Parent Information Leaflet Form

Introduction

We understand and appreciate that this is a very difficult time for you and that it may not seem a good moment to be talking about research. However we think it is important that you know about a study that this hospital is taking part in for babies born prematurely.

Short Title: PiPS: Probiotic in Preterm babies Study

Formal Title: The probiotic Bifidobacterium breve strain BBG−001 administered early to preterm infants to prevent infection, necrotising enterocolitis and death

Summary

This is a brief description of a research study designed to test whether giving probiotics to premature babies helps to protect them against serious illnesses. You have been given this leaflet because your baby has been, or may be, born 10 or more weeks early and we want to give you the opportunity to think about whether you would like your baby to take part in this study.

Children and adults have many bacteria in their gut that do not cause disease and are important for health. It is possible that if we give similar bacteria (probiotics) by mouth to premature babies soon after birth that other bacteria that can cause illness may be prevented from becoming established in the gut.

The number of babies that have been given probiotics is small; early results of studies are encouraging and probiotics appear to be safe, however we cannot be confident about this until they have been more widely used.

This hospital is one of about 20 helping in a study funded by the NHS through the Health Technology Assessment programme which will involve 1300 very premature babies and give a clear answer about whether probiotics are helpful or not.

The rest of this leaflet explains the study in more detail and describes what being in the study would mean for you and your baby. If, after reading this leaflet and discussing the study with the doctors and nurses in the neonatal unit, you decide to take part we will ask you to sign a consent form. Your baby will then enter the study and will receive either probiotic or an inactive substance that looks the same; this inactive substance is called a placebo. Probiotic or placebo will be continued once a day until shortly before you go home. Neither you nor the staff on the unit will know whether your baby is actually receiving probiotic.

The study does not involve any additional blood tests and should not cause your baby any pain or discomfort. We will collect information about your baby's progress in hospital but we do not currently have any plan to see you again after you have gone home.

Whether or not you decide to let your baby take part is entirely up to you. If you decide not to take part this will not affect the high standard of care your baby receives.

What problem are we trying to help?

Babies born as early as yours are at increased risk of infections and of other complications of prematurity; one of the most important of these is the illness necrotising enterocolitis that affects the gut. Usually these infections can be successfully treated with antibiotics but such illnesses often prolong a baby's stay in hospital and may increase the likelihood of life-long health problems. Occasionally they are so serious that the baby may need surgery or may even die.

There are a number of different ways in which the body protects us against infection; one of the most important is through the millions of bacteria that live in our gut. These are not germs that cause disease but are helpful bacteria that are essential for good health. Babies who are born at the expected time rapidly gain these bacteria from their mother and other members of the family. Babies born early have to be separated from their family and have few of these helpful bacteria; instead they are likely to have many other bacteria in their gut. Usually these other bacteria do not cause problems but they may cause infections that can be difficult to treat and be involved in the development of serious complications such as necrotising enterocolitis. They may also make it more difficult to digest milk which is very important for your baby's long term health.

It is possible that giving probiotics soon after birth will make the bacteria living in the gut of premature babies more like those of full-term babies and decrease the risk of them getting serious infections and necrotising enterocolitis.

What are probiotics and how much do we know about their use in newborn premature babies?

Probiotics are live micro-organisms, usually bacteria, that are taken by mouth and then multiply and live in the gut. There are lots of different probiotic bacteria, many of them have names beginning with Lactobacillus and Bifidobacterium and are contained in live yoghurt and a range of freely available health products.

There have been a number of studies giving probiotics to premature babies, the results suggest that giving probiotic might help babies to digest milk and to grow better, to have fewer episodes of serious infection and less necrotising enterocolitis. There have been no reports of complications. However the studies have all been small and none so far has been in the UK. In order to be clear whether or not probiotics are helpful and to be confident of their safety they need to be studied more widely.

Some studies have used just one type of probiotic and others have used mixtures. This study will use a single probiotic called Bifidobacterium breve strain BBG-001 (BBG). For the rest of this leaflet when we talk about probiotic this is the one we mean. The same probiotic has been given routinely to many thousands of newborn babies in Japan with no reported complications.

All of the earlier studies have mixed the probiotic in the baby's milk feeds; this has meant that babies who the doctors decide should not be fed have not been included in the studies. We think it is probably important, if probiotics are to be helpful, that they are given early, before other bacteria that may cause disease become established in the gut. In this study we plan to start probiotics early whether or not milk feeds have been started.

