

Information statement and consent form

HREC Project Number: HREC/17/RCHM/221

Research Project Title: The PEBBLES study: Prevention of Eczema, Food Allergy and Sensitisation Using a Skin Barrier Improvement Strategy

Principal Researcher: Dr Adrian Lowe

Version Number: 4 **Version Date:** 10/07/2018

Thank you for taking the time to read this **Parent/Guardian Information Statement and Consent Form**. We would like to invite your child to participate in a research project that is explained below. This document is 10 pages long. Please make sure you have all the pages.

What is an Information Statement?

These pages tell you about the research project. It explains to you clearly and openly all the steps and procedures of the project. The information is to help you decide whether or not you would like your child to take part in the research. Please read this Information Statement 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 health care worker.

If you would like your child to take part in the research project, please sign the consent form at the end of this information statement. By signing the consent form, you are telling us that you:

- understand what you have read
- 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 information and consent form to keep.

1. What is the research project about?

The skin of babies does not usually act as a very good barrier to allergens, like dust and foods. These allergens may be able to get through the skin and cause a child to become sensitive to these substances. Eventually allergies like eczema, asthma and hay fever may develop in some children. Allergies are a significant health problem in Australia. We think that by actively building up a baby's skin barrier, we might reduce their risk of developing these allergies.

In this world-first study, we aim to see if using an emollient cream called EpiCeram™ on the healthy skin of babies will *prevent* them from developing eczema and food allergy. If we can achieve this, it might reduce the risk of these children becoming sensitive to allergens, and from developing food allergies and other allergies later on in life, such as asthma.



EpiCeram™ is a unique product that contains the major building blocks of human skin. EpiCeram™ may help restore skin barrier function in children with eczema. Normal moisturisers can help manage eczema, but they do not help restore the skin's barrier function. Steroid creams (such as cortisone) can lessen the skin inflammation caused by eczema, but also reduce the skin barrier, which is not helpful.

EpiCeram™ is very effective in treating eczema: it has a similar effect on the symptoms of eczema as a moderate strength steroid cream, without the unwanted side effects.

Medications and drugs have to be approved for use in Australia by the government. The EpiCeram™ cream used in this project has not yet been approved for general use by the Therapeutic Goods Administration (TGA). The use of this cream is considered experimental in Australia. The Food and Drug Administration in the United States of America has approved EpiCeram™ for use by patients with eczema of *all ages*. EpiCeram™ is approved for use in babies for eczema; however, it has not yet been studied as a way of *preventing* babies developing eczema.

In our previous study of 80 infants, we found trends towards EpiCeram™ reducing risk of eczema and sensitisation to foods. We will now undertake a larger study to see if EpiCeram™ helps to prevent eczema and food allergy. A total of 760 newborn babies will take part in this project.

2. Who is funding this research project?

This project is fully funded by the National Health and Medical Research Council. PuraCap, the company who makes EpiCeram™ cream, are supplying the cream free of charge, but will play no other role in this research.

3. Why are we being asked to be in this research project?

We are asking you because you expressed an interest in this project, you are either pregnant or have a newborn child, and you, your partner, or one of your older children, have an allergic condition.

If you have reacted to any of the ingredients of EpiCeram™ cream in the past, we will not be able to enrol your child in this study. The ingredients of EpiCeram™ are: Capric Acid, Cholesterol, Citric Acid, Conjugated Linoleic Acid, Dimethicone, Disodium EDTA, E. Cerifera (Candelilla) Wax, Food Starch Modified Corn Syrup Solids, Glycerin, Glyceryl Stearate, Hydroxypropyl Bispalmitamide MEA (Ceramide), Palmitic Acid, PEG-100 Stearate, Petrolatum, Phenoxyethanol, Potassium Hydroxide, Purified Water, Sorbic Acid, Squalane, Xanthan Gum.

4. What does participation in this research involve?

Study length

This study will be for one year (from the birth of your child until they turn one year old).

Randomisation

At the first appointment (see below) we will randomly put your baby into one of two groups. These will be the “cream group” and the “no cream group”. This will be done by chance, similar to tossing a coin, so your baby will have an equal chance of being in either group.

