Participant Information Sheets and Consent Form

A Randomised Controlled Trial of Antenatal **Me**latonin Supplementation in Fetal Growth Restriction for Fetal Neuro**protect**ion.

The **PROTECT Me** trial

Project Sponsor	Monash Health
Principal Investigators	

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Location	<<insert site name>>
Project Number	<<insert site specific HREC number>>
Site Investigator	<<insert site investigator name>> <<insert site investigator affiliations>>

Part 1 What does my participation involve?

1 Introduction

You are invited to take part in this clinical trial (research project) because you are pregnant and your baby has been identified as having fetal growth restriction (FGR).

This Participant Information Sheet/Consent Form tells you about the research project. It will explain what participation involves. Knowing what is involved will help you decide if you would like to take part in the research, or not.

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 your partner, a relative, friend, or the doctor or midwife looking after you.

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 choose to take part.

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

- understand what you have read
- 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 these Participant Information Sheets and signed Consent Form to keep.

2 What is the purpose of this research?

The researchers are undertaking this research project in order to look at the use of *melatonin* as a way of protecting the developing brain of a baby with fetal growth restriction (FGR) during pregnancy.

FGR is a condition of pregnancy where the fetus (baby) does not grow at the rate that would be expected for their gestation. There are many causes of FGR, but the most common cause is because the placenta is not working as well as it could be. When compared to a placenta from a pregnancy that does not have FGR, a placenta from an FGR pregnancy is quite different. A placenta from a FGR affected pregnancy often does not receive or transport oxygen as easily to the fetus. This results in a relative lack of oxygen and the development of what is known as '*oxidative stress'* within both the FGR placenta, as well as within the FGR baby's body. *Oxidative stress* is believed to be harmful to a FGR baby's developing brain. For FGR babies during pregnancy, *oxidative stress* is one of the reasons why, after they are born, some FGR babies can have problems with their development and need extra support, especially if they were also born very early (preterm). For example, compared to those who did not have FGR, infants and children who had FGR are more prone to have poorer neurodevelopmental outcomes such as: learning disabilities, cerebral palsy and behavioural disorders. While not every baby who has FGR will be affected in this way, we know that FGR does increase the risk of conditions such as these occurring.

At this time, there are no treatments which can minimise, or even prevent, the adverse effects of *oxidative stress* on the developing brain of a FGR baby during pregnancy.

Our previous research work at Monash Health and Monash University has shown that *melatonin*, a naturally occurring hormone and powerful anti-oxidant, maybe useful as a potential treatment to protect the FGR baby's developing brain from *oxidative stress* during pregnancy. Therefore, a team of senior medical and scientific researchers, who are all recognised experts in their respective fields, have designed this research project. The aim of the research project is to find out if *melatonin* can reduce the effects of *oxidative stress* and **PROTECT** the baby's brain during pregnancy and ultimately lead to improved immediate and long-term (2 years) neurodevelopmental outcomes for the baby after it has been born.

The use of *melatonin* in human pregnancy as a potential therapy in FGR and pre-eclampsia (high blood pressure in pregnancy) has already been studied before at Monash. However, these two clinical research projects were small, preliminary, safety studies and while the results from both of these studies was encouraging, *melatonin* has not been used in a large, randomized, research project specifically for the purpose of fetal neuroprotection during pregnancy. Therefore, the use of *melatonin* in this research project is regarded as 'experimental'.

3 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 *Monash Health as well as <<insert study site name>>*.

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.

4 What does participation in this research project involve?

If you agree to participate in this research project, it will involve the following:

Consent

- We will ask you to read these Participant Information Sheets and sign the Consent Form.

To make sure that all the information obtained from the research project is reliable and the best it can be, we have chosen to undertake the research project as a *randomised controlled trial (RCT*). The RCT is regarded as the best way to test drugs, such as *melatonin*, for a specific purpose. The RCT method uses a process called 'randomisation' (like the flip of a coin) to allocate patients to the different study groups. Randomisation tries to make sure that the patients in each of the study groups are similar, and at the end of the research project, it allows us to interpret the results in a fair and appropriate way without jumping to conclusions.

The randomisation method of allocation means that you have an equal chance of being placed in either group. So as not to influence the results, neither you, the people caring for you or the researchers are able to choose the group that you are placed into.

