Participant Information Sheet/Consent Form

Interventional Study - *Adult providing own consent*

Box Hill Hospital

Title	Randomised, double-blind, placebo-controlled and parallel dose group trial to investigate efficacy and safety of multiple doses of oral BI 690517 over 14 weeks, alone and in combination with empagliflozin, in patients with diabetic and non-diabetic chronic kidney disease
Short Title	A study to test whether different doses of BI 690517 alone or in combination with empagliflozin improve kidney function in people with chronic kidney disease
Protocol Number	1378-0005
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 being asked to participate in this clinical research trial because you have chronic kidney disease (CKD).

Please read the following information carefully. It contains important information to help you decide whether to participate in this clinical trial. The trial staff will have a detailed discussion with you to inform you about the trial and the possible benefits and risks of your participation.

Ask questions about anything that is not clear at any time. You may take home an unsigned copy of this information to think about and discuss with your family, friends or personal doctor before you decide whether to participate or not.

After reading and discussing the information you should know:

- Why this clinical trial is being done;
- What will happen during the trial;
- Any possible benefits to you;
- The possible risks to you;

- Other options you could choose instead of being in this trial;
- How your personal information / health information will be protected during the trial and after the trial is over, and which data privacy rights you have;
- How your data and your biological samples will be collected, stored, processed, transferred and used;
- How your data will be part of the larger drug development program;
- What to do if you have problems or questions about this trial.

Your participation in this trial is voluntary. If you join this trial, you can still stop at any time. You have the right to not sign this consent form. If you do not sign, you cannot take part in this clinical trial. If you decide to participate, you will be asked to sign and date at the end of this form.

Your signature confirms that you agree and accept to take part in this trial and to the handling of your data as described in this form.

It is important that your personal doctor is aware that you are in a clinical trial because you may be taking a treatment that could affect your health. With your permission, we will notify him/her that you are taking part in this trial.

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

2 What is the purpose of this research?

The purpose of this trial is to look at whether a trial drug called BI 690517 is effective in improving kidney function in people who have CKD. The trial will also look at whether BI 690517 is effective in improving kidney function when taken together with another drug called empagliflozin, which may be used in the future, in people with CKD.

The kidneys perform several important functions; clearing (filtering) waste products from your blood; controlling blood pressure; making certain hormones; balancing certain chemicals (such as salts) in your blood; and removing excess fluid. In CKD these functions don't work so well.

It is common for people with CKD to be treated with a medication that blocks a biological system called the renin-angiotensin system (RAS). These treatments have meant some people do not need to start dialysis and have saved lives. However, despite taking RAS blockers, patients with kidney disease can still develop worsening of their condition. New treatments for CKD are therefore needed.

BI 690517 is new kind of medicine that inhibits an enzyme in your body called aldosterone synthase (AS). AS produces a hormone called aldosterone which has an influence on kidney function. If the aldosterone concentration is too high in your body this has negative effects on some minerals and water in your blood but also may lead to high blood pressure and damage the heart and the kidneys. By reducing aldosterone level there may be a benefit to your kidney disease. In the long run this may improve kidney function and slow or halt progress of kidney disease.

BI 690517 has not been approved as a treatment for any disease in Australia and therefore its use in this clinical trial is considered experimental. It has previously been tested in clinical trials with healthy volunteers and in a small number of patients with diabetic kidney disease.

In this trial three different doses of BI 690517 will be tested to see which is the best dose to be used for further development.

The second drug, empagliflozin, belongs to a class of drugs known as sodium glucose co-transporter 2 (SGLT-2) inhibitors. Empagliflozin works by causing glucose to be excreted in your urine. Your trial doctor can explain this in greater detail to you if you wish to have more information.

Empagliflozin was originally developed to treat people with diabetes and has recently been shown to have beneficial effects on the heart and the kidneys. It is expected that empagliflozin and other similar drugs will become an important part of the treatment regimen for patients with diabetes and CKD. Clinical trials of empagliflozin are also being conducted in patients with CKD who don't have diabetes and it is expected that empagliflozin will be recommended for these patients in the near future. Empagliflozin has been approved as a treatment for diabetes in Australia but not yet in patients with kidney disease and therefore its use in this clinical trial is considered experimental. It is marketed under the brand name Jardiance®.

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

3 What does participation in this research involve?

This trial compares the effects of the active trial drug BI 690517 with an inactive substance (placebo). A placebo is a substance that looks like the trial drug but contains no active drug. The trial will also investigate the effects of BI 690517 when it is given in combination with background empagliflozin or placebo.

The main method that will be used to investigate the effect of the trial drug BI 690517 is by testing your urine. We will measure Urine Albumin Creatinine Ratio (UACR) before you start taking trial drug and then at times throughout the trial. UACR shows whether you have albumin (protein) in your urine which is a sign of your kidney disease.

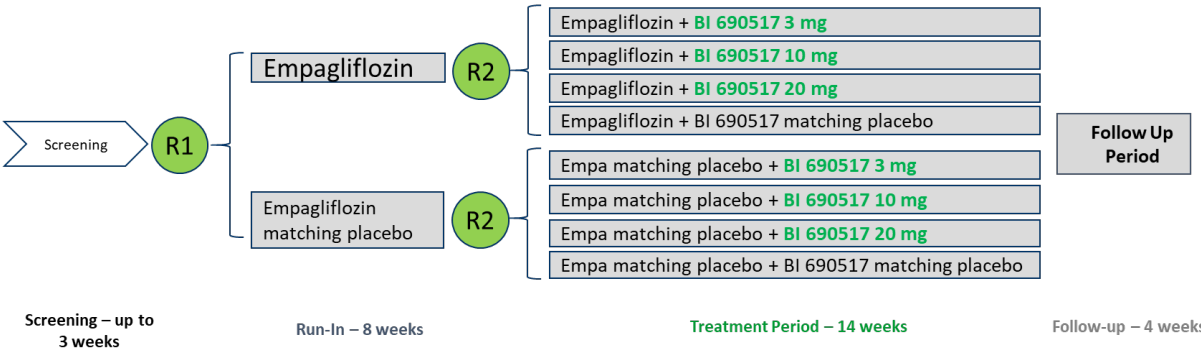

Figure 1. Study Flow Chart. (R1 – randomisation 1; R2 – randomisation 2)

After you are confirmed as eligible for the trial, you will be assigned randomly to receive background treatment with either empagliflozin or placebo (See figure 1 – R1). This process is

called randomisation. You will have a 50% chance of receiving empagliflozin and a 50% chance of receiving empagliflozin matching placebo. You will take the empagliflozin or placebo for 8 weeks to make sure you are stable on the background treatment before you start BI 690517 or BI 690517 matching placebo.

