Parent's Information Sheet

Study title:	**The EpiNet-*First* trials of new onset epilepsy**		
Locality:	**Auckland District Health Board**	Ethics committee ref.:	**14/NTB/56**
Lead investigator:	**Dr Peter Bergin**	Contact phone number:	**09 379 7440 ext 25663**

Your child is invited to take part in a research study to find out which of several anti-epileptic drugs is best for people who are starting treatment for epilepsy. Whether or not your child takes part is your choice. If you don't want your child to take part, you don't have to give a reason, and it won't affect the care your child receives. Your child will still receive normal care for his/her epilepsy. If you do want your child to take part now, but change your mind later, your child can pull out of the study at any time.

This Information Sheet will help you decide if you'd like your child to take part. It explains why we are doing the study, what his/her participation would involve, what the benefits and risks might be, and what would happen after the study ends. We will go through this information with you and answer any questions you may have. You do not have to decide today whether or not your child will participate in this study. Before you decide you may want to talk about the study with other people, such as family, whānau, friends, or healthcare providers. Feel free to do this. You are able to take as much time as you like deciding whether to participate in the study (though there may be a risk of further seizures while your child is not taking any treatment.)

If you agree to take part in this study, you will be asked to sign the Consent Form (on behalf of your child) on the last page of this document. You will be given a copy of both the Parent's Information Sheet and the Consent Form to keep. We will want to follow your child for at least 2 years.

This document is 9 pages long, including the Consent Form. Please make sure you have read and understood all the pages.

WHAT IS THE PURPOSE OF THE STUDY?

Epilepsy is a common neurological (brain) disorder. Approximately 2-3% of the population will be given a diagnosis of epilepsy by time they reach 60.

There are many drugs (i.e. medications) which are available to treat patients with epilepsy. All of these drugs have been shown to be helpful in reducing the likelihood of seizures, though they do not necessarily prevent all seizures in all patients. Unfortunately, doctors often cannot predict which drug will work best for a particular person. In fact some of them seem to have no effect at all in some patients.

In this research study - called The EpiNet-*First* series of Trials - we want to find out which of the various anti-epileptic drugs work best in people with new-onset epilepsy.

We will not be able to obtain enough patients in New Zealand alone to answer this question fully. This is therefore an international study.

WHAT WILL MY CHILD'S PARTICIPATION IN THE STUDY INVOLVE?

Your child has been invited as your doctor thinks he/she has developed epilepsy. Your doctor thinks that your child should start treatment with an anti-epileptic drug.

If you agree for your child to take part, then we will need to collect information about your child's epilepsy. Your child's doctor will fill in a form via the Internet to tell us what sort of seizures your child has, and whether your child has other health problems. Information will be transmitted via the Internet using a secure website, similar to those that are used by banks. We will not be collecting any personal information about your child, apart from name, date of birth, sex and hospital number. No material which could personally identify your child will be used in any reports on this study.

Your child will not need extra blood tests or any other samples taken for the study. Your child's doctor will decide what tests or investigations (e.g., EEG or brain scan), if any, your child should have.

If you agree for your child to take part, neither you nor your child's doctor will choose which anti-epileptic drug your child receives. Instead, the treatment your child will be offered will be chosen at random (by a computer, in a way that is similar to tossing a coin or rolling a dice). Once your child has been allocated an anti-epileptic drug both you and your child's doctor will know what it is.

If drugs are randomly chosen, then we can be confident that the groups of patients who receive the different drugs will be very similar. We can then follow the groups of patients to see if one group has a better outcome than the other groups.

All of the drugs we are studying have been used in New Zealand for many years, and are approved for the treatment of epilepsy. We know that they work well for most people, including children. We are now trying to find out if one is better than the others.

If your child's doctor has diagnosed your child as having focal seizures (seizures that begin in one part of the brain), your child will be enrolled into the **EpiNet-*First* Trial 1**. Your child will receive treatment, with either, carbamazepine, lamotrigine or levetiracetam.

If your child's doctor has diagnosed your child as only having generalized seizures, your child will be enrolled into the **EpiNet-*First* Trial 2.** Your child will receive treatment with either levetiracetam or valproate.

If your child has only generalized seizures, but valproate is not considered appropriate, your child will be enrolled into the **EpiNet-*First* Trial 3.** Your child will receive treatment with either levetiracetam or lamotrigine.

If your doctor has diagnosed your child as having epilepsy, but it is unclear what type of seizures your child has, your child will be enrolled into the **EpiNet-*First* Trial 4.** Your child will receive treatment with either levetiracetam or lamotrigine or valproate.