Randomisation

- Using randomisation, we will allocate you into **one** of the two study groups: either to receive *melatonin* tablets **or** to receive tablets that do not contain any *melatonin* ('a placebo').

Trial Intervention

- The intervention for this trial are tablets containing either: *melatonin* 10mg or 'a placebo', i.e. a tablet(s) that does **not** contain any *melatonin.* Taking part in the research project will require you to take the tablets three times a day, by mouth, until you have given birth
- We will ask you to keep a record of all the tablets you have taken and to also make a note of how the tablets make you feel.

Maternal blood sample collection

We would like you to allow us to collect some blood from you, at these time points:

- The first blood sample(s) will be collected from you before you take any of the trial tablets*
- Further blood samples will be collected at 48 hours (+/- 24 hours) and at 14 days (+/- 2 days) after you have started taking the trial tablets
- Around the time of birth, a further blood sample will be collected from you

* During and after your pregnancy, blood samples may be undertaken regularly (e.g. daily, alternate days, weekly) as part of your routine, clinical care. The doctors looking after you request for these blood samples to be taken because it is necessary to check your blood count, liver and kidney function while you are pregnant, to ensure that you are keeping well. This information is also important to the researchers, so for the purposes of the research project, we will record these blood results. We will always endeavour to collect any research blood tests at the time you are undertaking clinical tests if possible, however some extra blood tests may sometimes be necessary.

For the research project, blood collected from you during pregnancy and when you have your baby will be used to measure levels of *melatonin* and *oxidative stress* by the researchers. **N.B**. It is important to note that the results from these blood tests will not be used, or indeed useful, to help make any clinical decision or diagnosis, for you or your baby now, or in the future.

Each blood sampling for the research project will not exceed 20mL of blood, this volume is equivalent to approximately 1 (one) tablespoon. This volume of blood can safely be collected from you, in addition to any blood required for routine, clinical care, without risk of harm to you or your baby.

Sometimes it may be necessary to repeat a blood collection, for example, if a result is borderline or raised or not enough blood can be collected. If we need to collect any additional blood sample(s) from you for either routine, clinical care or the research project, we will explain the reason to you and only proceed with your (verbal) consent.

Participant (maternal) surveillance

- Fortnightly

- Take and record your blood pressure
- Record your weight
- Test your urine i.e. urinalysis (dipstick) to look for protein in your urine

Placenta and umbilical cord blood tissue collection

After you have given birth and the placenta has completely separated from both you and your baby, we would like to collect:

- A sample of blood (10mL, or less) from the umbilical cord

- A sample of the placenta

We do not need to touch your baby to be able to collect these tissue samples

These placenta and umbilical cord blood samples will be used to measure levels of *melatonin* and any markers of *oxidative stress*.

Ultrasound scans and Doppler waveform studies

All pregnancies with FGR will be closely monitored using ultrasound scans and Doppler waveform studies, and this will not change with your participation in the research project.

The ultrasound and Doppler studies that are a necessary component of the research project will include:

- On the day of recruitment
    - Ultrasound scan to measure your baby's growth
    - Ultrasound scan to measure the amniotic fluid ('waters') around your baby and a Doppler waveform study to measure the blood flow in different blood vessels in your baby and within the umbilical cord.
    - Doppler waveform study to measure the blood flow in your uterine (womb) arteries.

Thereafter, *at least*:

- *48 hours after taking the first dose of trial tablets*
    - *Ultrasound scan to measure the amniotic fluid ('waters') around your baby and a Doppler waveform study to measure the blood flow in different blood vessels in your baby and within the umbilical cord.*
    - *Doppler waveform study to measure the blood flow in your uterine (womb) arteries.*

- *Fortnightly (i.e. every 2 weeks)*
    - Ultrasound scan to measure your baby's growth
    - Ultrasound scan to measure the amniotic fluid ('waters') around your baby and a Doppler waveform study to measure the blood flow in different blood vessels in your baby and within the umbilical cord.
    - Doppler waveform study to measure the blood flow in your uterine (womb) arteries.

In addition:

- Permit us to record the information (measurements) from any other ultrasound scans and Doppler waveforms studies that are performed as part of your routine, clinical care during pregnancy.

Because ultrasound scans and Doppler studies are already undertaken as part of routine, clinical care in a pregnancy with fetal growth restriction (FGR), it is likely that we will not need to repeat these studies specifically for the purposes of the research project, as we can simply collect the information that we need from those 'routine' reports. However, if the ultrasound scan and/or Doppler studies have not been performed as part of your routine clinical care, then the researchers will arrange for the study to be performed specifically for the purposes of the research project.

