easternhealth

Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Box Hill Hospital

Title	A Phase II, randomized, double blind, parallel group,46 weeks dose-finding study of BI 456906 administered once weekly subcutaneously compared with placebo in patients with obesity or overweight
Short Title	A study to test whether different doses of BI 456906 help people with overweight or obesity to lose weight
Protocol Number	1404-0036
Project Sponsor	Boehringer Ingelheim Pty Ltd
Principal Investigator	Prof Christopher Gilfillan
Location	Box Hill Hospital – Arnold Street, Box Hill VIC 3128, Australia

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this research project. This is because you have been diagnosed with obesity or are overweight. The research project is testing a new potential treatment for people with obesity (significantly overweight). The new treatment is called BI 456906.

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 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 to take part, you might want to talk about it with a relative, friend or your local doctor.

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

If you decide you want 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
- Understand how data will be part of the larger drug development program
- Consent to take part in the research project

- Consent to have the tests and treatments that are described
- Consent to the use of your 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?

Health professionals use a calculation to determine if you are clinically overweight or if you have obesity. The usual way this is calculated is using the Body Mass Index (BMI). For the purpose of this study, when your calculated BMI is greater than 27, your doctor has classified you as overweight, and as the number gets higher this becomes more significant leading to a diagnosis of significantly clinically obese. There is no maximum weight limit for participants to take part in this study. The purpose of this trial is to find out whether the study drug BI 456906 helps people who have been classified as clinically overweight to obese to lose weight. This study intends to test different doses of the study drug to better understand how well people tolerate the treatment and the best dose to use in future studies to achieve weight loss.

Medications, drugs and devices have to be approved for use by the Australian Federal Government, by the Therapeutics Goods Administration (TGA). BI 456906 is an experimental treatment for obesity and is not approved for treatment of any other disease or condition in Australia or by any other authority elsewhere around the world, therefore its use in this research is considered experimental. This means that it must be tested to see if it is an effective treatment for weight loss.

3 What does participation in this research involve?

This trial compares the effects of the active study drug BI 456906 with an inactive substance (placebo). A placebo is a medication with no active ingredients or a procedure without any medical benefit. It looks like the real thing but is not.

You will be participating in a randomised controlled research project. This trial is testing different dosages of the study drug BI 456906. The research project is a double-blind study. This means that neither you nor your study doctor will know which dosage you are receiving. However, in certain circumstances your study doctor can find it out; for example, if it becomes necessary for your care.

We do not know which one may work best. To find out we need to compare different dosages. We put people into groups and give each group a different dosage. The results are compared to see if one is better. To try to make sure the groups are the same, each participant is put into a group by chance (random).

You will be assigned by random choice to receive either the study drug BI 456906 (at different dosages) or the placebo. This process is called randomisation. BI 456906 or the placebo will be given weekly by subcutaneous injections (2 syringes at each injection under the skin). The dose

will gradually increase up to week 20. After week 20 the dose will be the same for the remainder of this trial. You will have a one in five chance of being placed in any of the following groups:

Group A: dose increase up to 0.6 mg per week

Group B: dose increase up to 2.4 mg per week

Group C: dose increase up to 3.6 mg per week

Group D dose increase up to 4.8 mg per week

Group E: placebo injections

Please note that you will receive your first injections at the study site. You will also be trained on how to administer the injections. After the initial injections at the study site, you must administer the injections yourself (2 syringes at each injection site once a week). If you do not want to administer the injections yourself, you will discuss alternatives with the study doctor.

Your trial doctor will be told whether you received the trial drug BI 456906 or the placebo once the trial is finished worldwide. If you want to know what trial medication you were taking, please contact the trial doctor.

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.

TRIAL PROCEDURES

Time to be spent in the research project

Your participation in the trial will last approximately one year and require approximately 20 visits to the clinic or hospital (on site visits).

Should a new wave of the COVID-19 pandemic place you at risk when visiting the hospital/clinic, the site staff may decide to use phone or internet-based technology which allows you to talk with your doctor remotely, from home. If this is required, additional information will be provided and we will check if you are happy for this to occur.

Before the research project starts (screening):

The first trial visit will be a screening visit. The screening visit will include collection of information and testing as follows:

- Ask you to sign the Consent Form at the end of this document
- Demographics (year of birth, gender, age)
- Medical history and current health issues and symptoms
- Information about your mood. This information is collected because the study drug may have an effect on the activity of your brain, this is why you will be asked questions about your mood.
- Current and past medication use
- Physical examination

- Vital signs (breathing rate, temperature, pulse and blood pressure)
- Measurement of height, weight and waist circumference
- Blood and urine samples for safety laboratory tests, including one pregnancy test (if you are a woman) and SARS-CoV2 (Severe Acute Respiratory Syndrome - Corona Virus – 2) testing
- Infectious diseases testing, such as hepatitis B, hepatitis C (a disease that affects the liver) and HIV (a blood virus that may lead to AIDS). Your trial doctor/team will provide you with the necessary counselling and support before and after infectious disease testing
- Electrocardiogram (a test measuring electrical activity of the heart)

The results of the tests and/or questions at the screening visit will help the trial team decide whether you can continue in this research study. If these tests show that you are eligible to participate in the study, you will be able to continue. If you do not meet the eligibility criteria, you will not be able to continue. You should not go to another study site to be screened again.

