Participant Information Sheet

We invite you to take part in a research study called

The PEARL Study
Pregnancy and EARly Life

Before you decide whether to take part, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with relatives and friends if you wish. You are free to decide whether or not to take part in this study. If you choose not to take part, this will not affect the care you get from your own Doctors.

A copy of this Information Sheet is available in larger print if required. Contact details can be found on page 17.

Why are we doing this study?

The mission of the Quadram Institute Bioscience (QIB) is to understand how food and the gut microbiome (bacteria, fungi and viruses that live in our gut) are linked to the promotion of health and the prevention of disease.

The specific aim of The PEARL Study is to better understand the role of the gut microbiome during early life. Pregnancy and the first years of life are when the microbiome establishes, setting the foundation for future health; understanding this will help us identify ways to improve lifelong health and wellbeing.

We all carry millions of microbes in our gut and they usually cause us no harm. In fact, many of them have important health benefits. Babies are born with no (or very few) microbes in their gut and they acquire them early on in life, including directly from their mothers. A previous study (called BAMBI+) gave us valuable insights into how the gut works in babies, particularly how gut microbes help digest the baby's food releasing nutrients that encourage growth, and how they promote the baby's immune system helping them fight infection. We have also looked at how external factors, such as diet and antibiotics, affect the types of microbes found in the gut.

Our key focus in the PEARL Study is to determine how we can help establish a healthy gut microbiome in early life that will reduce the risk of infection, obesity and chronic inflammatory disease in later life.

Why am I being asked to take part?

Pregnancy and the first years of life are critical stages when the foundations for future health and wellbeing are being established. This will be the first study of its kind to compare the microbes in samples taken from you during and after your pregnancy, with those taken from your baby when he/she is born. This will help us understand how these microbes are transmitted from you to your baby. We want to determine what a 'healthy' microbial signature looks like in early life, so that we can begin to replicate this in new therapies that will give babies the best start in life.

We want to recruit 250 mums-to-be who are ***up to 22 weeks pregnant***.

When you attend your GP Surgery or Community Care setting to see the Community Midwife (Booking Appointment) which is normally at around 10 weeks, your Midwife will give you your Maternity Booklet containing all the information that will be recorded as you go through your pregnancy. To ensure you have plenty of time to consider whether you would like to take part in the study, inside this booklet will also be a PEARL Study Summary Participant Information Sheet. This very briefly describes the study and provides you with contact information should you wish to discuss the study further with the Study Researcher or request a full version of the information. The Midwife will also mention the study at the end of your appointment as they will be aware of the study and offer you a study flier.

Hospitals in England offer all pregnant women at least two routine ultrasound scans during pregnancy. You may be offered more than two scans depending on your health and your pregnancy (you can discuss this with your Midwife or your hospital Doctor).

1. Your first routine scan will be at the NNUH antenatal clinic for your Dating Scan (the date your baby will be due) at around 12-14 weeks. At this scan, you will also find out if you are going to have more than one baby.

2. The second routine scan will again be at the NNUH antenatal clinic for your routine Anomaly Scan at around 20 weeks (this scan checks for any abnormalities and is done routinely at this stage of your pregnancy).

The person who performs the scan (Sonographer) may offer you the study flier at the end of each scan.

Remember that even if you have already had your dating scan and your anomaly scan, you can still participate in the study as the first set of samples we would like to collect are not due until you are at 23 weeks*.

To be eligible for participation in this study, you need to be able to meet ***all*** *the Inclusion Criteria*:

Inclusion Criteria:

- You must be able to understand the study and provide signed and dated informed consent.
- You must be at least 18 years old at the point of consenting.
- You must be no more than 22 weeks pregnant.
- You must have a planned birth at the Norfolk & Norwich University Hospital (NNUH). **You can still be included in the study if you have a home birth as long as your maternity care has been provided by the NNUH.**
- You must have a BMI between 18 – 35 (your Midwife will calculate this for you using your height and weight and record it in your Maternity Booklet).
- You must be willing to provide samples over a period of 31 months (urine, stool {poo}, low vaginal swabs, skin swabs and breast milk (if breast-feeding this is optional). Blood samples are also optional. Also, from your baby, to collect stool and skin swabs.
- You must be willing to have a small freezer in which to store samples you collect until the end of the study.

If you meet ANY of the following exclusion criteria, you will not be eligible to take part, but we thank you for taking time to read this information sheet.

Exclusion Criteria:

- You are acting as a surrogate (planned pregnancy for the purpose of carrying the child on behalf of another woman).
- Planning to have your baby adopted or fostered or not living with you permanently.
- If you are living with or related to a member of the Research Study team.
- If you are a current smoker.
- If you have had an infection and needed to take antibiotics or antifungals or antivirals within the last 3 months.
- If you have taken steroids within the last 6 months, for example Prednisolone.
- If you are taking more than a daily dose (1 pot or container) of probiotics.
- If you have a history of polyps in your gut.
- If you have a long-standing gastrointestinal or liver function abnormality requiring on-going medical management or medication.
- If you have a history of cancer apart from squamous or basal cell carcinomas of the skin (skin cancer) that have been medically managed by local excision.
- If you have made any major changes to your diet in the last month (for example changed to vegan, vegetarian or stopped eating red meat).
- If you have a history of alcohol, drug or substance abuse.
- If you have a history of any liver problems, for example Hepatitis B or Hepatitis C.
- If you have any pre-existing medical condition that affect your immune system, for example Rheumatoid Arthritis, Type 1 Diabetes, Multiple Sclerosis, Asthma, Eczema or Psoriasis. **If you have not had any symptoms of Asthma, Eczema or Psoriasis in the last 5 years, you can still be included in the study.**
- If you have had major surgery of the gastrointestinal tract, apart from gall bladder or appendix removal, in the past five years.
- If you have had any major bowel surgery at any time.
- If you have a history of an inflamed bowel, for example Ulcerative Colitis, Crohn's Disease or Diverticulitis.
- If you have persistent, infectious gastroenteritis or persistent or long-term diarrhoea of an unknown cause.
- If you have long-term constipation.

If you are currently taking part in another study, you may still be eligible to take part in The PEARL Study. The Study Researcher will be able to tell you if you are eligible.

What will I need to do if I am eligible and decide to take part?

Over a period of approximately 31 months we will be asking you to do the following:

- Provide urine samples, stool (poo) samples, low vaginal swabs, skin swabs and colostrum/breast milk (if breast-feeding and if you are producing enough to feed your baby first) from yourself. Providing colostrum/breast milk is entirely optional. Low vaginal swabs are routinely taken for many other screens and these will not harm your baby. They are painless and you can do these yourself.
- Provide a sample of your baby's meconium (first poo sample), stool samples and skin swabs.
- Complete questionnaires about yourself and your baby.
- Allow 2mls cord blood to be taken at birth from the placenta once your baby's cord has been cut ***(this is optional)***.
- Provide a sample of blood – 4mls (less than 1 teaspoon) at either your 12 week scan, your 16 week routine appointment with the Midwife, the 20 week scan or when you have your 28 week routine bloods with your Midwife. ***All time points are optional***, you can give 1, 2, 3, 4 or no blood samples for research if you prefer. We request that you let the study researcher know if you provide a blood sample for research purposes each time so we know to come and collect the sample.
- Your health visitor will visit you at home after your baby is born to perform some routine checks and ask you some questions about your baby to ensure they are developing well. These checks are routinely performed between 9-12 months and between 27-30 months. We would like to collect the anonymised data from these two time points from your health visitor once they become available.

Details of why we require these samples, swabs and data are explained on pages 10-14. We will provide full instructions on how to collect and store samples and swabs.

We will supply you with a small freezer for the course of the study, to keep your samples in for each time point until a member of the Research team collects them from you at home. This will be within 4 weeks of freezing the samples. When we collect your frozen samples, we will also drop off your next collection pack containing everything you will need for your next set of samples. At the end of the study, the freezer is yours to keep. Alternatively, if you no longer want it, a member of the research team will come and collect it from you. The dimensions of the freezer are approximately 51 x 44 x 47.5 cm (H x W x D) and the weight is approximately 15.5 kgs.

We would like you to contact us at a convenient time once you are admitted to the NNUH for the delivery of your baby/babies so that we know to collect any samples or swabs that have been taken (these will be stored in a freezer on a different unit and will be collected by a study researcher). If you plan to give birth at the NNUH, but you actually give birth at another hospital, this is fine and you can still be included in the study. We would ask that you let us know as soon as it is convenient as you may still be able to provide swabs and samples after you and your baby/babies are discharged from hospital.

When can I be enrolled onto the study and what will happen next?

You can be enrolled onto the study at any point in your pregnancy ***up to 22 weeks***. Once we receive your reply sheet which is on page 18, we will contact you at a time convenient to you for an initial telephone conversation to discuss the study, check if you are eligible and answer any questions you might have. This

will take about 20 minutes. If you are happy with everything, you then have two options for when you can be enrolled:

1) If you are happy to speak to a Research Nurse immediately after your 12 or 20-week scan, then this can be arranged in advance when you speak to the Study Researcher. Alternatively, if you haven't already spoken to the Study Researcher, there will still be a Research Nurse in the waiting area who will be happy to speak to you if she/he is available. The Research Nurse will go through the study with you and use a Pre-consent checklist to make sure you have all the information you need to decide whether to enrol. You can ask as many questions as you need. The Research Nurse will show you instructions on how to collect your samples and swabs, how to store everything in the freezer provided and explain when samples will be collected from your home. There will also be a checklist for each collection time to remind you what you will need to collect. We will also show you the three types of questionnaires (one of which is optional) and the data collection forms that will be used. See pages 12-13 for why we are collecting this information.

If you are happy with everything and would like to enrol, we will ask you to sign a consent form. A copy will be sent to your GP and to the NNUH along with this PEARL Study Participant Information Sheet to be inserted into your personal medical records. You will also be given a copy to keep. We will also ask you to complete a Donated Equipment Disclaimer form for the freezer, which is standard practice. If you would prefer more time to think about the study, this is fine. You can come back to us later, so long as you have not passed your 22-weeks stage. You will need to allow about 1.5 hours for us to go through the study and show you everything. Your car parking charge will be waived.