Study treatment

If your baby is in the “cream group”:

- We will ask you to rub about 6 grams (a heaped teaspoon) of cream all over your baby's skin, including the face and hands. This needs to be done twice per day until they are six months old. We will show you how to do this. It is best if you rub the cream into your baby's skin at a regular time each day, particularly following his or her bath.
- Each tube of cream (90g) should last a little over seven and a half days (or just over a week). If you find yourself running out of cream, please call 1800 875 127, and we will organize more cream for you.
- We will ask you to record cream usage and any unusual signs/symptoms in the weekly online diary card we send you. This needs to be completed weekly for the 12-month study period.

- Please regularly check your baby's skin for any possible reactions to EpiCeram™. If your child develops a rash, reddening or other changes in skin colour, swelling, dryness, itching, flaking (scaling) or the skin becoming tender to touch, please contact us so that we can organise a time for one of our doctors to examine your baby's skin.

If your baby is in the "no cream group":

- We will ask you to follow your normal daily routine in caring for your baby's skin. If this includes the use of creams, oils (such as moisturiser or sunscreen), please make sure you record this information in the diary card provided.
- Record any unusual signs/symptoms in the weekly online diary card we send you. This needs to be completed weekly for the 12-month study period.
- Regularly check your baby's skin for any possible rashes. If your child develops a rash that concerns you, please contact us so that we can organise a time for one of our doctors to examine your baby's skin.

Visits and Procedures

Appointment 1:

When your child is between one day old to three weeks of age, we will organise an appointment either at The Royal Children's Hospital or on the maternity ward where you delivered your child. The appointment will take about two hours in total. We will:

- Ask you and your partner to complete a questionnaire about your allergy symptoms that you or your older children experience, and about your home. This will take about 20 minutes.
- Ask you to complete a questionnaire about your baby's birth. This should take about 10 minutes.
- Examine your baby's skin to find out how well your baby's skin acts as a *barrier* by placing a small device on your baby's forearm or forehead three times each for around 10 seconds. This test is painless and non-invasive.
- Give you an information pamphlet on how to prevent allergic disease in children, as endorsed by the Australasian Society of Clinical Immunology and Allergy (ASCIA).
- Randomly assign your baby to the "cream" or "no cream" group.
- **Optional aspects of the study:**
 - Perform a heel prick test, like the new born screening test, to collect a small amount of your baby's blood.
 - Take a sample of your baby's skin cells by placing small sticky discs on their skin and reapplying this disc for approximately 50 reapplications. Four of these discs will also be applied in one application to collect samples of your baby's skin oils. These tests are painless and non-invasive. The cells and oils will be analysed to see if they predict development of eczema. This sample will be sent overseas to the laboratory of our collaborators Dr John Common (Singapore) and Prof Donald Leung (United States of America) who will make sure that this information is kept as confidential as possible. This sample will be labelled with your child's code number only. It will not be possible for the testing laboratory to identify your child from their sample. Any samples sent overseas are not protected by Australian laws and regulations.

4-week contact

When your baby is 4 weeks old, we will contact you to arrange your baby's 6-week appointment at the Royal Children's Hospital. We will ask about your baby's health since the last study visit and query how much cream you have used (if you are in the "cream" group).

Appointment 2:

6 weeks after the first appointment we will ask you to come to The Royal Children's Hospital for a 60-minute long appointment. We will:

- Examine your baby's skin to find out:
 - How well your baby's skin acts as a *barrier* (in the same way as during appointment 1).
- Ask you to complete a questionnaire on the skin treatments you may have used for your baby.
- Give you more cream if you are in the "cream group" and supply you with a pre-paid, addressed satchel to send back all used and unused tubes of cream at the 6-month timepoint.
- **Optional aspects of the study:**
 - If you are breastfeeding we will ask for a sample of approximately 10-20ml of your breast milk.

