Participant Information Sheet

Parent/guardian

Your letterhead

Study title:	**Children's Anti-Inflammatory REliever (CARE) Study**		
Sponsor:	Medical Research Institute of New Zealand		
Locality:	*[Insert Locality]*	**Ethics committee ref.:**	20/NTB/200
Lead investigator:	*[Insert local PI name]*	**Contact phone number:**	*[Insert no.]*

INTRODUCTION

You and your child are invited to take part in a study to find out which of these two inhalers is better at preventing asthma attacks:

1. **Ventolin** 100 (salbutamol) inhaler, taken only when needed
2. **Symbicort Rapihaler** 50/3 (budesonide-formoterol) inhaler, taken only when needed

This information sheet will help you decide if you would like your child to take part. It sets out why we are doing the study and what your/your child's participation will involve. This includes what the benefits and potential risks might be, and what happens after the study ends.

You do not have to take part. If you choose not to, you don't have to give a reason, and it won't affect the care either of you receive. If you decide to take part now, but later change your mind, you and your child can leave the study at any time. If you do not take part, your GP will continue to manage your child's care and decide which inhaler(s) they are prescribed.

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 can also talk to one of the study team – their contact details are on page 10.

This document is 12 pages long, including the consent form at the end. Please make sure you have **read and understood all the pages**. If you agree to take part, you will be asked to sign an electronic copy of the consent form. You will be given a copy to keep.

SUMMARY

Most children with asthma use a blue reliever inhaler, such as **Ventolin**. New evidence for adults with asthma shows that **Symbicort** (a different type of reliever inhaler) is better, particularly at preventing asthma attacks. We want to find out if **Symbicort** is also better for children. To do this, we are inviting 380 children aged between 5 and 15 years old, with asthma, to take part in this year-long study.

If your child takes part, they will be given either a **Ventolin** or a **Symbicort** inhaler (this is chosen randomly). We will meet with you both 3 times and phone you 2 times, to ask some questions about their asthma and to do some breathing tests. Between visits, we will ask you to keep a record of any asthma attacks or time off school or work.

If your child's asthma is bad, or they have an asthma attack, we might want to give them an extra inhaler (**Flixotide** or **Seretide**) or increase how often they take their current inhaler.

WHAT INHALERS ARE USED IN THIS STUDY?

Inhaler	Symbicort Rapihaler (Budesonide-Formoterol)	Ventolin (Salbutamol)	Flixotide (Fluticasone)	Seretide (Fluticasone-Formoterol)
What does this inhaler look like? *[Study inhalers may differ slightly in colour.]*				
What's in it?	A beta$_2$-agonist (formoterol) which quickly opens up the airways. A weak inhaled steroid (budesonide) which reduces swelling in the airways.	A beta$_2$-agonist (salbutamol) which quickly opens up the airways.	A weak inhaled steroid (fluticasone) which reduces swelling in the airways.	A beta$_2$-agonist (salmeterol) which quickly opens up the airways. A weak inhaled steroid (fluticasone) which reduces swelling in the airways.
When should it be taken?	Only when needed (e.g. if wheezing). This inhaler can also be used every day to prevent asthma symptoms.	Only when needed (e.g. if wheezing).	Every day to prevent asthma symptoms.	Every day to prevent asthma symptoms.
Is this inhaler currently used by children with asthma?	No. This inhaler is used by children with asthma in Australia, but not in NZ.	Yes. These types of inhalers are the most commonly used by children with asthma.	Yes. This is the most common steroid inhaler prescribed for children with asthma.	Yes. This inhaler is used for children with difficult asthma.

WHO HAS APPROVED THIS STUDY?

This study has been designed by doctors who are asthma experts. It has been approved by the Northern B Health and Disability Ethics Committee (20/NTB/200) and registered with the Australian and New Zealand Clinical Trials Registry (http://www.anzctr.org.au/), reference ACTRN12620001091998. The full title of this study is: **Children's Anti-inflammatory REliever (CARE): An open-label randomised controlled trial of as-needed budesonide-formoterol vs salbutamol reliever therapy in mild childhood asthma.**

WHY HAS MY CHILD BEEN INVITED TO TAKE PART?

