384 Victoria Street
Darlinghurst NSW 2010
Australia

t: 61 2 9295 8100
f: 61 2 9295 8101

GARVAN INSTITUTE
Breakthrough Medical Research

Participant Information Sheet/Consent Form

Interventional Study – *Person Responsible*
Garvan Institute of Medical Research

Title	The Effect of a New GLP-1 agonist on Appetite and Gastric Emptying in Prader-Willi Syndrome
Short Title	ENGAGE PWS
Protocol Number	Version 2
Project Sponsor	The Garvan Institute of Medical Research
Coordinating Principal Investigator/ Principal Investigator	Prof. Lesley Campbell
Associate Investigator(s)	A/Prof. Alexander Viardot
Location	Garvan Institute of Medical Research

Part 1: What does participation involve?

1 Introduction

The participant is invited to take part in this research project. This is because the participant has been diagnosed with Prader-Willi syndrome (PWS). The research project is testing a new treatment for PWS. The new treatment is called exenatide extended-release (exenatide ER).

This Participant Information Sheet/Consent Form tells you about the research project. It explains the tests and treatments involved. Knowing what is involved will help you decide if you want the participant to take part in the research.

Please read this information carefully. Ask questions about anything that you don't understand or want to know more about. Before deciding whether or not the participant can take part, you might want to talk about it with a relative, friend or the participant's local doctor.

Participation in this research is voluntary. If you don't wish the participant to take part, the participant doesn't have to. They will receive the best possible care whether or not they take part.

If you decide you want the participant to take part in the research project, you will be asked to sign the consent section. By signing it you are telling us that you:

- Understand what you have read
- Consent to the participant taking part in the research project

- Consent to the participant having the tests and treatments that are described
- Consent to the use of the participant's personal and health information as described.

You will be given a copy of this Participant Information and Consent Form to keep.

2 What is the purpose of this research?

Exenatide ER belongs to a class of drugs called GLP-1 agonists, which help to control blood glucose levels in people with type 2 diabetes. These have been shown to have beneficial effects on appetite in PWS in the short term but when given to people with type 2 diabetes they slow the speed at which food moves through the stomach (gastric emptying), which may not be a good thing for people with PWS. The aim of this study is to find out whether the longer-term use of exenatide ER affects appetite and gastric emptying in adults with PWS. The results of this study may give us information about whether exenatide ER is a safe and effective treatment for excessive appetite and obesity in PWS in the future. Gastric emptying has only been measured a few times in people with PWS, and the results of these studies are unclear because it was measured in different ways and at different ages. We plan to use the most accurate test – gastric scintigraphy – to get the best information about gastric emptying in PWS.

Exenatide ER is approved in Australia to treat type 2 diabetes. However it is not approved to treat obesity. Therefore, it is an experimental treatment in people with PWS. This means that it must be tested to see if it is an effective treatment in PWS.

The results of this research will be used by the study doctor Amanda Hor to obtain a PhD degree. This research has been initiated by the chief investigator Professor Lesley Campbell.

3 What does participation in this research involve?

If you consent to the participant participating in the ENGAGE study, you will be asked to sign the Person Responsible Consent Form. The participant will be screened by one of the study doctors and, if eligible, they will be invited to begin the 12-week study, involving 12 injections of Bydureon (once weekly) and 4 visits to the Garvan Institute Clinical Research Facility. The timeline of the study period is as follows:

Before the treatment period begins, the participant will be invited to visit the Garvan Institute Clinical Research Facility on a scheduled day. During the visit they will take part in a study measuring the rate of gastric emptying (Visit 1).

The participant will be asked not to eat or drink anything other than water from midnight the night before. After arriving at the Garvan Institute at 8am, you will both be taken across the road to the nuclear medicine facility of St Vincent's Hospital.

The participant will be given a hospital gown to wear. A cannula will be placed in their arm and they will be asked to consume a scrambled egg meal within 10 minutes. They will then be asked to lie on a bench in a nuclear imaging room for ten minutes while the scintigraphy scanning is conducted. If desired, we can provide a laptop computer so that they can watch a DVD or listen to music while the scan is taking place, and you can stay in the room if you choose.

