Obtaining Informed Consent for the PiPS Clinical Trial

This leaflet is for health care professionals who are involved in seeking consent from parent's whose baby is eligible to take part in PiPS.

What is informed consent?

Informed consent is the process by which the parent, after discussing the study with a health care professional, voluntarily confirms their willingness for their baby to participate in the PiPS clinical trial.

Who is eligible to seek informed consent?

Consent can be sought and obtained by any health care professional who has received PiPS and GCP training, and who is registered to do so on the site delegation log. Please confirm with your site Principal Investigator whether you are able to obtain consent.

Who is eligible to give consent?

- Agreement to participate should ideally be sought from both parents of an eligible infant.
- Mothers automatically have parental responsibility for their children and can be the sole signatory on the consent form.
- Fathers may only act as sole signatory on the consent form if married to the mother when the child is born or if named on the birth certificate (**n.b.** the latter is unlikely to be relevant in this trial since it is rare to register the baby this early).
- Unmarried fathers do not automatically have parental responsibility for their child, but a court order or a 'parental responsibility agreement' can give it to them.

When and where should consent be taken?

Although babies can be randomised up to 48 hours after birth we are keen that they are recruited as soon as is feasible. Parents cannot formally give consent before the baby is born but whenever possible staff should try to begin the process of talking to parents about the trial before the onset of labour; the objective is to give them as much time as possible to consider their decision. If this has not been possible then they should be approached as soon as seems reasonable after birth.

If possible consent should be sought in a quiet area of the Unit away from the noise of the monitors and alarms. The person taking consent should use language which is easy to understand and which is free from jargon.

After telling the parent(s) about the trial and giving them an opportunity to ask their immediate questions a Parent Information Leaflet should be left with them to reinforce and expand upon what has been said. The Parent Information Leaflet should list the name and contact details of the local Principal Investigator and the designated local PiPS nurse as well as the contact details for the PiPS Trial Co-ordinator and the preterm baby charity Bliss. Bliss has agreed to be available as a source of independent advice and support for parents; the number of their helpline is given on the Information Leaflet.

Key points to be covered in discussion with parents

1. While preliminary results of studies of probiotics are encouraging, particularly in respect of reducing the incidence of NEC, the studies have been relatively small and we need bigger studies to be confident about whether or not probiotics are helpful.
2. In general probiotics are thought to be a very safe treatment. However the babies being recruited into this study are more preterm and younger than babies in other studies and at higher risk of complications like NEC; we need to be confident that it really is safe to give probiotics to this age group.
3. Neither the medical and nursing staff nor the parents will know whether the baby is receiving probiotic or placebo.
4. Parents may have heard or read about probiotics and be keen to give them to their baby. It is important to explain that the probiotic we are using in the study is different from those available commercially and that unlike them it is manufactured to a very high specification and that it contains a single probiotic bacterium so that we know exactly what the baby is receiving. Although a few neonatal units do sometimes use probiotics we do not believe that any of the products being used is manufactured to this high specification and during the course of the trial we would strongly discourage the use of any other probiotic product.
5. In order that the probiotic and placebo look identical the powders are resuspended in 1/8 strength Neocate, the baby receives 1ml of the intervention each day. It is important to explain this to parents, some of whom will have been advised that their baby is at such high risk of gut complications that feeds will be withheld. They should be reassured that the choice of Neocate has been made after wide consultation. Neocate is a synthetic product designed specifically to be tolerated by babies with compromised gut; it is inconceivable that 1ml of this very dilute product could cause NEC. Furthermore parents should be advised that this will not reduce the possibility of successful later breast feeding.
6. The objective will be to continue the intervention until 36 weeks post menstrual age even if the baby is transferred to another hospital.
7. The doctors looking after the baby will decide whether a dose of intervention should be withheld. In general we believe it is safe to give the intervention even on days when the baby is unwell – the only clear contraindication is the presence of intestinal perforation.
8. We will aim to collect 2 stool samples, one as close as possible to 2 weeks post-natal and one at 36 weeks post-menstrual age. These samples will be sent to the laboratory at the Royal London Hospital and analysed to check what bacteria are in the gut. We are requesting that these samples are retained for further investigations of the mechanisms of action of probiotics. This is described in the Parent Information Leaflet and specifically asked for by question 3 on the Consent Form - if the parents object to retention of the stool samples the baby can still be recruited and take full part in the trial.
9. No other samples are collected from participating babies.
10. It should be explained and is clearly documented in the Parent Information Leaflet that the investigators will extract data from the written case notes, from the electronic data held about the baby (e.g. SEND) and that details of results of microbiological investigations will be obtained directly from the hospital laboratory.
11. Parents can withdraw their baby from the study at any time and do not have to give an explanation. If this happens we would request that we can nonetheless use the baby's clinical data and collect outstanding stool samples.
12. It will not be possible to identify any individual baby in any presentation or report arising from the trial.

Important points to remember

- Parents who do not speak English should only be approached if an appropriate adult interpreter is available.
- Consent must be obtained before logging on to the Randomisation Website.
- Having gained consent the white copy is to be sent to the PiPS Trial Office (using the FREEPOST envelopes provided), the green copy is to be put into the Data Collection File, the yellow copy is to be given to the Parent and the green copy should be put into the babies medical notes with a Parent Information Leaflet.
- In the case of twins or triplets each infant must have a separate signed consent form. It should be explained to parents that the babies will be randomised as individuals; thus siblings may be in different arms of the trial.
- In the days following recruitment, and occasionally during the baby's stay, the clinical staff should confirm informally with the parents that they understand that their baby is in the trial and that they continue to consent to this and understand the trial design.

Recruitment of babies into multiple studies

There is no theoretical reason why babies should not be actively involved with other trials or non-intervention studies while participating in the PiPS trial. If investigators have any concerns they should contact the PiPS trial office who, if not able to answer the query immediately, will contact the Chief Investigator, Professor Kate Costeloe or designated deputy for advice.

Checklist

- ✓ Has the parent(s) had an opportunity to read the Parent Information Leaflet?
- ✓ Have you explained, and has the parent(s) understood, the aim of PiPS?
- ✓ Have you explained what the trial entails - proposed treatment and description of procedures?
- ✓ Have you explained the potential benefits and potential risks of taking part in PiPS?
- ✓ Have you explained what a placebo is?
- ✓ Have you explained what a 'randomised controlled trial' is?
- ✓ Have you explained that if the parent(s) decline, the baby's care is unaffected?
- ✓ Have you explained that the parents are free to withdraw their baby (i) at any time, (ii) without having to give a reason and (iii) without affecting their baby's medical care?
- ✓ Have you told the parent(s) that their GP will be informed of their baby's participation in PiPS?
- ✓ Has there been enough opportunity for the parent(s) to ask questions?