Your child has been invited to take part as they are aged between **5 and 15 years** old, **have asthma**, and **only use a reliever inhaler** for their asthma.

Before your child takes part in the study, **we will check very carefully to make sure it is safe for them**. They will not be able to take part if they:

- Have been admitted to hospital for more than 24 hours in the last year (or intensive care ever) due to their asthma
- **Used** more than one type of asthma inhaler in the last 6 months (e.g. **Flixotide**).
- **Used** more than 6 reliever inhalers (e.g. **Ventolin**) in the last year.
- Are pregnant (asthma symptoms may change, requiring different treatment).

WHAT WILL OUR PARTICIPATION IN THE STUDY INVOLVE?

The study will last for **1 year**, during which we will meet 3 times and phone you twice.

Screening visit (30 minutes) [60 minutes – selected sites only [substudy]

During this visit we will:

- Ask you and your child some questions about this information sheet to help improve how we explain our studies. This is optional. [include for selected sites only].
- **Explain the study** and answer any questions you have.
- Collect some **personal information** (e.g. your child's name and date or birth) and **medical information** (e.g. asthma history).
- Ask permission to **view your child's medical records** (GP, After Hours, ambulance, pharmacy, and hospital) during the study.
- Ask permission to use your child's **National Health Index (NHI) number** to check hospital admissions data and prescriptions against Ministry of Health records. This will provide us with more information about asthma attacks and medicines prescribed.
- For older children, we will ask some **personal questions**, such as whether they smoke or could be pregnant. These are important for safety reasons.

- Ask you to sign the **consent** form and your child to sign the assent form.

Visit 1 (1 hour)

During this visit we will:

- Ask **questions about your child's asthma**, including a short questionnaire of 5 questions.
- Ask you to fill in a brief **health economics questionnaire**. This will take 5 minutes.
- Measure your child's **height and weight**.
- Measure your child's **fractional exhaled nitric oxide** (**FeNO,** a gas normally breathed out) by getting them to blow into a tube. It tells us if there is swelling in your child's lungs.
- Ask your child to blow into a **spirometer**, which tells us how well their lungs are working.
- Give your child their **inhaler(s) and spacer**. We will show them how to use them. It is important that they only use these inhaler(s) during the study, unless told by a doctor.
- Give you and your child an **asthma action plan**. This will explain how to use the inhaler and spacer device, and when to get help if your child's asthma is worsening.
- Give you and your child a **log book and/or a mobile phone app** called MyCap. These can be used to record changes to your child's asthma (e.g. asthma attacks).
- **Write to your child's GP** telling them that your child is participating in this study.

The Screening visit and Visit 1 will be done at the same time, unless you would prefer to do them separately.

Visits 2 and 4 (30 minutes)

Visits 2 and 4 will be done over the phone at 3 months and 9 months. During these visits we will ask **questions** about your asthma. We will send replacement inhalers to you.

Visit 3 (30 minutes)

This visit will take place at 6 months, during which we will:

- Ask **questions** about your child's asthma, including the short questionnaire.
- Check your child's **inhaler technique** and provide new inhalers, if required.
- Ask you to fill in a brief health economics questionnaire.

Visit 5 (1 hour)

During this visit we will:

- Ask **questions** about your child's asthma, including the short questionnaire.
- Ask you to complete a **brief health economics questionnaire**.
- Measure your child's **height and weight**.

- Do a **FeNO test** and blow into a **spirometer**.
- Collect your child's study inhalers and provide them with **new inhalers**.
- **Write to your child's GP** telling them that your child has completed the study.

This visit will take place at 12 months or when you withdraw your child from the study.

What should we do between visits?

Between visits you should **carry on as usual**. This means your child should continue to use their inhaler when they need to. We will send you monthly email or text reminders to fill in the logbook or MyCap app. If you are worried about your child's asthma, you should contact their GP who will continue to look after them during the study.