What is the purpose of the study?

The purpose of this study is to find out whether giving BBG to babies born 10 or more weeks early, reduces episodes of blood stream infection and necrotising enterocolitis. We will also study whether there is increased survival and whether babies are likely to leave hospital sooner if they receive probiotic.

Why has my baby been chosen?

All newborn babies are at some risk of infection and of necrotising enterocolitis but this risk is much greater in very premature babies, we are therefore inviting parents of babies born 10 or more weeks early to take part in this study.

This hospital is one of about 20 in England involved with this study. We are aiming to include 1300 babies; we need this number to be confident of finding out whether probiotics are helpful or not.

Does my baby have to take part?

You do not have to agree to your baby taking part in this study. If you decide not to take part it will not affect in any way the quality of care you and your baby receive. Similarly if you decide that you would like your baby to take part and then change your mind your baby can be taken out of the study at any time without you having to give a reason.

What will happen to my baby if I agree to take part?

Because we are studying the effect of giving probiotic early we are asking you to make your initial decision about whether your baby should take part within 48 hours of birth. We realise that this may put you under increased stress and apologise for this; we would not do this if we didn't believe it was important. We will discuss the study with you again during the course of your baby's stay in hospital to make sure that you understand what is happening and that you continue to agree to your baby taking part. There will always be someone available with whom you can discuss the study, sometimes this will be by phone.

If you agree that you would like your baby to take part in this study, your baby will be put into one of two groups; one group will receive probiotic and the other will receive a dummy product that looks the same, this dummy product is called a placebo. Your baby will have a 50/50 chance of being put into either of these groups. The allocation of your baby to a group will rely on chance (rather like tossing a coin). Neither you nor the staff caring for your baby will know which group your baby is in. This is the only way we can be sure that we test probiotic fairly. The first dose of probiotic or placebo will be given as soon as is practicable for the ward staff after you have signed the consent form; this may not be until the following morning.

The probiotic and the placebo are supplied to us as granules which we mix with fluid, we then put a few drops down the baby's feeding tube. We will do this once each day until your baby reaches 36 weeks of gestation (36 + 0 days). Because it is important that nobody knows which product your baby is receiving we mix both probiotic and placebo with a very dilute preparation of a special infant formula called Neocate so that they still look the same. Neocate is an infant formula that is very easy to digest and is made especially for babies with gut problems; it is not made from cow's milk. For this study Neocate is being used at 1/8 of full strength. This does not provide any significant nutrition for your baby and is so dilute that it cannot pose any risk to the gut even in those babies that the doctors decide should not be fed. This will in no way reduce your chances later of successfully breast feeding your baby.

If your baby is unwell the doctor in charge locally will decide whether or not doses are missed out.

If your baby is discharged home earlier than 36 weeks the probiotic or placebo will be stopped a few days before. If your baby is transferred to a different hospital before 36 weeks we will aim to continue to give the product; if the new hospital is not already involved in the study we will provide training to the staff to enable this to happen.

If your baby sucks well and is able to have the feeding tube removed earlier than 36 weeks the probiotic or placebo will be given directly into the mouth with a syringe once a day before a feed.

Two weeks after birth and again at 36 weeks (if your baby is still in hospital) we will collect a sample of your baby's stool. These samples will be sent to the microbiology laboratory at Barts and the London Hospital, London E1 where they will be tested to check whether or not your baby has been successfully colonised with probiotic and what other bacteria have colonised the gut.

If you agree the remaining stool sample will then be deep frozen and stored for later testing in a related study for which we have not yet secured funding. The additional tests are designed to help us understand the effects of probiotics.

No extra blood tests or injections are necessary and all other aspects of your baby's care will be entirely at the discretion of the local doctors and nurses.

Unless there is a specific medical reason why not, it is hoped that mothers of babies in the study will provide breast milk for their babies since human breast milk promotes the multiplication of BBG.

What are the possible side effects of the treatment?

There are no reported side effects associated with the probiotic being used for this study. However all babies in the study will be monitored very closely throughout the study by the staff on the Neonatal Intensive Care Unit.

What information will be collected about me and my baby?

