



Information statement and consent form

HREC Project Number: 38236

Short Name of Project: Pilot study of CBD in children with ID

Full Name of Project: Pilot study of cannabidiol (CBD) in children with Intellectual Disability (ID) and Severe Behavioural Problems (SBP)

Principal Researcher: Associate Professor Daryl Efron, Consultant Paediatrician, The Royal Children's Hospital

Version Number: 2.0

Version Date: 31 October 2018

Thank you for taking the time to read this **Participant Information Statement and Consent Form**. We would like to invite your child to take part in a research project that is explained in this form.

This form is 10 pages long. Please make sure you have all the pages.

What is an Information Statement and Consent Form?

An Information and Consent Form tells you about the research project. It explains exactly what the research project will involve. This information is to help you decide whether or not you would like your child to take part in the research. Please read it carefully.

Before you decide if you want your child to take part or not, you can ask us any questions you have about the project. You may want to talk about the project with your family, friends or a health care worker.

Taking part in the research project is up to you

It is your choice whether or not your child takes part in the research project. You do not have to agree if you do not want to. If you decide you do not want to take part, it will not affect the treatment and care your child gets at The Royal Children's Hospital or from their paediatrician.



Signing the form

If you want your child to take part in the research, please sign the consent form at the end of this document. By signing the form you are telling us that you:

- understand what you have read
- have had a chance to ask questions and received satisfactory answers
- consent to your child taking part in the project.

We will give you a copy of this form to keep.

What is the research project about?

Our research project is a *pilot study*. A pilot study helps us to prepare for a bigger study. In a pilot study, we look at how the study works, as well as how a study treatment affects people.

Children with **Intellectual Disability** (ID) can also have **Severe Behavioural Problems** (SBP). SBP can have an effect on their families and carers, and can also affect their health care, education and the management of their disability.

At the moment, dealing with SBP is difficult. There are drugs that can be used to treat SBP, but these are not always effective. These drugs can also cause serious side-effects.

Parents and doctors are interested in using **medical cannabis** as a treatment for SBP in children with ID. However, there is not enough evidence to know if cannabis works for these patients.

In this study, we are testing a treatment called CBD100 (cannabidiol). CBD100 is a legal cannabis extract, which does not appear to have the same intoxication, addiction, or withdrawal effects seen in THC-containing cannabis. It may be helpful in improving behaviour, and may also have fewer side effects than existing medications. We hope to find out if CBD100 works and if it is safe. We aim to recruit 10 children with ID and SBP to take part in this pilot study.

Because this is a pilot study, we are also collecting information to help us understand how we can run a bigger trial. The information we collect may help us to do a large trial to show whether CBD100 is safe and helpful for reducing SBP in children with ID.

1. Who is running the project?

This project is being led by Associate Professor Daryl Efron. The project plan was written by staff of the Murdoch Children's Research Institute, including A/Prof Efron.

The company Tilray are supplying the study drug.

This project will be run at the Royal Children's Hospital, Melbourne (RCH). The research team for this project includes doctors and researchers at the RCH.

2. Why is my child being asked to take part?

We are asking your child to take part in the project because they:

- are aged between 8 and 16 years
- and**
- have ID
- and**
- have SBP.

3. What does my child need to do in this project?

Your child will be in this study for 17 weeks. Your child will need to visit the hospital on five occasions.

The study is in three parts:

- Screening period: Up to 14 days
- Treatment period: 74 days (9 days up titration, 8 weeks maintenance, 9 days down titration)
- Post-treatment follow up: 30 days

a) Screening

We first need to check that your child is suitable for this study. To do this, we will need to do some tests and procedures.

These tests and procedures are:

Test/Procedure	What will happen?
Medical history	We will ask you some questions about your child's medical history including about their ID and SBP, and other illnesses they may have had. We will ask you about medications your child may have taken in the past to help manage their SBP, and any medication they are currently taking for any reason.
Physical examination	We will examine your child to check their overall health. We will measure their temperature, heart rate, breathing rate and blood pressure, and also their height and weight.
Parent/carer survey	We will ask you to complete a questionnaire about your child and their disability, and how this affects their life. We will also ask you some questions about your family and what supports you have for your child.
Blood collection	We will collect some blood by pricking your child's finger. We may need to put a needle into a vein in your child's arm to collect blood. We will test your child's blood to see if there are any health concerns for your child that could be a problem if they took CBD.
ID assessment	We will do an assessment of your child's level of intelligence using an IQ test. Your child will need to do things like answer questions, look at pictures, and work with blocks.

b) Baseline

If your child is eligible for the study, then they will be invited back to the hospital for a baseline visit. This could be up to two weeks after the screening visit. At the baseline visit we will collect information about your child before we give them the study drug.