If you are eligible at this stage, you will plan your next visit to the site. The site staff will give you a "3-day food diary" in paper. Before the second visit, you will be asked to record in this diary everything you eat and drink during 3 entire days (over 2 weekdays and 1 weekend day). The trial team will give you detailed instructions on how to record that information.

If you are interested in participating in a genetic banking sub-study, your trial doctor will provide you with a separate information sheet and consent.

Additional project procedures to be performed before you receive the study drug

The trial team needs to find out about your health before you begin receiving the study drug. This is called the baseline visit. In addition to the results from the screening visit, some examinations will be repeated at the baseline visit that will help the trial team to decide whether you can continue in this trial.

This visit includes collection of information and testing as below:

- Changes in your health and symptoms since your first visit
- Changes in medication use since your first visit
- Physical examination, vital signs
- Weight and waist circumference measurement
- Urinary pregnancy test

Based on all these results, the investigator will confirm if you are eligible to enter the treatment period. If this is the case the following procedures will be done:

- Blood samples will be taken for safety laboratory tests to see if your body is producing antibodies against BI 456906, and for biomarkers. The optional sample for genetic banking will be taken if you consented for it.
- You will have to complete some participant questionnaires related to eating behaviour and physical functioning.

- You will receive your first injections. You will also be trained on how to do the injections by yourself. It is important to take all medication regularly during the trial. You must do the injections (2 syringes at each injection) once a week. If you do not want to do the injections yourself, you will discuss alternatives with the study doctor.
- You will receive an instruction sheet describing how to store and handle the study drug syringes. You will get additional material like a cooler bag for transport, a special container for used syringes etc.
- You will have an interview with study staff who will prepare for you a diet and exercise program to follow during the trial.
- You will receive a paper diary to record your food intake daily.
- You will be given instructions to load one app on your smartphone that will be used as an electronic diary to record your weekly injections, your home measurement of weight, and your daily physical activity, as described later in this document. If you do not have a smartphone, you will be given one for the duration of the trial.
- You will receive a weight scale to enable home weight weekly measurements

Treatment period:

There may be a break between treatments so that medications that you were taking before the trial are cleared from your body before you start the new study treatment.

The treatment period will last for 46 weeks. During the first 20 weeks the dose will be gradually increased. During that period, you will have one visit every 2 weeks. You will get instructions on what to do if you have side effects affecting your digestive tract. There will be some flexibility in the dose increase schedule between week 10 and 20. Your study doctor may decide to delay the next dose increase to make sure you can tolerate it. Once you have reached the target dose, you will continue the treatment until week 46, with on-site visits every 4 weeks.

In the section "**What are the possible risks and disadvantages of taking part?"** of this document you will find a more detailed description of the different trial tests and procedures including related risks.

END OF TREATMENT VISIT

After you have been taking the trial medication for the full duration of the trial, or if you decide to stop taking the trial medication, you will have an "End of Treatment" visit, one week after the last injection. You will not receive any more trial medication. At this visit your trial doctor will discuss your future care and any medications you require.

FOLLOW-UP PERIOD/VISIT

You will not take any trial drug during the "Follow-up Period". After your final Follow-up Visit you will have completed the trial. After you have completed the trial, you will be offered standard medical care. Any side effects that continue after your last dose of the trial drug will be followed until considered resolved by the trial doctor. The trial staff will inform the Sponsor of any side effects evaluated as being trial-related and occurring after you have completed the trial.

The visit schedule tests and trial procedures are described in the below table. Boxes marked with an X show what will happen at each visit. Descriptions of these procedures and their related risks are listed in the section "**What does participation in this research involve?"**

Visit	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	EOT	F-up
Week of treatment	Screening (up to 3 months before visit 2)	0	2	4	6	8	10	12	14	16	18	20	24	28	32	36	40	44	46	Drug discontinuation	EOT+ 4w
Approximate length of time needed	**3h30**	**3h**	**1h 45**	**2h 15**	**1h 45**	**2h15**	**1h45**	**2h15**	**1h45**	**2h15**	**1h45**	**2h15**	**2h15**	**2h**	**2h15**	**2h**	**2h**	**15 min**	**45 min**	**2h30**	**45 min**
Be trained to inject the drug		X																			
Physical examination	X	X		X		X		X		X		X	X	X	X	X	X		X	X	X
Vital Signs, weight and blood tests	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	X
Electro-cardiogram	X	X	X	X	X	X	X	X	X	X	X	X	X		X					X	
Blood sample for optional biobanking		X								X				X						X	
Diet and exercise interview		X		X		X		X		X		X	X	X	X	X	X		X	X	
Collection of 3days food intake		X										X								X	
Questionnaires in clinic	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X	X		X	X	
Self-administered questionnaires	X	X										X							X	X	

Additional costs

This trial is funded by the sponsor, Boehringer Ingelheim.

