would involve, what the benefits and risks to you might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not you will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this.

If you agree to take part in this study, you will be asked to sign the Consent Form on the last page of this document. You will be given a copy of both the Participant Information Sheet and the Consent Form to keep.

This document is six pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHY HAVE I BEEN INVITED TO PARTICIPATE?

Is this study suitable for me?
We are inviting you to take part because you are already taking one or two diabetes medicines (like metformin and/or gliclazide), but your diabetes may be improved with an extra treatment. We are inviting you to try two common diabetes medicines to see which one improves your diabetes the best and which one suits you. We will check your medical records first, to see if these medications are suitable for you.

You will not be able to take part in the study if you:

- have type 1 diabetes
- have had a change in diabetes medications or dose within the last 3 months
- have only been diagnosed with type 2 diabetes for less than 12 months
- are currently taking insulin or have been treated with insulin in the last 3 months
- are treated with steroid medication, rifampicin, gemfibrozil, phenytoin or carbamazepine
- have heart failure and feel short of breath during ordinary activities
- have a history of bladder cancer, diabetic ketoacidosis or pancreatitis
- are pregnant, breastfeeding or planning to become pregnant in the next 1 year
Do I have to take part?
Whether you decide to take part or not is entirely up to you. Your decision will not affect the medical care you receive in any way. If you agree to take part, you are free to withdraw at a later stage, without giving a reason.

**WHY ARE WE DOING THIS STUDY?**

We are trying to understand why some diabetes medicines do not work well for some people so that we can help to choose the most effective medicine for different people with diabetes in the future.

We know that the response to these medications can be variable and their effect may be different between individuals. We are trying to understand whether this response is different in Maori and Pacific people (compared to those of other ethnicities) and if it would be possible to predict if a medicine is more likely to work for someone based on their ethnicity, body weight, lipid levels and genetics. If we could predict which medicine is likely to work for a person, we could choose the most effective treatment, avoiding ineffective medicines and unnecessary side effects.

**WHO IS DOING THIS RESEARCH?**

This study is being led by researchers from: the University of Auckland in collaboration with several diabetes specialists, general practitioners and health providers around the North Island, including Auckland District Health Board.

If you have questions about the study, please contact:

- Assoc Prof Rinki Murphy, lead researcher of the study
  - Phone: (09) 923 6313
  - Email: R.Murphy@auckland.ac.nz or
- Dr Ryan Yeu/ Dr Rebecca Brandon
  - Phone: 0272617559
  - Email: T2Dmed@auckland.ac.nz

**STATEMENT OF APPROVAL**

This study has been approved by the Health and Disability Ethics Committees (HDEC) reference number 18/STH/242.

**IF I AGREE TO TAKE PART, WHAT WILL I BE ASKED TO DO?**

This study is looking at two standard diabetes medications: vildagliptin and pioglitazone, which can be added when one or two other medicines (like metformin and/or glipizide or gliclazide) are not enough to maintain good blood sugar levels.

You will be randomly assigned to take one medicine for 4 months then you will crossover to the other one for 4 months, in the order sent to you by the research pharmacist.
Baseline screening and consent visit 1:
Following a detailed discussion of the two study medications (vildagliptin and pioglitazone), if you agree to participate you will be asked to sign the consent form (copy attached). Your routine diabetes blood tests and medical history will be checked to confirm you are suitable to take part. We will ask you to complete a brief questionnaire about your diabetes. We will measure your height, weight and blood pressure.

We will ask you to have a baseline fasting blood test for biochemical and genetic analysis to find out if there are any blood or gene variants that could explain or predict your response to treatment with either of the two study medications. After you have had this test, our study pharmacist will courier you 4 months of one study medication followed by 4 months of the other study medication (vildagliptin or pioglitazone in random order).

Research visit 2: (4 months after starting study medication 1)
We will ask you to have a fasting blood test just before your appointment to check on your response to the first medication. We will ask you about your experience with the first study medication and any changes to your health or other medications. We will ask you to complete a brief questionnaire about your diabetes. We will measure your weight and blood pressure.

Research visit 3: (4 months after starting study medication 2)
We will ask you to have a fasting blood test just before your appointment to check on your response to the second medication. We will ask you about your experience with the first study medication and any changes to your health or other medications. We will ask you to complete a brief questionnaire about your diabetes. We will measure your weight and blood pressure. We will record your preference for which study medication you would like to continue and with your permission, we will check on the prescribing decision made by your GP and your blood glucose control 6 months later. Your participation in this study will be completed and you will be asked to see your usual doctor and/or nurse for your ongoing diabetes care.

Will my GP be told I am in the study?
Yes, we will inform your GP that you are in the study and the results from this study so that they know what medication you are taking and the information from the study may help with your treatment choice after the study has finished.

If I need an interpreter, can one be provided?
Unfortunately, we do not have funding to provide interpreters, which is why people not confident in reading and writing English will not be able to participate.

What are the possible benefits and risks of this study?

What are the benefits of taking part?
By participating you may help us to choose more personalised and effective treatment for people with type 2 diabetes in the future and in some cases your own study results may help you and your doctor decide on your ongoing diabetes care. There may also be no direct benefit to you.

Are there any risks in taking part?
The treatments being used in this study are medications that are regularly prescribed for people with diabetes. In the screening visit we will check that it is safe for you to take both of the medications being tested. We will provide a specific guide which describes the medications and what to do if you
experience any side effects. The common side effects include dizziness, leg swelling and headache. Hypoglycaemia (low blood sugar) is also a possibility if you are also taking sulfonylurea medications such as gliclazide or glipizide. Uncommon side effects include constipation, pancreatitis and hepatitis. The research team will carefully monitor you for any adverse effects and withdraw you from the study or transfer you to the next medication if necessary. As with your standard diabetes care, the blood tests may be uncomfortable, but they will be carried out by experienced staff.