Once enrolled you will then be given your Phase 1 Trimester 1, or Trimester 2 collection pack (depending on how many weeks pregnant you are). This will contain labelled collection packs and questionnaires with instructions for collecting and storing samples. You can opt to receiving your questionnaires via an online link if you wish.
The Trimester 1 pack will contain two labelled blood bottles (purple top) if you would like to give a blood sample at week 12 and/or week 16. The Trimester 2 pack will contain two labelled blood bottles (purple top) if you would like to give a blood sample at week 16 and/or week 20. The study researcher will explain the blood bottles and ensure you have the correct blood bottle for any of your routine appointments. The Trimester pack 3 will contain one blood bottle (purple top) if you would like to give a blood sample at week 28. If you would like to give a blood sample at any of these 4 time points, please take the marsupial bag (plastic see-through bag) containing the blood bottle and blood request form with you to your routine pregnancy appointment. Remember to hand this in to the phlebotomist/Midwife who will take this blood sample.

You will also be given a study carry card with your unique identification number and contact details for the study Researchers. This is the size of a credit card and we ask that you carry this with you for the duration of the study. We will make a note of how many weeks pregnant you are and your Estimated Date of Delivery so that we know when to pick up your samples. We will also ask you

how many babies you are expecting so that we can give you the right number of collection pots, swabs and questionnaires to collect samples and data from your baby/babies.

We would also like to place a study sticker within your Maternity Booklet. The reason for doing this is because it is going to be a busy time when you are admitted in to hospital to give birth. The person (Midwife or Doctor) who will be with you during labour and birth will see the sticker and be able to help you with collecting your samples at a convenient time during labour or around birth (when possible). Phase 2 on pages 8-9 explains this in more detail. You will also receive a sticker at the consenting meeting to put on your sample freezer to remind you and anyone in your household not to put any food items in this freezer. If you encounter any technical problems with the freezer during the study, we would ask that you contact the study Researcher as soon as possible.

Lastly, we will provide you with a freepost Study Withdrawal Postcard. Should you wish to withdraw from the study at any point, please complete this and send it back to us.

If the Research Nurse is not available and you would like to speak to someone while you are at the hospital, please call Shelina Rajan on **01603 255149** or **07876 182564**. Shelina is the Clinical Studies Officer for the PEARL Study and will be happy to speak to you.

2) If you prefer to speak to us about the study when you are not attending for your 12 or 20-week scan, we can arrange an appointment to meet you at the at the QI Clinical Research Facility, providing you have not passed your 22-weeks stage. The same process will apply as described above. As this is a specific appointment about the study, mileage will be reimbursed at the rate of 45p per mile. Your car parking fee will also be waived and again, you will need to allow 1.5 hours.

Extra Consent

Once you have consented to the study, we will also ask you to read the Norwich Biorepository Information Sheet about the storage of your samples at the end of the study. This is a tissue bank where all the participants' samples are frozen, stored securely, and made available to other Researchers to use in future ethically-approved research. We will also provide you with a separate consent form for the samples from your baby to be stored in the same way. You and your baby's samples will be stored anonymously so there will be no link to either of you. You can choose whether or not to sign the consent form for this when you sign the study consent, or you can take time to think about it. No additional samples or swabs will be taken for this purpose.

The study will last approximately 31 months and is divided into 3 collection phases:

Phase 1: Pregnancy

Trimester 1. We would like you to collect a urine sample, a stool (poo) sample, a skin swab and a low vaginal swab at week 12. The low vaginal swab will not cause any harm to your baby.

Trimester 2. As described for Trimester 1 but at week 23, with a Health Questionnaire and a CDCP (Centre for Disease Control and Prevention) Pregnancy Questionnaire. We would also like you to complete another questionnaire relating to personal food choices called Participant Dietary Preferences and Perceptions Questionnaire. This questionnaire is entirely optional.

Trimester 3. As described for Trimester 1 but at week 30. These samples will be taken by yourself at home, stored in your sample freezer and picked up by the Researchers within 4 weeks of them being frozen.

You will have an extra 7 days from each timepoint to collect your samples and complete the questionnaires.

We would also like to collect a small additional sample of blood for research (4mls) each time you have your routine blood tests. The routine blood tests are offered at 12, 16, 20 and 28 weeks. The research bloods are optional and you can opt to donate 1, 2, 3, 4 or no research samples at all.

All of the routine pregnancy scans, blood and urine samples that you provide as part of your care during this antenatal period are really important to maintaining the health of you and your baby. The results of these tests are also very helpful to us for the PEARL study. On the consent form we ask for your permission to use these results in the PEARL study – all results will be anonymised. The reasons why we are asking to use these are explained on pages 13-14.

For Phase 1 you will be given your first collection pack which will be either the Trimester 1 or Trimester 2 collection pack (depending on when you are enrolled on to the study). At the meeting you have with the Study Researcher or Research Nurse, the pack will contain everything you need including a checklist and sample collection and storage instructions. Your next Trimester collection packs (2nd or 3rd) will be delivered to you when we come to collect your samples from the first pack. Collection will be within 4 weeks of samples being frozen.