We will tell you if we find out new information, which may affect your child's health or willingness to continue in the study. If required, we will ask you/ your child to sign an updated consent/ assent form to indicate you are willing to continue in the study.

Can we contact the study team between visits?

You can phone or email a member of the study team between at any point during the study. We may want to arrange an extra visit if:

- You are worried about your child staying in the study or would like them to stop.
- You are worried that your child will run out of inhalers before the next visit.
- Your child has an asthma attack requiring steroids (liquid, tablets or injection).
- Your child becomes pregnant (they will need to be withdrawn from the study).

Can I choose which inhaler my child is given?

No. Your child has a **50:50 chance** of getting either **Ventolin** or **Symbicort**. We will use specialised computer software to randomly choose which inhaler they get. This means that we will only know which inhaler your child gets after the computer decides.

What happens if my child has an asthma attack during the study?

You should get help straight away if you think your child is having an asthma attack.

After your child has been treated, you should contact a member of the study team. If your child was prescribed steroids or admitted to hospital we will want to make sure they are using the right inhalers. If they are using **Ventolin**, we will add a preventer inhaler (**Flixotide** or **Seretide**). If they are using **Symbicort**, we will increase how often they use it.

POSSIBLE RISKS AND BENEFITS OF THIS STUDY

Are there any side effects of the inhalers?

- Unfortunately, **all medicines can cause side effects**. Possible side effects for the inhalers used in this study are listed below. Some of the terms can be a bit confusing – you can talk

to a member of your study team if you have any questions about what they mean.

- **Most people don't experience any side effects**, but some people do. If your child experiences any new or unusual symptoms, or you are worried, you can **contact the study team**. You should not let this delay you getting help if required.
- Some of the side effects can be prevented by **using a spacer** with the inhaler, and **rinsing the mouth** with water after use.
- The risk of not treating asthma is greater than the risk of side effects from an inhaler.

Ventolin:

Common (1 in 10 to 1 in 100 people)	Awareness of heart beating, headache, shaking, blushing.
Uncommon (1 in 100 to 1 in 1,000 people)	Heart beating fast, mouth and throat irritation, muscle cramps, problems sleeping.

Symbicort Rapihaler:

Common (1 in 10 to 1 in 100 people)	Awareness of heart beating, headache, slight shaking, mild sore throat, irritation in the mouth and throat after long term regular use, cough, dry mouth.
Uncommon (1 in 100 to 1 in 1,000 people)	Heart beating fast, feeling sick, muscle cramps, dizziness, light headedness, feeling tired, thirsty, restless, problems sleeping.

Flixotide:

Common (1 in 10 to 1 in 100 people)	Mild sore throat, irritation in the mouth and throat after long term regular use*, bruising.
Uncommon (1 in 100 to 1 in 1,000 people)	Skin rash, itchy skin, feeling sick.

Seretide:

Common (1 in 10 to 1 in 100 people)	Mild sore throat, irritation in the mouth and throat after long term regular use, headache, muscle cramps, joint pain.
Uncommon (1 in 100 to 1 in 1,000 people)	Shaking, anxiety, problems sleeping, skin rash, itchy skin, heart beating fast, bruising, feeling tired, thirsty.

Is it safe to give steroid inhalers to children?

Inhaled steroids are one of the most important medicines used to treat asthma. They are **very safe** in children, even when taken for a long time.

What are the risks associated with spirometry and FeNO testing?

Your child may feel slightly breathless or dizzy for a short time after the breathing tests. We will monitor them throughout the tests and if they feel unwell they can stop.

What are the benefits of being involved in this study?

During the study, you will play an active role in your child's care. They will receive regular, careful attention and education from a team that includes doctors and the top asthma experts in New Zealand. By taking part, and helping us find out which inhaler is best (**Symbicort** or **Ventolin**), you will be helping people with asthma all over the world.

FUNDING THE STUDY

- The study is being paid for by the Health Research Council of New Zealand and Cure Kids.
- The **Symbicort** inhalers are being provided by AstraZeneca, the company who make them.
- You will not incur any costs for taking part in this study. We will reimburse you $50 per in-person visit for transport costs. Your child will receive a $30 gift card or book voucher (koha) at Visit 3, and a certificate at Visit 5, as a thank you for taking part in the study.

