PARENT/GUARDIAN INFORMATION SHEET
IRAS ID: 300524

STUDY TITLE

Biomarkers in preschool children with wheeze to **TA**rget therapy w**I**th inha**L**ed c**OR**ticosteroids (**TAILOR**): a feasibility study".

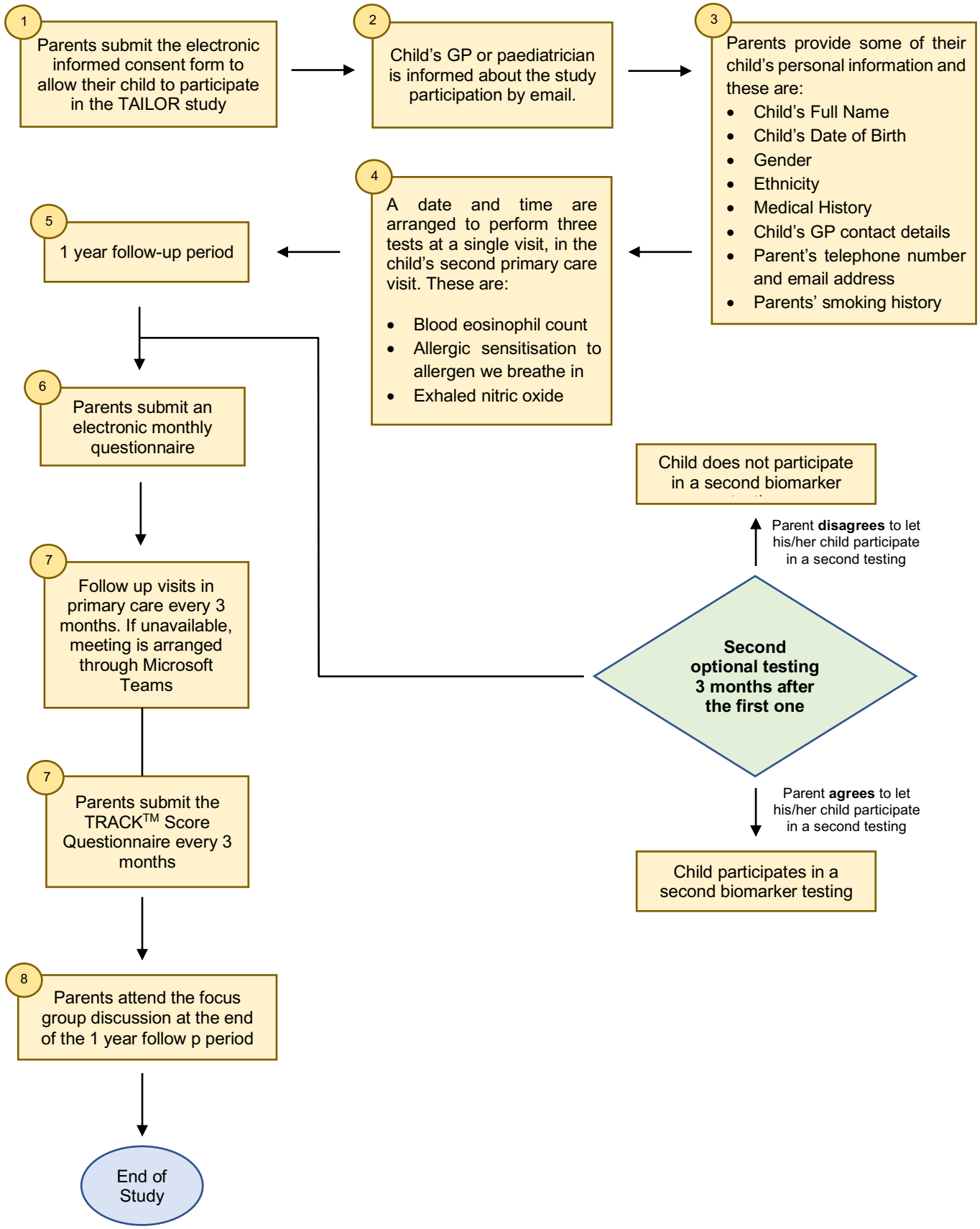
You are being invited to participate in a research study which will be contributing to the PhD research project of Mr. Andreas Perikleous and involves preschool children. Before you decide if you want your child to participate or not, it is important for you to understand why this research is being done and what it involves. Please take time to read the following information carefully and discuss it with others if you wish.

BACKGROUND INFORMATION ABOUT THE STUDY

You are being asked to read this leaflet because your child has had attacks of wheezing. This is a common condition in preschool children and affects their quality of life. Some but by no means, all preschool children have an inflammation (Type 2 inflammation) in their airways caused by a specific type of cells that are also present in the blood and are called eosinophils. It has been shown that inhaled steroids that many preschool children with wheeze are being prescribed only work when there is Type 2 inflammation. As a result, since ICS do not have any effect if this type of inflammation is not present, many children are being unnecessarily exposed to side effects. It is difficult to diagnose Type 2 inflammation by taking a history of symptoms and examining the child. So other indicators are needed that can help us identify this type of inflammation and only give ICS to children who will benefit. These indicators are commonly known as biomarkers, and we are trying to find out if they are useful.