After 8 weeks of background treatment with empagliflozin or empagliflozin matching placebo, you will be randomised again to receive one of three doses of the active drug BI 690517 or BI690517 matching placebo, on top of the treatment you were receiving in the first part (See figure 1 – R2). **There will be a 75% chance that you will be assigned to the active trial drug (BI 690517) and a 25% chance that you will be assigned to placebo.** You will continue to receive this medication for 14 weeks.

This is a double-blind trial. This means that nobody (including you and your doctor) will know if you are receiving the trial drugs (BI 690517 and empagliflozin) or the matching placebo. This way the results of the trial will not be favoured one way or another. If it becomes necessary for your care, your trial doctor will be able to find out whether you are taking the placebo or the trial drug(s).

The different tablet strengths of BI 690517 are in different sizes. The placebo tablets will also come in different sizes to match the BI 690517 strengths. You will need to take 3 tablets of BI 690517 or BI 690517 matching placebo, plus the empagliflozin or empagliflozin matching placebo tablet, **in total 4 tablets**.

In this clinical trial competitive enrolment will be used. This means that when a target number of participants have started treatment in the clinical trial, all further enrolments will be closed. It is possible that you could be in the screening phase when this happens. If you meet all the requirements for entering the run-in phase of the clinical trial, you will be able to continue in the trial.

STUDY PROCEDURES

In Table 1 of this document you will find a detailed overview and schedule of all the visits which lists the trial tests and procedures planned at each visit.

In Table 2 of this document you will find a more detailed description of the different trial tests and procedures including related risks.

The trial doctor or the trial staff will go through the information with you.

INDURATION OF THE TRIAL

Your participation in the trial will last approximately 29 weeks and require approximately 12 trial visits.

The trial is split into four periods:

1. **Screening Period** (up to 3 weeks)
2. **Run-in Period** (8 weeks)
3. **Treatment period** (14 weeks)

4. Follow-up Period (4 weeks)

You may need to come for additional visits to those specified in Table 1: Visit Schedule, if the doctor feels it is necessary to check your health, or if you need to change dose of medication.

Home Sampling (urine collection)

Home sampling is when you collect your urine at home. However, this does not have to be done at home, you are able to collect the urine anywhere. There are two types of urine sampling in this trial: First Morning Void (FMV) urine which will be used to measure your UACR, and 24-hour urine collection, which will be used to investigate the possible effects of BI 690517 on a hormone in your urine called cortisol.

Several times during the trial you will be asked to collect your urine first thing in the morning. This is called the First Morning Void (FMV) urine. The first morning void is the urination after you wake up to start your day. If you wake up in the middle of the night to urinate, e.g. at 4am and then go back to sleep, this urine does not need to be collected. However, if you are an early riser and get up 'for good' e.g. at 4am, this would qualify as your First Morning Void urine. Of course, there may be times when you might go back to bed after your usual wake up time. In this case you should collect the urine at your usual wake up time.

You will always collect First Morning Void urine over 2 consecutive days. Sometimes you will collect FMV urine 1 day before the trial visit and on the day of the trial visit. Where the visit is conducted in the clinic, you have to bring all your collected urine to the clinic on the day of the second urine sample.

At other times you will collect FMV urine at home when you do not have a trial visit. This will be the day before the home sampling timepoint and the day of the home sampling timepoint.

A courier may collect your urine samples from your home. The trial team will go through the details about how the samples should be prepared and collected from your home. The trial team will discuss with you beforehand about who will package the samples for collection and how these will be collected by the courier. Please see section "Section 16 What will happen to information about me?" to see what contact details will be provided to the courier and how this will be used.

Twice during the study, you will also be asked to collect all of the urine you produce over a 24-hour period. This is called the 24-hour urine collection. The first 24-hour urine will be collected during the Run-In Period before you start treatment with BI 690517 / matching placebo, and the second sample will be collected just before the end of the Treatment Period. You will need to bring all your 24-hour collected urine to your next visit at the clinic, which will be a few days later.

You will receive collection cups and containers for each FMV and 24-hour urine collection. You can ask your trial nurse or doctor to give you a collection pan or funnel if you think this will help you. The urine samples should be kept as cool as possible, preferably in the fridge, if not then the coolest place possible until you can take them to the clinic, or until a courier can collect them. They should not be frozen. You will receive training on how to do the sampling and will also receive a detailed Urine Home Sampling Guide. If you have any questions about how or when to collect your urine, please ask your trial doctor or nurse.

1) Screening Period - Before the clinical trial starts:

The first trial visit will be a screening visit at the clinic. At the screening visit you will be trained on how to collect your urine at home and what to do with the samples after you have taken them. Screening assessments may be conducted over more than one day. Please see Table 1 for details of the visits and procedures during the screening period.

The results of the tests and questions during the screening period will help your doctor to decide whether you can continue. If these tests show that you are eligible to participate in the trial, you will be able to continue in this trial. If you do not meet the eligibility criteria, you will not be able to continue.

In some circumstances your trial doctor may suggest you to be screened again (re-screened) at a later date. If you wish to be re-screened your trial doctor would go through everything with you again and ask you to sign a new consent form.

You must not go to another trial site to be screened again so that you can participate in this trial.

At the end of the screening period, you will need to collect your FMV urine samples at home before you start taking the trial drug in the Run-in Period. You will be asked to collect urine the day before Visit 2 and in the morning of Visit 2.

2) Run-in Period

If you are eligible for the trial, you will be randomised to receive either empagliflozin or empagliflozin matching placebo at Visit 2 and you will start the Run-in Period. You will be asked to take this trial drug once a day in the morning for a period of 8 weeks. Your first dose will be given in the clinic. Please see Table 1 for details of the visits and procedures during the run-in period.

You will also be provided with paper copies of the following trial diary cards

- 'Participant PK Diary Card'
    - You will need to record the exact times you take your trial drug on the two days before each of your trial visits.
- 'Participant 24-hour Urine Diary Card'
    - You will need to record the start date and time and the stop date and time of the 24-hour urine collection.

Visit 3 will be a phone or video call from your trial nurse or doctor. At visit 4 (one week before the start of the Treatment period), you will have blood tests to confirm whether you are eligible to start taking the trial drug (BI 690517 or BI 690517 matching placebo).

You will be asked to collect your FMV urine for two days in a row on three occasions in the run-in period as follows:

- 8 and 7 days before visit 4 (2 weeks before start of treatment period)
- 1 day before, and the day of, visit 4 (one week before start of treatment period)

- 1 day before, and the day of, visit 5 (start of treatment period)

You will also do 24-hour urine collection sometime between Visit 4 and up to 3 days before Visit 5.

