Parents /Guardians Information and Consent Form

Trial of Optimal Therapy for Pseudomonas Eradication in Cystic Fibrosis

(www.torpedo-cf.org.uk)

Your child is being invited to take part in a research study. Before you decide whether or not 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 others if you wish.

- **Part 1** tells you the purpose of the study and what will happen if your child takes part
- **Part 2** gives you more detailed information about how the study will be organised

Please ask us if there is anything that is not clear or if you or your child would like more information. Take time to decide whether or not you wish to take part.

Part 1

1) What is the purpose of the study?

People with Cystic Fibrosis are at risk of developing infection in their lungs. If this should happen then a common cause of infection can be a bacteria or germ called *Pseudomonas aeruginosa*. Usually when this bacteria is first found in the sputum or cough swab patients are treated with antibiotics to get rid of (eradicate) the bacteria. There is a choice of treatment that can then be used to eradicate the bacteria – either antibiotics taken by mouth (orally) or given directly into the vein usually in the arm or the back of the hand (intravenously, IV), each given in association with three months of inhaled antibiotic treatment through a machine called a nebuliser which allows you to inhale the medication as a mist directly into your lungs.

It is generally accepted that these treatments are essential to try to get rid of the *Pseudomonas* from the lung and the doctor for your child would normally choose one of these methods to treat your child if they had Pseudomonas in the lungs. However, we do not know for sure which of these treatments is the best to help get rid of this type of infection.

The only way to find out which of these two treatments is the most helpful is to compare the two treatments in adults and children with Cystic Fibrosis (CF). This type of study is called a Randomised Controlled Trial (RCT).

We have therefore designed a study to compare the two different antibiotic treatments. If you and your child agree to take part your child will be randomly allocated to one of two groups;

Treatment A) 14 days IV ceftazidime and IV tobramycin*
Treatment B) 3 months oral ciprofloxacin*
**Both treatments will be given in conjunction with 3 months inhaled (nebulised) colistin*

2) Why has my child been chosen?

This study will recruit 280 patients from CF centres throughout the UK.

Your child has been asked to take part in this study because your CF centre has recently indentified that your child has *Pseudomonas aeruginosa* infection of the lungs.

3) Does my child I have to take part?

No, taking part is voluntary. It is up to you and your child to decide whether or not to take part, or drop out at any time, without giving a reason. A decision to leave the study or a decision not to take part will not change the standard of care your child receives now or in the future. The study doctor may also ask your child to stop taking part in the study at any time if they feel it is necessary.

4) What will happen to my child during the study?

The total study duration is 24 months, with a minimum follow-up period of 15 months. Study visits will take place every three months and should normally be scheduled to take place at the same time as normal hospital visits.

Screening

If you and your child are happy to take part, and are satisfied with the explanations from your research team, you and your child will be asked to sign a consent form at the first clinic visit. You will be given a copy of the signed information sheet and consent forms to keep. Once consent has been taken, you/your child will be asked some questions about their medical history, and a physical examination will be carried out. This will be performed by your usual CF team and will add approximately 45 minutes to the consultation time.

Treatment Allocation

Half (50%) of the people in the study will be given IV treatment (Treatment A) and the other Oral treatment (Treatment B), so there is a 50/50 chance of your child getting either treatment group. You and your child will not be able to choose which treatment your child gets. The decision of which of the two treatments you receive will be made by chance (this is called 'randomisation').

Treatment A: treatment will be given intravenously over a period of 14 days, with each intravenous treatment lasting no more than 1 hour at a time. Three blood tests will be taken during the course of their treatment to monitor how well their kidneys are working and to check that they are getting the correct amount of tobramycin. These tests are carried out routinely as part of standard care for all patients receiving tobramycin. During the 14 day treatment period your child will usually have to stay in hospital as an inpatient. It is sometimes possible to give some of this treatment at home and you could discuss this with your CF team.

Treatment B: treatment will be given as a liquid/tablet which your child will need to take twice daily for 3 months.
**Both treatments will be given in conjunction with inhaled colistin for 3 months*

During treatment your child will be asked to complete a daily treatment diary. The aim of this treatment diary is not to check that your child has taken all their medication but will be used to keep an accurate record of what medication was taken when. You and your child will also be provided with a short health diary which will allow you to record how many times your child has seen their GP or other people involved in their care. This will allow the study team to assess how the study treatment impacts on you and your child.

Follow up

After your child has stopped receiving treatment you and your child will be required to attend hospital for a follow up visit every 3 months up to a maximum of 24 months after entering the trial. During these visits your child will have an examination performed by your usual CF team, who will perform lung function measurements (spirometry) if your child is old enough, and your child will be asked to provide sputum and / or cough samples.