After the 10-minute scan, the participant can have a 50-minute break in a nearby waiting room. It would be best if they didn't do any strenuous activity at this point, but walking around a little is fine. Three

more 10-minute scans will be done at 1, 2 and 4 hours after eating the meal, with a break between each. During the 4 hours we will take blood samples via the cannula to measure levels of blood glucose, insulin, hormones and lipids.

After the gastric emptying study, we will perform a dual-energy X-ray absorptiometry (DXA) scan in a nearby room to assess body composition (the amount of fat tissue and muscle tissue). This is a scan that is commonly used to assess bone density in relation to osteoporosis. The participant will be asked to lie on a bench similar to that used in the gastric emptying study while the scanning is done. This will take about 5 minutes. We will also ask them to complete a 20-minute learning and memory test on a tablet. They will not be able to eat anything during the 4-hour study, but we will supply a healthy lunch afterwards.

After the participant has completed the first study visit, it will be time for them to start the 12-week Bydureon treatment period. You will be shown how to prepare the drug and perform the subcutaneous injection. The injection should be given once a week, on the same day each week.

After 4 weeks of the Bydureon treatment period, the participant will be asked to undergo a second gastric emptying study (Visit 2). This is because we want to find out whether taking this drug changes gastric emptying speed. The second gastric emptying study will be conducted in exactly the same way as the first. If the gastric emptying speed of the participant has slowed significantly compared to their first measurement, it may not be safe to continue using this drug, and we will discontinue the treatment. If, on the other hand, gastric emptying speed has not changed significantly, they will continue with Bydureon treatment for 8 more weeks.

At the end of the treatment period, the participant will come back to the Garvan Institute Clinical Research Facility to participate in a third gastric emptying study (Visit 3), which will be exactly the same as the previous two, as well as the same learning and memory test. After this visit, the study will be completed. However, to get as much information as possible about the effectiveness of this drug, we would like to measure the body weight of the participant once more 12 weeks after the conclusion of the study (Visit 4).

Results from the study will be monitored monthly by a doctor who is not involved in this project.

The participant will be participating in an open-label study. In an open-label study both you and the participant know that the participant is receiving the treatment.

This research project has been designed to make sure the researchers interpret the results in a fair and appropriate way and avoids study doctors or participants jumping to conclusions.

There are no additional costs associated with participating in this research project, nor will you or the participant be paid. All medication, tests and medical care required as part of the research project will be provided to the participant free of charge.

You or the participant may be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visits, up to $300.

It is desirable that the participant's local doctor be advised of the decision to participate in this research project. If the participant has a local doctor, we strongly recommend that you inform them of the participant's participation in this research project.

4 What does the participant have to do?

During the course of the study, the participant should continue with their normal diet and exercise habits. They can take their regular medication and can still donate blood if they wish. Participants would be restricted from taking part in the study if they become sick or have a major change in their treatment, living environment or body weight. You will be responsible for helping the participant to take the drug weekly and in accordance with the instructions provided.

5 Other relevant information about the research project

We anticipate that a total of 40 participants will be taking part in this study. 20 of these will be non-PWS control subjects, who will attend Visit 1 but will not enter the treatment arm of the study. This study involves researchers from the Garvan Institute of Medical Research, St Vincent's Hospital Sydney and Royal Prince Alfred Hospital, and all study procedures will be conducted at either the Garvan Institute of Medical Research or St Vincent's Hospital. This study will build on findings from another study previously conducted at the Garvan Institute of Medical Research, which investigated the effects of a single injection of a shorter-acting form of exenatide on appetite in PWS.

6 Does the participant have to take part in this research project?

Participation in any research project is voluntary. If you do not wish to take part, you do not have to. If you decide to take part and later change your mind, you are free to withdraw from the project at any stage.

If you do decide to take part, you will be given this Participant Information and Consent Form to sign and you will be given a copy to keep.

Your decision whether the participant can take part or not take part, or take part and then withdraw, will not affect your routine treatment, or your relationship with the Garvan Institute of Medical Research or St Vincent's Hospital Sydney.

7 What are the possible benefits of taking part?

We cannot guarantee or promise that the participant will receive any benefits from this research; however, possible beneficial effects may include improvement in appetite, behaviour and/or body weight.

8 What are the possible risks and disadvantages of taking part?

Medical treatments often cause side effects. The participant may have none, some or all of the effects listed below, and they may be mild, moderate or severe. If the participant has any of these side effects, or you are worried about them, talk with the participant's study doctor. The participant's study doctor will also be looking out for side effects.

