ADULT INFORMATION SHEET

Evaluating the biological activity of a single dose of encapsulated oral semaglutide in healthy adults over a period of one week

Why are we doing the study?

Semaglutide is a medication used in Type 2 diabetes management and can also help with weight loss. We want to see how a single dose of semaglutide in a capsule form (encapsulated oral semaglutide) will affect blood glucose and insulin responses when a person who is healthy is subjected to an intravenous glucose tolerance test (IVGTT).This is an investigator-led study and sponsored by The Kids Research Institute Australia (The Kids). It will be conducted in Perth Children's Hospital with the study medication being provided by Diabetology Limited. This study is a first-in-human trial investigating encapsulated oral semaglutide.

Why are we asking you?

We are asking you to take part in this study because we need to test it in people without diabetes first, and you are a healthy adult aged between 18-60 years old.

<u>You can participate in this study if you:</u>

- Healthy with no medical conditions.
- Are a female and have a negative serum pregnancy test (blood test) at screening and will practice effective birth control during the study period.
- All male patients must agree to practice effective contraceptive methods during the course of the study.
- Are willing to comply with all study investigations

<u>However, you cannot participate in this study if at the screening visit, we find out that you:</u>

- Are a female who is pregnant or breastfeeding or plan to breastfeed during the course of the study.
- Are involved in a weight loss program and are not in the maintenance phase
- Have started on weight loss medication within 3 months prior to screening.
- Have had or plan to have bariatric surgery during the course of the study.
- Have a history of gastrointestinal disorders or delayed gastric emptying
- Have a history of pancreatitis.
- Have a history of cardiac disease.
- Have abnormal liver function, thyroid function and lipid profile.
- Evidence of infectious diseases.
- Have a history of a tumor or cancer within the past 5 years .
- Are using recreational or illicit drugs or have had a recent history (within 1 year of screening)
- Have a drug or alcohol abuse or dependence. (Alcohol abuse includes heavy alcohol intake >3 drinks per day or >14 drinks per week or binge drinking).

- Are using cannabinoid products during the 1 week prior to each visit.
- Are enrolled in another clinical trial involving an investigational product within 30 days of the screening visit.
- Have any condition or other factor (at the Investigator's discretion) that makes you unsuitable for enrolment into the study.

Who is carrying out the study?

The study is being carried out by **Professor Timothy Jones** and the research team of the Children's Diabetes Centre, The Kids.

What will the study tell us?

This study will tell us how one dose of encapsulated oral semaglutide will affect blood glucose response and insulin response, during an intravenous glucose tolerance test (IVGTT), over 7 days, as compared to before taking the study medication.

Do you have to take part?

No, you do not have to take part in this study. Participation in this study is entirely voluntary. You may withdraw from the study at any time by contacting any member of the research team and signing the withdrawal of consent form at the end of this document.

What will you be asked to do if you decide to take part in this study?

If you take part in this study will need to attend Outpatient-D at Perth Children's Hospital on six separate occasions. You will be paid for your time, travel, parking and meal as follows: $150 for the screening visit and $170 for each of the 5 IVGTT sessions.

What happens at each study visit and how long each visit takes is outlined in the study schedule below:

Visit Sequence	Visit Duration	Visit assessments/investigations
VISIT 1 (within 14 days before Visit 2) **SCREENING**	Approx 2h	**THIS IS A FASTING VISIT.** **Please fast for 8h for this screening visit, but you can have water to drink.** At this visit: • We will confirm that you understand what the study involves. • We will take your medical history to ensure that you meet the inclusion criteria and do not meet the exclusion criteria. • We will then have you sign the Informed Consent. • We will measure your height, weight, and vital signs. • If you are a female, we will ask you when your last menstrual period was. We will also do a serum pregnancy test as a study requirement. • We will take 8mL of blood for investigating your lipid profile, liver function, thyroid function, HbA1c and c-peptide. • We will provide you with two data logs to collect information about any adverse events/illnesses you may have until the next visit, and any medication that you might take. • We will provide you with EMLA (numbing cream) for use before each of the following visits, if you require it. • We will also advise all females to practice effective