A very important aspect of this study involves assessing how your child's health or any treatment your child may receive affects his/her quality of life so our research nurses will ask you and your child to fill in a questionnaire that asks your child about how he / she is feeling. This questionnaire will be repeated at 3 months, 15 months and 24 months afterwards. The questionnaires will be completed when you and your child attend for your child's treatment or follow-up appointments and will take approximately five minutes to complete. It is very important for you and your child to answer all the questions in the questionnaire for us to accurately assess the impact of the treatment upon you.

5) What if my child is pregnant or plans to become pregnant or is breastfeeding?

Your child should not take part in this study if they are pregnant, or if they plan to become pregnant during the first three months of the study during which time they will be receiving the *Pseudomonas* eradication treatment. There is no reason from the study point of view that your child should not become pregnant after this initial three months.

6) What are the alternatives for treatment?

The treatments used for this trial are part of standard NHS care and are both used for the treatment of Pseudomonas infections in the lungs of CF patients. If you decide not to participate in the study, then your doctor will discuss treatment options with you.

7) What are the side effects of the treatment?

There are side effects to all types of medicines:

If your child receives intravenous antibiotics there is a small risk that they will developed an allergic reaction to the antibiotic, in some rare cases tobramycin can cause kidney problems. However, if your child is going to receive IV treatment they will be closely monitored by their clinician. Your child will have a blood test at the start of treatment to check their kidney function is normal and that they are getting the correct amount of tobramycin. Your child will also have two further blood tests taken during their treatment to carefully monitor the levels of antibiotic in their body. These are routine tests carried as part of standard care for all patients that receive tobramycin. Tobramcyin can rarely affect hearing.

Ciprofloxacin can make skin more sensitive to the sun and therefore more prone to sunburn, you should use sun screen when you know your child will be in the sun. Other common side effects are feeling sick and development of diarrhea. Ciprofloxacin can rarely cause joint pain.

The CF doctor taking care of your child will fully explain the possible side effects for both treatments with you and your child before treatment begins. Should any side effects develop then your child should stop taking the study medication and you should discuss alternative treatment

with his/her CF team who may feel that it is safe to continue or may wish to give your child a different treatment.

8) What are the possible disadvantages and risks of taking part?

Both of these forms of treatment are available to your child whether or not you take part in this study. The study will cause you and your child a little added inconvenience because of the additional questions that you will be asked at a maximum of nine clinic visits.

9) What are the possible benefits of taking part?

Both treatments that will be used in the TORPEDO-CF trial have been shown to eradicate Pseudomonas infection from the lungs of CF patients. However, this cannot be guaranteed. The information we get from this study may help us to improve future treatments for CF patients whose lungs have become infected with *Pseudomonas aeruginosa.*

10) What if there is a problem?

Any complaint about the way your child has been dealt with during the study or any possible harm your child might suffer will be addressed either by your own CF team or by the study team if necessary. The detailed information on this is given in Part 2.

11) Will my child's participation in this study be kept confidential?

Yes. All information which is collected about your child during the course of this research will be kept strictly confidential. We will inform your child's GP and the Medicines for Children Research Network Clinical Trials Unit (CTU) of your child's participation in the study. Other than this, any information about your child that leaves the hospital will have his/her name and address removed so your child cannot be identified from it. The detailed information on this is given in Part 2.

12) Contact for Further Information

Please feel free to ask your child's doctors any questions about the study or about any of the treatments described above.

This completes Part 1 of the Information Sheet.
If the information in Part1 has interested you and you are considering participation, please continue to read the additional information in Part 2 before making any decision.

Part 2

13) What if new information becomes available?

Sometimes during the course of a research project, new information becomes available about the treatments/drugs that are being studied. If this happens, your child's research doctor will tell you and your child about it and discuss with you whether you and your child may want to continue participation in the study. If your child decides to withdraw his/her consent the research doctor will make arrangements for your child's care to continue. If you and your child decide to continue in the study you and your child will be asked to sign an updated consent form.

Also on receiving new information your child's research doctor might consider it to be in your child's best interests to withdraw him/her from the study. Your child's doctors will explain the reasons and arrange for his/her care to continue.

If the study is stopped for any other reason, your child will be told why and your child's continuing care arranged.

14) What happens if I change my mind?

If at any point you and your child decide to withdraw from the study your child will continue to be treated according to local practice with your child's usual CF team. If you and your child decide to withdraw from study treatment we would like to continue to follow up and collect data as part of his/her normal clinic visit collect to be used in the study. However, if you decide to withdraw from the trial completely no more date will be collected about your child from that point.

All data collected up until the time of withdrawal will be anonymised and included in the study analysis.

15) What if there is a problem?

If you and your child have a concern about any aspect of this study, you should ask to speak with CF team taking care of your child who will do their best to answer your questions. If you and your child remain unhappy and wish to complain formally, you can do this through the NHS Complaints Procedure. Details can be obtained from the hospital.