There may be side effects that the researchers do not expect or do not know about and that may be serious. Tell the participant's study doctor immediately about any new or unusual symptoms.

Many side effects go away shortly after treatment ends. However, sometimes side effects can be serious, long lasting or permanent. If a severe side effect or reaction occurs, the participant's study doctor may need to stop the participant's treatment. The participant's study doctor will discuss the best way of managing any side effects with you.

- Blood sampling: The participant may experience slight pain when we insert the needle for blood sampling. If you wish, we can apply an anaesthetic cream to the skin before inserting the needle. There is a slight chance of skin irritation and/or bruising, however these are usually temporary and are expected to resolve completely.

- Exenatide ER injection: The weekly subcutaneous injection of exenatide ER could cause slight pain, minor bruising and/or itching of the skin. Occasionally, a small, painless bump or hardening of the skin can form at the injection site. These are harmless, and usually disappear within a few weeks.

- Exenatide ER treatment: Some people who take exenatide ER experience mild to moderate nausea. This usually decreases over time. Other possible side effects include vomiting, diarrhoea, constipation and low blood sugar levels. These symptoms are unlikely to occur; if experienced, they are not usually harmful. Nevertheless, we will be monitoring the participant closely throughout the course of the study.

- Scintigraphy and DXA scanning: If the participant has participated in other research studies involving x-rays or nuclear medicine tests in the last 5 years, please inform one of the study coordinators of the details. This research study involves exposure to a very small amount of radiation. As part of everyday living, everyone is exposed to naturally occurring background radiation and receives a dose of about 2 millisieverts (mSv) each year. The effective dose from this study is about 1.22 mSv. At this dose level, no harmful effects of radiation have been demonstrated as any effect is too small to measure. The risk is believed to be very low.

If participation in this study were to uncover a medical condition of which you or the participant were unaware, the study doctor would discuss this with you both and provide an appropriate referral. Then depending on the seriousness of the condition, the study doctor would make a decision as to whether participation in the research project would be continued. The research team will pay for any necessary treatment of side effects.

The effects of exenatide ER on the unborn child and on the newborn baby are not known. Because of this, it is important that research project participants are not pregnant or breast-feeding and do not become pregnant during the course of the research project. The participant must not participate in the research if the participant is pregnant or trying to become pregnant, or breast-feeding. If the participant is female and child-bearing is a possibility, the participant will be required to undergo a pregnancy test prior to commencing the research project. If the participant is male, the participant should not father a child or donate sperm for at least 1 month after the last dose of study medication.

Both male and female participants are strongly advised to use effective contraception during the course of the research and for a period of 1 month after completion of the research project. You or the participant should discuss methods of effective contraception with the participant's study doctor.

If the participant does become pregnant whilst participating in the research project, you should advise the participant's study doctor immediately. The participant's study doctor will withdraw her from the

research project and advise on further medical attention should this be necessary. The participant must not continue in the research if she becomes pregnant.

You should advise the participant's study doctor if the participant fathers a child while participating in the research project. The participant's study doctor will advise on medical attention for the participant's partner should this be necessary.

If the participant becomes upset or distressed as a result of their participation in the research, the study doctor will be able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research project team. This counselling will be provided free of charge.

9 What will happen to the participant's test samples?

Blood will be collected from the participant in this study so that we can measure levels of appetite-regulating hormones. Blood samples will be stored in a freezer with secure access at the Garvan Institute of Medical Research in a re-identifiable (coded) way. Access to codes allowing the re-identification of samples will be stored on a password-protected secure server, with only members of the research team having access. Remaining blood samples will be disposed of as biological waste after 15 years.

11 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the participant's study doctor will tell you about it and discuss with you whether you want the participant to continue in the research project. If you decide to withdraw the participant, their study doctor will make arrangements for their regular health care to continue. If you decide that the participant can continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, the participant's study doctor might consider it to be in the participant's best interests to be withdrawn from the research project. If this happens, the doctor will explain the reasons and arrange for the participant's regular health care to continue.

10 Can the participant have other treatments during this research project?

Whilst the participant is participating in this research project, they may not be able to take some or all of the medications or treatments they have been taking for their condition or for other reasons. It is important to tell the participant's study doctor and the study staff about any treatments or medications the participant may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell the participant's study doctor about any changes to these during the participant's participation in the research project. The participant's study doctor should also explain to you which treatments or medications need to be stopped for the time the participant is involved in the research project.