Collection and use of information about you and your baby

- To assist us to understand and present the results from our research project we will need to collect relevant information from your hospital records and those of your baby with regard to: your health, pregnancy (including ultrasound and Doppler studies), birth and postnatal period and then subsequently, your child up to 2 years of age.

- Permit us to use the final, combined, results (only) from all the participants in this research project in the planning of future, related research projects for which HREC (Human Research Ethics Committee) approval will be sought and obtained.

Follow-up of your baby

- General assessment

  Following birth, for one week, we would like to record your baby's wellbeing. This will include asking you to keep a daily record of their sleep and feeding patterns. This can be done by permitting the researchers to access your baby's feeding charts or, if you prefer, we can give you a form and you can complete the information in collaboration with nursing staff. Should your baby go home before they are 1 week of age, then we ask for you to record their sleep-feed cycles.

- Neurological assessments

  The purpose of the research project is to find out if the administration of *melatonin* to the mother during pregnancy, protects the developing brain of her baby. Therefore, it is important that we are able to do some neurodevelopmental assessments on your baby after they have been born. These assessments will include:

- Magnetic Resonance Imaging (MRI) is a medical imaging procedure that uses a magnetic field and radio waves to take pictures of the body's interior. It is a very safe and a non-invasive procedure. This means that no ionizing radiation (unlike the case with x-rays) is used to create images. The images are analysed by a specialist doctor called a clinical radiologist. For the research project, the MRI will be performed once. The MRI will be carried out on your baby around the date your baby would have been due.

- General Movement Assessment (GMA) is a non-invasive measure of spontaneous infant movements; the movements are assessed using video recordings collected through a smartphone App called Baby Moves. For the research project, the GMA will be performed three times. The first time will be around the date your baby would have been due. The second at 12 weeks corrected age (± 1 week) and the third time will be at 14 weeks corrected age (± 1 week). This will involve you collecting a three-minute video of your baby using the App.

  For many babies who are born early, the GMA assessment is already part of their routine, clinical care and will be performed while they are in hospital, in which case there may not be a need to repeat it for the research project. However, if your baby has already gone home when the GMAs are due, and you do not wish to use the App to perform the GMA, you have the option to come back to the hospital to undertake these studies.

- Bayley Scales of Infant and Toddler Development 4th edition (Bayley-4): performed around 2.5 years (± 6 months), corrected age. The Bayley-4 assesses developmental functioning of infants, including assessment of, for example, movement, thinking and response to situations around them. The Bayley-4 may require a single visit back to the hospital.

- Infant Toddler Social-Emotional Assessment (ITSEA): performed around 2.5 years (± 6 months), corrected age. The ITSEA is a social-emotional and behavioral assessment. This is a questionnaire you can complete from home.

The results of any of the neurodevelopmental assessments performed on your baby/child will be discussed with you, by your treating doctors while your baby is in hospital. After you have gone home, when you return for follow up assessments as part of this research project, the results will be explained to you. Should there be any concerns, this will be discussed with you and ongoing care arranged with the appropriate services.

You will be provided with a Monash Health car parking exemption permit for any follow-up visit required as part of this research project. The exemption permit is for a one time use only and will allow you to park in a Monash Health car park without the need to pay.

Inform your General Practitioner (GP)

- Permit us to send a letter to your GP (family doctor) to inform them that you have taken part in this clinical trial.

Optional component of the research project

The following is an optional, extra component of the research project, this means that if you choose not to do it, you do not have to, but you can still take part in the research project.

Use of tissue samples (maternal blood, umbilical cord blood and placenta) and/or de-identified data/information, in any future, pregnancy/birth fetal growth restriction (FGR) related research projects.

Following the laboratory analysis of your tissue samples (i.e. blood, placenta and umbilical cord blood) for this research project, if any of the tissue samples are left over, instead of throwing them away in the bin as medical waste, we would like to ask you if you would consider allowing us to keep the remaining tissue and your associated de-identifed data (information), to use in any future, pregnancy/birth FGR related, research projects.