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

You will be reimbursed for any reasonable travel, parking, meals and other expenses associated with the research project visit.

It is important that your personal doctor (usually your general practitioner or GP) is aware that you are in a clinical trial because you may be taking a treatment that could affect your health. By signing this document, you agree for your GP to be notified of your participation in this study and of any clinically relevant information noted by the study doctor in the conduct of this study.

4 What do I have to do?

- You must tell your trial doctor if you have previously participated in this trial, have been in another clinical trial in the past year, or are currently in another clinical trial. While participating in this trial, you should not take part in another clinical trial, or in this trial at another site. This is to protect you from possible injury arising from such things as extra drawing of blood samples, potential medication interactions, or other hazards.

- You will receive a Trial Identification Card. It is important that you carry this card with you at all times. If you are treated by another doctor (for example, in an emergency), it is important that you tell them of your participation in this trial by showing this card.

- If you are treated by another doctor, it is important that you tell the trial staff about your treatment and what happened.

- You must follow the trial instructions provided by the trial staff, come to all scheduled trial visits, and be reasonably available for any scheduled telephone or video visits.

- You must follow the diet and exercise regimen prepared for you. You must record your daily food intake in a paper diary and record physical activity in your e-diary as instructed.

- At the beginning of the treatment period, after 20 weeks, and after the 46 weeks of treatment, you must record in detail all of what you eat and drink during three entire days.

- You must store and inject the trial medication as instructed by the trial staff. You will receive written instructions to help you. You must record all the injections in your e-diary.

- You must remember to bring your unused trial medication and all empty containers to each of your on-site visits and explain if there is any lost or missing trial medication.

- You must call/tell the trial doctor if you experience any side effects or if you feel unwell, even if you think that it has nothing to do with this trial.

- You must tell the trial doctor about all prescription and non-prescription drugs, herbal preparations and food supplements that you are taking or planning to take. There may be some foods that you should avoid while on this trial and your trial doctor will review this information with you.

5 Other relevant information about the research project

We estimate that approximately 30 people will participate in this trial in Australia and about 350 worldwide.

6 Do I 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 to take part or not to take part, or to take part and then withdraw, will not affect your routine treatment, your relationship with those treating you or your relationship with Eastern Health.

7 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital. Other options are available; these may include, for example, lifestyle modifications such as exercise and dietary changes, or other clinical trials. Your study doctor will discuss these options with you before you decide whether or not to take part in this research project. You can also discuss the options with your local doctor.

8 What are the possible benefits of taking part?

We cannot guarantee or promise that you will receive any benefits from this research; If you join this research study, you may or may not lose weight.

Medically significant weight loss (approximately 10 percent of initial weight) can lead to:

Reductions in

- blood pressure
- cholesterol

- blood glucose (sugar)

If you are taking medications for one or more of the above listed conditions, dosages may need to be adjusted as your overall health improves.

Other benefits may also be obtained. Increasing activity level can favourably affect the above conditions and has the additional benefit of helping you sustain weight loss. Weight loss and increased activity may provide psychological and social benefits.

You may not personally benefit from participating in this trial, but you may contribute to new information that may benefit other patients and provide the medical and scientific community with information about treatment for obesity.

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

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

There are risks to taking part in any clinical trial. If you will receive the placebo, you will only receive diet and exercise counselling and will not receive an active treatment for your condition. Your condition might become worse, stay the same, or improve during the course of this trial.

If you receive active trial drug, then side effects are more likely to occur. Some of those side effects can be treated. Some may go away when you stop taking the trial drug. Some can be mild, but others may continue longer or become permanent. Some may be life-threatening or fatal.

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

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, your study doctor may need to stop your treatment. Your study doctor will discuss the best way of managing any side effects with you.

As with any drug, an allergic reaction can occur. Allergic reactions can be mild or more serious and can even result in death. Common symptoms of an allergic reaction are rash, itching, skin problems, swelling of the face and throat, or breathing difficulties. If you think you are having an allergic reaction, call the trial doctor right away. If you are having trouble breathing, call 000.

Gallstone disease

Being overweight or obese may make you more likely to develop gallstones (which increase the risk of gall bladder disease), especially if you are a woman. People with obesity or who are overweight may have higher levels of cholesterol in their bile, which can contribute to the formation of gallstones. Losing weight very quickly and/or a large amount may raise your chances of forming

gallstones as it can prevent the gallbladder from emptying properly. Several factors may raise your chances of having problems with gallstones in patients with obesity or who are overweight. These factors include:

- Gallstones that you had but without any symptoms
- Rapid weight loss
- A large amount of weight loss
- Long term very low-calorie diet

If you have gallstones without symptoms, talk with your trial doctor about how to lower your chances of developing more or larger gallstones or lower the risk of developing acute gallstone disease.

Common symptoms of acute gall bladder disease include severe pain in your upper right or center abdomen that can spread to your right shoulder or back, fever, nausea or vomiting. If you think you are having an acute gall bladder disease, call the trial doctor right away. If you are having trouble breathing, call 000.