The **EpiNet-*First*-Trial 5** is for patients with seizures of uncertain nature for whom valproate is not appropriate. Your child will receive treatment with either levetiracetam or lamotrigine.

After treatment has been started your child will be followed up at 3, 6 and 12 months, and at 6 month intervals thereafter, depending on how well your child is responding to treatment. For some of these follow-ups, we will see your child in a clinic, but for other reviews we may contact you by phone or e-mail.

You will also be asked to complete a brief questionnaire (on behalf of your child) at the start of your child's treatment and again after 3 months, and then at 6 month intervals for at least the next 2 years.

You will be asked to keep a diary of any seizures that may occur. In particular, we will want to know whether your child has further seizures, and if so, how often they occur. **It is important that you record all the seizures your child has as accurately as you can.** We will also want to know whether your child experiences side effects from the treatment, and if so, how severe they are. If it turns out that the treatment does not control your child's seizures or causes major side effects, the treatment can be stopped and another treatment started. If this happens we would still like to collect information about your child's progress.

Your child will probably be started on a low dose of the anti-epileptic medication and this will be gradually increased over the first few weeks. If your child continues to have seizures, then the dose may be increased. If your child continues to have more seizures or your child gets side-effects from the treatment, then this anti-epileptic medication will be stopped. It will be replaced with a different medication. If this happens we would still like to collect information about your child's progress.

To ensure that the information we collect is meaningful, **it is very important that your child does actually take the drug that is prescribed as reliably as possible**. You can stop your child's medication if your child has troublesome side effects, or if you change your mind, but **we need to know if your child stops taking it**. We could be misled if patients do not take the medication prescribed, and we do not know this, since we then will draw the wrong conclusion about the effectiveness of the different medications. If your child experiences troublesome side effects, tell your doctor, and discuss with him or her whether your child should continue it.

The study will start in 2014 and we plan to recruit over 3,600 patients with epilepsy (internationally and over the five EpiNet-*First* trials); we wish to follow up everyone who has taken part in the study for at least 2 years.

Your child's clinical treatment will not be affected by taking part in this study your child will receive routine clinical care.

WHAT ARE THE POSSIBLE BENEFITS AND RISKS OF THIS STUDY?

What are the side effects of the antiepileptic drugs being tested?

We will not be giving your child any experimental drugs. All the drugs that we are using are standard medications that are known to be safe and effective in people with epilepsy; they are registered in New Zealand for the treatment of epilepsy, and are approved by New Zealand's drug supervising agency, Medsafe, for this purpose.

However, there are side effects to all types of medicines and there is still a small risk that your child could have some sort of adverse reaction to a medication, though this risk will not be increased by taking part in the research study. In other words, your child is likely to have the same risk even if your child does not take part in this trial. Similarly, there is a very small chance that a person with epilepsy can die during a seizure; however, once again, this risk will not be increased by taking part in the research study.

Side Effects
Some anti-epileptic drugs may cause dizziness, sedation (sleepiness), nausea or diarrhoea, clumsiness, or double or blurred vision in some patients, particularly if the dose is too high. However, many people do not get any side effects from their anti-epileptic medicine, particularly if the medicine is introduced slowly. If side effects do occur, they often settle over the first few days or, weeks after a patient starts the drug. Occasionally, anti-epileptic drugs can cause mood changes; sometimes people feel less motivated or less enthusiastic about their activities. Some people put on weight or get thinning of the hair with anti-epileptic drugs. Some drugs can cause a reversible tremor.

If your child develops any of the side effects mentioned here, or any other possible side effects, and you are concerned, you should contact your hospital doctor or nurse (contact details can be found on your child's seizure diary).

Allergies and hypersensitivity reactions
Some people turn out to be allergic to one or more anti-epileptic drugs. Allergic reactions most commonly happen in the first few weeks after the treatment is started. The most common sign of an allergy is a skin rash. This is most likely with carbamazepine and lamotrigine; approximately one in twenty people will develop a skin rash with each of these drugs. Patients typically develop a rash that looks like a measles rash. The rash is usually a minor nuisance, but it can develop into a more severe allergic reaction. If your child develops a rash you should contact your hospital doctor or nurse (contact details can be found on your child's seizure diary). If you cannot get hold of anyone, and you have a rash that is getting worse, you should stop your child taking the drug immediately. Some genetic factors seem to increase the risk of a serious allergic reaction to carbamazepine, particularly in Asian patients.

Sexuality and reproductive issues for women
There is an interaction between some anti-epileptic drugs and the combined oral contraceptive pill. Carbamazepine reduces the effectiveness of oral contraceptives, and lamotrigine may also do so. Women who are sexually active and taking carbamazepine or lamotrigine should therefore consult their doctor or family-planning services before stopping or starting an oral contraceptive medication. Levetiracetam and valproate do not interact with the oral contraceptive pill.