3) Treatment Period

At Visit 5 you will have the second randomisation, this time to receive the trial drug (BI 690517 or placebo). You will be asked to take the trial drug (BI 690517 or BI 690517 matching placebo) along with the background trial drug (empagliflozin or empagliflozin matching placebo) once a day in the morning for a period of 14 weeks. You will have 6 visits during the Treatment Period (Visits 5-9 and End of Treatment visit). At each visit you will be asked to take your daily dose during the visit.

There will be regular visits during the treatment period where some tests will be performed. You will also be asked to collect 24-hour urine within the week before the End of Treatment visit and FMV urine samples at home on several occasions:

- 1 day before, and the day of, visit 8 (Week 6)
- 1 day before, and the day of, visit 9 (Week 10)
- 15 days and 14 days before the End of Treatment visit (Week 12)
- 8 days and 7 days before the End of Treatment visit (Week 13)
- 1 day before, and the day of, the End of Treatment visit (Week 14)

You will also be asked to record the exact times you take your trial drug(s) on the two days before each of your trial visits on the 'Participant PK Diary Card', and record the start date and time and the stop date and time of the 24-hour urine collection on the 'Participant 24-hour Urine Diary Card'.

Drugs like BI 690517 can sometimes cause potassium levels in your blood to rise. Your doctor will monitor your potassium levels closely and may decide to reduce your dose of trial drug. If your potassium levels continue to be high despite reducing the dose, your doctor may decide that you should stop taking BI 690517 or BI 690517 matching placebo completely. In this case you may still continue to take the background empagliflozin or empagliflozin matching placebo for the remainder of the trial.

Your doctor will also monitor you closely for signs of adrenal insufficiency. Adrenal insufficiency occurs when the adrenal glands don't make enough of the hormone cortisol. Cortisol levels in your blood naturally vary over the course of the day so it is important your blood samples are taken in the morning. If the cortisol levels are below a certain level you will be asked to return to the clinic for an ACTH Challenge Test (as described in Table 2: Description of study procedure and risks).

After you have been taking the trial drugs for the full duration of the trial, you will have an 'End of Treatment' (EoT) visit. You will take your last dose of study medication in clinic at this visit but then you will not take any more trial drug for the remainder of the trial. If you decide to stop taking the trial drug(s) before you reach the end of the treatment period, you will also have an EoT visit,

but you will not take any trial drug at this visit. At this visit your trial doctor will discuss your future care and any medications you require.

4) Follow-up Period

After the End of Treatment visit, you will enter the "Follow-Up period" to further assess any adverse events, and investigate the effects of the study medications after they have been stopped. You will not take any trial drug during this period. There are two visits in the follow up period. Please see Table 1 for details of all of the tests performed.

You will be asked to collect FMV urine samples at home between the follow up visits on the following occasions:

- 6 and 7 days after the first Follow-up Visit (at Week 16)
- 13 and 14 days after the first Follow-up Visit (at Week 17)

After the final follow-up visit (FUp2) you will have completed the trial. You will then be offered standard medical care.

If you decide to stop taking the background study medication (empagliflozin or empagliflozin matching placebo) during the Run-In Period and you never start any treatment in the Treatment Period, you will only need to come to the first follow-up visit (FUp1) after EoT and then you will have completed the trial. If you decide to stop taking the study medication (BI 690517 or BI 690517 matching placebo) early during the Treatment Period, you should complete all follow-up visits.

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.

Table 1: Visit Schedule

- Boxes marked with an X show what will happen at each visit. If there is a number this shows how many times this is done.
- HS stands for Home Sampling, a visit to the clinic is only required if you need to return your urine samples. For examples, visit 3.1, 9.1, 9.2, FUp1.1 and FUp1.2.
- Descriptions of these procedures are listed in Table 2.

	Screening (up to 3 weeks)	**Run-in Period (8 weeks)**				**Treatment Period (14 weeks)**								**Follow-up Period (4 weeks)**			
Weeks before / after starting treatment with BI 690517 / placebo	**-11**	**-8**	**-4**	***-2***	**-1**	**0**	**1**	**2**	**6**	**10**	***12***	***13***	**14**	**15**	***16***	***17***	**18**
Visit (EoT = End of Treatment; FUp1 = Follow-up visit 1; FUp1.1 = Follow-up visit 1.1; FUp1.2 = Follow-up visit 1.2; FUp2 = Follow-up visit 2)	**1**	**2**	**3**	***3.1***	**4**	**5**	**6**	**7**	**8**	**9**	***9.1***	***9.2***	**EoT[e]**	**FUp1**	***FUp 1.1***	***FUp 1.2***	**FUp 2**
Type of Visit (C = clinic; H = home; HS = Home Sampling; T = telemedicine)	**C**	**C**	**T**	***HS***	**H**	**C**	**H**	**C**	**C**	**H**	***HS***	***HS***	**C**	**C**	***HS***	***HS***	**H**
Approx. visit duration (in hours)	**2.5**	**2**	**0.5**	**-**	**4**	**4**	**2**	**2**	**4**	**2**	**-**	**-**	**4**	**2**	**-**	**-**	**2**
Medical History (including historical kidney-related data if available)	X																
Height	X																
Weight	X					X			X				X				
Physical Examination	X	X				X			X				X	X			
Vital Signs – blood pressure & heart rate	X	X			X	X	X	X	X	X			X	X			X
Electrocardiogram (ECG)	X					X			X				X	X			
Pregnancy test (if applicable) – blood at visit 1, urine at all others	X		X			X			X	X			X				X

	Screening (up to 3 weeks)	Run-in Period (8 weeks)				Treatment Period (14 weeks)								Follow-up Period (4 weeks)			
Weeks before / after starting treatment with BI 690517 / placebo	**-11**	**-8**	**-4**	***-2***	**-1**	**0**	**1**	**2**	**6**	**10**	***12***	***13***	**14**	**15**	***16***	***17***	**18**
Visit (EoT = End of Treatment; FUp1 = Follow-up visit 1; FUp1.1 = Follow-up visit 1.1; FUp1.2 = Follow-up visit 1.2; FUp2 = Follow-up visit 2)	**1**	**2**	**3**	***3.1***	**4**	**5**	**6**	**7**	**8**	**9**	***9.1***	***9.2***	**EoT[e]**	**FUp1**	***FUp 1.1***	***FUp 1.2***	**FUp 2**
ACTH Challenge Test[a]	X					(X)	(X)	(X)	(X)	(X)			(X)				
Training on home sampling	X																
Urine collection at home – first morning void (2 consecutive days)		X		X	X	X			X	X	X	X	X		X	X	X
Urine collection at home – 24-hour sample (at least 3 days before the visit)						X							X				
Urine sample – safety	X[b]	X			X	X	X	X	X	X			X	X			X
Blood test – safety and eGFR	X	X			X	X	X	X	X	X			X	X			X
Blood test – cortisol	X					X	X	X	X	X			X	X			X
Blood test – biomarkers		X				X			X				X				X
Blood test – pharmacogenomic						X											
Blood test – pharmacokinetic (PK)[c]		X			4X	4X	X	X	4X	X			4X				
Blood test – aldosterone					4X	4X	X		4X	X			4X	X			X
Optional biobanking (blood test & urine sample)		X				X			X				X				X
Complete trial diaries prior to the visit					X	X	X	X	X	X			X				
Medication kit(s) provided		X				X		X	X	X							
Return medication kit					X[d]	X	X[d]	X	X	X			X				