We will send you a reminder message 1 day before the start of <u>each</u> collection time point throughout the study to remind you when to take your samples and store them in the freezer provided. When your samples are ready to collect we would ask you to reply to the reminder message saying "Done" so that we know they have been taken. If we do not receive a message saying "Done" from you by day 5 of the 7 day collection window, we will send the reminder message again. If we still haven't heard from you by day 8 (1 day after your collection window finishes), we will give you a call.

We will also send you a reminder message 1 week before we will be picking up your samples and again the day before so you are aware of when this will be. We will check the hospital systems before sending each reminder message to make sure that you or your baby haven't been admitted with any serious medical issues. If we see admissions of a serious nature we will not send you any reminder messages at this point. This to avoid causing any further distress to you at this time.

To ensure you have everything you need on time, your Phase 2 collection packs (Birth, Week 1 and Week 3) will all be delivered together when your Trimester 3 samples and swabs are collected by the Researchers. To avoid any confusion, each pack will be labelled clearly.

You will need to bring your Maternity Booklet to hospital when you are admitted, so if you keep the Birth collection pack and your Maternity Booklet together, you won't forget either of them 😊

Phase 2: Birth and the First 3 weeks after birth

We would like to collect swabs and samples from yourself and your baby. In the case of multiple births, we will link each of your babies to you and collect and store each baby's samples and swabs separately. We realise that the time around labour, birth, and the period after labour can be quite an emotional time for new parents. We also realise that there may be a period of time when your baby needs some specialist care in the Neonatal Intensive Care Unit (NICU). The Midwife and NICU Specialist Nurses will be very sensitive to your needs and to those of your baby throughout this time and will only ask for samples when it is appropriate to do so.

If you have opted for a home birth, samples you have collected at home can be stored at home in the freezer provided and collected by appointment by the study researcher. In the case of a water birth either at home or at the NNUH, we would request that samples be collected either before entering the birthing pool or within 7 days of giving birth. No samples will be requested whilst you are in the birthing pool.

Low Vaginal Swab Collection During Labour/ Delivery.

- For normal vaginal delivery: You will be asked if you agree to have this swab taken by the Midwife or Obstetrician. It will be exactly the same as the ones you have taken yourself during pregnancy (inserted 2cm into the vagina). The Midwife or Obstetrician would collect this swab at a time convenient and appropriate to you during labour, but before you give birth. If there is any reason it cannot be taken before birth or you prefer not to have this taken during labour, then you can have up to 7 days to provide this yourself, and it will be collected from your home by the Researchers at the end of Week 3.
- For delivery by Caesarean Section: We would still like to obtain a low vaginal swab even if you have a C-Section. As part of routine clinical care prior to a C-Section, it is usual practice to have a catheter inserted which drains any urine produced directly in to a bag (your Midwife or Doctor will discuss this with you if appropriate). This may provide an opportunity for collection of the swab. The consent form you sign agreeing to taking part in the study will give you the option to agree to having this swab taken at the time of delivery. Even if you agree on the consent form, you can change your mind later, and you will still have up to 7 days to provide it, as described above if you prefer.

- **Umbilical Cord Blood at Birth.** At birth, we would like to collect 2mls of umbilical cord blood, which is blood that remains in the placenta and in the attached umbilical cord after childbirth; you can opt out of this if you wish to.
- **Within the First 7 Days after Birth**. From yourself, we would like you to collect a urine sample, a stool sample and a skin swab (plus the low vaginal swab if we were not able to collect this at the time of delivery). We realise this is quite an emotional time for you and will ensure these requests are handled sensitively. If you are breast feeding and are producing enough milk for your baby, we would also like you to collect up to 1ml of colostrum or up to 5mls of breast milk depending on how soon after birth you are able to provide a sample (your Midwife will explain the difference between

colostrum and breast milk). From your baby we would like you to collect their first stool sample, known as meconium (ideally collected between 46-72 hours after birth), and, where possible, a skin swab. The reasons why we are collecting these samples are detailed on pages 10 to 12.

Weeks 1 and 3 after birth. From yourself, we would like you to collect a urine sample, a stool sample, a low vaginal swab and a skin swab at week 1 and again at week 3. From your baby we would like you to collect a stool sample and a skin swab at week 1 and again at week 3. If your baby is still in NICU at weeks 1 and 3, all samples from you and your baby will be sensitively requested by the Specialist Nurse.

If you are at home with your baby at weeks 1 and 3, we would ask that you collect the swabs and samples from yourself and from your baby and store them in the freezer for the Researchers to collect. There will also be a CDCP questionnaire about your baby to complete. We realise this can be quite an overwhelming time for you so please do not worry if these are a bit late. For this reason, you will have an extra 7 days to provide each of the week 1 and week 3 samples.

Any swabs, samples and questionnaires that could not be collected at the time of birth or prior to discharge, we will ask you to take these home with you so that you can collect them at home. The collection pack will have everything you need including a checklist and sample collection and storage instructions. All the Phase 2 packs (Birth, Week 1 and Week 3) will be picked up together at the end of Week 3 and your Month 4 pack dropped off.