Women may develop irregular periods with valproate.

Most anti-epileptic drugs increase the risk to an unborn baby. These risks must be balanced against the risks of uncontrolled seizures. If you have any questions or concerns, your doctor will discuss this further with you.

Anti-epileptic drugs may cause abnormalities in the baby called congenital malformations. These might include a cleft lip, cleft palate, heart defects, or spina-bifida. For lamotrigine, carbamazepine and levetiracetam the risk is about 3% (3 in 100). For valproate the risk may be as high as 10% (1 in 10). There is also evidence that valproate may result in the baby having learning difficulties. For these reasons, we do not recommend that women of childbearing age take valproate, if they are in a sexual relationship.

When the drug allocated to your child is dispensed there will be a full information sheet in the packaging which is supplied by the manufacturer. This sheet will add to the information given about your drug in this Parent's Information Document.

What are the possible disadvantages and risks of taking part?

There are risks associated with epilepsy, and risks associated with the medicines that are prescribed to control epilepsy, but there are no risks that are directly associated with the research itself. Your child may end up taking a medication that is different from the one your doctor would have prescribed if your child was not taking part in this research. It is possible that your child may have a worse outcome - either because of side-effects, or because the medication prescribed is less effective than the one your child may otherwise have received. On the other hand, your child may have a better outcome. The reason we are doing the study is to find out which of the medications is best. If your child has been invited to take part in this study, then your doctor thinks that any of the medications your child might receive would be appropriate for him/her.

What are the benefits of taking part?

By your child taking part you will help doctors learn whether one of the drugs we use to treat epilepsy is better than the other drugs. We hope that the results of this study will help us to improve the treatment of epilepsy in children and young people in the future.
We cannot say if your child will benefit directly from this research study; your child may end up taking a drug that is less effective or has a higher risk than another drug, or your child may end up taking a drug that is shown to be the best one. Your child will be monitored more closely than would be the case if you did not take part in this research study.

If you wish, you may ask a friend, family or whanau member to help you understand the risks and / or benefits of this study and any other explanation you may require. If you need an interpreter, one can be provided, though this may require that you come back to another appointment.

WHO PAYS FOR THE STUDY?

The study is funded by the Neurological Foundation of New Zealand and the New Zealand Health Research Council. It is being run in your hospital, and is being organised by The EpiNet steering group and the Auckland District Health Board.

You can find out more about the EpiNet Research Project at this website: www.epinet.co.nz

There will not be any costs to you for participating nor any payments made to you.

WHAT IF SOMETHING GOES WRONG?

If you have any concerns about any aspect of this study, you should speak with your child's hospital doctor (consultant).

If your child was injured as a result of treatment given as part of this study, which is unlikely, your child would be eligible for compensation from ACC just as if your child was injured in an accident at work or at home. You will have to lodge a claim with ACC, which may take some time to assess. If your child's claim is accepted, your child will receive funding to assist in their recovery.

If your child has private health or life insurance, you may wish to check with your child's insurer that taking part in this study won't affect your child's cover.

If harm occurs to your child and is due to someone's negligence, you may have grounds for legal action for compensation against the treating District Health Board or Hospital. In the event of defective product you may have grounds for legal action for compensation against the manufacturer. However, in both cases you may have to pay your legal costs.

If you have any queries or concerns regarding your child's rights as a participant in this study you may wish to contact a Health and Disability Advocate, telephone

- Northland to Franklin 0800 555 050

- Mid and lower North Island 0800 42 36 38 (4 ADNET)
- South Island except Christchurch 0800 377 766
- Christchurch 03 377 7501

WHAT ARE MY CHILD'S RIGHTS?

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

Yes. Only people working on the study or working to ensure the study is run correctly will have access to the data. All information collected about your child during this study will be confidential and will be stored securely and not destroyed until 10 years after the study has finished.

We will tell your child's GP that your child is taking part in this study.

What if new information becomes available?

Sometimes during the course of a research study, new information becomes available about the drugs that are being studied. If this happens, your child's hospital doctor will tell you about it and discuss with you whether you want your child to continue in the study.

WHAT HAPPENS AFTER THE STUDY OR IF WE CHANGE OUR MIND?

Taking part is completely voluntary. If you decide that you do not want your child to take part, or after an original decision to take part you decide to withdraw your child from the study, this is alright. You do not have to give a reason and it will not affect the standard of care your child receives now or in the future.

