**Participant Information Sheet/Consent Form – Parent/Guardian**

**Project Title**: Probiotic dose-response study in extremely preterm infants: A randomized controlled trial

**Principal Investigator**: Dr Chandra Rath, Neonatal senior registrar

**Student Researcher**: Dr Chandra Rath

**Associate Investigator(s):** A/Prof Shripada Rao, Dr Gayatri Jape, Prof Sanjay Patole

**Location:** Neonatal Intensive Care Unit, King Edward Memorial Hospital, Subiaco, Western Australia, 6008.

**What is the research about?**

Premature babies (born before 8 months of pregnancy) are at risk necrotising enterocolitis (NEC), a potentially serious inflammatory condition of the bowel, as well as hospital acquired infections, and poor nutrition. Complications of prematurity such as these, especially NEC, increase the risk of death, and long‐term disability. The risk of these complication is high especially in extremely premature babies born before 28 weeks of pregnancy. Probiotics are beneficial bacteria which have been shown to significantly reduce the risk of death, NEC, and hospital acquired infections whilst facilitating nutrition in very premature babies. Probiotic supplementation for very premature babies is a standard practice in all neonatal intensive care units (NICU) in Australia, New Zealand and many units in other countries.

We currently administer a daily dose of 3 billion probiotic bacteria for premature babies in our unit using a product imported from Japan, under a special permission from the Australian government. This dose is based on our research using this product and studies of other probiotics. This study is designed to assess if a dose higher than 3 billion bacteria per day is more effective whilst being safe in reducing inflammation and improving the balance of beneficial versus potentially harmful bacteria in the gut of extremely premature babies.

Specifically, the proposed study will compare the dose of 3 billion against 6 and 9 billion bacteria per day in extremely premature babies using the stool (poo) samples. We think that babies who receive higher dose of probiotics will have reduced gut inflammation and better intestinal bacteria and overall health compared to those who receive lower dose.

**What happens if I decide for my baby to participate?**

If you decide to let your baby take part in this research, we will ask you to sign the consent form. By signing you agree that you have understood what you have read and what has been discussed. Signing the consent confirms that you agree for your baby to participate in the research project and have their health information used as described. Please take your time and ask any questions you may have before you decide what to do. You will be given a copy of this information sheet and the consent form to keep.

If you decide to allow your baby to participate in our study, we will collect 2 stool samples from your baby. The first sample will be collected before and the second sample will be collected 4 weeks after starting the probiotic supplementation. The samples will be kept in a deep freezer at KEM Hospital, Subiaco, Western Australia before sending them to a specialised laboratory in University of New South Wales, Sydney for analysis. Whether your baby will receive the probiotic at a dose or 3 or 6 or 9 billion bacteria per day will be decided randomly to avoid bias and generate scientifically robust results.

**What are the potential benefits and risks?**

This study is designed to assess if a probiotic dose higher than the currently used dose of 3 billion bacteria per day is safe and more effective in reducing inflammation and improving the balance of beneficial versus potentially harmful bacteria in the gut of extremely premature babies. The results of this study will add significant knowledge for using the most appropriate dose of probiotics in premature babies. Whether your baby will have the proposed benefits or not is uncertain.

As for risks, probiotics have been extensively studied in premature babies in many NICUs across the globe. It is important to note that doses much higher than 3 billion per day (e.g. 9 billion) have been used in very premature babies. No major adverse effects related to probiotic supplementation have been noted in these studies. Occasionally, some babies may develop abdominal distension and regurgitation after probiotic supplementation. If required, we will stop the supplementation in such cases. There have been reports of infections caused by the probiotic bacteria. However, these infections are easy to diagnose and treat, and most agree that the significant benefits of probiotics outweigh the rare risk of this complication. We will be carefully monitoring your baby for probiotic infection and treat promptly if required. It is possible that your baby may develop a side effect that we do not know about yet.

**What if I don't consent or withdraw consent 'during the study'?**

Taking part in this study is voluntary. It is your choice whether to allow your baby to participate in this study or not. The standard of care provided to your baby will not be affected in anyway if you decide not to participate in the study or withdraw from the study at any stage. You do not have to give us a reason for your decision at any stage.

**Who will have access to my baby’s information?**

The research team and a representative of the CAHS Ethics Office will have access to the information we collect in this research. The collected information will be re-identifiable (coded). This means that we will remove identifying information on any data or sample and replace it with a code. Only the research team will have access to the code to match the data or sample to your baby’s name, if required. Any information will be confidential and used only for this study. We can let others know this information only if required by the law or as per your request.

# What happens with the results of the research?

The results of this study will be presented in scientific conferences and published in a peer-reviewed journal. The presentations and publications will not have any identifiable information to protect participant confidentiality. Results of the study will be provided to you if you wish.

**Who can I talk to if I need more information?**

Dr Chandra Rath can be contacted on 0452549299 to answer any questions you may have about your baby’s participation in this research. This study has been approved by the human research ethics committee of Perth Children’s Hospital, Western Australia. If you have any concerns and/or complaints about this study, you may contact the Executive Director Medical Services CAHS on 0864562222 Your concerns will be brought to the attention of the ethics committee.

**Consent Form:** Parent/Guardian

**Title**: Probiotic dose-response study in extremely preterm infants: A randomized controlled trial

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**Associate Investigator(s):** A/Prof Shripada Rao, Dr Gayatri Jape, Prof Patricia Conway, Prof Sanjay Patole

**Student researcher**: Dr Chandra Rath

* I have read, or had read to me, the information statement version listed above, and I understand its contents.
* I believe I understand the purpose, extent and possible risks of my baby’s involvement in this project.
* **I voluntarily consent to my baby taking part in this research project.**
* I have had an opportunity to ask questions and I am satisfied with the answers I have received.
* I understand that this project has been approved by Perth Children’s Hospital Human Research Ethics Committee and will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007) – updated March 2014.
* I understand I will receive a copy of this Information Statement and Consent Form.

**OPTIONAL CONSENT**: I do/ I do not consent to the storage and use of my baby’s

information in future ethically approved research projects that are related to this project.

**Baby’s name:**

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**Parent’s name Parent’s signature Date**

Declaration by researcher: I have supplied an Information Sheet and Consent Form to the

participant who has signed above, and believe that they understand the purpose, extent and possible risks of their involvement in this project.

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**Research team member’s name** **Research team member’s signature** **Date**

Note: All parties signing the Consent Form must date their own signature.

Interventional Study Participant Information Statement and Consent Form

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**Research team member’s name Research team member’s signature Date**

**Note:** All parties signing the consent form must date their signature.

Interventional Study Participant Information Statement and Consent Form