Study Drug BI 456906

Taking BI 456906 may cause you to have nausea and/or vomiting, sometimes with severe intensity. You will receive additional guidance to appropriately manage adverse events during the study.

Although nausea or vomiting are known to be transient and self-limiting, these can sometimes significantly bother your daily life and might cause additional adverse effects such as being overly tired and being dehydrated.

If below symptoms or signs persist because of nausea or vomiting, please contact your trial doctor and nurse on the number presented below. Always remember in a medical emergency dial 000, and make sure you disclose you are in a research project.

- Not urinating very much, or dark yellow or brown pee
- Rapid heartbeat or rapid breathing
- Feeling dizzy
- Sleepiness, lack of energy, confusion or irritability
- Fainting

The study doctor or the trial staff will go through the description of the known side effects with you. They will answer any questions you might have about the severity and frequency of risks and other potential discomforts. You will be monitored carefully to check for these risks. Your study participation may be stopped if any signs of drug toxicity or other damage occurs.

You need to tell your trial doctor or a member of the trial team immediately if you experience any side effects.

Study Drug known side effects:

Very common: More than 1 in 10 risk (>10%)	
Gut	Decreased appetite
	Feeling full after eating a small amount of food
	Indigestion
	Feeling sick in your stomach (nausea)
	Frequent, loose or liquid bowel movements (diarrhea)
	Vomiting
	Air (gas) in the belly (abdominal distention)
	Belching (eructation)
Nose and Throat	Inflammation of the nose and throat (like the common cold)
Heart	Irregular heartbeats

Common: between 1 -10 out of 100 risk (1-10%)	
Gut	Stomach pain
	Constipation (decreased bowel movement)
Breathing system	Burning sensation in the throat or chest
Heart	Abnormal heart rhythms
	Fast heart beats
	Extra heart beats
Generalised symptoms	Tiredness

Risks of trial procedures

The table below lists the required procedures and the associated risks. The trial staff will describe the trial procedures and related risks to you. Please ask any questions you might have. In addition, there may be risks which are not known at this time.

Procedure	**Description**	**Risks**
Blood tests	Approximately 524 mL (26¼ tablespoons) of blood for the whole trial will be drawn to test your blood for - Safety and liver function - Biomarkers	• mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. • small risk of light-headedness and/or fainting. • rarely the puncture site can become infected or nerves may

Procedure	Description	Risks
	- Immunogenicity - Pharmacokinetic At each visit, approximately 15-50 mL (just under 1 to 3 tablespoon) of your blood will be taken from a vein in your arm. You may be asked to return for additional blood tests at any time if your study doctor believes they are necessary.	be damaged causing long-lasting abnormal sensations, impaired sensation of touch and persistent pain. • Frequent blood tests may cause anemia (low red blood cell count) that may need a blood transfusion.
SARS-CoV-2 test	The viral test that shows if you are currently infected with the COVID-19 virus. The most common method of collecting a sample is to swab the back of your nose. It is done once at screening visit.	This test may be uncomfortable and rarely causes a mild nose bleed.
Mandatory HIV and hepatitis testing	You will be screened for HIV (the 'AIDS' virus) and hepatitis B and C using a blood test. Before the tests are done, you will receive information and counselling.	If a test shows you have HIV or hepatitis B or C, this may surprise or upset you. You will have follow-up counselling and receive independent medical advice. If your test results are positive, your study doctor must notify government health authorities. Signing the consent form means that you agree to have this testing; it will not be done without your consent.
Pregnancy test	This test measures the hormone ß-hCG that is present in your blood or urine when you are pregnant. You cannot participate in a clinical trial if you are pregnant or planning to become pregnant.	As with any blood tests (see above)
Urine test	A urine drug test is done at screening to look for drugs that may contra-indicate your participation in the trial. Urine tests for your general health and look for red blood cells, protein, sugar and infection in the urine.	Nil

Procedure	Description	Risks
Physical examination	A routine manual examination your trial doctor performs to check your overall health.	Nil
Blood pressure test	This measures the pressure in your arteries as your heart pumps.	The squeezing of an inflated blood pressure cuff on your arm may be uncomfortable. It usually takes only a few seconds.
ECG (electrocardiogram)	This measures the electrical activity of your heart.	Mild skin irritation may occur from the ECG electrode pads or when removing these pads from your chest.
Genetic testing	Some blood samples will be used to analyse your genetic information. You can think of genetic information as a large instruction book that your body reads to understand how it should be built and function. All humans have the same instruction book in their body but some words or letters may be different from one person to the other. Some of those differences have no effect on your health but others can influence the likelihood of developing a disease or affect how medicine to treat a disease will work. If genetic analyses are done, they may involve all or part of your genetic information. In this study, the test will study genes associated with obesity, its related diseases, and the way the study drug works in the body.	These tests are not intended to be used for an individual diagnosis. Your results will be combined with data from a large number of other individuals. These tests are not suited to make a decision about your medical treatment. Therefore, neither you nor your study doctor will be informed about these research results.
Diet and Exercise Counseling	Diet and exercise counseling will be provided by a dietitian or a trial staff member to help you to improve your blood sugar levels. At every visit, the trial staff will remind you to follow your diet and exercise plan.	You may not like following a diet and exercise plan.