The tissue(s) that you donate for any future, related FGR research could one day be used for genetic testing to learn about the role genes play in FGR. Genes are the basic "instruction book" for the cells that make up our bodies and may be passed on from generation to generation within families. Since the significance of any future genetic tests is not known for you, we will not release the results of any genetic testing nor will the results be used in the planning of your clinical care, or that of your child.

However, in the future, before any other researcher can access and use your tissue samples or data (information), they must apply for and be given, Human Research Ethics Committee (HREC) approval before they are permitted to use the tissue and data for their research project.

Optional substudy of the research project

The following is a substudy within the research project and is also completely optional. You can choose not to take part in this substudy but still participate in the research project and/or in another optional component of the study.

We would also like to invite you to complete a questionnaire about fetal movements. This will help to determine the effect of early fetal growth restriction (FGR) and antenatal melatonin therapy on maternal-reported fetal movement strength, frequency and pattern.

If you agree to participate in this substudy, you will be asked to complete a questionnaire on 3 occasions: at enrolment, 2 weeks after randomization and at 34 weeks gestation.

This questionnaire is a modified version of a fetal movement tool preciously used in two New Zealand pregnancy studies and takes around 5-10 minutes to complete.

The questionnaire will be administered electronically, where possible, using the REDCap system. If you don't have email / internet access, a hard copy questionnaire will be available.

5 Do I have to take part in this research project?

No, you don't. 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 research project at any stage.

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 <<insert study site name>>.

If you decide to take part, you will be given this Participant Information and Consent Form to sign, and subsequently, a signed copy of these documents to keep.

6 What are the alternatives to participation?

You do not have to take part in this research project to receive treatment at this hospital.

Please note that whether you choose to participate in the research project, or not, your routine clinical care does not change, this may include: a need to have regular ultrasound and Doppler studies performed as well as the collection of blood sample(s).

7 What are the possible benefits of taking part?

There will be no clear benefit to you from your participation in this research project. However, we hope that the findings from the research project may change, and improve, the care of mothers with a FGR pregnancy in the future.

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

- Melatonin

Melatonin has previously been tested in pregnant women in research projects and in women undergoing assisted reproduction, e.g. IVF (in vitro fertilization) procedures. These research studies also include those that have previously been conducted at Monash Health. Here, at Monash Health, we have used *melatonin* in two other, small studies as a potential new treatment for mothers who had problems in their pregnancies, such a pre-eclampsia (high blood pressure in pregnancy) and fetal growth restriction (FGR). These mothers received *melatonin* at similar doses to this trial. In those other studies women took melatonin for many days, or weeks. No side effects or adverse effects of melatonin on either a mother or her baby has been reported.

Animal studies to specifically investigate harmful effects of the use of melatonin during pregnancy have not shown any damage to the mother or fetus. These animal studies have used doses of

melatonin that would be equivalent to a 100-times higher than the dose that we use in this study. As a result of this, *melatonin* has been assigned a TGA (Therapeutic Goods Administration) category B3 – a safe drug.

Melatonin has an excellent safety profile. As with any other medicine it can cause adverse reactions. These are considered to be **rare** i.e. likely to occur in fewer than 1 in 1,000 patients, and may include:

Irritability, nervousness, insomnia, abnormal dreams, anxiety, migraine, lethargy, psychomotor hyperactivity (restlessness associated with increased activity), dizziness, somnolence (tiredness), high blood pressure, indigestion/reflux, mouth ulceration, dry mouth, hyperbilirubinaemia (changes in the composition of your blood which could cause yellowing of the skin or eyes (jaundice), inflammation of the skin (dermatitis), night sweats, pruritis (itching), rash, dry skin, pain in extremities, menopausal symptoms, asthenia (feeling of weakness), chest pain, excretion of glucose in urine, excess proteins in the urine, abnormal liver function, weight gain, reduced number of white blood cells in the blood, decreased number of platelets in the blood, high level of fatty molecules in the blood, severe chest pain due to angina, feeling your heartbeat (palpitations). low serum calcium levels in the blood, altered mood, aggression, agitation, crying, stress symptoms, disorientation, early morning awakening, increased sex drive, depressed mood, depression, loss of consciousness or fainting, memory impairment, disturbance in attention, dreamy state, 'pins and needles' feeling (paresthesia), reduced visual acuity (visual impairment), blurred vision, watery eyes, dizziness when standing or sitting, vertigo, hot flushes,, blistering in the mouth, tongue ulceration, gastrointestinal upset, vomiting, abnormal bowel sounds, flatulence (wind), salivary hypersecretion (excess saliva production), halitosis (bad breath), abdominal discomfort, gastric disorder, inflammation of the stomach lining, eczema, erythema (skin rash), psoriasis, nail disorder, arthritis, muscle spasms, neck pain, night cramps, pain, thirst, passing large volumes of urine, presence of red blood cells in the urine, urination during the night, and abnormal blood electrolytes.