- Heel prick test as per Visit 1.
- Take a sample of your baby's skin cells and oils the same way as the previous visit

6-month contact:

When your baby is 6 months old we will contact you by phone or email. We will:

- Ask you to complete a questionnaire on the skin treatments you may have used for your baby.
- If your baby is in the cream group, we will ask you to return all the cream tubes (used and unused) to us via the supplied prep-paid and addressed post satchel.
- Provide you with the ASCIA guidelines regarding the recommended introduction of solid foods.

Appointment 3:

When your child is 12 months old we will ask you to come to The Royal Children's Hospital for the last 60-minute long appointment. During this follow-up appointment, we will:

- Examine your baby's skin using the same assessments described above.
- Do a skin prick test on your baby. This is an allergy scratch test to find out if your baby has a sensitivity to common substances (allergens) such as dust, cat hair, rye grass, and foods (milk, egg and peanut).

The test is done by placing drops of each substance on your baby's back and then gently pricking the outer layer of skin. If your baby has a sensitivity to the allergen an itchy bump will appear, much like a mild mosquito bite. We will measure any reactions to the substances after 15 minutes.

Please avoid giving your baby any medications that contain antihistamines (commonly used in cold or allergy treatments) for 72 hours before you come to the appointment, as these can interfere with the skin prick test. Please tell us if you have used an antihistamine within the three days prior to the test. The histamine used as a control prick and the allergens in this project have not yet been approved by the Therapeutic Goods Administration (TGA) in Australia. Therefore, their use is considered experimental here. The Department of Allergy at the RCH routinely uses allergens and histamine on children suspected to have allergic diseases. The allergens have been approved for use in Europe and are widely used there.

Children who are sensitised to certain foods during the skin prick testing will be offered an appointment to attend the allergy clinic at the Royal Children's Hospital where they will undergo a food challenge to determine if they are allergic to those foods. This will be conducted under the supervision of a Doctor who has been specifically trained to manage oral food challenges and you will be provided with detailed instructions prior to your appointment. This will be at no cost to you. These results will be recorded for the study.

- **Optional aspects of the study:**
 - If you are breastfeeding, we will ask for a sample of approximately 10-20ml of your breast milk.
 - Heel prick test as per Visit 1.
 - Take a sample of your baby's skin cells and oils the same way as the previous visit
 - Saliva sample. We'd like to collect a saliva (spit) sample from your child. We plan to use the sample to extract genetic material to study known and yet to be discovered genes involved in the development of allergy and lung disease, as well as for measuring proteins that are associated with allergies.

Before all appointments we ask that you:

- Don't use any skin moisturiser on your baby for 24 hours prior to the appointment, including the study cream (if you are in the cream group).
- Don't wash your baby's forearms or forehead with soap or bath oils on the day of the appointment.
- Please advise us if you have applied topical corticosteroids on your baby's forearms or forehead during the one week before the appointment, as these treatments can influence the readings of our tests and we will need to re-schedule your appointment.

Your responsibilities

If you enrol your child into this study, you will be asked to attend an initial appointment when your baby is one day to three weeks of age (at either the maternity ward where you gave birth or at the Royal Children's Hospital), to attend two appointments at the Royal Children's Hospital (when your child is six

weeks and 12 months of age) and to complete a weekly online diary card for the duration of the study. If your child is allocated to the cream group, you will be responsible for applying the cream twice per day until they are six months of age.

Optional consent

The following parts of the study are all optional - your baby can still participate without you agreeing to these aspects of the research. Please tick the boxes on the consent page to tell us if you would like to take part in these parts of the study.

- Heel prick test: We'd like to perform a heel prick test at each visit, like the new born screening test, to collect a small amount of your baby's blood. We will measure biomarkers such as vitamin D level that may relate to risk of allergic disease.
- Breast milk sample: If you are breastfeeding, we would like to collect a sample of the mother's breast milk at visits 2 and 3. We will examine aspects of these samples (including fatty acids, bacteria or bugs, and contaminants from the environment) to see if they influence the risk of allergies in your child.
- Saliva sample: We'd like to collect a saliva (spit) sample at the final 12-month visit. We plan to use the sample to extract genetic material to study known and yet to be discovered genes involved in the development of allergy and lung disease.
- Finally, we would like to keep in contact with you to monitor your child's development in the future.