Procedure	Description	Risks
Questionnaires	Interviews will be done to assess **CSSRS (Columbia-Suicide Severity Rating Scale):** You will be asked to answer questions to see if you have suicidal thoughts or behaviours. It will take about 5-10 minutes to complete. You will be asked to complete 4 questionnaires about: • Your mental health • Your eating behaviour • Your ability to do normal daily activities It is important that you complete the questionnaires yourself and not ask others to do it for you.	You might find the questionnaires are long, or upsetting, or tiring. You may feel emotionally distressed. You might not like some of the questions or feel uncomfortable answering them. You do not have to answer any questions that make you feel uncomfortable. If you have suicidal thoughts or behaviour, the trial doctor will advise you to see a psychiatrist.

Information on pregnancy and breast feeding

For female participants

The effects of BI 456906 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. You must not participate in the research if you are pregnant or trying to become pregnant, or breast-feeding. If you are female and child-bearing is a possibility, you will be required to undergo a pregnancy test prior to commencing the research project.

Female participants must avoid pregnancy during the course of the research and for a period of 5 weeks after the last study drug intake. You should discuss effective methods of avoiding pregnancy with your study doctor.

Women who are able to become pregnant and their male sexual partner is able to father a child have to use two forms of effective contraception, where at least one form is a highly effective method of birth control, for the entire period of the trial and until 5 weeks after the last dose of trial drug. The male partner must use a condom or be vasectomised with documented absence of sperm. The female participant must use one highly effective method of contraception. Your trial doctor will talk to you about the best method of birth control for you.

The study drug may interfere with the capacity of your body to absorb oral contraceptives. If you are using oral contraceptives, you should change to any of the non-oral contraceptives listed below.

A list of acceptable methods of highly effective contraception is indicated in the table below.

Acceptable methods of highly effective contraception
Combined (oestrogen and progestogen containing) hormonal birth control that prevents ovulation (intravaginal, transdermal) + Male partner using condom or vasectomised
Progestogen-only hormonal birth control that prevents ovulation (injectable, implantable) + Male partner using condom or vasectomised
Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS). + Male partner using condom or vasectomised
Bilateral tubal occlusion + Male partner using condom or vasectomised
Complete sexual abstinence (not to have male-female vaginal sex)

You may choose complete sexual abstinence from male-female sex. If you choose abstinence (not to have sex) as your method of birth control, you must completely avoid having vaginal sex with a male partner.

The following abstinence methods are not acceptable: periodic abstinence, for example, calendar, ovulation, symptothermal (signs of ovulation), post-ovulation methods; declaring abstinence while receiving the study drug and withdrawal.

If you do become pregnant whilst participating in the research project, you should advise your study doctor immediately. Your study doctor will withdraw you from the research project and advise on further medical attention should this be necessary. You will be asked to continue to participate in trial visits. Your health and your baby's health will be monitored throughout your pregnancy. Even if you are no longer in the trial, your trial doctor will contact you after your baby is born to find out about the baby's health.

For male participants

Contraception is not required for male participants.

10 What will happen to my test samples?

The biological samples collected from you during the trial as described under the section "Trial Procedures" will be stored, processed, and used under your code number for the purposes of this trial for analyses as follows:

Routine Safety and Pregnancy testing samples:

Blood and urine will be collected for routine safety and blood for pregnancy tests (for women of child bearing potential) and will be sent to a central laboratory for analysis. Leftover samples will be destroyed once the tests are completed. The urine pregnancy testing will be done at the trial site. The samples will be destroyed at the trial site once the results are known.

Use of Drugs Testing:

This research project involves the collection of information about your use of drugs. Participation in the research project includes urine analysis to determine the presence of some recreational drugs such as cannabis, cocaine, opiates etc. The test may reveal that you have previously used illegal drugs. That information will be stored in a re-identifiable (or coded) format. In the event that Eastern Health is required to disclose that information, it may be used against you in legal proceedings or otherwise.

Infectious Disease Testing:

Blood will be taken to see if you have infectious diseases, such as hepatitis B, hepatitis C (a disease that affects the liver), HIV (a blood virus that may lead to AIDS) and a swab taken of the back of your throat and nasal passage will be tested for SARS-CoV-2 (a virus that may lead to COVID-19 disease). This is because the study doctors need to know if it is safe for you to enter the study. You will receive information and counselling before the test. If a test shows you have HIV or hepatitis or Covid-19, or any other reportable diseases, you will have follow-up counselling and medical advice. If your test results are positive, the study doctors are required by law to notify government health authorities. Signing the consent form means that you agree to have this testing; it will not be done without your consent.

Infectious disease samples will be destroyed once the tests are completed.

Biomarker samples (in blood):

In this trial, non-genetic and genetic biomarker testing will be done.

Non-genetic biomarker testing will be done to measure cardio-metabolic markers (e.g. satiety and liver related biomarkers) to see if there are changes before and after receiving the study drug. Proteins play specific roles for various body functions.