As with any medication, there may be side effects caused by *melatonin* administration that the clinical staff caring for you do not expect or do not know about. Tell your doctor or midwife immediately about any new or unusual symptoms that you get. Please also advise your research midwives via <<insert study coordinator email address>>.

If you are taking any medications, please tell the member of the research team, because some types of medication should not be combined with *melatonin* and as a result you would not be eligible to take part in this research study.

- <u>Maternal blood sample collection</u>

The total volume of blood that you are being asked to provide to this research project, will not cause you harm. With the exception of the blood sample that we collect from you around the time of birth, we will try to collect most/all of the other research blood samples at the same time as the blood is being taken, or an intravenous cannula ('bung') is being sited, as part of your routine, clinical care.

Having a blood sample taken may cause you some discomfort or bruising. Sometimes, the blood vessel may swell, blood may clot in the blood vessel, or the area could become inflamed. Rarely, there could be a minor infection or bleeding. If this happens, it can be easily treated.

- <u>Ultrasound scans and Doppler waveform studies</u>

Both ultrasound and Doppler waveform studies have a strong safety record. For women who have a baby with FGR, frequent ultrasound scans and Doppler studies are an integral component of routine, clinical care. No adverse event from ultrasound in pregnancy has been reported.

- Follow-up of your baby

There are no risks to you or your baby related to any of the follow up assessments for the research project. The results of any of the neurodevelopmental assessments performed on your baby/child will be discussed with you, by your treating doctors while your baby is in hospital, and after you have gone home, results will be provided to you and if any concerns are identified, these will be discussed with you and ongoing care arranged with the appropriate services.

- Other

As with any research project, there may be additional risks that the researchers do not expect or do not know about.

If you do become upset or distressed as a result of your participation in this research project, the researcher is able to arrange for counselling or other appropriate support. Any counselling or support will be provided by qualified staff who are not members of the research team and will be provided free of charge. In addition, you may prefer to suspend or end your participation in the research project if distress occurs.

9 What will happen to my tissue samples?

The tissue samples being collected for this research project are: your (maternal) blood, an umbilical cord blood sample and some placenta. These tissue samples will be collected from you and then stored in The Ritchie Centre, Hudson Institute of Medical Research and the Department of Obstetrics and Gynaecology, Monash University.

- All provided tissue samples will be de-identified immediately at the time of collection and allocated a unique code. This means that any information which could identify you, such as: your name, address, date of birth and hospital record number will be removed before your tissue sample(s) go to the laboratory for the scientists to process.

After the scientists in the laboratory have finished looking at your tissue sample(s) for this research project, should any of your tissue sample(s) remain, instead of throwing the remaining tissue(s) away, we would like to ask you to consider allowing us to keep them for use in any future, pregnancy/birth FGR related research project being undertaken in the department. However, In the future, before your tissue can be used in this way, the researchers must obtain Human Research

Ethics Committee (HREC) approval for their research project before they would be allowed to access and use your tissue sample(s).

On the Consent Page of this document you can indicate your agreement for 'future use' of your tissue if that is something you would like to do. If you would prefer not to allow your tissue(s) to be used in this way, after the scientists have looked at your tissue for this research project, should any remain, we will simply throw it away as clinical waste.

10 What if new information arises during this research project?

Sometimes during the course of a research project, new information becomes available about the treatment that is being studied. If this happens, the researchers will tell you about it and discuss with you whether you want to continue in the research project. If you decide to withdraw, your Principle Investigator will make arrangements for your regular health/clinical care 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, the Principle Investigator might consider it to be in your best interests to withdraw you from the research project. If this happens, the Principle Investigator will explain the reasons and arrange for your regular health/clinical care to continue.

11 Can I have other treatments during this research project?

It is important to tell the researchers 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 the researchers about any changes to these during your participation in the research project.