		contraception from this visit to the last visit.
Visit Sequence	**Visit Duration**	**Visit assessments/investigations**
VISIT 2 (Day minus2)	Approx 3.5h	**THIS IS A FASTING VISIT.** **Please fast for 10h for this visit, but you can have water to drink during this time. During this time, you are to avoid cigarettes, alcohol, caffeine, and vigorous exercise.** This visit will happen at approximately 8am. On arrival we will measure your vital signs, and ask you details of any adverse events (eg: headaches, nausea) and of any drugs you may have taken for these adverse events. And if it is OK to proceed with the study procedures, we will give you the **placebo** capsule with 100ml water (Time 0). After which we will insert an IV cannula in one of your arms for the IVGTT testing. This involves administering a set amount of intravenous glucose, through the drip in your arm, to see how your body responds to the glucose. **You are having a placebo today, so that we can see how your body responds to the IVGTT, when you only swallow the capsule without the study drug*. <u>IVGTT</u>: • The IVGTT will be done 2h after having taken the **placebo** capsule. The IVGTT takes 1h and involves the collection of 2 mL of blood (each for BGL and Insulin testing) at the following time points: -5, 0, 5, 15, 25, 35, 45, and 60 min post-administration of the IV glucose via the cannula. The total blood volume collected during this meal challenge is 32mL. • Once the IVGTT is completed you will have a meal before you are discharged.
VISIT 3 (Day 0)	Approx 3.5h	**THIS IS A FASTING VISIT.** **Please fast for 10h for this visit, but you can have water to drink during this time. During this time, you are to avoid cigarettes, alcohol, caffeine, and vigorous exercise.** This visit will happen at approximately 8am. On arrival we will measure your vital signs, and ask you details of any adverse events (eg: headaches, nausea) and of any drugs you may have taken for these adverse events. If you are a female, we will do a urine pregnancy test, and we will proceed with the visit only if it is negative. And if it is OK to proceed with the visit procedures, we will give you the **study medication** with 100ml water (Time 0). We will then insert an IV cannula in one of your arms for the IVGTT testing. This involves administering a set amount of intravenous glucose, through the drip in your arm, to see how your body responds to the glucose. <u>IVGTT</u>: • The IVGTT will happen at the same time or approximately the same time each day. The IVGTT takes 1h and involves the collection of 2 mL of blood (each for BGL and Insulin testing) at the following time points: -5, 0, 5, 15, 25, 35, 45, and 60 min

		post-administration of the IV glucose via the cannula. The total blood volume collected during this meal challenge is 32mL. • Once the IVGTT is completed, you will have a meal before you are discharged.
Visit Sequence	**Visit Duration**	**Visit assessments/investigations**
VISIT 4 (Day 1) VISIT 5 (Day 4) Visit 6 (day 6)	Approx 3.5h	**THESE ARE FASTING VISITS.** **Please fast for 10h for these visits, but you can have water to drink during this time. During this time, you are to avoid cigarettes, alcohol, caffeine, and vigorous exercise.** These visits will happen at approximately 8am. On arrival we will measure your vital signs, and ask you details of any adverse events (eg: headaches, nausea) and of any drugs you may have taken for these adverse events. And if it is OK to proceed with the IVGTT, we will insert an IV cannula in one of your arms for the IVGTT testing. This involves administering a set amount of intravenous glucose, through the drip in your arm, to see how your body responds to the glucose. <u>IVGTT</u>: • The IVGTT will happen at the same time or approximately the same time each day. The IVGTT takes 1h and involves the collection of 2 mL of blood (each for BGL and Insulin testing) at the following time points: -5, 0, 5, 15, 25, 35, 45, and 60 min post-administration of the IV glucose via the cannula. The total blood volume collected during this meal challenge is 32mL. • Once the IVGTT is completed you will have a meal before you are discharged.

Is there likely to be a benefit to me?

There is likely no benefit to you. However, should we find any abnormal results from the blood tests the investigator will discuss these results with you, and email a discharge summary with your test results to your general practitioner. You GP can then act on these results as needed.

Is there likely to be a benefit to other people in the future?

The findings of this pilot study may add to the research data regarding improved type 2 diabetes management, with regards to treatment mimicking natural physiology and with less side-effects.

What are the possible risks and/or side effects?

Although this is the first time humans have been given this drug in this way, however encapsulation is commonly used to deliver drugs. Further, semaglutide in tablet form is approved and used for type 2 diabetes management. Therefore, the risk from taking semaglutide in this form is not considered high.

You may feel nauseous or have diarrhoea with the study drug. Should this happen, we will prescribe you with appropriate medication to relieve the symptoms.

There is small risk of bruising, bleeding or skin reaction at the insertion of the cannula for the intravenous glucose testing and the blood test at the screening visit. We will reduce this risk by appropriate location of the cannula insertion site, and following hospital guidelines for insertion of the cannula. Some people feel faint with cannulation, so we will do the cannulation while you are lying on a bed.