At this visit we will do the following procedures:

Test/Procedure	What will happen?
Physical examination	We will examine your child to check their overall health. We will measure their temperature, heart rate breathing rate and blood pressure, and also measure their height and weight.
Medication check	We will ask you about any medications your child is taking.
Side effect monitoring	We will ask you to complete a questionnaire about possible side effects of CBD100 as a baseline, so we can compare with when they are taking the medication.

c) Randomisation

We will put your child into one of two groups:

- Group 1. *Treatment group*. In this group your child will be given CBD100
- Group 2. *No treatment group*. In this group your child will be given placebo drug. A placebo is a medication with no active ingredients. It looks like the real thing but is not.

This will be done by chance, like tossing a coin, so your child has an equal chance of being in either group.

We can't choose which group your child is put in, and neither can you or your child. For the duration of the study neither you nor any of the researchers will know what group your child is in.

d) Treatment

We will give your child their first dose of study drug at the hospital on the same day as the baseline visit. Your child will need to stay at the hospital for an hour after we give them the study drug to make sure they are OK.

We will give you a supply of the study drug to take home with you, and also diary cards to complete to record your child's doses of study drug and symptoms. At each visit, you will need to return all unused study drug, as well as completed diary cards and empty drug bottles.

Over the first nine days we will increase your child's dose of study drug every three days. Then the dose will remain the same from days 10 to 66, after which the dose will be reduced over the next 9 days and then stopped.

At day 10 and day 66, your child will need to return to the hospital for an examination.

On Day 38, you will need to attend the hospital to collect another supply of the study drug. Your child does not need to attend this visit. They will also not need to attend the visit on Day 74.

The procedures that will be done at each visit are shown in the table below.

	Screening	Baseline/ Day 1	Day 10	Day 38	Day 66	Day 74	End of study phone call (Day 104)
		First dose, increased for 9 days	Stable dose	Mid-way	Dose decreased for 9 days	End of treatment	
Medical history	X						
Physical examination	X				X		
Comorbidity assessment	X						
Behaviour assessment	X						
Parent/carer survey	X						
Blood collection	X		X		X		
ID assessment	X						
Medication check	X	X	X		X		X
Side effect monitoring		X	X		X	X	X
Provide supply of study drug		X	X	X	X		
Provide diary		X	X		X	X	
Collect diary			X		X	X	X
Visit length (hours)	2-3 hours	1 ½ hours	1 hour	½ hour	1 hour	½ hour	

e) Post-treatment Follow Up

30 days after your child's last dose of study drug, we will call you at an arranged time for an end of study check.

f) Questionnaires

At various times throughout the study you will be asked to complete questionnaires that provide us with important information about your family wellbeing, your child, and any physical symptoms your child may experience during the study. These questionnaires will be sent via email as a secure web-link, and can be completed on your home computer or tablet. The questionnaires will be sent to you on Days 1, 10, 66 and 104.

g) Study samples

This study involves the collection of blood samples. These will be used to make sure there are no side-effects, and also for research purposes.

We will test these samples at the Royal Children's Hospital Laboratory Service. The samples will be destroyed once the laboratory tests have been done.

h) Other treatment

It is important to tell us about any treatments or medicines your child may be taking. This includes prescription medicines, over-the-counter medicines, vitamins or herbal medicines. If there are any changes to these while they are in this study, you must let us know.

During the study, your child may not be able to take some or all of the medicines or treatments they usually take for their condition. We will tell you which treatments or medicines need to be stopped while your child is in the study.

i) Informing your child's GP

You should tell your child's GP that your child is taking part in this research study.

j) Reimbursement

Your child will not be paid to take part in this research project. We will give you parking vouchers when you come to the hospital for research study visits.

k) After the study

If you are interested, we can only inform you whether your child was given the study drug or placebo after all the results of this research study have been finalised. The study drug is available through the Special Access Scheme with approval on a case-by-case basis due to exceptional clinical circumstances. This product is not currently subsidised, meaning that families must fund the cost themselves. If you wish to apply for approval for cannabidiol through this scheme, you could discuss this with your child's paediatrician.

l) Alternatives to participation

Your child does not have to be in this study. There are alternative treatments for your child, including the standard treatment for SBP. This treatment includes anti-psychotic and other psychotropic medications

4. Can my child stop taking part in the project?

Your child can stop taking part in the project at any time. You just need to tell us so. You do not need to tell us the reason why. If your child leaves the project we will use any information already collected unless you tell us not to.

We may also stop the study for a variety of reasons. We may need to take your child off the study treatment for the following reasons, such as if:

- we believe that it is in their best interest
- they have side effects from the treatment that are considered too severe
- your child becomes pregnant

- your child does not follow instructions or come to planned study visits
- the sponsor stops the study unexpectedly.

If your child leaves the study early, we will need to reduce their dose of study drug slowly. We will explain how to do this. It is important that you do not just stop giving your child the study drug without talking to us.

New information may become available that might affect your decision to let your child stay in the study. If we learn any new information, we will talk to you about it.

5. What are the possible benefits for my child and other people in the future?

We cannot guarantee that your child will get any benefits from this project. However, the study drug may help with your child's SBP.

Information from this study will be used to plan a larger study of CBD100 (or a similar product).