We will need to collect standard clinical information about your pregnancy, the condition of your baby at birth and progress throughout the hospital stay. This information will be collected from the baby's written and electronic case record. The study will not involve you in any interviews or questionnaires. In order to get accurate results from all samples taken by the medical staff to check for infection, we will contact the hospital microbiology laboratory directly since the detail needed for the study is not always available in the case notes.

After your baby has completed the study, records maintained by the NHS Information Centre and NHS Central Register maybe used to help us contact you in future and to provide information about your baby's health status.

What are the possible disadvantages of taking part?

We believe that this intervention is safe and that there are no disadvantages for you in taking part in this study whichever group your baby is in.

We will need to collect information about you and your baby.

What if new information becomes available?

There is currently a lot of interest in the use of probiotics for premature babies and other studies in other countries using slightly different probiotics are underway. We will be monitoring any results emerging from these studies closely and will inform you if any important new information becomes available during the course of the study that might make you change your mind about your baby's involvement.

What if something goes wrong?

The chance of anything going wrong as a result of taking part in this study is very small. However we are required to tell you the following:

If your baby is harmed and this is due to someone's negligence, then you may have grounds for legal action for compensation against Queen Mary, University of London in respect of any harm arising out of the participation in the Clinical Trial or the NHS in respect of any harm which has resulted from the clinical procedure being undertaken.

Will my taking part in this study be kept confidential?

Your GP will be told that you took part in the study.

Your details and the information collected for the study will be kept securely and will only be seen by the study organisers and people from the regulatory authorities whose job is to ensure that studies such as this are carried out safely. They may also need to look at your baby's notes to check that the information collected for the study is correct. Information about you or your baby will not be used for any purpose other than to answer these research questions.

Although we currently have no plans to collect any further information about your baby after discharge from hospital we will retain your contact details in case anything emerges from this or any other study of probiotics that makes it important that we contact you again. The NHS has a central register (based at the General Register Office) that would be able to tell us if you have left the NHS and through which we would be able to locate you.

What will happen to the results of the research?

At the end of the study the results will be analysed and published in an international journal. We will send you a copy of the final results of the study. A copy of the full journal article can be requested from the National Perinatal Epidemiology Unit. You and your baby will not be identified in any report or publication arising from the study.

Who is organising and funding the research?

The study is being run jointly by Barts and the London School of Medicine at Queen Mary, University of London and by the National Perinatal Epidemiology Unit, University of Oxford.

The study is funded by the NHS through the National Institute for Health Research (NIHR) Health Technology Assessment (HTA) programme.

Who has reviewed the study?

All research that involves NHS patients or staff, information from NHS records or uses NHS premises or facilities must be approved by a NHS Research Ethics Committee before it goes ahead. Approval cannot guarantee that you will not come to any harm if you take part. However approval does mean that the Committee is satisfied that your rights will be respected, that the risks have been reduced to a minimum and that balanced against the possible benefits it is reasonable for babies born as early as yours to take part. The committee has also checked that we are giving you sufficient information to make an informed decision about taking part.

Thank you for reading this leaflet. The doctor or nurse who gave it to you will be pleased to discuss it with you and to provide further information if that would be helpful. Alternatively the contact details of the study's Principal Investigator in your NHS hospital and the Study Co-ordinator are provided below.

What if I have any concerns?

If at any stage you have any concern or query about this study or the way it has been carried out, you should contact the Principal Investigator (the name and contact details are below), or you may contact the hospital complaints department.

Information is also available on the study website at: www.npeu.ox.ac.uk/pips

If you would like to contact an independent organisation to discuss the inclusion of babies in research studies without reference to this particular study we suggest that you contact the premature baby charity Bliss. Their address is:

Bliss, 9 Holyrood Street, London SE1 2EL
Freephone Family Support Helpline: [redacted]
Website: www.bliss.org.uk

Name and contact details of local contact:

Name and contact details of Study Co-ordinator:

[redacted] (PiPS Trial Co-ordinator)

National Perinatal Epidemiology Unit, Clinical Trials Unit
University of Oxford
Old Road Campus
Headington
Oxford
OX3 7LF

[redacted]

(To be printed on headed paper)

INFORMATION SHEET FOR PARENTS AND GUARDIANS

Title: Evaluating the reliability of standardised two-year neurodevelopmental data collected during NHS follow-up in children born preterm (REC reference: 10/H07020/35)

Short title: Reliability of two-year neurodevelopmental assessment in preterm infants

We would like to invite your child to take part in a research study.
This information sheet explains why this study is being carried out and what it involves. Please read it carefully and discuss it with others if you wish. Ask us if there is anything that is not clear. Take time to decide whether or not you would like your child to take part.