	Screening (up to 3 weeks)	Run-in Period (8 weeks)				Treatment Period (14 weeks)								Follow-up Period (4 weeks)			
Weeks before / after starting treatment with BI 690517 / placebo	**-11**	**-8**	**-4**	***-2***	**-1**	**0**	**1**	**2**	**6**	**10**	***12***	***13***	**14**	**15**	***16***	***17***	**18**
Visit (EoT = End of Treatment; FUp1 = Follow-up visit 1; FUp1.1 = Follow-up visit 1.1; FUp1.2 = Follow-up visit 1.2; FUp2 = Follow-up visit 2)	**1**	**2**	**3**	***3.1***	**4**	**5**	**6**	**7**	**8**	**9**	***9.1***	***9.2***	**EoT[e]**	**FUp1**	***FUp 1.1***	***FUp 1.2***	**FUp 2**
Review any side effects/medication changes	X	X	X		X	X	X	X	X	X			X	X			X

[a] ACTH Challenge Test will be performed at screening, but may also need to be performed during the study to exclude adrenal insufficiency.

[b] Also includes spot UACR

[c] At the PK visits marked 'X', a blood sample will be taken before the daily dose of trial drug. At the visits marked '4X', a blood sample will be taken before you take your daily dose of trial drug, then afterwards at 30 minutes, 1 hour and 2 hours. Usually when more than one blood sample is taken a catheter can be used so you don't have to have a needle inserted each time – please see Table 2 for further information or ask the trial team.

[d] You should bring your medication kits with you to all visits, but you will not return them at visit 4 and visit 6

[e] If you stop trial drug(s) early you will be asked to have an End of Treatment visit. If you stop your trial drug(s) during a scheduled visit or you were still taking trial drug up to a day before then you will be asked to complete all assessments. If you have stopped taking the trial drug(s) during the Run-In Period or if the EoT visit is scheduled for a later date then you may not need to have all the biomarker, PK and aldosterone samples collected at the EOT visit or Follow up visits. We would still like you to do the 2 days of FMV urine sampling as this may provide some useful information.

COURIER AND TELEMEDICINE

Courier

You may have the option to have a courier company come to collect your trial medication from the clinic and deliver it to you personally at your home. Any urine samples collected can also be taken by courier, who will come and collect the samples from your home. Please see section "Section 16 What will happen to information about me?" to see what contact details will be provided to the courier and how this will be used.

The trial drug is intended only for you and must be stored out of the reach of children. Please keep all empty boxes/blisters and any unused, leftover trial drug. This should be returned at your next visit or this may be collected by a courier.

Your trial team will discuss all of these details with you before any courier visits your home. You can change your mind about whether you do/do not want to have your urine samples and/or trial medication sent to and from your study site at any time without having to give a reason.

Telemedicine

Telemedicine is the name given when technology is used to connect with participants without having to visit the trial site. In this trial we will use this to refer to phone calls, video calls or messaging participants. Every participant will be asked to provide a phone number to the trial team so that they can get in touch with you, for example to discuss taking the trial drug, the urine collection, to discuss your general health and/or to arrange/rearrange visits. You will also have their phone number if you need to contact them, please see section 20 "Further Information and who to contact". The use of video calls may be offered to you, you can choose whether you would like to use them.

MODIFICATION OF TRIAL PROCEDURES

Protection of our trial participants is of the highest importance. During the trial, in the event of disruption (e.g. pandemic), it may be necessary to modify how your trial visits are conducted. Before changes are made, the trial doctor will provide you with additional information for you to review and consider. You can then decide whether you agree to continue in the trial. If you want to know more details about these possible modifications, please ask your trial doctor.

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. Please ask the study staff for more details.

If you decide to participate in this research project, the study doctor will inform your local doctor.

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. You should also 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 available for any scheduled telephone visits. You should call the trial staff as soon as possible in case you are not available for the visit to arrange for an alternative visit.

- You must collect and store your urine samples at home as instructed by the trial staff.

- You must store and take the trial drug as instructed by the trial staff, in particular:
    - During the run-in period, you must take one tablet of empagliflozin or empagliflozin matching placebo daily
    - During the treatment period, you must take one tablet of empagliflozin or empagliflozin matching placebo daily and three tablets of BI 690517 or BI 690517 matching placebo daily (4 tablets in total).
    - The tablets should be taken at the same time every day, in the morning (after urine collection on the days you need to collect urine). They should be taken with a glass of water. They can be taken with or without food.
    - **There must be at least 12 hours between doses.** You should try not to miss any doses. If you do miss a dose and it is more than 12 hours since your last dose, do not take double the dose the next time, but continue as usual at the next planned intake.
    - **Do not take your trial drug the morning of your visits.** The trial staff will give you the trial drug during the visit.

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

- Do not throw the study drug in the bin or flush it into the toilet. Do not give your study drug to any other person to take and keep the study drug out of the reach of children and others who cannot read the label.

- You should not make any changes to your non-study medication(s) or dose without talking to your study doctor first.

- You should inform the study doctor or study staff of any surgeries that are or will be planned during this study.

- You should avoid drastic changes to your diet and lifestyle, including unusual or strenuous exercise.

- **For two days prior to visits with pharmacokinetic (PK) and/or aldosterone sampling (see Table 1), you must record the dates and times when you took your trial drug in the diary provided. You should also record the start and stop dates and times for the 24-hour urine collection.**

- You do not need to come fasted to trial visits, however at the visits where there are post-dose PK samples taken, you should only drink water and not eat food from the time of the first PK sample (approx. 30 mins before the dose) until the last PK sample (2 hours after the dose).

- 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 medications and 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 7 people will participate in this trial in Australia and at least 552 participants worldwide.

As an optional part of this trial, you are being asked to participate in an optional biobanking. 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 trial procedure.

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 include receiving standard treatment such as lifestyle changes and/or taking part in another clinical trial. 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; however, possible benefits may include your kidney disease will be more closely monitored during this trial which may be beneficial.

Through your participation in this research project, you may contribute new information that may benefit other patients and provide the medical and scientific community with information about treatment for chronic kidney disease.