**WHO PAYS FOR THE STUDY?**

Funding to undertake this study is provided by Health Research Council of New Zealand. Both study medications will be prescribed in accordance with current guidelines for diabetes treatment. We will cover all dispensing and courier costs of the study medications. We will provide you with a koha of $60 once you have completed the study.

**WHAT IF SOMETHING GOES WRONG?**

If you were injured in this study, which is unlikely, 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 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 MY BLOOD SAMPLE AND MEDICAL INFORMATION BE USED FOR?**

**Do I have to give blood samples to take part?**

Yes. Blood tests that are important for your clinical care such as blood glucose, kidney function, liver tests, and cholesterol will be analysed by your local laboratory and copied to you and with your permission to your GP. An extra research blood sample will be collected at the start of the study for biochemical and genetic analysis to find out if there are any blood or genetic markers that may be used to explain or predict your response to treatment with either of the two study medications. Your DNA will only be tested for genes/gene variants that are thought to be important in medication response, and will not be screened for genes currently known to be predictive of disease or any other reason.

We respect your cultural beliefs. You may hold beliefs about a sacred and shared value of all or any blood/tissue samples collected. The tikanga/cultural expectations associated with storing your blood and genetic samples/tissue and/or sending your samples overseas should be discussed with your family/whanau as appropriate. There are a range of views held by Māori around these issues; some iwi disagree with storage or genetic analysis of samples citing whakapapa and advise their people to consult prior to participation in research where this occurs. However, it is acknowledged that individuals have the right to choose. If you change your mind later, just let us know, and we will either return or appropriately dispose of your sample and remove your data.

**Will my taking part in the study be kept confidential?**

No one outside the small group of researchers doing the study will know any of your details. When the results of the study are published in a journal for other doctors and scientists to see, no information about individual people or family/whānau is used. If further information is required we may need to access your medical records. All of your medical information collected for the study stays strictly private and in very secure storage. All information stored about you will have your name, address and other identifying details removed. Your identifying and contact information will be stored separately from all other information we
collect from you. No one will be able to identify you from anything we record. All computers used will be password protected.

**WHAT HAPPENS AFTER THE STUDY OR IF I CHANGE MY MIND?**

Participation in this study is entirely voluntary. You can decide to stop taking the study medications or withdraw from the study at any time. If you decide to stop taking the medications, the researchers may invite you to attend a follow-up assessment and ask you to contribute to the study at a reduced level. If you decide to completely withdraw your consent from further research participation no further information will be collected about you.

A decision to withdraw from the study at any time will not affect the standard of your continued medical care.

**WHAT HAPPENS TO MY SAMPLES AND INFORMATION AFTER THEY HAVE BEEN COLLECTED?**

All specimens will be stored in secure freezers at the University of Auckland. We will know exactly where each specimen is stored. Certain substances will be measured in the samples to see if differences may be linked to effectiveness of the two study medications. We expect all samples to be used up, but if there is any leftover sample this would be destroyed according to good laboratory practice standards. If you wish an appropriate karakia to be used to dispose of these blood samples when the study data analysis has ended, please indicate your wish on the consent form. All specimens will be coded with a code that does not identify you.

Your samples and data will be kept until the end of the analysis for up to 15 years (in case there are delays in funding for the testing). After this time they will be destroyed.

**WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?**

Thank you for considering your participation in this study

Ngā Tāngata hei whakapānga atu - If you have any questions, concerns or complaints about the study at any stage, you can contact:

Assoc Prof Rinki Murphy, lead researcher of the study  
Phone: (09) 923 9192  
Email: R.Murphy@auckland.ac.nz

Local investigator contact:

Dr Ryan Yeu or Dr Rebecca Brandon  
Phone: 0272617559  Email: T2Dmed@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@hdc.org.nz

If you require Māori cultural support talk to your whānau in the first instance. Alternatively, you may contact the administrator for He Kamaka Waiora (Māori Health Team) by telephoning 09 486 8324 ext 2324

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

Phone: 0800 4 ETHICS  
Email: hdecs@moh.govt.nz
Consent Form

<table>
<thead>
<tr>
<th>Please tick to indicate you consent to the following:</th>
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<tbody>
<tr>
<td>I have read and I understand the Participant Information Sheet.</td>
</tr>
<tr>
<td>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.</td>
</tr>
<tr>
<td>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.</td>
</tr>
<tr>
<td>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 medical care.</td>
</tr>
<tr>
<td>I consent to the research staff collecting and processing my relevant information, including information about my health.</td>
</tr>
<tr>
<td>If I decide to withdraw from the study, I agree that the information collected about me up to the point when I withdraw may continue to be processed.</td>
</tr>
<tr>
<td>I consent to my GP or current provider being informed about my participation in the study and of any significant abnormal results obtained during the study.</td>
</tr>
<tr>
<td>I understand that my participation in this study is confidential and that no material, which could identify me personally, will be used in any reports on this study.</td>
</tr>
<tr>
<td>I know who to contact if I have any questions about the study in general.</td>
</tr>
<tr>
<td>I agree to genetic and biochemical analysis of my blood sample to be used for predicting diabetes medication response.</td>
</tr>
<tr>
<td>I wish to have my blood samples disposed of with appropriate karakia</td>
</tr>
<tr>
<td>I wish to receive a summary of the results from the study</td>
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<tr>
<td>I am happy to be contacted for future research study</td>
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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: ________________

Type 2 Diabetes Medication Study PIS, Version 3 ADHB 08.04.19