1. What is the purpose of the study

The long-term health outcome of children born preterm is important. All preterm infants are seen after their discharge from hospital and have their development checked. The doctors carrying out this assessment use different methods that may not be comparable. If children participate in a research study, they may have a repeat assessment.

The purpose of this study is to establish how reliable the routine check is in comparison to a detailed assessment carried out by specially trained examiner. Our secondary goal is to be able to reduce the requirement for a second assessment if children participate in research studies in the future.

2. Why has my child been chosen

We are approaching the families of children born in London at less than 30 weeks gestation (more than 10 weeks before their due date), who are being seen in a hospital follow-up clinic.

3. Does my child have to take part?

This is entirely up to you. Your decision will not affect the standard of care your child receives.

4. What is involved in joining the study?

We will invite you to bring your child for a special appointment at your local hospital, at a time convenient to you. During this session, we will examine movement, speech and problem-solving skills through play and also examine muscle tone. The assessment will be done by a specially trained doctor and does not involve any invasive, unpleasant or painful testing. Most children find the assessment enjoyable and fun. We will also ask you to fill in two questionnaires about your child's social skills and behaviour. The session will last approximately 90 minutes and your child will be with you the whole time. The study will not require you to do anything else and your child's involvement will stop after this appointment. We will reimburse the cost of travel for the hospital visit.

We will compare the results of this assessment with the check carried out in your child's normal hospital follow-up clinic. To do this, we will require your permission to look at your child's medical records.

In the future, we hope to assess the reliability of the assessment at 2 years in predicting future development. We would therefore also like to ask for your permission to contact you in the future.

5. Are there any benefits from taking part?

Your child will receive a detailed assessment of his/her skills and development. We will send a copy of the results to your child's hospital paediatrician and your GP.

There is a possibility that your child may be found to have difficulties in a particular area. If so, your paediatrician will explain what this means, and arrange for further assessments and help to improve your child's abilities should this be necessary.

Some difficulties only become apparent as a child grows older. Therefore your child should continue to receive assessments as recommended by your paediatrician. If you are concerned about your child's development at any time it is important you discuss this with your paediatrician, GP or health visitor.

6. Are there any disadvantages of taking part

The tests used in this study are used around the world to assess children. They involve play and puzzles in a structured way. Most children find them fun but if your child becomes bored or tired we can have a break or stop if you wish.

7. What if there is a problem?

We are required to inform you that there are no special compensation arrangements in the unlikely event of something going wrong. If you are harmed due to someone's negligence, you may have grounds for a legal action. If you have concerns about the way you have been treated during this study, you should inform the Chief Investigator, Professor Neena Modi (contact information below). The normal NHS complaint mechanisms are also available to you and you may contact the Imperial Academic Health Sciences Centre Joint Research Office.

8. What will happen if I do not want my child to continue with the study?

If you do not wish your child to carry on with the study, you can withdraw him/her at any time, without giving reason. This will not affect the care your child receives.

9. Will details about my child be kept confidential?

All information collected about your child during the course of the study will be kept confidential.

10. What will happen to the results of the research study?

The results will be presented at medical conferences and published in scientific journals. No participant will be identified in any presentation or publication.

11. Who is funding and organising this study?

The study is funded by the National Institute for Health Research as a component of the Medicines for Neonates Programme. It is led by the Section of Neonatal Medicine at Imperial College London.

12. Who has reviewed this study?

This study and information sheet has been reviewed and approved by *(Research Ethics Committee)*.

Thank you for reading this. Please do not hesitate to contact us if you have any questions.

[redacted]
Email: [redacted]

Dr [redacted]
Tel: [redacted]
E-mail: [redacted]

Dr [redacted]
E-mail: [redacted]

Professor [redacted]

UK Neonatal Collaborative Necrotising Enterocolitis Study

(REC reference: 11/LO/1430)

UK Neonatal Collaborative
NECROTISING ENTEROCOLITIS STUDY

This study is a component of the NIHR funded "Medicines for Neonates" Programme*, which aims to use operational electronic data to support neonatal services and research. The "**UK Neonatal Collaborative NEC (UKNC-NEC) Study group**" are neonatal teams committed to entering high quality electronic data.