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

There are risks to taking part in any clinical trial. If you receive a placebo, you will not receive an active treatment for your condition. Your condition might not improve, or it could get worse during the course of this trial.

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

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.**

You will be monitored carefully to check for these risks. Your trial 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 as soon as possible if you experience any side effects.

Taking BI 690517, empagliflozin or placebo or the use of Synacthen® (or equivalent) for the ACTH challenge test may cause you to have one or more of the adverse events (or side effects) listed below. The trial doctor or the trial staff will go through the description of the adverse events with you. Please ask any questions you might have. In addition to the adverse events listed, there is always the risk of developing adverse events which are not known at this time.

BI 690517

The trial drug BI 690517 has been used in trials with healthy volunteers and in a trial with participants who had diabetic nephropathy, a type of diabetic kidney disease. If you receive the trial drug BI 690517 it may cause you to have one or more of the adverse events listed below. The list includes adverse events that are considered related to trial drug as well as those that are not, for example they could be caused by the participant's general health.

Adverse events frequently observed with compounds like BI 690517 may include, but are not limited to:

- hyperkalaemia (increase in potassium levels in the blood),
- insomnia
- dizziness
- syncope (fainting)
- headache
- tachycardia (rapid heartbeat)
- atrial fibrillation (irregular heartbeat)
- hypotension (low blood pressure)
- cough
- diarrhoea
- nausea
- constipation
- vomiting
- muscle spasms
- back pain
- renal impairment (decrease in kidney function)
- asthenia (lack of energy)
- change in blood test results including:
    - increase in blood urea, creatinine and testosterone levels, or
    - decrease in sodium levels in the blood

BI 690517 may cause overproduction or underproduction of some other hormones from your adrenal gland. Your adrenal function will be monitored at regular intervals. You should contact your doctor immediately if you have symptoms such as weakness, weight loss, abdominal pain or low blood pressure.

Empagliflozin

In research studies carried out so far, empagliflozin has been given to more than 13,000 patients with type 2 diabetes.

The side effects in this section are listed by frequency. Frequencies are defined as:

- Very common (more than 10% risk that this will happen)
- Common (between 1% and 10% risk that this will happen)
- Uncommon (between 0.1% and less than 1% risk that this will happen)
- Rare (between 0.01% and less than 0.1% risk that this will happen)

The side effects observed with empagliflozin include:

Very common:

- Low blood sugar (hypoglycaemia) when used with a class of blood sugar lowering drugs called sulphonylurea (sulfonylurea) or insulin

Common:

- Urinary tract infections
- Genital infections
- Itching, also known as pruritus
- Increase in urination frequency or amount of urine
- Thirst
- Blood lipids increase. This laboratory test measures the cholesterol and other related substances in your blood
- Allergic skin reactions (e.g., skin rash, raised red itchy areas)
- Constipation
- Symptoms and signs of volume depletion (decrease of water in the body) such as hypotension (low blood pressure), syncope (fainting) (uncommon). If you are older than 75 years, these symptoms may occur more often (common).

Uncommon:

- Ketoacidosis (a life-threatening condition with increased chemicals called ketones in the blood)
- Painful urination, also known as dysuria
- Blood creatinine increase and glomerular filtration rate decrease. These laboratory tests are frequently used to assess how kidneys are working
- Increase in haematocrit. This laboratory test is used to measure the percentage of red blood cells in the blood

Frequency Unknown:

- Angioedema (swelling of your face, lips and throat that may cause difficulty breathing or swallowing)
- Bacterial infection that destroys the tissue under the skin ("Fournier's Gangrene" which is a type of necrotising fasciitis) in the area between your anus and genitals (perineum)
- There have been reports of pyelonephritis (inflammation of the kidney) and urosepsis (a serious and potentially life-threatening condition where the infection coming from the urinary tract is being spread in the blood)

In 24-week trials, treatment with empagliflozin resulted in a mean systolic blood pressure decrease up to 4.8 mmHg. Your blood pressure will be checked at each visit to monitor this.

In 24-week trials, treatment with empagliflozin resulted in a mean body weight decrease up to 2.2 kg. Your body weight will be monitored throughout the trial.

In addition, as with all drugs, empagliflozin may cause an allergic reaction that could become serious and require immediate treatment in a hospital or emergency room.

Empagliflozin is still a relatively new medicine and is still being studied, and therefore there may be other side effects which are currently unknown.

Hypoglycaemia

Symptoms of low blood sugar (hypoglycaemia) can be as follows: sudden outbreaks of sweating, palpitations (rapid heartbeat), trembling, feeling of hunger, restlessness, paleness, headaches, sleepiness, anxiety, uncertainty, problems with vision and speech, signs of paralysis and abnormal sensations. Sustained and severe cases of low blood sugar can lead to loss of self-control or unconsciousness.

Hyperglycaemia

Opposite of hypoglycaemia, you could also experience hyperglycaemia (high blood sugar levels) if you have underlying diabetes or pre-diabetes. This is only a problem for a patients' health if blood sugar levels are extremely high and are left like this for a long time. If you notice being more thirsty or needing to urinate more often, you may have high blood sugar levels.

Ketoacidosis

Ketoacidosis is a serious problem that happens to people with diabetes when chemicals called "ketones" build up in their blood. In extreme cases, it can be fatal. It occurs mainly in people with diabetes who make little or no insulin, which is the hormone that allows the body to use sugar as a source of energy.

Normally, the body breaks down sugar as a source of energy. However, in people with diabetes who do not make sufficient insulin, the body is unable to use sugar. Instead the body burns fat as a source of energy; but burning fat can cause too many ketones to be made, and when they build up in the blood, they can be toxic.

You can reduce your chances of getting ketoacidosis if you avoid losing too much water (dehydration) and do not start any diet with very low carbohydrate intake (low-carb diet, e.g. Atkins diet) since such diets might increase the production of ketones in your body. In case you have already started a low-carb diet, you should stop that diet. Reducing alcohol intake also reduces your risks of developing ketoacidosis.

If you are on insulin therapy, you can reduce your chances of getting ketoacidosis by taking your insulin exactly as directed, and measuring your blood sugar often to make sure it is not too high or too low.

Your risk for ketoacidosis might be increased

- if you have fever
- if you had ketoacidosis in the past
- if you have or have had problems with your pancreas, including pancreatitis or surgery on your pancreas.

It is important that you inform your trial doctor about such conditions.

