Department of Pediatrics
Patan Hospital, PAHS, Lalitpur
Tel:+977-1-5227778

Department of Pediatrics
TU Teaching Hospital, IOM, Maharajgunj
TelM+977-1-4412303

Department of Pediatrics
John Radcliffe Hospital,
Oxford University, UK
Tel: +44(01)1865234239

Parent information sheet and consent form

Study Title: Optimising DPT-Containing Vaccine Infant Immunisation Schedules in Nepal

Why are vaccines important?

Vaccines help protect our bodies against diseases. When a child comes into contact with a disease against which they have been vaccinated, their body will be able to recognise and fight the disease. Without vaccines, children are at increased risk of catching many serious diseases.

Why do we want to do a study?

The World Health Organization (WHO) recommends that all children receive a number of different vaccines at specific ages. The DPT containing vaccines (DPT-Hep B- Hib) protects against 5 diseases, they are diphtheria, tetanus, whooping cough, hepatitis B and diseases like pneumonia and meningitis caused by a bug called Haemophilus influenzae type b (Hib.) Many countries around the world give this vaccine at different time points however it is not known which schedule is best.

The purpose of this study is to help identify the best possible schedule for DPT containing vaccine or alternative schedules, which will provide the best level of protection against the diseases when children are young. To do this, the DTP-containing vaccine will be given according to 5 different schedules, with a booster at 9 or 12 months of age. These schedules have been proven safe and effective and are being used in different countries. The 5 schedules will be compared to see if any one schedule is better than the others. The results of this study will be used to help develop potential new childhood vaccination schedules

Your child will receive all the other vaccines which are currently given routinely: BCG/Polio vaccines, Pneumococcal vaccine, Japanese Encephalitis, Measles and Rubella vaccine; Although the timing of each vaccine may be slightly different from what you have learnt about the National Immunization program. Additionally, we will give vaccines for typhoid, and chicken pox. The study doctor/nurse will talk to you about all the vaccines that your child

receives. All vaccines will be given according to the different schedules (See table 1) and your child may fall in any of five schedules shown in the table.
The study will be conducted in 2 countries (Nepal and Uganda). Approximately 900 children will be enrolled in each country.

What does the study involve?

The study involves your child attending for up to 3 more visits than they usually would over the same time frame, for vaccinations. They may have up to 4 blood tests. They will also receive, with your permission, 2 additional vaccines (for typhoid and varicella) which they would not usually receive and will protect them against two additional diseases which are common in childhood and can result in hospital admission.

During the study, you and your child will attend up to 10 visits at the study centre over a 2-year period, depending on the vaccination schedule your child is allocated to. The study team will monitor the growth of your child and draw no more than 4 samples of blood, at different times over 2 years, to assess the body's response to the vaccine.

If you decide that you want your child to take part, you will be asked to sign an informed consent form. You will be given a copy of the signed form to keep, and the original will stay at the study centre.

At the first visit the study doctor will record your child's date of birth, gender race/ethnicity and ask you some questions about your child's medical history and current health status. Your child will be assigned to one of the 5 vaccination schedule groups. He/she /will have an equal chance of being assigned to any of the different vaccine schedules and booster groups. This will be determined at random by a computer. No one will influence which schedule your child follows during the study. We will explain in more detail the schedule your child has been allocated to. Your child will then either receive their first set of vaccines or be asked to come back at 8 weeks of age. The study doctor/nurse will inform you about the schedule you are assigned to and give you a health card and this will show the different time points your child will come for study visits.

At each study visit a physical examination will be performed to check your child's overall health; if needed they will take a blood sample and give any vaccines that are due. The study doctor will also ask about any illness' and medications your child has since the last study visit.

Table 1: vaccines schedules up to 24 weeks of age

Schedule One			
6 weeks	**10 weeks**	**14 weeks**	
Consent & randomisation **DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**DPT, HepB-Hib** **PCV** **Polio (oral)** **Rota**	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV**	

Schedule Two			
6 weeks	**10 weeks**	**14 weeks**	
Consent & randomisation **DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**Polio (oral)**	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	

Schedule Three			
6 weeks	**8 weeks**	**16 weeks**	**20 weeks**
Consent & randomisation	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**Polio (oral)**

Schedule Four			
6 weeks	**8 weeks**	**12 weeks**	**16 weeks**
Consent & randomisation	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**DPT, HepB-Hib** **Polio (oral)** **Rota**	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV**

Schedule Five			
6 weeks	**8 weeks**	**16 weeks**	**24 weeks**
Consent & randomisation	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**DPT, HepB-Hib** **PCV** **Polio (oral) &** **FIPV** **Rota**	**DPT, HepB-Hib** **Polio (oral)**

Table 2: vaccine schedules 9 months – 2 years

Booster Group 1				
9 months	**10 months**	**12 months**	**15 months**	**24 months**
DPT, HepB-Hib **Measles-Rubella** **PCV**	**Typhoid**	**Japanese encephalitis**	**Measles-Rubella**	**Varicella**

Booster Group 2				
9 months	**12 months**	**13 months**	**15 months**	**24 months**
Measles-Rubella **PCV**	**DPT, HepB-Hib** **Japanese encephalitis**	**Typhoid**	**Measles-Rubella**	**Varicella**

Booster Group 3				
9 months	**12 months**	**13 months**	**15 months**	**24 months**

Measles-Rubella PCV	**DPT, HepB-Hib Typhoid**	**Japanese encephalitis**	**Measles-Rubella**	**Varicella**

Booster Group 4				
9 months	**12 months**	**13 months**	**15 months**	**24 months**
Measles- Rubella PCV	**DPT, HepB-Hib Typhoid Japanese encephalitis**		**Measles-Rubella**	**Varicella**

What will happen to the blood samples taken from your child?