STUDY BACKGROUND

Preventive strategies for Necrotising Enterocolitis (NEC) remain elusive; feeding practices are widely believed to influence susceptibility but have not been tested adequately in randomised controlled trials. Most baseline incidence data come from small studies using varying case-definitions. Surveillance of NEC is also important for assessing temporal trends and geographical variation.

STUDY AIMS

1) To establish an objective case-definition for NEC that is applicable nationally and internationally
2) To determine the incidence of NEC over a large geographically defined population
3) To identify enteral-feed related antecedents that precede the onset of NEC.

METHODS

This study will utilise anonymised NHS electronic data captured as part of clinical care using the neonatal.net NHS platform (widely known as the "Badger system") from all babies admitted over 18 months (starting Nov 2011) throughout the country.

WHAT IS REQUIRED FROM NEONATAL UNITS IN THE UKNC-NEC STUDY GROUP?

Only to ensure completion of the following electronic fields on all neonatal admissions:

Static data

(Enter once on all babies)

- Birth weight
- Gestational age
- Sex
- Mother's race
- Antenatal steroids
- Gastrointestinal anomalies

Daily data

(Enter daily on all babies)

- Most recent weight
- Enteral feed (Type/ Fortifier/Volume)
- Medications (COX inhibitors/ Antibiotics)
- Lines in situ (Umbilical arterial line)
- Packed red cell transfusion

"Abdominal x-ray performed" ad-hoc form

- ONLY TO BE COMPLETED for babies who have an abdominal x-ray to investigate abdominal signs

If your unit would like to contribute to the study or would like further information, please contact :
Dr [redacted] Clinical Research Fellow, Neonatal Data Analysis Unit, Department of Medicine, Imperial College London, Chelsea & Westminster campus , Fulham Road, London SW10 9NH [redacted]

*** Medicines for Neonates Programme Senior Investigators:**

[redacted]

NDAU Neonatal Data Analysis Unit | Imperial College London | MfN Medicines for Neonates | Chelsea and Westminster Hospital NHS Foundation Trust

Version 1, July 2011

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

Are you the parent or carer of a baby who has spent time on a neonatal unit?

If so we would love to hear from you!

In neonatal care, a lot of data is routinely collected from your baby. Some of this information could be very useful to health researchers but at the moment it is not automatically used for this purpose.

We would like you to answer our questionnaire, so we can hear your views on the subject: Who (if anyone) would you be happy to see your baby's data and for what sort of research?

We would love to hear from fathers as well as mothers who currently have or have recently had a baby in neonatal care. Users of languages other than English can be supported to take part in the survey.

What do I need to do to take part?

Please let one of the nurses know you are interested.

A research nurse will be able to tell you more about the survey, provide you with the questionnaire and help you fill it in if you would like.

There is also an information leaflet available to answer any questions you may have.

NDAU
Neonatal Data Analysis Unit

MANCHESTER 1824

More information
If you would like more information regarding the project please contact:
[redacted] Children's Research Nurse
Tel: [redacted]
Mobile [redacted]

Bliss
for babies born too soon, too small, too sick

What is the purpose of the study?

In neonatal care, a lot of data is routinely collected from your baby. A lot of this information could be very useful to health researchers but at the moment it is not automatically used for research purposes.

'Data' refers to all sorts of information that is collected, from birth weight to drugs administered, to the progress your baby is making and so on. This might be recorded in a database or on paper notes. We are asking only about information, not tissue samples etc.

'Research' refers to the process of collecting, ordering and evaluating information in order to provide further understanding, new knowledge and/or a basis for decision making and action or change.

Please note that we are not asking to use your baby's data. We are interested in hearing what you think. There are no 'right' or 'wrong' answers.

Where and when is the research taking place?

The survey is taking place in a number of neonatal units across England, in London, the North West and Yorkshire. It will run from Oct 2011 to Oct 2012.

What are the advantages of taking part?

The subject of data sharing for research purposes is high on the agenda in health care and so now is an opportunity to make your voice heard.

Are there any disadvantages of taking part?