6. What are the possible risks, side-effects, discomforts and/or inconveniences?

Medical treatments often have side effects. Your child may have none, some or all of the side effects listed below. These side effects may be mild, moderate or severe. We will also be looking out for side effects.

There may be side effects that we do not expect or know about. Please tell us immediately if your child gets any new or unusual symptoms. If a severe side effect or reaction occurs, we may need to stop your child's treatment.

Many side effects go away shortly after treatment ends. However, sometimes they can be long lasting or permanent.

If your child experiences any symptoms listed below, or if you notice something different about their body, please call us straightaway. We will assess whether these symptoms are related to the study drug.

CBD100

We don't know completely what side effects children with ID may have from taking CBD100, or how likely it is that they will have side effects.

In other studies of CBD100, researchers have seen the following side effects:

- drowsiness, or sleeping for increased lengths of time
- change in appetite
- diarrhoea
- nausea and vomiting
- change in liver function on blood tests

Blood tests

There are no major risks associated with a blood test. It is possible your child may feel some pain or discomfort during the test. We can use a numbing cream before the needle to reduce this. There may be a little bruising, swelling or bleeding where the needle enters the skin. Some people can feel light-headed when blood is taken.

Reproductive risks

Because of the age-range of participants in this study, it is possible that your child may have started or gone through puberty. The following information is important if your child is able to become pregnant or father a baby:

- The effects of the study drug on an unborn or newborn baby are not known.
- If your child is pregnant, she cannot take part in this study.
- If your child becomes pregnant during the project, we need to be told immediately.

Compensation for Injury

By signing the consent form, you are not giving up any legal rights to seek to obtain compensation for injury.

7. What will be done to make sure my child's information is confidential?

In this study we will collect and use personal and health information about your child for research purposes. Any identifying information that we collect about your child will be treated as confidential. It will be used only in this project, unless we say otherwise. We can disclose the information only with your permission, except as required by law.

All information will be stored securely in the Australian Paediatric Pharmacology Research Unit (APPRU) at The Royal Children's Hospital.

The information will be re-identifiable. This means that we will remove your child's name and give the information a special code number. Only we can match your child's name to their code number, if it is necessary to do so.

As the participants in this project are under 18 years old, we will keep their information at least until the youngest participant turns 25 years old. Alternatively, we will keep their information for at least 15 years after the study has closed – whichever date is latest.

You have the right to access and correct the information we collect and store about your child. This is in accordance with relevant Australian and/or Victorian privacy and other relevant laws. Please contact us if you would like to access this information.

The Royal Children's Hospital and Murdoch Children's Research Institute are research partners. This means that the two organisations share research information with each other.

The following people may access information collected as part of this research project:

- the research team involved with this project
- The Royal Children's Hospital Human Research Ethics Committee.

These groups may need to inspect and/or copy your child's research records for data analysis. They may also want to check that study procedures are followed correctly. Your child's name and personal details will not be released unless required by law.

Some of the information collected as part of this research may be important for your child's medical treatment and health. The following information will be placed in your child's hospital medical record and/or sent to your child's doctor to help the people who care for them:

- your child's participation in this study

We will tell your child's pediatrician if there are any abnormal test results that they need to know about.

At the end of the study, we may present the results at conferences. We may also publish the results in medical journals. This will be done in such a way that your child cannot be identified.

8. Will we be informed of the results when the research project is finished?

We will send you a summary of the overall project results. The summary will be of the whole group of research study participants, not your child's individual results.

9. Who should I contact for more information?

If you would like more information about the project, or in the case of an emergency, please contact:

Name: Associate Professor Daryl Efron

Contact telephone: 03 9345 4563

Email: Daryl.Efron@rch.org.au

You can contact the Director of Research Ethics & Governance at The Royal Children's Hospital Melbourne if you:

- have any concerns or complaints about the project
- are worried about your child's rights as a research participant
- would like to speak to someone independent of the project.

The Director can be contacted on (03) 9345 5044.

CONSENT FORM**HREC Project Number:** 36236**Short Name of Project:** Pilot study of CBD in children with ID**Version Number:** 2.0 **Version Date:** October 31 2018

- I have read this information statement and I understand its contents.
- I understand what my child and I have to do to be involved in this project.
- I understand the risks my child could face because of their involvement in this project.
- I voluntarily consent for my child to take part in this research project.
- I have had an opportunity to ask questions about the project and I am satisfied with the answers I have received.
- I understand that this project has been approved by The Royal Children's Hospital Melbourne Human Research Ethics Committee. I understand that the project and any updates will be carried out in line with the National Statement on Ethical Conduct in Human Research (2007).
- I understand I will receive a copy of this Information Statement and Consent Form.

Child's Name_____
Parent/Guardian Name_____
Parent/Guardian Signature_____
Date_____
Name of Witness to
Parent/Guardian's Signature_____
Witness Signature_____
Date

Declaration by researcher: I have explained the project to the parent/guardian who has signed above. I believe that they understand the purpose, extent and possible risks of their child's involvement in this project.

Research Team Member Name_____
Research Team Member Signature_____
Date

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