IF SOMETHING GOES WRONG

If your child is injured in this study, which is unlikely, they will be eligible for compensation from ACC just as they would be if they were injured in an accident at school or at home. This does not mean that their claim will automatically be accepted. You will have to lodge a claim with the ACC on their behalf, which may take some time to assess. If this claim is accepted, you will receive funding to assist in your child's recovery.

LOOKING AFTER YOUR INFORMATION

This part of the information sheet outlines what information will be collected, where it will be stored, how it will be used, and who has access to it.

Data collection

- During the study we will collect information about your child. We will also need to collect some basic information about you (e.g. your name and address). We only collect data that is relevant to the study.
- We will link study information with Ministry of Health records using your child's NHI number. This will allow us to check hospital admissions and prescription data.
- You can also use a free mobile app called MyCap to record information about your child's asthma. This is optional – you do not have to use this app. We do not share your or your child's information with any third parties.
- **Your child cannot take part in the study if you do not want us to collect any of this information.**

- You can ask the study team to stop collecting information about you and your child at any time. This will end your child's participation in this study. **Information collected up until this point will continue to be used**. This is to protect the quality of the study.

Data storage and access

- The table below outlines the **type of information** collected from you and your child during the study, **where it is stored** and **who has access** to it. The groups in **green** are only allowed to access your and your child's information to make sure the study is being run properly, the information is correct, and is being stored safely.

Type of information		Storage	Access
Identifiable information – *this can be linked back to you and your child (e.g. name or NHI)*			
Source data	• Information collected from you and your child (including log book) • Medical records • Study test results • Information you submit on MyCap	• **Electronic:** stored securely at study sites, on servers in Wellington, NZ, and Sydney, Australia • **Paper:** stored securely under restricted access at study sites	• Study staff • Study monitors • Ethics committee, regulatory authorities and AstraZeneca, if the study is audited • You and your child
Ministry of Health records	• Hospital admissions • Prescriptions	• Secure servers in Sydney, Australia and Wellington, NZ	• The Sponsor and study monitors
Deidentified (coded) information – *linked back to you/your child through your study ID only*			
Study database	• Results of tests and some information collected from you and your child. Data is moved here to be analysed	• Stored securely by MRINZ on servers in Sydney, Australia	• The Sponsor and study monitors • The study statistician
Safety data	• Side effects	• Shared with AstraZeneca, the company that makes Symbicort	• AstraZeneca Staff (cannot link back to identifiable data)

- **You and your child can ask to see any information** we have about you and your child. If you think some of our information is wrong, you can ask us to change it.

- After the study is finished, **other researchers may ask us to share the coded data**. We check each request to make sure they meet MRINZ standards and only use the data for research purposes. We will never share information that identifies you or your child.

Will you keep our data private and confidential?

- Information collected about you and your child is kept private and confidential, as per the law. Health information will only be given away if required by law.
- We will do our best to protect your privacy. Although the risk of people inappropriately accessing your child's data is very small, we cannot guarantee absolute confidentiality. We will tell you if your or your child's privacy has been breached, and take appropriate action.
- We are required to store information for 10 years after the youngest child in the study turns 16 years old, or for 15 years from the end of the study, whichever is greater. After this time, all confidential information will be destroyed.

What will you do with our data?

- Collected data will be analysed to find out which inhaler is better at preventing asthma attacks in children with asthma. We will publish our results in medical journals and online. We hope that this will lead to improve care for children with asthma.

WHAT HAPPENS IF WE CHANGE OUR MINDS?

- If you agree to your child taking part in the study but later change your mind, you and your child can stop at any time. Equally if your child no longer wants to continue in the study, they can stop. Neither of you have to give a reason.
- If you decide you no longer want to continue with the study inhalers but are happy to continue with the study visits, we will stop the inhalers and continue your child's follow up for the full year.
- If you or your child no longer want any study follow up you can let us know verbally and you do not have to attend a leaving visit. However, if you agree, we can arrange a final visit to discuss any questions you may have and collect your inhalers. Otherwise we will ask you to post the study inhalers back to us.
- If your child experiences any side-effects during the study we may also ask if we can continue to check in on you until the side-effects have resolved.
- If you do withdraw your child from the study, all the information provided up to the point of them leaving will be kept and included in the final study results.