12 What if I withdraw from this research project?

If you decide to withdraw from the project, please notify a member of the research team. They will organise for you to sign the Withdrawal of Participation Form. Your withdrawal from this research project will in no way affect your routine clinical care, your relationship with those treating you, or your relationship with <<insert study site name>>.

If you do withdraw your consent during the research project, the researchers will not collect any further tissue samples (i.e. maternal blood, umbilical cord blood or placenta) or additional personal information from you. Although you should be aware that any tissue samples or personal information that may have already collected, will be retained and form part of the research project final results. This is necessary to ensure that the results of the research project can be measured properly and to comply with the law. If you do not want the researchers to do this, you must tell them before you join the research project.

13 Could this research project be stopped unexpectedly?

It is unlikely this research project will be stopped unexpectedly but it would be stopped if:

- We discovered that participants in the research project were being compromised in any way.
- The sponsor of the research project, Monash Health, makes a request for the research project to stop.

14 What happens when the research project ends?

Once your baby/child has completed the GMA Bayley Scales of Infant and Toddler Development 4th edition (Bayley-4) and Infant Toddler Social-Emotional Assessment (ITSEA), performed at 2 years, corrected age, your participation in the research project will end. The research project itself will conclude once we have recruited 336 mothers and babies and all the data ('information') collection has been completed.

If you would like a summary of the findings from this research project, please inform the named researcher:

Name	Doctor Kirsten Palmer B.Biomed Sci, MBBS (Hons), PhD, FRANZCOG
Position	Obstetrician and Maternal Fetal Medicine Fellow, Monash Health Research Fellow, Monash University Department of Obstetrics and Gynaecology.
Telephone	Via Monash Medical Centre Switchboard: +61 3 959 46666
Email	kirsten.palmer@monash.edu

15 Other relevant information about the research project

Additional costs
There are no additional costs associated with participating in this research project, nor will you be paid. All the trial tablets i.e. *melatonin or* placebo and investigations that are required to be performed as part of this research project, will be provided to you free of charge.

Research related follow-up visits
You will be provided with a Monash Health car parking exemption permit for any follow-up visit required as part of this research project. The exemption permit is for a one time use only and will

allow you to park in a Monash Health car park without the need to pay.

Part 2 How is the research project being conducted?

16 What will happen to information about me?

By signing the Consent Form, you consent to: the collection and use of your blood samples and any relevant information about you and your baby/child, that is required for the conduct of this Human Research Ethics Committee (HREC) approved research project.

Any information collected about you will only be disclosed to the researchers who are analysing your blood samples, with your permission, except as required by law. Any information will always be disclosed to them in a de-identified form, that is without your personal details, for example: name, initials, date of birth, address, telephone number or hospital record number being attached to it.

Any information obtained in connection with this research project that can identify you will remain confidential. This information will be stored in a locked filing cabinet and password-protected database, accessible only by the research team that have been approved by the Human Research Ethics Committee (HREC).

After the research project has been completed, the information will be securely stored for 23 years by the principal investigator, as currently recommended by the National Health and Medical Research Council (NHMRC) and Monash Health HREC. After this time, all the information will be disposed of in a secure and confidential manner.

In accordance with relevant Australian and Victorian privacy and other relevant laws, you have the right to request access to the information collected and stored by the research team about you. You also have the right to request that any information with which you disagree be corrected.

Please contact the research team member named at the end of this document if you would like to access your information.

Your health records and any information obtained during the research project are subject to inspection (for the purpose of verifying the procedures and the data) by the relevant authorities and authorised representatives of the Sponsor, Monash Health or as required by law. By signing the

Consent Form, you authorise release of, or access to, this confidential information to the relevant named research personnel and regulatory authorities as noted above.

- Information about your participation in this research project will be recorded in your hospital records
- A letter will be sent to your GP (family doctor) to inform them that you have taken part in this research project.
- It is anticipated that the results from this research project will be published and/or presented in a variety of forums. In any publication and/or presentation, information will be provided in such a way that you cannot be identified, except with your permission.

Should you choose to agree to allow us to keep any remaining tissue(s) for use in any future, pregnancy/birth FGR related research project being undertaken in the department, your information (data) will also be kept with it. This is because, future researchers who may use your tissue(s), will also need to understand and interpret their results. Any researcher must obtain Human Research Ethics Committee (HREC) approval for their research project before they would be allowed to access and use your tissue sample(s) and its associated data/information.