When taking empagliflozin, ketoacidosis could occur even at normal or near-normal glucose levels. Signs and symptoms of ketoacidosis include:

- nausea (feeling sick)
- vomiting (being sick)
- abdominal (tummy) pain
- loss of appetite
- shortness of breath
- rapid heartbeat (tachycardia)
- rapid breathing, where you breathe in more oxygen than your body actually needs (hyperventilation)
- low blood pressure (hypotension), which can make you feel dizzy and lightheaded
- a noticeable smell of ketones on your breath, which is often described as smelling like pear drops or nail varnish remover (not everyone is able to smell ketones)
- mental confusion
- unconsciousness (coma)
- general malaise
- any other unspecific symptoms

If ketoacidosis is suspected, hospital treatment is needed, so you should immediately refer yourself to hospital and/or your trial doctor, or contact an emergency physician if you think you might have it.

Necrotising fasciitis of perineum (Fournier's Gangrene)

Necrotising fasciitis of perineum is an extremely rare serious bacterial infection that destroys the tissue under the skin (necrotising fasciitis) in the area between your anus and genitals (perineum) that can cause death. Necrotising fasciitis of the perineum has happened in women and men who take SGLT2 inhibitor including empagliflozin. Necrotising fasciitis of the perineum may lead to hospitalisation and may require multiple surgeries. Seek medical attention immediately if you have fever or you are feeling very weak, tired or uncomfortable (malaise) and you develop any of the following symptoms in the area between and around your anus and genitals:

- pain or tenderness
- swelling
- redness of skin (erythema)

An antidote, a treatment to counter-act the effects of empagliflozin, is not available. If you have side effects or adverse events from empagliflozin, they will have to be treated as symptoms occur.

Synacthen® (or another brand) – for ACTH Challenge Test

Serious side effects:

Anaphylactic shock or severe allergic reaction symptoms may include redness or pain at the injection site, rash, itching, hives or flushing, dizziness, feeling or being sick, difficulty breathing, and swelling of the face, lips, tongue or other parts of the body, feeling very unwell. This tends to be more severe in people who suffer from allergies (especially asthma). For these reasons, you will be monitored carefully for 30 minutes after the injection. If you have had an allergic reaction with Synacthen® (or another brand), you should never receive Synacthen® Ampoules or similar medicines again and you will not be able to participate in this study.

- bleeding into the adrenal gland (small glands above the kidneys) which may result in sudden stomach or back pain, weakness, fainting, loss of appetite and feeling or actually being sick
- blood clot (symptoms may include pain, swelling, redness, warmth and tenderness in the area of the clot depending on location in the body)

If you experience any of these at any time, tell your doctor straight away or go immediately to the nearest hospital accident and emergency department.

There are other side effects which may occur with Synacthen®. They usually occur after using Synacthen® for a long time, which will not happen in this trial. Your trial doctor will explain the known risks and discomforts to you. There may be other risks of ACTH challenge test that are currently unknown.

INFORMATION ON BIRTH CONTROL

For Female Trial Participants

No studies have been done on empagliflozin in pregnant women or women who are nursing their infant. It is not known if BI 690517 or empagliflozin are safe for pregnant women, unborn babies

and infants who are nursing and it is possible that if BI 690517 or empagliflozin is given to a pregnant woman it might harm the unborn child. Animal studies with drugs similar to empagliflozin (other SGLT-2 inhibitors) have identified a risk to kidney development when that drug was taken during the second or third trimester of pregnancy. Empagliflozin has not been similarly tested in humans.

As with any trial drug, the effect of BI 690517 or empagliflozin on the unborn child is unknown and unforeseeable.

If you decide to take part in this trial and you are able to become pregnant, you must be willing to have a pregnancy test done before you take trial drug, regularly during the trial and at the end of the trial. You must also avoid becoming pregnant while you take part in this trial. You cannot participate in this trial if you are pregnant, breastfeeding, or plan to become pregnant during your trial participation.

You must use two methods of birth control throughout the trial, and for a period of at least 7 days after last trial drug intake. One of these should be a barrier method, such as a condom. The other should be a highly effective method of birth control. Your trial doctor will talk to you about which of the following methods of birth control are suitable for you. Examples are:

- Combined (oestrogen and progestogen containing) hormonal birth control that prevents ovulation (oral, intravaginal, transdermal).
- Progestogen-only hormonal birth control that prevents ovulation (oral, injectable, implantable).
- Intrauterine device (IUD) or intrauterine hormone-releasing system (IUS).
- Bilateral tubal occlusion
- Abstain from male-female sex. Abstinence is only acceptable if this is part of your usual lifestyle. Periodic abstinence e.g. calendar, ovulation, symptothermal, post-ovulation methods; declaration of abstinence for the duration of exposure to trial drug; and withdrawal are not acceptable.

You do not need to use birth control to be in this study if you are not able to get pregnant due to being postmenopausal (2 years without your period without another medical cause) or have had one of the following: both ovaries removed, a hysterectomy (removal of the uterus), or both fallopian tubes removed.

If you are pregnant or think you could be pregnant, it is important for you to tell the trial doctor or trial staff immediately. If you become pregnant during the trial, you will discontinue trial drug and 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 Trial Participants

The effect of empagliflozin and BI 690517 on sperm is unknown. Because the study drugs may affect an unborn child, you should not father a child while taking part in this study. You should tell your partner that you are participating in this research study.

If you decide to take part in this study, and your female sexual partner is able to become pregnant, then you must be vasectomised with documented absence of sperm or you must use a condom or abstain from male-female sex while you are taking the study drugs and for 7 days after the last dose of drug. Abstinence is only acceptable if it is part of your usual lifestyle. If you choose abstinence (not to have sex) as your method of birth control, you must completely avoid having vaginal sex with your partner. Periodic abstinence e.g. calendar, ovulation, symptothermal (signs of ovulation), post-ovulation methods, declaration of abstinence while taking the study drugs, and withdrawal are not acceptable.

Contraception is not mandatory for your female sexual partner.

You should tell your female sexual partner that you are participating in this trial. If your partner becomes pregnant, you must tell the trial doctor about the pregnancy. The trial doctor will ask you for your female partner's contact information and consent to obtain information on the pregnancy and the outcome for the mother and baby and notify the Sponsor (Boehringer Ingelheim) of the pregnancy.

Risk associated with the study procedures

The trial doctor or the trial staff will go through the description of the trial procedures and related risks with you. Please ask any questions you might have. In addition to the risks listed, there is always the chance of developing risks which are not known at this time.

Table 2: Description of study procedure and risks

Procedure	Description and Risks
ACTH challenge test	**Description:** • This tests the function of your adrenal glands which are located near your kidneys. • ACTH is the abbreviation for adrenocorticotrophic hormone, which is a hormone released by the pituitary gland. • It stimulates the production and release of cortisol (a steroid hormone) which is produced by adrenal glands. • An initial blood sample is collected and then synthetic ACTH (Synacthen® or equivalent) is injected into a muscle or a vein. • An additional blood sample is taken 30 minutes after the ACTH injection to evaluate if your body produces enough cortisol which is a signal that your adrenal gland is working correctly.