Phase 3: 4 – 24-months after birth

Month 4. From yourself, we would like you to collect a urine sample, a stool sample, a skin swab and a low vaginal swab. If possible and applicable, we would also like you to collect up to 5mls of expressed breast milk. From your baby, we would like you to collect a stool sample and a skin swab. There will also be a CDCP Questionnaire about your baby to complete. We would also like you to complete another questionnaire relating to personal food choices called Participant Dietary Preferences and Perceptions Questionnaire. This is the same questionnaire you completed when you were pregnant and again is entirely optional.

Months 8, 16, 20 & 24. From your baby we require a stool sample and a skin swab to be collected at each time point. There will also be a CDCP questionnaire about your baby to complete. From yourself we do not require any samples or swabs, but there will be the same Dietary Preferences Questionnaire (optional) and a Health questionnaire to be completed at 24 months. This will be the same as the one you completed when you were pregnant.

At each of the Phase 3 time points, you have an extra week to collect your baby's stool sample, skin swabs and questionnaires. These samples should be placed in your sample freezer and they will be picked up within 4 weeks of the samples being frozen.

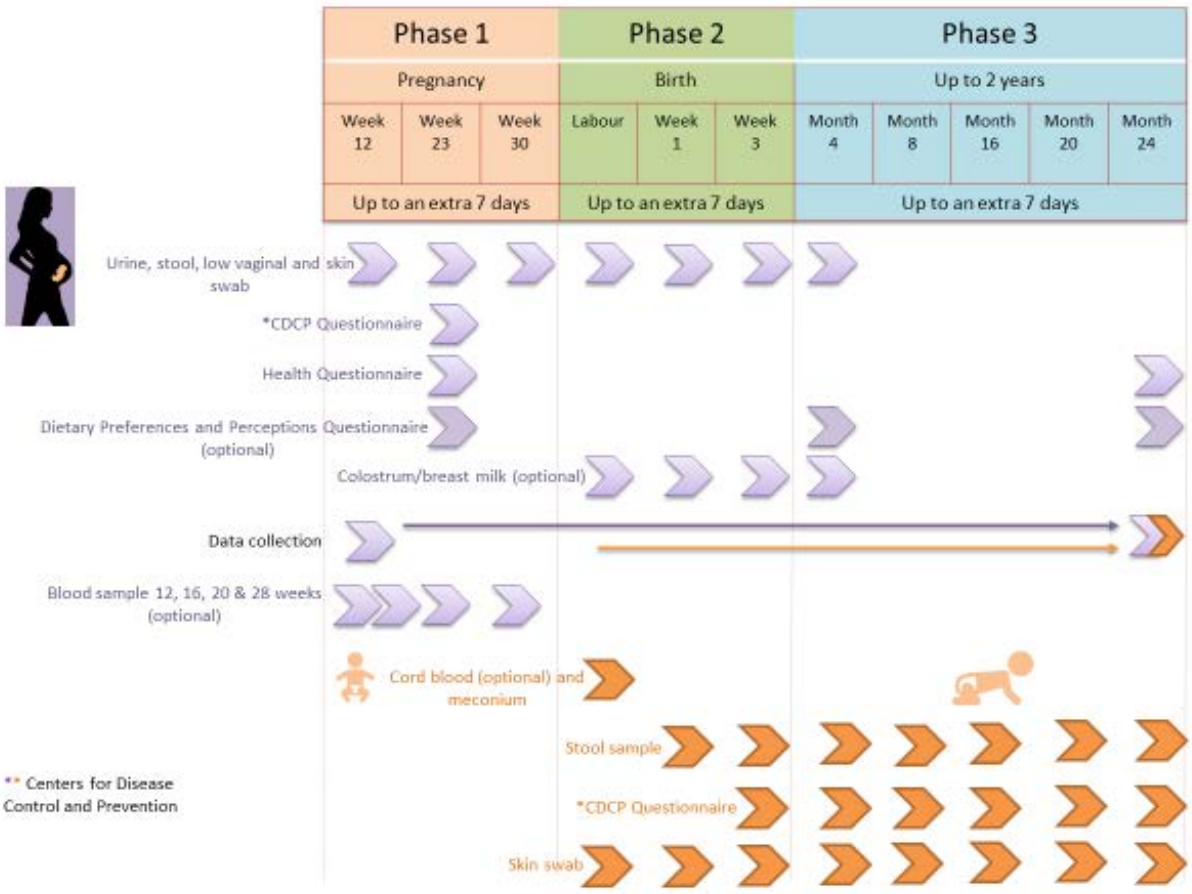
For Phase 3 the collection pack for each time point will be clearly labelled and delivered to you when your previous samples are picked up by the Researchers. The packs will contain everything you need including a checklist and sample collection and storage instructions.

In the event of your freezer breaking down, please contact the study researcher as soon as possible.

To keep you up to date with how the study is progressing and to inform you of any related news, we would like to send you a 1-page newsletter once a year, around December. You will have the option of receiving this either as a link or with your collection pack as appropriate.

Please let us know in good time if any of your contact details change, e.g. change of address, phone number whilst you are on the study. This is so we can make sure your frozen samples are picked up and your collection packs are delivered in good time. Please also let us know if you change your GP up to 6 months after you complete the study so we can collect data which is relevant to you and your baby taking part in the study. Thank you.