STUDY VISITS AND PROCEDURES

Procedures	Appointments and Surveys			
	SCREENING/Visit 1	Visit 2	Survey	Visit 3
Age (days/months)	One day – three weeks	6 weeks	6 months	12 months
Allergy questionnaire	X			
Baby's birth questionnaire	X			
Skin assessment	X	X		X
Randomisation	X			
Study cream dispensing	X	X		
Participant survey	X	X	X	X
Diary card		X	X	X
Skin prick test				X
Food challenge				X
Optional Procedures				
Breast milk sample		X		X
Skin sample	X	X		X
Heel prick test	X	X		X
Saliva sample				X

Other treatment

If you wish to do so, you may use any other creams, oils (such as moisturiser or sunscreen) on your baby's skin, except as noted in the 'before all appointments' section. Please make sure you record this information in the online diary card and if you are in the "cream" group, also continue applying the study cream daily.

Informing your GP

Please feel free to inform your GP that you are involved in this project, and that he or she may contact us to discuss your involvement on the contact details on page 9.

After the study ends

We would like to keep in contact with you at the end of the study. Please let us know on the consent form if you are happy for us to do so. We are not able to offer you any supply of the study cream after your child turns six-months of age as it is not yet approved for use within Australia and is only available for use during the six-month study period.

Withdrawal of study treatment

You may elect to stop applying the study cream at any time. If this occurs, we would ask you to let us know and to return all of the unused cream. Even if you decide to stop using the cream, we would still like to have you attend the follow-up appointments, if you are willing to do so.

5. What are our alternatives to taking part?

Participation in a research project is voluntary. It is your choice to let your child take part in this research. You do not have to agree if you do not want to.

If you give your consent and change your mind, your child can withdraw from the project. You do not need to tell us the reason why you or your child want to stop being in the project. However, please tell us if your child plans to leave the research study so we can let you know if there are any health risks or special requirements linked to withdrawing. If your child leaves the study, we will use any information already collected unless you tell us not to.

Whatever your decision, it will not affect any treatment or care your child gets, or your family's relationship with The Royal Children's Hospital, the maternity hospital you delivered your child at, or The University of Melbourne.

Your alternatives to taking part in this study may include standard management of your child's skin, and to treat any symptoms if they develop.

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

There may be no direct benefit to you or your baby. We will provide the best available advice on how to minimise the risk that your baby will develop allergic disease, as endorsed by the Australasian Society of Clinical Immunology and Allergy. These strategies might reduce the risk that your baby develops eczema, hay fever and asthma. If your baby is in the "cream group" the use of the cream may further reduce the risk of eczema and food allergies.

We hope that our research will benefit other people in the future by providing a new cream for the prevention of eczema.

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

There is a small risk that your baby's skin will not be able to tolerate the cream and a rash will develop. We believe this is unlikely as the cream contains the major building blocks of human skin, and this did not happen to any child in our previous study. If a reaction happens, we will ask you to come to The Royal Children's Hospital so that one of the study dermatologists can examine your baby's skin, and establish the best way to manage this rash. This will be at no cost to you.

There are also no major risks associated with the heel prick test. There is a slight risk of bruising and infection but this is quite rare. This test is performed on almost all newborns and may cause slight discomfort.

The skin prick test is not painful but it may cause discomfort, as it can cause a bump that is itchy for about the first 15 minutes. These bumps go down within an hour or two. We will tell you how to manage the itch if your baby is distressed. Skin prick tests are very safe, but there is a small risk (about 1 in 10,000) of a serious allergic reaction. If this occurs the reaction will be treated immediately with the appropriate medicines.

The food challenge will only be performed on children who exhibit signs of sensitivity to a certain food. If your child does require a food challenge, this will occur at a separate appointment at the Royal Children's Hospital and you will be provided with detailed instructions beforehand. This challenge will be closely supervised by a Doctor who has been specifically trained to manage oral food challenges. There is a risk of allergic reaction with oral food challenges. The reaction may be mild (rash, facial swelling, vomiting, diarrhoea, tummy pain) or severe (involving breathing problems or low blood pressure or collapse). If this does occur your child will be treated immediately with the appropriate medication. This visit will be at no cost to you. Very rarely patients may die as a result of an allergic reaction.