Genetic testing will look at DNA (deoxyribonucleic acid), RNA (ribonucleic acid), or other gene products, like proteins in your cells. Genes are a part of your DNA which determines things like the colour of your hair or eyes. Your genes affect how you respond to drugs. RNA carries instructions from DNA to make proteins. Every cell in your body uses proteins to perform certain functions.

- Genetic testing of DNA will be done to assess certain genes known to have mutations (changes to the structure of a gene) that may cause obesity.
- Genetic testing to identify genes from RNA that are involved with the way the study drug works in the body, how the body responds to the drug, and how severe the disease may be.

Other non-genetic biomarker testing may be done. At this time, it is not known what testing will be done.

Please note that any collection, storage and transfer of data related to your samples in the context of research projects entails the risk of breaches of confidentiality (e.g., the possibility of identifying you), particularly regarding your genetic information. These risks cannot be completely excluded and rise with increasing amounts of linked data, especially when you make further genetic information available on the internet about yourself. This risk is very low since your participation in the trial and all data and results of the trial are confidential.

Pharmacokinetic (PK) and Anti-Drug Antibodies/Neutralising Antibody (ADA/NAb) Samples

Blood will be taken for PK testing to see how your body uses the study drug and how fast or slow it moves through or out of your body, and for ADA/NAb testing to measure your immune response to the study drug (when the body detects and defends itself against substances that appear unknown and harmful).

After completion of the clinical trial, the leftover samples from the biomarker, PK and ADA/NAb testing may be used for explorative biomarker investigations not yet specified or for additional testing to see how the study drug reacts over time. These samples will be discarded after the testing is completed but not later than 5 years after the trial is over and the sponsor completes a report that contains the trial results.

If you do not want your samples to be stored for the additional testing, you cannot participate in this trial.

Optional Samples

As an optional part of this trial, you are being asked to allow the collection and storage of blood samples for potential future scientific research. You will be provided with a separate consent form with information so that you can decide whether or not you want to participate in this optional part.

The samples or parts of them may be transferred to the Sponsor, its research partners and service providers (like clinical research organisations or laboratories) including companies belonging to the Boehringer Ingelheim Group of Companies.

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, your study doctor will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your study doctor will make arrangements for your regular healthcare to continue. If you decide to continue in the research project you will be asked to sign an updated consent form.

Also, on receiving new information, your study doctor might consider it to be in your best interests to withdraw you from the research project. If this happens, he/she will explain the reasons and arrange for your regular healthcare to continue.

12 Can I have other treatments during this research project?

Whilst you are participating in this research project, you may not be able to take some or all of the medications or treatments you have been taking for your condition or for other reasons.

The study drug may affect the absorption of any other oral medication that you may take, therefore, in these circumstances the study doctor may request for additional tests to be performed to make sure the oral medication that you are taking are still effective and safe. If this is not possible, you may not be able to participate in the study or to continue the treatment with the oral medication.

It is important to tell your study doctor and the study staff about any treatments or medications you may be taking, including over-the-counter medications, vitamins or herbal remedies, acupuncture or other alternative treatments. You should also tell your study doctor about any changes to these during your participation in the research project. Your study doctor should also explain to you which treatments or medications need to be stopped for the time you are involved in the research project.

It may also be necessary for you to take medication during or after the research project to address side effects or symptoms that you may have. You may need to pay for these medications and so it is important that you ask your doctor about this possibility.

13 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team before you withdraw. This notice will allow that person or the research supervisor to discuss any health risks or special requirements linked to withdrawing. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled. Leaving the trial will not affect your future medical care.

You should be aware that data collected by the sponsor up to the time you withdraw 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.

Listed below are three possible scenarios when you could stop your trial participation. Your trial doctor will discuss these scenarios with you.

- **You may stop trial drug, but agree to continue participation and/or continue to be contacted**

If you decide to stop taking the trial medication, you may still continue to participate in trial visits. You will be asked by the trial staff to return to clinic for the End of Treatment visit, and then every 4 weeks to measure body weight until the end of the planned treatment period, and to come to the site for a final assessment at the initially planned end of treatment date. The collected information is important for the scientific value of the trial to interpret the trial results correctly. You are free to refuse this regular contact. Your decision will not affect your future medical care. If you do not come to site visits anymore, site staff will contact you at the initially planned end of treatment to get some information on your health status and weight.

- **You may stop trial drug and participation completely and withdraw your consent**

You have the right to withdraw your consent at any time. If you decide to stop trial medication and participation, then the final assessments such as weight and waist measurement, physical examination, laboratory tests, and electrocardiogram (ECG) should be completed as soon as possible. This is important for your safety and well-being. In addition, you must return all unused trial medication. After the final assessments, no further information about you will be entered into the trial database.

All data that had already been collected up to the time of withdrawal of your consent, including data gathered at any of your final assessments, will still be used to ensure the correct completion and documentation of the clinical trial and comply with applicable law.

Samples collected for the purpose of this trial and not yet analysed will be destroyed.