A summary of all the collection time points is provided in the figure below.



What we would like to collect from you as the mother and why.

- **<u>Stool samples</u>** It is now well known that the types of microbes you have in your gut, and therefore your stool, influence many important processes in your body. These include digestion of food, programming of the immune system, and helping to prevent invasion of pathogenic microbes.

Importantly, the beneficial microbes that you have in your gut change during pregnancy in preparation for the birth of your baby. Taking these samples allows us to see which microbes you pass on to your baby and how different factors e.g. antibiotics, may alter these microbes.

- **Urine – 20mls** Taking urine samples allows us to identify any microbial products present that could be linked to processes such as immune development in yourself and your baby/ babies.

- **Blood- 4mls (optional)** We know that certain microbes help programme your immune system. By examining blood samples, we can see how your microbes are shaping what types of immune cells you have in your blood.

- **Skin swab** Like your gut, your skin is also home to lots of different types of microbes, which may also be passed on to your baby/ babies after they are born during skin-to-skin contact. By taking a skin swab to determine what microbes mum has we can see whether any of these also 'turn up' on your baby's skin, or in their developing gut.

- **Low vaginal swab** If your baby is born via a natural birth, one of the first places it will pick up its new microbes is from the birthing canal. Taking a low vaginal swab allows us to find out what bacteria are present over the course of your pregnancy and then whether these beneficial bacterial are passed on to your baby/ babies after birth.

- **Colostrum/Breast milk (optional)** Previous studies have shown that breast milk may also contain microbes that are passed on to a baby during feeding. We would like to examine breast milk for these microbes and also for the presence of other dietary factors that could help 'feed' and maintain particular bacteria within the baby's gut.

Another reason for collecting all of these swabs and samples is to perform what we call host genotyping. This allows us to better understand how the genes that you and your baby have influence the types of bacteria that they have in your and your baby's gut. Previous studies have identified a variety of genes that may influence what types of microbes are found in the gut and on skin; as each of us (apart from identical twins!) have different genes, we would like to find out how these differences relate to the differences in the microbes present in mum and baby.

Please be assured, we will NOT be performing any kind of genetic testing on you for diseases or conditions and the genotyping we do has no clinical relevance to you or your relatives. Therefore, there is no need for you to receive the results of this test. Please note, we will only ask you to provide colostrum/breast milk if you are breast feeding and if you are producing enough to feed your baby first.

What we would like to collect from your baby and why.

- **Cord blood 2mls (optional)** Cord blood is the blood shared between mum and her baby and we would like to look at this to see if there are any beneficial microbial factors that might be linked to you and your baby's developing immune system.

- **Meconium sample** Meconium is your baby's first poo! As it is the first, we would like to analyse it to identify which are the first microbes that colonise your baby's gut.

- **Stool samples** Colonisation of microbes during the first phases of life is very important for healthy development of a baby. Thus, over the course of the first two years of life, we would like to analyse your baby's poo samples to understand how these microbes change over time, and how different diets (e.g. moving from milk to solid foods) changes the types of bacteria present.

- **Skin swabs** Skin microbes are also important for healthy development. We would like to see how these microbes change over time and whether any also find a home in your baby's gut.

Health Questionnaires.

Many different factors, including what you eat and whether you have had a course of antibiotics, can influence what types of microbes you have in different parts of your body (e.g. gut and skin). The Health questionnaire answers that you provide will help us determine how these factors might be affecting your microbes, and whether this, in turn, influences which bacteria are passed on to your baby.

You will receive the Health questionnaire with your Phase 1 Trimester 2 collection pack and then again with your Phase 3 24-month collection pack. We will show you a copy before we consent you to the study.

Centre for Disease Control and Prevention (CDCP) Questionnaires.

These questionnaires include a set of approved questions designed to capture lots of information from pregnant mums about their diet and lifestyle and then about their baby when they arrive. CDCP questionnaires were developed in America and are quite lengthy. The good thing is (and with CDCP's permission) that we have shortened them a lot so now they only have questions that are specifically relevant to the PEARL study. A CDCP questionnaire will be requested for you to complete for yourself at Trimester 2, then again for your baby at 3 weeks after birth, then at 4, 8, 16, 20 and 24 months after birth.

Dietary Preferences and Perceptions Questionnaires.

This 6-page questionnaire will help us understand your motivations for your dietary choices and health needs during and after pregnancy, and how this links to your gut microbes. There is not much research about mums-to-be food choices and this information is important to shape dietary advice during and after pregnancy and how to promote a healthy microbiome. There is a section at the end of this questionnaire

asking how you rate elements of your personality, for example extraverted and enthusiastic which may link in to your food choices. We appreciate that you are completing two other questionnaires, so for this reason, this questionnaire is optional. If you wish to complete the questionnaire, they will form part of your collection pack at Trimester 2 and then again at 4 months and 24 months after giving birth.

All the questionnaires are available in paper and digital format. You can opt for paper versions of these questionnaires, which will be provided in your collection pack and will be collected with your frozen samples. If you opt to complete the questionnaires online, a link will be sent in the appropriate reminder message. We will show you a copy of all the questionnaires before we consent you to the study.