WHAT HAPPENS AFTER THE STUDY?

- Once your child completes the study, or if they leave the study early, we will give them a new reliever inhaler. This inhaler may be different to the one they used during the study, depending on the asthma guidelines at the time. We will not be able to provide **Symbicort Rapihalers**.

- The decision of what inhaler your child will continue to use after the study will depend on their usual doctor. We will advise you to make an appointment with their GP to review their asthma and provide them with a new prescription for inhalers. We will inform their GP that they have completed the study.
- We can send you a summary of the results. There will be a delay in getting these to you as it will take several months from the end of the study to analyse the data.

WHO TO CONTACT FOR MORE INFORMATION

If you would like to take part in this study, or to talk to a member of the study team:

Name: <<INSERT HERE>>

Phone: <<INSERT HERE>>

E-mail: <<INSERT HERE>>

If you want to talk to someone who isn't involved with the study:

Name: Nationwide Health and Disability Advocacy Service

Phone: 0800 555 050

Fax: 0800 2 SUPPORT (0800 2787 7678)

Email: advocacy@advocacy.org.nz

For Māori health support please contact:

Name: <<NAME AND LOCATION OF SUPPORT SERVICE>>

Phone: <<INSERT HERE>>

Email: <<INSERT HERE>>

The health and disability ethics committee that approved the study:

Name: Health and Disability Ethics Committee (HDEC)

Phone: 0800 4 ETHIC (0800 4 38442)

Email: hdecs@health.govt.nz

Consent Form

parent/guardian

Your letterhead

Participant ID:	

Please tell us if you need an interpreter

Please read the statements below and sign at the end if you agree (consent):

I have read, or have had read to me in a language I am fluent in, and I understand the Participant Information Sheet.
I have been given sufficient time to consider whether or not my child should participate in this study.
I have had the opportunity to use a legal representative, whānau/ family support or a friend to help me ask questions and understand the study.
I am satisfied with the answers I have been given regarding the study and I have a copy of this consent form and participant information sheet.
I understand that taking part in this study is voluntary (my choice) and that I may withdraw my child from the study at any time without this affecting my, or my child's, medical care.
I consent to the research staff collecting and processing my and my child's information, including information about my child's health.
I consent to my child's National Health Index (NHI) number being used to link study information with Ministry of Health records on hospital admissions and prescription data.
I understand that my and my child's participation in this study is confidential and that no material, which could identify me and my child personally, will be used in any reports on this study.
If my child withdraws, or is withdrawn, from the study, I agree that the information collected about me and my child up to the point when they are withdrawn may continue to be processed.
If my child withdraws, or is withdrawn, from the study, I agree that the study team may continue to access my child's medical records for a maximum of 18 months from Visit 1 to obtain and use information relevant to this study.
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.
I agree to a sponsor-approved representative, 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.
I understand the compensation provisions in case of injury during the study.
I know who to contact if I have any questions about the study in general.
I understand my child's responsibilities as a study participant.

[An electronic signature is equivalent to a wet ink signature]

Declaration by <u>parent/guardian</u> of the participant:

I hereby consent to my child taking part in this study.

Name of child (participant): _____

Name: _____

Signature: _____ Time & Date: _____

Declaration by member of <u>research team</u>:

I have given a verbal explanation of the research project to the parent(s)/guardian(s) of the participant (child), and have answered their questions about it. I believe that the participant's parent(s)/guardian(s) understands the study and has given informed consent to participate.

Name: _____

Signature: _____ Time & Date: _____

Declaration by the <u>interpreter</u> (if applicable):

I have provided a true and accurate translation of the research project to the parent(s)/guardian(s) of the participant (child).

Name: _____

Signature: _____ Time & Date: _____