11 What if I withdraw the participant from this research project?

If you decide to withdraw the participant from the project, please notify a member of the research team before you withdraw them. This notice will allow that person or the research supervisor to further discuss any health risks or special requirements linked to withdrawing.

If you do withdraw the participant during the research project, the study doctor and relevant study staff will not collect additional personal information from the participant, although personal information already collected will be retained to ensure that the results of the research project can be measured properly and to comply with law. You should be aware that data collected by the sponsor up to the time you withdraw the participant will form part of the research project results. If you do not want them to do this, you must tell them before you join the research project.

14 Could this research project be stopped unexpectedly?

This research project may be stopped unexpectedly for a variety of reasons. These may include reasons such as:

- Unacceptable side effects
- The drug being shown not to be effective
- The drug being shown to work and not need further testing

12 What happens when the research project ends?

Continued supply of exenatide ER will not be available to participants after completion of the study. You and the participant will receive a summary of the results of the study by email or post, whichever you prefer, within 6 months of completion of data collection. If requested, we can provide you with a copy of any scientific papers that we will publish using this research project's data and discuss them with you.

Part 2: How is the research project being conducted?

13 What will happen to information about the participant?

Collected data will be stored as electronic files on a password-protected secure server at the Garvan Institute of Medical Research and as paper files in a locked filing cabinet. They will be stored in a re-identifiable (coded) way, with access to codes allowing re-identification restricted to members of the research team. Data will be stored for 15 years after collection, after which time it will be destroyed. You are being asked to provide consent for the use of data for this project only. This project does not involve the establishment of a database.

By signing the consent form you consent to the study doctor and relevant research staff collecting and using personal information about the participant for the research project. Any information obtained in connection with this research project that can identify the participant will remain confidential. Collected data will be stored as electronic files on a password-protected secure server at the Garvan Institute of Medical Research and as paper files in a locked filing cabinet. They will be stored in a re-identifiable (coded) way, with access to codes allowing re-identification restricted to members of the research team. Data will be stored for 15 years after collection, after which time it will be destroyed. This project does not involve the establishment of a database.

The participant's information will only be used for the purpose of this research project and it will only be disclosed with your permission, except as required by law.

It is anticipated that the results of this research project will be published and or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that the

participant cannot be identified, except with your permission. Participants' data will not be presented individually but as a group.

In accordance with relevant Australian and NSW privacy and other relevant laws, you have the right to request access to the participant's information collected and stored by the study team. You also have the right to request that any information with which you disagree be corrected. Please contact the study team member named at the end of this document if you would like to access the participant's information.

14 Complaints and compensation

If the participant suffers any injuries or complications as a result of this research project, you should contact the study team as soon as possible and you will be assisted with arranging appropriate medical treatment for the participant. If the participant is eligible for Medicare, they can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

15 Who is organising and funding the research?

This research project is being conducted by Professor Lesley Campbell and has been funded by a philanthropic donation.

No member of the research team will receive a personal financial benefit from the participant's involvement in this research project (other than their ordinary wages).

16 Who has reviewed the research project?

All research in Australia involving humans is reviewed by an independent group of people called a Human Research Ethics Committee (HREC). The ethical aspects of this research project have been approved by the HREC of St Vincent's Hospital Sydney (reference number HREC/15/SVH/437). This project will be carried out according to the National Statement on Ethical Conduct in Human Research (2007). This statement has been developed to protect the interests of people who agree to participate in human research studies.

17 Further information and who to contact

The person you may need to contact will depend on the nature of your query. If you want any further information concerning this project or if you have any medical problems which may be related to your involvement in the project (for example, any side effects), you can contact either of the study doctors—Dr Alexander Viardot on 0405 457 732 or Dr Amanda Hor on 0433 166 088—or any of the following people:

For matters relating to general information and scheduling:

Name	Dr Louise Purtell
Position	Study co-ordinator
Telephone	0448 910 267
Email	l.purtell@garvan.org.au

For matters relating to research at the site at which the participant is participating, the details of the local site complaints person are:

Name	Prof. Lesley Campbell

Position	Chief investigator
Telephone	9295 2622
Email	l.campbell@garvan.org.au

If you have any complaints about any aspect of the project, the way it is being conducted or any questions about being a research participant in general, then you may contact:

Reviewing HREC approving this research and HREC Executive Officer details

Reviewing HREC name	St Vincent's Hospital Sydney Human Research Ethics Committee
HREC Executive Officer	
Telephone	8382 2075
Email	sarah.charlton@svha.org.au

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Consent Form - *Adult providing own consent*

Title	The Effect of a New GLP-1 agonist on Appetite and Gastric Emptying in Prader-Willi Syndrome
Short Title	ENGAGE PWS
Protocol Number	Version 2
Project Sponsor	The Garvan Institute of Medical Research
Coordinating Principal Investigator/ Principal Investigator	Prof. Lesley Campbell
Associate Investigator(s)	A/Prof. Alexander Viardot
Location	Garvan Institute of Medical Research

Declaration by Person Responsible

I am the Person Responsible for *[Participant's Name]* (the Participant).

I have read the Participant Information Sheet or someone has read it to me in a language that I understand.

I understand the purposes, procedures and risks of the research described in the project.

I have had an opportunity to ask questions and I am satisfied with the answers I have received.

I believe that the participation of the participant in this study is not contrary to their best interests.

I freely agree to the participant participating in this research project as described and understand that I am free to withdraw the participant at any time during the research project without affecting their future health care.

I am aware of my responsibilities as the Person Responsible for the participant and I understand that I will be assisting the participant in meeting their responsibilities whilst they are participating in this study.

I understand that I will be given a signed copy of this document to keep on behalf of the participant.

I give permission for the participant's doctors, other health professionals, hospitals or laboratories outside this hospital to release information to the Garvan Institute of Medical Research concerning the particpant's disease and treatment for the purposes of this research project. I understand that such information will remain confidential.

Name of Participant (please print) _____

Name of Person Responsible (please print) _____

Relationship of Person Responsible to Participant

Signature of Person Responsible _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Declaration by Study Doctor/Senior Researcher

I have given a verbal explanation of the research project, its procedures and risks and I believe that the participant has understood that explanation.

Name of Study Doctor/ Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

I consent to the storage and use of blood and tissue samples taken from me for use, as described in the relevant section of the Participant Information Sheet, for this specific research project.

Name of Participant (please print) _____

Name of Person Responsible (please print) _____

Relationship of Person Responsible to Participant _____

Signature of Person Responsible _____ Date _____

Name of Witness* to Participant's Signature (please print) _____

Signature _____ Date _____

* Witness is not to be the investigator, a member of the study team or their delegate. In the event that an interpreter is used, the interpreter may not act as a witness to the consent process. Witness must be 18 years or older.

Name of Study Doctor/ Senior Researcher† (please print) _____

Signature _____ Date _____

† A senior member of the research team must provide the explanation of and information concerning the research project.

Note: All parties signing the consent section must date their own signature.

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Form for Withdrawal of Participation - *Adult providing own consent*

Title	The Effect of a New GLP-1 agonist on Appetite and Gastric Emptying in Prader-Willi Syndrome
Short Title	ENGAGE PWS
Protocol Number	Version 2
Project Sponsor	The Garvan Institute of Medical Research
Coordinating Principal Investigator/ Principal Investigator	Prof. Lesley Campbell
Associate Investigator(s)	A/Prof. Alexander Viardot
Location	Garvan Institute of Medical Research

Declaration by Person Responsible

I wish to withdraw the participant from taking part in the above research project and understand that such withdrawal will not affect the participant's routine treatment, relationship with those treating them or their relationship with the Garvan Institute of Medical Research.

Name of Participant (please print) _____

Name of Person Responsible (please print) _____

Relationship of Person Responsible to Participant _____

Signature of Person Responsible _____ Date _____

[In the event that the participant's decision to withdraw is communicated verbally, the Study Doctor/Senior Researcher will need to provide a description of the circumstances below.]

Declaration by Study Doctor/Senior Researcher†

I have given a verbal explanation of the implications of withdrawal from the research project and I believe that the participant has understood that explanation.

Name of Study Doctor/ _____

Senior Researcher[†] (please print) _____

Signature _____ Date _____

[†] A senior member of the research team must provide the explanation of and information concerning withdrawal from the research project.

Note: All parties signing the consent section must date their own signature.