What are the possible discomforts and/or inconveniences?
Some people feel may find the phlebotomy and cannulation uncomfortable. To minimise the discomfort, we can provide you with a tube of numbing cream and show you how to use it, before coming in for the IVGTT visits.

Where is our information kept?
All paper records will be stored in locked cabinets in the The Kids office space on Level 6W of Perth Children's Hospital.
Electronic data will be stored on password protected The Kids REDCap database and an electronic study folder in a limited access secure Perth Children's Hospital server.
All biological samples will have destroyed as per PathWest protocol, once the results have been checked and any verification required is performed.
Your data will be stored for 15 years after the grouped results are published; after which it will be destroyed as per The Kids research data management policies.

What about your privacy?
Your personal data will only be identified by a unique code, and only the investigators and the research team specific to the study will be able to link your results to you. Publications and presentations about the results of this study will not identify anyone by name. We will inform you of the results and publication via email.
However, we will inform your general practitioner (GP) that you are participating in the study. We will also inform them of any abnormal results from the blood tests, so that they can provide you with the necessary management or care.

Who has approved the study?
The South Metropolitan Health Service (SMHS) Human Research Ethics Committee have approved this study smhs.hrec@health.wa.gov.au; Reference number (PRN): RGS00000006856.This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2023) produced by the National Health and Medical Research Council of Australia. This statement has been developed to protect the interests of people who agree to participate in human research studies.

Reviewing HREC name	South Metropolitan Health Service Human Research Ethics Committee
HREC Executive Officer	Ethics Coordinator
Telephone	08 6152 2064
Email	SMHS.HREC@health.wa.gov.au

Who to contact for more information about this study:
If you would like any more information about this study, please contact:

Name:	Niru Paramalingam
Contact no:	08 6456 4611
Email:	niru.paramalingam@health.wa.gov.au

Who to contact if you have any concerns about the organisation or running of the study?
If you have any concerns or complaints regarding this study, you can contact the following:

Complaints contact person:	CAHS Manager of Research Ethics & Governance
Contact no:	08 6456 8639

Your concerns will be drawn to the attention of the Ethics Committee who is monitoring the study.

What to do next if you would like to take part in this research:
If you satisfy the inclusion and exclusion criteria listed in this information sheet and you would like to take part in this study, please contact Niru on 08 6456 4611, to make an appointment for the screening visit. You will sign the consent form for participation in this study when you attend this appointment.

THANK YOU FOR READING THIS INFORMATION SHEET

ADULT CONSENT FORM

Evaluating the biological activity of a single dose of encapsulated oral semaglutide in healthy adults over a period of one week

Principal Investigator: Professor Timothy Jones *Chief Coordinating Investigator, The Kids.*

- ☐ I have read, or have been read to me, the information statement version above and I understand its contents.
- ☐ I believe I understand the purpose, extent, and possible risks of my involvement in this study.
- ☐ I voluntarily consent to taking part in this study and I understand that I may withdraw from the study at any stage.
- ☐ I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- ☐ I agree that research data gathered from this study may be published, provided that names are not used.
- ☐ I understand that this study has been approved by the South Metropolitan Health Service Human Research Ethics Committee and will be carried out in line with the National Statement on Ethical Conduct in Human Research (2023).
- ☐ I understand I will receive a copy of this Information Statement and Consent Form.

| --- | --- | --- |
| Participant's Name | Participant's Signature
(If deemed to be a mature minor) | Date |

Declaration by researcher:
I have supplied an Information Sheet, version listed as above, and Consent Form to the participant who has signed above, and believe that they understand the purpose, extent and possible risks of their involvement in this project.

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| Researcher's Name | Researcher's signature | Date |

Government of Western Australia
Department of Health
Child and Adolescent Health Service

The KIDS RESEARCH INSTITUTE AUSTRALIA

ADULT WITHDRAWAL OF CONSENT FORM

Evaluating the biological activity of a single dose of encapsulated oral semaglutide in healthy adults over a period of one week

Principal Investigator: Professor Timothy Jones *Chief Coordinating Investigator, The Kids.*

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, or my relationship with my health care provider. Please note that all the data collected in this study and the samples collected will be destroyed, and not used for the study purposes. However, if you withdraw from the study after taking the study drug, you will followed-up for adverse events and medication use for a week from having taken the drug. This is so that if any of the adverse events may be related to the study drug, we need to report this to the Board that is monitoring the safety of the study.

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Participant's Name (If deemed to be a mature minor)	Participant's Signature	Date

Declaration by researcher:
I have discussed the early withdrawal of the participant from this research project.

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Researcher's Name	Researcher's signature	Date