The questionnaire will take 15-20 minutes of your time and some of the questions may be upsetting. As parents, we appreciate what a difficult time this is and we make it clear on the questionnaire which questions we think may cause upset. You are free to skip any questions that you do not wish to answer.

Is the questionnaire anonymous?

The information you give us will not be seen by anyone other than the researchers at the University of Manchester. You will have the option of supplying your name and address and letting us know if you want to be contacted in future regarding this or related research.

How many parents will be taking part in the study?

We are hoping to receive 1525 completed questionnaires altogether.

Am I eligible to take part in the study?

If you have, or have had, a baby in neonatal care, we would love to hear from you. We are keen for both mothers and fathers (and other carers if appropriate) to complete a questionnaire independently of one another. So both you and your partner (if you have one) can fill in a separate questionnaire.

What will happen if I don't want to carry on with the study?

If you decide to take part and then later change your mind, either before or during the study, you can withdraw. However, once the questionnaire has been filled in and sent back it will have been anonymised, therefore withdrawing will not be an option as we will not be able to trace the questionnaire back to you.

Who is organising and funding the study?

Funded by the National Institute for Health Research, it is part of a much bigger project that involves the Neonatal Data Analysis Unit (NDAU) based at Imperial College, London. This project is led by [redacted] and [redacted] at The University of Manchester, in partnership with Bliss.

This questionnaire has been designed by a group of parents (both mothers and fathers) who have all had babies in neonatal care in recent years. Whilst we have all spent time with our babies in neonatal care, we all have different views on who we would want to have access to our babies' data, depending for example on the purposes of the research and how/when we were asked.

Can I find out what the findings are from the research?

Yes. You will be given the option of providing us with your contact details so that we can post or e-mail you with the findings at the end of the study. Alternatively, they will be published on the Bliss website at www.bliss.org.uk

What if there is a problem?

If you have concerns about any aspect of this study, please ask to speak to the research nurses who will do their best to answer your questions.

If they are unable to resolve your concern or you wish to make a complaint regarding the study, please contact a University Research Practice and Governance Co-ordinator on [redacted] or [redacted]. Alternatively, email: [redacted]

Should any distress arise, the Bliss helpline [redacted] may be of use.

Chelsea and Westminster Hospital NHS
NHS Foundation Trust

What do I have to do if I agree to take part?

If you are willing and able to take part, then a research nurse will ask you to sign a consent form. You will then be given a copy of the questionnaire.

You will be given the choice of filling in the questionnaire yourself or having a research nurse fill it in with you. The research nurse will ensure that anything you say is kept confidential.

Interpreter services are available should you or your partner require them.

Again, confidentiality is guaranteed. If you wish to complete the questionnaire on your own, you can do so on the unit. It should take around 15-20 minutes to fill in. A pre-paid envelope will be provided addressed to The University of Manchester so that the questionnaire can be sent back and it will not be seen by the staff at the hospital.

Why do the questions refer to one baby when I have had a multiple birth?

For consistency of style we use 'baby' in the singular. However we do appreciate that a number of parents completing the questionnaire will have more than one baby in neonatal care at this time. Please bear with us on this.

More Information

If you would like more information about the project please contact:

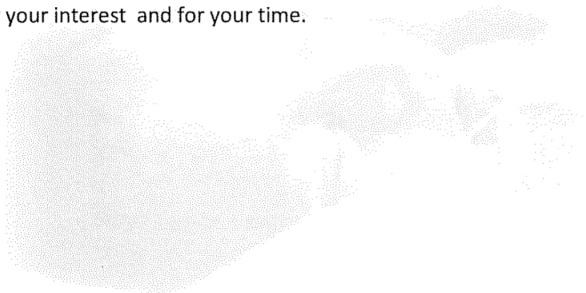
[redacted]esearch Nurse
Tel: [redacted]
Mobile: [redacted]
Email: [redacted]

Data Sharing in Neonatal Services

We would like to invite you to take part in a new research study from the University of Manchester and Bliss (the charity for babies born too soon, too small, too sick.) It is a questionnaire survey that has been designed by a group of parents, both mothers and fathers, who have all had babies in neonatal care in recent years.

Before you decide whether or not to participate, please read this booklet, as it explains why the research is being carried out and what it will involve. Feel free to ask us if there is anything that is not clear or you want to know more about.

Thank you for your interest and for your time.



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