17 Injury

If you suffer any injuries or complications as a result of participating in this research project, you should contact the researchers 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 hospital.

18 Who is organising and funding the research?

The research project has been initiated by Professor Euan Wallace, Carl Wood Professor and Head of Department of Obstetrics and Gynaecology, Monash University and will be led by Doctor Kirsten Palmer, Monash Health and Monash University. Professor Wallace and Doctor Palmer are working with a multi-disciplinary team of Monash Health and Monash University, senior medical and scientific researchers, who are all recognised experts in their respective fields. The project has been funded by several, different research awards made to the researchers for the purposes of furthering research into fetal growth restriction (FGR) and fetal neuroprotection. These include awards from: Equity Trustee's, Monash University and The Cerebral Palsy Alliance.

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

19 Further information and who to contact

The person you may need to contact will depend on the nature of your query.

If you would like any further information concerning this research 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:

Lead Principal investigator:

Name	<<insert site investigator name>>
Position	<<insert position of site investigator>>
Telephone	<<insert site investigator phone number>>
Email	<<insert site investigator email address>>

Study coordinator:

Name	<<insert site study coordinator>>
Position	<<insert study coordinator position>>
Telephone	<< insert study coordinator phone number>>
Email	<<insert study coordinator email address>>

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	<<insert name of HREC>>
HREC Executive Officer	<<insert name and role of HREC representative>>
Telephone	<<insert HREC phone number>>
Email	<<insert HREC email address>>

Consent Form

The **PROTECT Me** trial

A Randomised Controlled Trial of Antenatal **Me**latonin Supplementation in Fetal Growth Restriction for Fetal Neuro**protect**ion.

Project Sponsor	Monash Health
Project Number	<<insert site specific HREC number>>
Location	<<insert site name>>
Principle Investigators	<<insert site specific investigator/s>>

Declaration by Participant

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree to participate in this research project as described and I understand that I am free to withdraw at any time during the research project without it affecting my future health care.
- I understand that my General Practitioner (GP) will be informed of my participation in this research project.
- I understand that I will be given a signed copy of this document to keep.

Optional component of the research study

Select **one** box only:

☐ I agree to the use of my tissue samples (maternal blood, umbilical cord blood and placenta) and de-identified data/information in this research project only.

☐ I agree to the use of my tissue samples (maternal blood, umbilical cord blood and placenta) and de-identified data/information, in this research project and also in any future, pregnancy/birth fetal growth restriction (FGR) related research project, which has sought and received, HREC approval. I understand that any future, related research may involve genetic testing.

Name of participant (Please PRINT):

Signature: Date:

Declaration by 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 the 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.

<<insert logo here>>

Consent Form (baby/child)

The **PROTECT Me** trial

A Randomised Controlled Trial of Antenatal **Me**latonin Supplementation in Fetal Growth Restriction for Fetal Neuro**protect**ion.

Project Sponsor	Monash Health
Project Number	<<insert site specific HREC number>>
Location	<<insert site name>>
Principle Investigators	<<insert site specific investigator/s>>

Declaration by Participant

- I have read the Participant Information Sheet or someone has read it to me in a language that I understand.
- I understand the purposes, procedures and risks of the research described in the project.
- I have had an opportunity to ask questions and I am satisfied with the answers I have received.
- I freely agree for my baby/child to participate in this research project as described and I understand that I am free to withdraw my baby/child at any time during the research project without it affecting the future health care of my baby/child.
- I understand that my General Practitioner (GP) will be informed of my baby/child's participation in this research project.
- I understand that I will be given a signed copy of this document to keep.

Name of participant (baby/child) (Please PRINT):

Name of Parent/Guardian (Please PRINT):

Signature of Parent/Guardian: Date:

Declaration by 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 the 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.

<<insert logo here>>

Form for Withdrawal of Participation

The **PROTECT Me** trial
A Randomised Controlled Trial of Antenatal **Me**latonin Supplementation in Fetal Growth Restriction for Fetal Neuro**protect**ion.

Project Sponsor	Monash Health
Project Number	<<insert site specific HREC number>>
Location	<<insert site name>>
Principle Investigators	<<insert site specific investigator/s>>

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 <<insert study site name>>.

Name of Participant (please PRINT):

Signature: Date:

In the event that the participant's decision to withdraw is communicated verbally, the researcher will need to provide a description of the circumstances below.

Declaration by the 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 the 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.