Data Collection from your GP and hospital records.

We don't want to miss any helpful information about you and your baby during the study. This means that not only would we like to record the progress of your pregnancy, but also any associated events that might happen to you and your baby throughout pregnancy, labour, birth and up to 2 years after birth. We would like to collect data from your GP and hospital records over the course of the study that relate to any change in you or your baby medical history, any treatments, infections, alternative therapies, hospitalisations, vaccinations and medications. This information can then be linked to the data on microbes that we collect from the samples/swabs and the information in the questionnaires that you provide us with, from yourself and from your baby. We would like to collect your hospital admission data one month after you have been discharged from hospital. The rest of the data will be collected from your GP records after you have completed the study. We will show you these questionnaires before we consent you to the study.

Data collection from your health visitor.

Once you are discharged from hospital following the birth of your baby, you will routinely be seen by a health visitor at home who will check that your baby is growing and developing as expected. When your baby is aged between 9-12 months and between 27-30 months, your health visitor will complete a set of questions with you to see how your baby's development is progressing. We would like to ask your permission to access this data from these two time points. This will help us to see if there are any links with your baby's microbes and general development. We will collect this anonymised data from the health visitor once it becomes available so you will not need to do anything.

Why are we asking your permission to use results from routinely collected pregnancy scans, blood and urine tests?

Pregnancy scans, blood and urine will be collected routinely as part of your clinical care. There may be times when your Doctor advises some additional tests, for example if you are diabetic or develop diabetes during pregnancy (your Midwife or hospital Doctor will be able to advise you). Routine tests are done/offered at the following time points:

- Week 10 (Booking Appointment). This is when you see your Midwife and a Full Blood Count (FBC), your Blood Group, antibodies, *Rubella* status and routine screening tests will be collected.

- Week 12 Dating Scan. This is when you will be offered a routine Combined Test to look for any abnormalities (your Midwife or hospital Doctor will discuss this with you).
- Week 16 routine tests with your Midwife. You may be offered the routine Quadruple Test (your Midwife or hospital Doctor will discuss this with you).
- Week 20 Anomaly Scan.
- At 28 weeks your FBC and antibodies tests will be repeated.
- Urine tests are routinely performed at various time points throughout your pregnancy by your Midwife and at the hospital.

By agreeing for us to have access to results from the routine tests described above and from any additional tests, will help us to determine the role that you and your baby's microbes may have on different health outcomes. This has the potential to help us develop new health-promoting diet- and microbe-based therapies in the future.

Are there any benefits to taking part?

The information we obtain from this study will help us to better understand how the transfer of a mother's gut microbiome to her baby might influence that baby's health as they develop during pregnancy and early life.

Will my GP be informed?

Yes, it is routine practice for us to inform your GP that you are participating in a study at QIB. This is one of the things that you are agreeing to when you sign the consent form to take part in the study.

Are there any risks or side effects from participating in this study?

There can be a small amount of discomfort associated with taking blood. This generally only occurs on insertion of the needle. You should not experience pain during the procedure or afterwards. You may develop a small bruise at the site where the blood sample was taken but this will fade like any bruise. If you are taking any medication to thin your blood, please tell the phlebotomist (person taking blood) in advance.

There are no known risks to you taking low vaginal swabs during pregnancy.

Do I get paid for doing this?

Participating in this study is entirely voluntary. However, we do recognise that being involved in the study may cause you some inconvenience, particularly during Phase 2 of the study.

As a thank you for participating in the study, a 'Love-To-Shop' voucher to the value of £20 will be posted to your home address at the end of the study for your time and any inconvenience.

PRIVACY NOTICE

Will my taking part in this study be kept confidential?

QIB is the sponsor for this study based in the United Kingdom. We will be using information from you and/or your medical records in order to undertake this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. QIB will keep identifiable information about you for 15 years after the end of the study in a secure archive at the QIB or designated secure off-site location.

Your rights to access, change or move your information are not affected, as we need to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw or you are withdrawn from the study, we will keep the information about you that we have already obtained. To safeguard your rights, we will use the minimum personally-identifiable information possible. You can find out more about how we use your information by contacting Shelina Rajan at pearl@quadram.ac.uk

All information collected about you during this study will be kept strictly confidential. We follow Ethics and Research Governance and Good Clinical Practice (GCP) requirements.

The study will comply with EU General Data Protection Regulation (GDPR) and the UK Data Protection Act 2018. The legal bases used under the regulation that we employ to process your personal information is for tasks carried out in the public interest, which this study and associated research is.

Your personal information will be stored in locked filing cabinets at the QIB. Suitable security measures and precautions are also taken for any confidential or personal data processed or stored electronically.

Once enrolled on to the study, you will be issued with a unique study identification number. Your baby will also have unique study identification numbers. These numbers will be used to protect your personal information and samples so that no one will be able to work out they are yours. These codes are also kept in a locked filing cabinet at QIB separate from your personal information.

Any communication, relating to the study, to you or from you that is sent or received on the study mobile phone will be handled in accordance with the terms set out by the QIB Data Protection Officer.