As part of the study your child will have a total of 4 blood draws over 2 years. Table 2 below shows possible timings for each blood draw The exact timing of each blood draw will be allocated at your first visit. We will take no more than 5mls of blood each time. Your child's samples will be labelled with a code that will allow your child's identity to be anonymised.

Table 3: Blood draw timing

Blood draw timing			
Blood 1	**Blood 2**	**Blood 3**	**Blood 4**
6-24 weeks	**24 weeks -28 weeks**	**9 months or 12 months**	**10 months – 24 months**

All blood samples will be stored at Patan Hospital or Tribhuvan University Teaching Hospital and some will be shipped to laboratories in Europe to help understand how well the vaccines work. At the end of the study, anonymised left-over samples will be stored for future analysis unless you request for them to be destroyed. No additional tests will be performed without the approval of the Nepal Health Research Council (NHRC)

At any time during the study or after the study has finished you may ask for your samples to be destroyed. Information obtained from the samples will continue to be kept and used for the purposes agreed by you in this document.

What are the possible disadvantages or risks of taking part in the study?

Most children who receive vaccines remain entirely well. Some children may develop redness, swelling and pain at the site of injection and some irritability, sleepiness or reduced feeding. Children can develop fever and may develop vomiting or diarrhoea. There have been very rare reports of prolonged crying, rashes and allergic reactions. The study staff are trained and equipped to deal with these. There are no additional risks beyond those that are normally possible with routine immunisations.

In some groups the infant will get a particular vaccine later than national schedule and you may worry that there is possibility of Vaccine Preventable Disease but such risk is negligible.

Your child will be continually followed to monitor for any untoward events. We will ask you to report any symptoms of illness in your child.

The blood test may be uncomfortable. However, painless creams will be offered to minimise discomfort. Only experienced doctors and nurses involved in the study will be drawing blood from your child after adequate preparation. After the blood draw there may be a small bruise which should fade in a few days.

What are the possible benefits of taking part in this study?

During the study your child will receive the routine vaccines in the Nepal vaccine programme. In addition, your child will also receive typhoid and chicken pox vaccines free of charge which are not currently the part of the national immunization schedule and have to be bought at expensive prices by the parents. If your child has a fever or other symptoms of illness during the 2 years of the trial, they will be able to access routine medical care and treatment through the study hospital by designated paediatricians and doctors for the study and all costs will be covered by the study. If your child is sick, please contact the study Dr on telephone number ……. and they will arrange to see you and your child at the study site.

Your child's participation in this study will help generate information to help optimize vaccine schedule that will prevent these vaccine preventable diseases better in children of this country and the world in future.

You will receive 500 NRS to cover travel costs for each scheduled study visit

What else do I need to know?

If you decided to take part representatives of the ethics committee and regulatory authorities may read your child's study records to check that the study is being carried out properly. The results of your child's tests and the information we collect about your child (also called study data) will be shared with other researchers who are in alliance with us in other countries. This will not however include any personal identification information. Your child's privacy and personal information will be protected using measures which follow Data Protection Act in Nepal. The data collected will be used for research related to infection and immunity. We will inform you of any changes to the study. The study team may contact you at a later date via telephone or email in connection with this study or other studies.

Taking part in this study is entirely voluntary, and you can withdraw from the study at any time by contacting the research team at the hospital. You do not need to give a reason, it will not affect your child's routine care and your child will receive their vaccines in the normal way. If you choose to withdraw from the study, we will make sure your child completes the routine vaccine programme. We will still use the information you gave us before your withdrawal.

The study sponsor has insurance to cover the costs of research-related injuries providing that your child followed all the instructions and advice of the study doctor and did nothing to cause or contribute to the research-related injury.

What if you have any additional question who should you contact ?

If you or your child have a question, concern or complaint about any aspect of this study, you should ask any of the study doctor, …… on telephone number: ……. or a member of the research team who will do their best to help or you or you can contact the Lead Investigators, Dr Meeru Gurung (Patan) on phone number: ……... or Dr Arun Sharma (IOM) on phone number: ……... If you have any concerns or complaints about the research you may contact the ethical review board of NHRC. (Ramshah Path, Kathmandu, Nepal, P.O.Box 7626 Phone:- **977-1-4254220**, Fax : 977-1-4262469 / 977-1-4268284, Email : **nhrc@nhrc.gov.np**)

By signing this consent form, you are giving permission for the processing and use of your child's personal information for this study.

Please note that, once your child commences the study, the data collected cannot be deleted for a number of years due to legal requirement to retain the data for 15 years.

University of Oxford is organising this study as the study sponsor and is responsible for your child's anonymised study data in accordance with applicable Data Protection laws.

Who has reviewed the study?

This study has been reviewed and approved by the Nepal Health Research Council Research Ethics Committee, The Institutional Review Boards at Patan Academy of Health Sciences, Patan and the Institute of Medicine, Tribhuvan University and the University of Oxford Tropical Research Ethics Committee (OxTREC)