If you decide to stop your child's treatment, your child can still remain in the study, and this is what we would recommend. This means that we would still collect information about any new treatment your child takes, and whether your child has further seizures. However, if you want to stop your child being in the study altogether, you can withdraw your child completely, and no more information will be collected about your child. All information collected up until this time will be included in the study analysis, unless you request that it is not included. We will continue to communicate with your child's GP in the usual manner.

When people who have started in a research study withdraw from the study, it does weaken the study. Therefore, if you think it is likely that you will withdraw your child from the study before it finishes (which will take at least 2 years), it would be better if your child does not join at the beginning. Similarly, if you are not prepared to give your child any medicine to stop his/her seizures, then it would be better if your child does not take part in the research study.

If you are happy with your child's medication, even after the study has ended, your child is able to continue taking the treatment as he/she would in usual clinical practice.

What will happen to the results of the study?

We will publish the results of this study in a scientific medical journal. Your child's confidentiality will be ensured at all times and will not be identified in any publication. A short summary of the study will be provided on our website (www.epinet.co.nz).

The study data will be stored indefinitely within the on-line database (EpiNet). The data will only be removed if you withdraw consent for your child.

Who has reviewed this research study?

The science and ethics of this study were reviewed and approved by the Health and Disability Ethics Committee (HDEC).

WHO DO I CONTACT FOR MORE INFORMATION OR IF I HAVE CONCERNS?

If you have any questions, concerns or complaints about the study at any stage, you can contact:

Dr Peter Bergin, Chairman of the EpiNet study Group
Consultant Neurologist, Neurology Department, Auckland City Hospital
Phone: 09 379 7440 x 25663

If you want to talk to someone who isn't involved with the study, you can contact an independent health and disability advocate on:

Phone: 0800 555 050
Fax: 0800 2 SUPPORT (0800 2787 7678)
Email: advocacy@hdc.org.nz

If you require Māori cultural support, talk to your whānau in the first instance. Alternatively you may contact the administrator for He Kamaka Waiora (Māori Health Team) on:
Phone: 09 486 8324 ext 2324

or

If you have any questions or complaints about the study you may contact the Auckland and Waitematā District Health Boards Maori Research Committee or Maori Research Advisor by telephoning: 09 4868920 ext 3204

You can also contact the health and disability ethics committee (HDEC) that approved this study on:

Phone: 0800 4 ETHICS
Email: hdecs@moh.govt.nz

Consent Form

Centre Name:

Name of Investigator:

Trial Number: ||__|__|__|__|__|__|__|__|

Patient's date of birth |__|__|/|__|__|/|__|__|__|__|

If you need an INTERPRETER, please tell us.

Please tick to indicate you consent to the following

I have read, or have had read to me in my first language, and I understand the Parent's Information Sheet.	Yes ☐	No ☐
I have been given sufficient time to consider whether or not I want my child to participate in this study.	Yes ☐	No ☐
I have had the opportunity to use a legal representative, whanau/ family support or a friend to help me ask questions and understand the study.	Yes ☐	No ☐
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and information sheet.	Yes ☐	No ☐
I understand that taking part in this study is voluntary (our choice) and that my child may withdraw from the study at any time without this affecting my child's medical care.	Yes ☐	No ☐
I consent to the research staff collecting and processing my child's information, including information about my child's health.	Yes ☐	No ☐
If I decide to withdraw my child from the study, I agree that the information collected about my child up to the point when I withdraw may continue to be processed.	Yes ☐	No ☐
I consent to my child's GP or current provider being informed about my child's participation in the study and of any significant abnormal results obtained during the study.	Yes ☐	No ☐
I understand that my child does not have to keep taking treatment if it appears to be harmful to him / her.	Yes ☐	No ☐
I agree to an approved auditor appointed by the New Zealand Health and Disability Ethic Committees, or any relevant regulatory authority or their approved representative reviewing my child's relevant medical records for the sole purpose of checking the accuracy of the information recorded for the study.	Yes ☐	No ☐
I understand that my child's participation in this study is confidential and that no material, which could identify my child personally, will be used in any reports on this study.	Yes ☐	No ☐
I understand the compensation provisions in case of injury during the study.	Yes ☐	No ☐
I know who to contact if I have any questions about the study in general.	Yes ☐	No ☐
I understand my child's responsibilities as a study participant.	Yes ☐	No ☐

Name of Participant:

Declaration by parent/caregiver of participant:

I hereby consent for my child to take part in this study.

Parent's/Caregiver's name: _____

Signature: _____ Date: _____

Declaration by member of research team:

I have given a verbal explanation of the research project to the participant's parent/caregiver, and have answered the parent/caregiver's questions about it.

I believe that the participant's parent/caregiver understands the study and has given informed consent for his/her child to participate.

Researcher's name: _____

Signature: _____ Date: _____