There are no major risks associated with the saliva test. The genetic analysis to be undertaken in this study is for medical research and is not the same as a clinical genetic test. We will not be giving any results or information from the genetic analysis. The genetic analysis does not involve information that is relevant to your child's future health.

All of the other tests involved in this project cause no pain and have no known risks or side-effects.

The study may involve unforeseen risks. If any new information about risks and/or side effects becomes known during the project, we will tell you what they are.

The cost associated with travel may also be an inconvenience. When you arrive at our clinic we will provide you with a voucher to pay for your parking as you exit the car park. The time taken to complete a survey, and bring your baby to The Royal Children's Hospital for up to three appointments (depending upon where you have your initial appointment) may also be inconveniences.

This project needs you to follow a set of strategies to help prevent the development of eczema. This may take a small amount of additional time in the care of your baby each day which could be an inconvenience.

8. What will be done to make sure my family's information is confidential?

Any information we collect from you and your child will remain confidential. We will use this information only for this research project. Only the researchers involved with this project and The Royal Children's Hospital Ethics Committees can have access to this information. The Therapeutic Goods Administration (TGA) may also require access to this information to assess the safety of the EpiCeramTM cream. We can disclose your information and your child's information only with your permission, except as required by law. You have the right to look at, and ask correction of, your information and your child's information in accordance with Victorian and other privacy legislation.

The information we collect will be re-identifiable. This means that we will remove your names and give the information a special code number. Only the research team can match your names to your code numbers, if it is necessary to do so.

We will keep the information in a password protected database stored on the servers at the University of Melbourne. All electronic files that contain results from these tests will also be password-protected. Skin oil and cells, breast milk, blood spots and saliva samples will be stored securely at the Murdoch Children's Research Institute Biobank Facility, Royal Children's Hospital.

We would like you to consider allowing us to store and use your breast milk and your child's blood spot, saliva samples and skin oil and cell samples and data for future allergy-related research. Any future research project will be approved by an Ethics Committee. The samples will be kept indefinitely if you give your permission. If you consent to us using these samples and data for future research, it is likely that we will send these samples and data to other states and overseas to be analysed in the laboratories of our collaborators. Our collaborators will make sure that this information is kept as confidential as possible. Any samples and data that we send will be labelled with your child's code number only. It will not be possible for the testing laboratories to identify you or your child from their sample. Any samples and data sent overseas are not protected by Australian laws and regulations. Please tick the box on the consent form if you agree to allow this or not.

We will store the information collected from this project until the youngest participant turns 25 years old. We will destroy the information after this time.

We will present these results at scientific conferences and publish them in scientific journals. The results will not identify any individuals and will show only group information.

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

Yes! We will send you a summary of the results when the project is finished. This will be around January 2023. The results will be of group findings. It will give no individual results. In the meantime, we will send you an annual project newsletter to know how things are progressing.

10. What happens if my child is injured during the project?

If you suffer any injury or complication as a result of this research project, contact the study team as soon as possible. The study team will help to arrange appropriate medical treatment for you. If you are eligible for Medicare, you can get medical treatment to treat the injury or complication as a public patient in any Australian public hospital at no cost to you.

11. Will my child be able to claim compensation if injured?

In the unlikely event that your child suffers an injury as a result of taking part in this project, hospital care and treatment will be provided by the public health service at no cost to you.

If you would like more information about the project or if you need to speak to a member of the research team in an emergency, please contact the Study Coordinator:

Name: Shaie O'Brien

Contact telephone: 1800 875 127

If you have any concerns and/or complaints about the project, the way it is being conducted or your rights as a research participant, and would like to speak to someone independent of the project, please contact:

Director
Research Development & Ethics
The Royal Children's Hospital Melbourne
Telephone: (03) 9345 5044.