Procedure	Description and Risks
	Risks: • As with all blood sampling, there is a risk of mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. • Furthermore, there is a small risk of light-headedness and/or fainting. • In rare cases, the puncture site can also become infected or nerves may be damaged, inducing long-lasting abnormal sensations (paresthesia), impaired sensation of touch and persistent pain. • For further information regarding risks of ACTH administration please refer to Section 9 "What are the possible risks and disadvantages of taking part?"
Blood tests	**Description:** • This is a diagnostic test of your blood that may be used to ensure your safety by checking that your organs are functioning normally. • Blood samples will be drawn from a vein in your arm. • The table below shows the approximate number of blood samples that will be drawn over the course of the trial and the approximate volume of blood collected. • If you participate in the optional biobanking additional blood will be collected. This is detailed in the separate consent form. **Risks:** • As with all blood sampling, there is a risk of mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. • Furthermore, there is a small risk of light-headedness and/or fainting. • In rare cases, the puncture site can also become infected or nerves may be damaged, inducing long-lasting abnormal sensations (paraesthesia), impaired sensation of touch and persistent pain. • Frequent blood collection may cause anaemia (low red blood cell count), which may create a need for blood transfusions.

Procedure	Description and Risks

	Volume per blood draw (ml)	Number of blood draws	Estimated Total amount (ml)
Safety	Between 8 ml *(1.5 teaspoons)* and 18.5 ml *(3.5 teaspoons)* depending on the visit	11	135
Cortisol	2.5 *(0.5 teaspoons)*	10	25
Pregnancy *(if applicable)*	5 *(1 teaspoon)*	1	5
Biomarkers	4 *(1 teaspoon)*	5	20
Pharmacogenomic	8.5 *(1.5 teaspoons)*	1	8.5
Pharmacokinetic (PK)	2 *(0.5 teaspoons)*	35	70
Aldosterone profile	6 (*1 teaspoon*)	20	120

eGFR is analysed from the safety samples

It is expected that in total approximately 390ml will be taken over the course of a trial. This figure may vary slightly as there may also be occasions where a blood draw needs to be repeated. The total amount is less than a single blood donation (470ml).

Vital signs: heart rate and blood pressure	**Description:** • The act of taking vital signs is the recording of pulse rate (or heart rate) and blood pressure. • A blood pressure test measures the pressure in your arteries as your heart pumps. **Risks:** • These are routine procedures with little risk. • When the blood pressure test is done the squeezing of an inflated blood pressure cuff on your arm may be uncomfortable. It usually takes only a few seconds.
ECG (electrocardiogram)	**Description:** a painless test which measures the electrical activity of your heart. **Risks:** there may be some skin irritation from the ECG electrode pads or pain when removing these pads from your chest.

Procedure	Description and Risks
Physical examination	**Description:** A routine manual examination your trial doctor performs to check your overall health. **Risks:** This examination generally produces little pain or discomfort.
Pregnancy test	**Description:** • A pregnancy test measures a hormone in the body called human chorionic gonadotropin (HCG). This hormone is present in your body when you are pregnant. • A pregnancy test is done using your blood or your urine. You cannot participate in a clinical trial if you are pregnant or planning to become pregnant. **Risks:** • As with all blood sampling, there is a risk of mild pain, local irritation, bleeding or bruising (a black and blue mark) at the puncture site. • Furthermore, there is a small risk of light-headedness and/or fainting. • In rare cases, the puncture site can also become infected or nerves may be damaged, inducing long-lasting abnormal sensations (paresthesia), impaired sensation of touch and persistent pain.
Urine test (urinalysis)	**Description:** • Urine tests for safety are used to look for the presence of red blood cells (high levels of protein) which may indicate a kidney problem and excreted minerals that can cause kidney stones. • A sample of your urine is also likely to be checked for bacteria that cause infection. **Risks:** Because this procedure involves normal urination, there should not be any discomfort and no known risks.
First Morning Void (FMV) urine	**Description:** The First Morning Void urine sample is the first urination of the day. Urine collected for the First Morning Void sample will be analysed for Urine Albumin Creatinine Ratio (UACR). **Risks:** Risks as described above for “Urine Test”
24-hour urine collection	**Description:** • 24-hour urine collection is performed by collecting a person's urine in a special container over a 24-hour period. • The 24-hour collection may begin at any time during the day, however, it is common to start the collection the first thing in the morning. It is important to collect all urine in the following 24-hour period. **Risks:** Risks as described above for “Urine Test”

10 What will happen to my test samples?

The biological samples collected from you during the trial as described under the section "Study Procedures" and Table 1 and 2 will be stored, processed, and used under your code number for the purposes of this trial for analyses.

- Blood samples for safety, estimated glomerular filtration rate (eGFR) and pregnancy test (if applicable)
  - These will be collected by the site staff and sent to a laboratory.
  - The safety and pregnancy samples are used to monitor your health and to make sure it is safe for you to participate/continue in the trial. eGFR is used to see how healthy your kidneys are.
  - After they have been analysed the samples will be destroyed.
- Blood samples for pharmacokinetics
  - These will be collected by the site staff and sent to a laboratory.
  - They are used to show how your body absorbs, breaks down, and removes the trial drug in the blood.
  - The samples may be used after analysis for further investigations. They will be discarded no later than 5 years after signature of the final clinical trial report.
- Blood samples for aldosterone (and cortisol and other steroid hormones)
  - Plasma samples will be collected by the site staff and sent to the Sponsor and other members of the Boehringer Ingelheim Group of Companies and those working with the Sponsor.
  - The samples will be used to measure the amount of aldosterone (and other steroid hormones) over time.
  - The samples may be used after completion of the clinical trial for further investigations related to this. They will be discarded no later than 2 years after the last patient has completed the trial.
- Blood samples for biomarkers
  - This will be collected by the site staff and sent to a laboratory.
  - Biomarkers are biological molecules that help to show how healthy your kidneys are.
  - The samples will be discarded no later than 2 years after the last patient has completed the trial.
- Blood sample for pharmacogenomics testing
  - This will be collected by the site staff and sent to a laboratory.
  - This test looks at a special type of molecule called deoxyribonucleic acid, or DNA for short. DNA is what your genes are made of.

- Looking at your DNA and how you respond in this trial and comparing it to other participants' DNA and how they responded might help to explain why responses to medicines or the intensity of side effects vary from person to person. These tests may also help to learn more about kidney disease.
- The samples will be analysed and destroyed no later than 2 years after the last patient has completed the trial.