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

- **Your trial doctor may decide that you must stop**

Your trial doctor might decide to stop your trial drug or trial participation early without your consent when, in the trial doctor's judgment, it is in your best health interest to do so. It might also happen that your trial doctor asks you to discontinue study drug because it is found that the benefit/risk ratio is not favourable anymore (e.g. another disease occurs, or you cannot make the injections regularly).

Some of the reasons why this might happen are listed below:

- Your condition worsens or does not improve and an alternative treatment is medically indicated.
- The trial treatment or procedures are found to be unsafe or ineffective.
- Your inability to take the trial drug / participate as instructed.
- Cancellation by the Sponsor or regulatory authority.
- Or any other unforeseen reasons that make it necessary to stop your participation in the trial.

If you are removed from the trial, the trial doctor will explain to you why you were removed.

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
- Decisions made in the commercial interests of the sponsor or by local regulatory/health authorities.

15 What happens when the research project ends?

After completion of the study, you will not receive any more study medication. Your trial doctor will discuss your future care and any medications you require.

The results of the trial will be published on Boehringer Ingelheim's Trial Web site (http://trials.boehringer-ingelheim.com). The results may also appear in other clinical trial registries in countries in which the trial is conducted such as http://www.ClinicalTrials.gov. The results will not include information that can identify you.

The results of the trial may also be published in a professional journal or presented at scientific meetings. Your identity will not be disclosed in those presentations.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

Use of Your Personally Identifiable Information

The part of your personal information that directly identifies you, such as your name and address, will remain at the trial site and can be accessed by the trial doctor and other people at the site who are assisting with the trial or your care. This information may also be checked at the trial site by the

- Sponsor, or the Sponsor's representatives (including monitors hired by the Sponsor through a service provider),
- ethics review board/committee that reviewed the ethical aspects of this trial, and/or
- domestic or foreign regulatory agencies such as the U.S. Food and Drug Administration (FDA) and the Therapeutic Goods Administration (TGA) that approve medicines.

These persons check that the trial is carried out correctly at the trial site. They are bound by a duty of confidentiality.

Coding of Your Data

Your personally identifiable information and health information collected in this clinical trial will be labelled with a unique code number. Coded data may also include data/information such as images (e.g. x-rays, CT-scan, MRI and EEG). The code number will be used in place of your name and other information that directly and easily identifies you. Only the trial site will have the link between your personal information and the coded data. This link will not be provided to the Sponsor; only your coded data will be sent to the Sponsor. The Sponsor will take measures to

protect the confidentiality and security of your coded data and your privacy in accordance with current law.

To support the review of your data, your trial doctor may code and share data/information from your medical records. This will be limited to specific information relating to this trial.

Use of Your Coded Data and Biosamples

Your coded data and biosamples are needed for the Sponsor, its research partners and service providers (like clinical research organisations or laboratories), companies belonging to the Sponsor's group, regulatory authorities such as drug regulators, reimbursement agencies and ethics review boards to develop the drug, get permission to introduce and keep it on the market, monitor its safety and get it covered by health insurance. The data will be used in this study and in related research activities necessary for the drug development program in order to:

- understand how the trial drug and similar drugs work in the body and the study drug mode of action
- better understand yours, related diseases and associated health problems
- develop diagnostic tests for, or drugs to treat, yours and related diseases
- learn from past studies to plan new studies or improve scientific analysis methods
- publish research results in scientific journals or use them for educational purposes

The coded data may be transferred within your country or to other countries (including but not limited to Singapore and Germany) for analysis. Where the data protection rules in other countries are not as strict as the rules in your country, the sponsor will adopt appropriate measures to provide an adequate level of protection according to Australian law.

In case another organisation takes over development or commercialisation of the trial drug, your coded data or biosamples may be transmitted to them. They will then have to protect your data and biosamples in the same way as described herein.

Incidental Findings

The Sponsor will search for results that are related to the research question outlined in the trial protocol. To do so, researchers will obtain results by combining your data with data from other trial participants. Nevertheless, other results which may be of medical importance specifically for you and other trial participants may also occur (these are called incidental findings). In case of incidental findings that are considered medically actionable because they have clear and immediate medical significance to your health, the Sponsor will take all justifiable efforts to inform your trial doctor. Your trial doctor may then discuss the impact of these incidental findings with you. If you are <u>not</u> interested in receiving this information, please let your trial doctor know.

Sharing of Your Anonymised Data

The Sponsor is convinced that access to trial data advances clinical science and medical knowledge and is in the best interest of patients and public health, provided that patient privacy is protected. Therefore, the Sponsor may share with credible researchers an anonymised set of your trial data, but only for specified and approved scientific research. Anonymisation means that the

Sponsor will adopt certain measures to avoid your identification through the trial data. In particular, the Sponsor will delete the unique code to your data, so that it is impossible to trace back the anonymised data to your coded data.

Storage of Your Coded Data

All coded data, including yours, will be kept by the Sponsor. Only your trial doctor will be able to link your unique code number to you. This link will remain at the trial site for a maximum of 30 years and will then be destroyed by the trial doctor. After that it is not possible to link your unique code number directly back to you.