Access to your personal records is restricted to the study team, study nurses, NHS medical staff and your GP.

All research is subject to inspection and audit and, although your records may be accessed for this purpose, any personal information is held anonymously and remains confidential.

Please note that QIB Clinical Research Facility (CRF) has CCTV cameras in use for security purposes. Cameras on the outside cannot identify who specific individuals are who enter and leave the building. However, cameras within the public areas of the building would be able to identify individuals. This is the same security system that operates in most organisations and is designed to protect the public and staff.

To discuss any data protection policy or compliance related queries, please contact the QIB Data protection officer on dpo@nbi.ac.uk or call 01603 450067.

During participation in the study, you may receive a letter from the Study Researcher inviting you to attend the CRF to provide an audio/video recording of your experience of taking part in the study. This material will be used to promote public awareness of the study and we will always respect your rights to privacy and

anonymity where expressed. We may also ask you to provide anonymised quotes for use in research reports and publications. This is completely optional. You may decline this invitation and it will not affect your participation in the study.

What happens when the research study ends?

Findings of this study will be reported in the scientific literature. ***No individual's data will be identified***.

What will happen to my samples?

All data and samples will be anonymised. Half of all the samples we collect from you will be stored securely at the QIB. The other half will be anonymised and stored at the Norwich Biorepository for back-up purposes. At the end of the study, any samples that are not used at the QIB will be kept anonymised and stored at the NBB for future ethically-approved research.

What if relevant new information becomes available or changes to the study are made?

If this happens, we will tell you. If changes to the study have to be made, you may be asked to sign another consent form.

Will I be told the results of the study?

The results of the study will be published in scientific journals and presented at national and international scientific meetings. We are unable to tell you any of your individual results since it is only possible to draw conclusions from the group as a whole.

At the end of the study, we will provide feedback of what we have found as a result of your help and what it may mean for future research. We will update our websites to fill you in on all the exciting research that we have performed on your precious samples.

What if there is a problem?

If you have a concern about any aspect of the study, you should ask to speak to the Clinical Studies Officer Shelina Rajan on **01603 255149** or **07876182564** who will try to answer your questions. If you remain unhappy and wish to complain formally, you can do this through the chairperson of the Human Research Governance Committee (HRGC) at the QIB – Dr Antonietta Melchini antonietta.melchini@quadram.ac.uk 01603 255030.

What if something happens to me while I am on the study?

If you are harmed by taking part in this research project there are no special compensation arrangements. If you are harmed due to someone's negligence, you may have grounds for legal action, but you may have to pay for it. Regardless of this, if you wish to complain or have any concerns about the way you have been treated whilst taking part in this study at the NNUH clinics, there will be a local hospital complaints procedure that you can follow. The PALS (Patient Advice and Liaison Service) is a confidential service designed to

support patients, relatives and carers. Their website is pals@nnuh.nhs.uk and the office has an answerphone which is available 24 hours a day: **01603 289036** or **01603 289045**.

QIB accepts responsibility for carrying out trials and as such will give consideration to claims from participants for any harm suffered by them as a result of participating in the trial, with the exception of those claims arising out of negligence by the participant. QIB has liability insurance in respect of research work involving human participants.

Please note that the Institute will not fund any legal costs arising from any action unless awarded by a court.

Who has reviewed this study?

To protect your safety, rights, wellbeing and dignity the study has been reviewed by the QIB Human Research Governance Committee (HRGC) and an independent group called the London-Dulwich Research Ethics Committee (REC) which is made up of Expert and Lay members.

RECs review research proposals and give an opinion about whether the research is ethical. They also look at issues such as the participant involvement in the research. The committees are entirely independent of research sponsors (the organisations responsible for the management and conduct of the research), funders and the researchers themselves. This enables them to put participants at the centre of their review.

What should I do now?

If you are interested in taking part in the study and would like to know more, then please complete the reply sheet below and return it in the Freepost envelope provided.

Alternatively, you can complete this form online at www.quadram.ac.uk/pearlstudy

If you would like to speak to someone in the first instance or require a copy in larger print, please contact the Clinical Studies Officer Shelina Rajan on **01603 255149** or **07876182564** or email pearl@quadram.ac.uk

If you are not interested in taking part in the study or you are not eligible, you need not do anything. No one will contact you about the study.

Thank you for taking the time to read this information.

Quadram Institute
Science Health Food Innovation

The PEARL Study
Pregnancy and EARly Life

I am interested in finding out more information about this study.
Please complete the sections below with your personal details and return in the Freepost envelope provided. Alternatively, you can register your interest by completing this form online at www.quadram.ac.uk/pearlstudy or by e-mailing pearl@quadram.ac.uk

Name: ……

Address: ……

……

Date of birth ……

Daytime telephone number ……

Evening telephone number ……

Mobile telephone number ……

I am happy for a message to be left via my daytime/evening number YES/NO

*Please circle as applicable

Preferred day(s)/time(s) to call ……

E-mail address (optional) ……

Expressing an interest to take part does not commit you to taking part in the study.

For office use only If participating, please indicate above how the patient would like to be contacted during the study using contact details provided.

NHS
Norfolk and Norwich University Hospitals
NHS Foundation Trust