If your child is harmed by taking part in this research project, there are no special compensation arrangements. If your child is harmed and this is due to someone's negligence, then you may have grounds for a legal action for compensation against the NHS Trust where your child was being treated but you may have to pay for your legal costs. The normal National Health Service complaints mechanisms should be available to you (if appropriate).

In the event of defective product then you may have grounds for a legal action for compensation against the manufacturer, but you may have to pay for your legal costs.

16) Will my child's participation in the study be kept confidential?

All information which is collected about your child during this study is considered confidential and giving this information to anyone else (called a third party) is not allowed with the exceptions noted below. The paper files used to record information in this study will be labeled with a unique trial number. Medical information may be given to your child's doctor or other appropriate medical personnel responsible for your child's welfare.

In order to confirm that the appropriate informed consent has been taken, copies of you and your child's signed consent forms will be sent to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU) in the University of Liverpool. The University of Liverpool is registered as a Data Controller with the Information Commissioner and will ensure that your child's confidentiality is preserved.

Your child's NHS number will be used by the MCRN CTU to request information from your hospital about any microbiology results (cough or sputum samples) generated for the purpose of this study and for a maximum of 12 months prior to your child taking part in the study.

If you and your child decide to take part in the study, some parts of your child's medical records and the data collected for the study will be looked at by an authorised person from University Hospitals Bristol NHS Foundation Trust who are sponsoring the study. They may also be looked at by representatives of regulatory authorities or by authorised people from other NHS bodies to check that the study is being carried out correctly. Your child's medical records will be checked in the hospital and will not be removed. All authorised individuals will have a duty of confidentiality to your child and nothing that could reveal your child's identity will be disclosed outside of the research site. By signing the consent form you and your child will be giving permission for this to happen. In the event of the study results being sent to health authorities, or published, all your child's records will be kept confidential and your child's name will not be disclosed to anyone outside the hospital.

All documents and files relating to the study will be stored confidentially either at your local site or at the MCRN CTU or both for up to a maximum of 15 years. Nobody outside of the study will have access to the results of your child's tests and we will not reveal the information to your family, unless you request it. If you are agreeable, we will notify your child's GP that your child is involved in the study and a copy of this information sheet will be forwarded to them. The results of this study will be published, but it will not be possible to identify individual patients who have participated in the study.

17) Involvement of the General Practitioner?

With your consent, the study doctor will write to your child's GP to let them know of your child's involvement in the study. The study doctor may also ask for further medical information from your child's GP about his/her if necessary

18) What will happen to any samples my child gives?

As a part of the main study, sputum and/or cough swab samples will be taken as part of routine clinical care. These samples will be used to screen for a range of bacteria including *Pseudomonas aeruginosa*. If *Pseudomonas aeruginosa* is isolated from your child's sputum or cough sample, then isolates will be collected and transferred to an external laboratory. These isolates will be used only for the purposes of the TORPEDO-CF trial and for future Cystic Fibrosis related research. These isolates will not be used for any commercial purposes. This external laboratory will do some additional testing of the *Pseudomonas* isolates.

The samples will be kept in a secure place until we need them; nobody outside of the study (expect for MCRN CTU staff and your Hospital) will have access to **any** confidential information that you give to us. Confidential details (such as your child's name, address and GP details) will be kept locally and not made available to researchers.

Your child's sample will be coded and the researchers carrying out tests on the samples will not be given information they do not need to carry out the tests and analyse the results. Coded is not the same as anonymous. It will be possible to use the codes to identify that a result is from your child's sample. However, we do not plan to do this unless there is a good research reason to do so. We will maintain this information so that we can properly manage the samples donated. For instance, sometimes we may need to update our record of your child's clinical details to help us interpret the results of tests.

19) What will happen to the results of the study?

The results are likely to be published in the six months following completion of the study. Your child's confidentiality will be ensured at all times and will not be identified in any publication. At the end of the study the results can be made available to you and your child's GP if you wish.

20) Who is organising and funding the Research?

University Hospitals Bristol NHS Foundation Trust is sponsoring this study; they have assigned the day to day running of the study to the Medicines for Children Research Network Clinical Trials Unit (MCRN CTU) in the University of Liverpool.

This study is funded by the Health Technology Assessment programme of the Department of Health. Each collaborating site has been allocated funds for provision of general office supplies and to support nurse time and pharmacy costs.

21) Who has reviewed the study?

The study has been reviewed for scientific content by expert members of the Heath Technology Assessment program of the Department of Health review committee and a Multi-Centre Research Ethics Committee has reviewed the study for ethical considerations.

THANK YOU FOR READING THIS INFORMATION SHEET.
WE HOPE YOU HAVE FOUND THIS SHEET HELPFUL