Rights under Data Protection Laws

You have the right to review which personal data the trial site and Sponsor store about you. You can also request that incorrect personal data is corrected or that processing is restricted.

In order to exercise your rights, please contact the trial site staff using the contact details listed in Section 20, who will align with the Sponsor. You can also ask to receive the personal information you have provided for the trial in a standardised electronic format or to have them transmitted to another person of your choice. You can also contact your local data protection authority in case of questions or concerns about the handling of your personal data. In some cases, your rights can be limited under applicable laws, especially where they conflict with the conduct of the trial and mandatory archiving requirements. In this case you will be informed accordingly.

Clinical Trial Websites and Publication

A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. law. This website will not include information that can identify you. At most, the website will include a summary of the results. You can search this website at any time.

17 Complaints and compensation

If you suffer 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. If you are eligible for Medicare, you can receive any medical treatment required to treat the injury or complication, free of charge, as a public patient in any Australian public hospital.

There are two avenues that may be available to you for seeking compensation if you suffer an injury as a result of your participation in this research project:

- The pharmaceutical industry has set up a compensation process, with which the Sponsor of this research project Boehringer Ingelheim Pty Ltd has agreed to comply. Details of the process and conditions are set out in the Medicines Australia Guidelines for Compensation for Injury Resulting from Participation in a Company-Sponsored Clinical Trial. In accordance with these Guidelines, the sponsor will determine whether to pay compensation to you, and, if so, how much. The research staff will give you a copy of the Guidelines together with this Participant Information and Consent Form. If you have any

questions about the Guidelines, please ask to speak to the Manager of Eastern Health Office of Research & Ethics on (03) 9895 3398.

- You may be able to seek compensation through the courts.

18 Who is organising and funding the research?

This research project is being conducted by Boehringer Ingelheim and sponsored and funded in Australia by Boehringer Ingelheim Pty Ltd.

Boehringer Ingelheim may benefit financially from this research project if, for example, the project assists Boehringer Ingelheim to obtain approval for a new drug.

By taking part in this research project, you agree that your samples (or data generated from analysis of these materials) may be provided to Boehringer Ingelheim. Boehringer Ingelheim may directly or indirectly benefit financially from your samples or from knowledge acquired through analysis of your samples.

The sponsor will be owner of the trial results. If commercial products or other valuable discoveries result from research using your samples and/or data, these products and discoveries may be owned, patented, licensed, or otherwise developed for commercial sale by sponsor, other researchers, or companies. If this should occur, you will not receive any financial benefits or compensation or other proprietary interest from any commercial products or discoveries that may result from such research.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Boehringer Ingelheim, the study doctors or their institutions, there will be no financial benefit to you or your family from these discoveries.

Eastern Health will receive a payment from Boehringer Ingelheim Pty Ltd for undertaking this research project.

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

19 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 Melbourne

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.

Approval to conduct the Research has also been given by the institution responsible for supervising the standard of care where the research will be carried out.

20 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 the principal study doctor on (03) 9092 6753 or any of the following people:

Clinical contact person

Name	Vanessa James
Position	Study Coordinator
Telephone	(03) 9194 7573
Email	vanessa.james@monash.edu

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

Complaints contact person

Name	Eastern Health Office of Research and Ethics
Position	Manager
Telephone	(03) 9895 3398
Email	ethics@easternhealth.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 Melbourne
HREC Executive Officer	The Deputy Director of Research
Telephone	03 9231 2394
Email	research.ethics@svhm.org.au

Local HREC Office contact (Single Site - Research Governance Officer)

Name	Eastern Health Office of Research and Ethics
Position	Manager
Telephone	(03) 9895 3398
Email	ethics@easternhealth.org.au

easternhealth

Consent Form - *Adult providing own consent*

Box Hill Hospital

Title	A Phase II, randomized, double blind, parallel group,46 weeks dose-finding study of BI 456906 administered once weekly subcutaneously compared with placebo in patients with obesity or overweight
Short Title	A study to test whether different doses of BI 456906 help people with overweight or obesity to lose weight
Protocol Number	1404-0036
Project Sponsor	Boehringer Ingelheim Pty Ltd
Location	Box Hill Hospital – Arnold Street, Box Hill VIC 3128, Australia

Consent Agreement

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 give permission for my doctors, other health professionals, hospitals or laboratories outside this hospital to release information to Eastern Health concerning my disease and treatment for the purposes of this project. I understand that such information will remain confidential.

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

I freely agree to participate in this research project as described and understand that I am free to withdraw at any time during the study without affecting my future healthcare.

I understand that I will be given a signed copy of this document to keep.

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

Declaration - for participants <u>unable</u> to read the information and consent form

See Note for Guidance on Good Clinical Practice CPMP/ICH/135/95 Section 4.8.9. A legally acceptable representative may be a witness*.

Witness to the informed consent process

Name (please print) _____

Signature _____ Date _____

* Witness is <u>not</u> to be the Investigator, a member of the study team or their delegate. Witness must be 18 years or older.

<u>Declaration by Study Doctor/Senior Researcher†</u>

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.