- Urine Sample collected during the visit
  - Urine will be collected during the visit, processed by the site staff and sent to a laboratory.
  - You should only need to provide one sample for all of the following tests: safety, biomarkers and (if applicable) pregnancy.
  - The samples for safety and pregnancy will be destroyed after analysis.
  - The samples for biomarker analysis will be destroyed once a separate biomarker report has been written no later than 2 years after the last patient has completed the trial.

- Urine samples collected at home
  - These are the samples mentioned in section "Trial Procedures" that you will collect yourself.
  - The samples will be sent to a laboratory for analysis.
  - After they have been analysed the samples will be destroyed.

To minimise the amount of blood and urine taken, where possible the samples mentioned above will be collected in one or two tubes and then separated out by the site staff.

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.

Overseas Laboratory	
Central Laboratory	LabCorp (Asia) Pte. Limited 1 International Business Park #01-01 The Synergy Singapore 609917

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. 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.

13 What if I withdraw from this research project?

You may choose not to take trial drug or to leave this trial completely at any time. 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.

It is important that you tell the trial doctor if you are thinking about stopping or have decided to stop so your trial doctor can evaluate the risks of stopping treatment with BI 690517, empagliflozin or placebo. If you need to stop either the background medication or the study medication, for example if you have side effects, it may be possible to continue to take the other medication for the rest of the trial.

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 all trial drugs, you will be asked to come in for an End of Treatment visit (EoT). After the EoT visit Follow-Up Visit 1 (FUp1) will be performed a week later. This visit is important so that we can follow-up on any adverse events (side effects) you may have had. There is one further visit Follow-Up Visit 2 (FUp2) which is the last visit in the trial. In between FUp1 and FUp2 you will also be asked to perform home-sampling – please see the 'Trial Procedures' section and Appendix A. If you're willing you will be asked to do these visits and home-sampling so that we can collect information about how your kidneys are functioning during this time.

- **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 drug and participation, then the final assessments (End of Treatment) listed in Appendix A should be completed as soon as possible. This is important for your safety and well-being. In addition, you

must return all unused trial drug. 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.

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

Your trial doctor might decide to stop your trial drug(s) or trial participation early without your consent when, in the trial doctor's judgment, it is in your best health interest to do so. Some of the reasons why this might happen are listed below:

- Your condition worsens or does not improve or you need to take an alternative treatment that is not allowed in the trial.
- The trial treatment or procedures are found to be unsafe or ineffective.
- Your inability to take the trial drug / participate as instructed.
- You become pregnant
- Cancellation by the Sponsor or regulatory authority.
- Or for 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/treatment being shown not to be effective
- The drug/treatment 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 the treatment ends you will not be able to continue receiving the study drug. Your study doctor will speak with you about your treatment options after the study ends.

A description of this clinical trial will be available on http://www.ClinicalTrials.gov. 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.

The results of the trial will be published on the sponsor's trial website (http://trials.boehringer-ingelheim.com). The results may also appear in other clinical trial registries in countries in which the trial is conducted. 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, remain at the trial site, in paper or electronically, and can be accessed, by the trial doctor and other people who are assisting with the trial and your care.

This information may also be checked 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 Therapeutic Goods Australia (TGA), the U.S. Food and Drug Administration (FDA) and European Medicines Agency (EMA) that approve medicines.

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

Courier collections/ deliveries

When couriers are used during this trial the trial team will provide the courier with your name and your address. After delivery/ collection, the record of your name and address will be deleted from the courier's system. Only your trial doctor or a member of their team will be able to link the shipment information to your identity.

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 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 EU 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 patients. Nevertheless, other results which may be of medical importance specifically for you and other trial patients 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 and his/her team (e.g the study nurse). 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 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.

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.

- 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 Pty Ltd.

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

By taking part in this research project you agree that samples of your blood or tissue (or data generated from analysis of these materials) may be provided to Boehringer Ingelheim Pty Ltd.

Boehringer Ingelheim Pty Ltd may directly or indirectly benefit financially from your samples or from knowledge acquired through analysis of your samples.

You will not benefit financially from your involvement in this research project even if, for example, your samples (or knowledge acquired from analysis of your samples) prove to be of commercial value to Boehringer Ingelheim Pty Ltd.

In addition, if knowledge acquired through this research leads to discoveries that are of commercial value to Boehringer Ingelheim Pty Ltd, 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.

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	Gabrielle Garner
Position	Study Coordinator
Telephone	(03) 9094 9523
Email	gabrielle.garner@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
HREC Executive Officer	HREC Executive Officer
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

Eastern Health

Consent Form - *Adult providing own consent*

Box Hill Hospital

Title	Randomised, double-blind, placebo-controlled and parallel dose group trial to investigate efficacy and safety of multiple doses of oral BI 690517 over 14 weeks, alone and in combination with empagliflozin, in patients with diabetic and non-diabetic chronic kidney disease
Short Title	A study to test whether different doses of BI 690517 alone or in combination with empagliflozin improve kidney function in people with chronic kidney disease
Protocol Number	1378-0005
Project Sponsor	Boehringer Ingelheim Pty Ltd
Principal Investigator	Prof Christopher Gilfillan
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 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
- Other research that is closely related to this research project

By signing this consent section, I agree to the use of my tissue samples for genetic testing, as outlined in the relevant Section 10 “What will happen to my test samples” of the Participant Information Sheet.

I agree that the trial doctor or trial staff can contact me by phone and/or video calls and I will provide information about my health status.

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.

<Optional (You do not have to answer Yes to still participate in the trial):

Yes	No
☐	☐

I agree to the courier company visiting my home to deliver study drug and pick up urine samples, and that for this purpose, my contact details will be passed on to the third-party courier company.

Declaration by Participant – for participants who have read the information

Name of Participant (please print) _____

Signature _____ Date _____

Declaration - for participants unable 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 not to be the Investigator, a member of the study team or their delegate. 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.

Eastern Health

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

Box Hill Hospital

Title	Randomised, double-blind, placebo-controlled and parallel dose group trial to investigate efficacy and safety of multiple doses of oral BI 690517 over 14 weeks, alone and in combination with empagliflozin, in patients with diabetic and non-diabetic chronic kidney disease
Short Title	A study to test whether different doses of BI 690517 alone or in combination with empagliflozin improve kidney function in people with chronic kidney disease
Protocol Number	1378-0005
Project Sponsor	Boehringer Ingelheim Pty Ltd
Principal Investigator	Prof Christopher Gilfillan
Location	Box Hill Hospital – Arnold Street, Box Hill VIC 3128, Australia

Declaration by Participant

I wish to withdraw from participation in the above research project and understand that such withdrawal will not affect my routine treatment, my relationship with those treating me or my relationship with Eastern Health.

Name of Participant (please print) _____

Signature _____ 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.