In this study we want to measure three potential biomarkers; we will not make any change in your child's treatment. The first biomarker is blood eosinophils. These can be measured very easily by taking only one drop of blood from a finger prick sample and measuring it through a point of care test (like the blood drop used to measure sugar levels in children with diabetes). The second biomarker is to find out if the child has allergic sensitization to allergens that are breathed in and these will be house dust mite, grass pollen, tree pollen, cat and dog hair. Finally, the third biomarker that is going to be used in this study is a molecule that is produced in high quantities from airways of preschool children with Type 2 inflammation and wheeze, which is called nitric oxide (NO). This is easily obtained, by having children breathe through a mask connected to a collection bag. The breath is collected and FeNO is measured from the bag sample later on.

STUDY FLOWCHART



WHY HAS MY CHILD BEEN CHOSEN?

We have asked you to read this because your child has been diagnosed with wheezing by a doctor.

DOES MY CHILD HAVE TO TAKE PART?

It is up to you to decide whether your child will take part or not and you do not have to give a reason if you decide you do not want your child to take part. A decision not to take part, will not affect the standard of care your child receives. Indeed, your child's treatment will be as determined by your doctor and will not be changed at all by taking part in the study.

CAN I STOP MY CHILD BEING PART OF THIS STUDY EVEN IF I INITIALLY AGREE?

If you do decide to take part, you will be given this information sheet to keep and be asked to sign an electronic consent form. If you decide to take part, you are still free to withdraw at any time and without giving a reason. A decision to withdraw at any time, will not affect the standard of care your child receives. Indeed, your child's treatment will be as determined by your doctor and will not be changed at all by taking part in the study.

WHAT WILL HAPPEN IF MY CHILD TAKES PART?

After the informed consent sheet is signed, we will ask you to give us the contact details of the child's GP or paediatrician, to inform him/her about child's participation in this study through a letter sent to his/her email along with this patient information sheet. In addition, we will ask you to provide us some personal information and these are shown in table below:

LIST OF PERSONAL DATA OBTAINED	
a) Child's Full Name	e) Medical History
b) Child's Date of Birth	f) Child's GP contact details
c) Gender	g) Parents' smoking history
d) Ethnicity	h) Parent's telephone number and email address

Then we will show you a video of four different clips of children making extra sounds during breathing to confirm the respiratory sounds you are describing.

WHAT TESTS WILL MY CHILD HAVE?

We will arrange a date and time to perform three tests at a single visit, in their second primary care visit. Below are the tests we are going to perform:

1. **Blood eosinophil count** (number of eosinophils in the blood). To do this we will take a single drop of blood from a finger prick sample (like the blood drop taken many times a day by people with diabetes to measure sugar levels).

2. **Atopic sensitisation to allergens we breathe in.** These will be house dust mite, grass pollen, cat and dog hair. The method is very safe and simple and is used in routine clinical practice. A tiny drop of allergen solution will be placed on the child's skin on either his/her back, leg or arm and scratched, and whether a small skin wheal results, is determined 20 minutes later. We will also do a test with a blank drop and histamine to check the test has been done properly. The blank drop will not create a wheal, but histamine will, and will be compared with the other 4 allergens above. The wheal diameter will be measured with a specialised metric ruler. The wheals usually disappear within an hour and if the child feels itchy, an antihistamine cream will be applied.

   Please note that for this test to be performed, children should not be taking an antihistamine treatment 72 hours prior to the commence of the test.

3. **Exhaled nitric oxide.** This is a molecule that is produced in high quantities in the inflamed airways of preschool children with wheeze. In order to measure this, we will ask your child to breathe normally into a sample bag that will be collected for later analysis. We will do this test twice

Please note that all samples will be destroyed after use, and they will not be retained.

If your child has been prescribed oral corticosteroids, the tests will be performed 2 weeks after the treatment stops, so that our results are not affected by corticosteroids.

There will be one test visit at the start of the study and a second **optional** testing 3 months after the first one. Please note that your child does **not** have to participate in the second testing.

The tests will take no longer that 1 hour in total. We will not ask for your child's treatment to be changed in any way, but we would like to know how your child is responding to whatever treatment has been suggested by your doctor. To do this, we will be sending a monthly electronic questionnaire by email or SMS, regarding your child's wheezing episodes and ask you to fill this in. We would also like to see you and your child face-to-face to assess their progress every 3 months during the 1-year

follow-up period. For your convenience, if a face-to-face meeting in primary care is not feasible, we can arrange a video meeting through Microsoft Teams.

WHAT DO YOU AND YOUR CHILD NEED TO DO?

The children do not need to change **anything** in their lifestyle or treatment. They will continue their daily routine and treatment as before. The only restriction is that the child should normally not participate in another medical or scientific clinical trial.

Parents/carers will only be asked to:

- bring their child in primary care every 3 months in the 1-year follow-up period, but if not feasible, video meetings can be arranged with Microsoft Teams.
- complete a short monthly electronic questionnaire/diary sent by email or SMS.
- attend the focus group discussion at the end of the 1-year follow-up period.

All the above will be performed as far as possible to suit the parents' convenience.

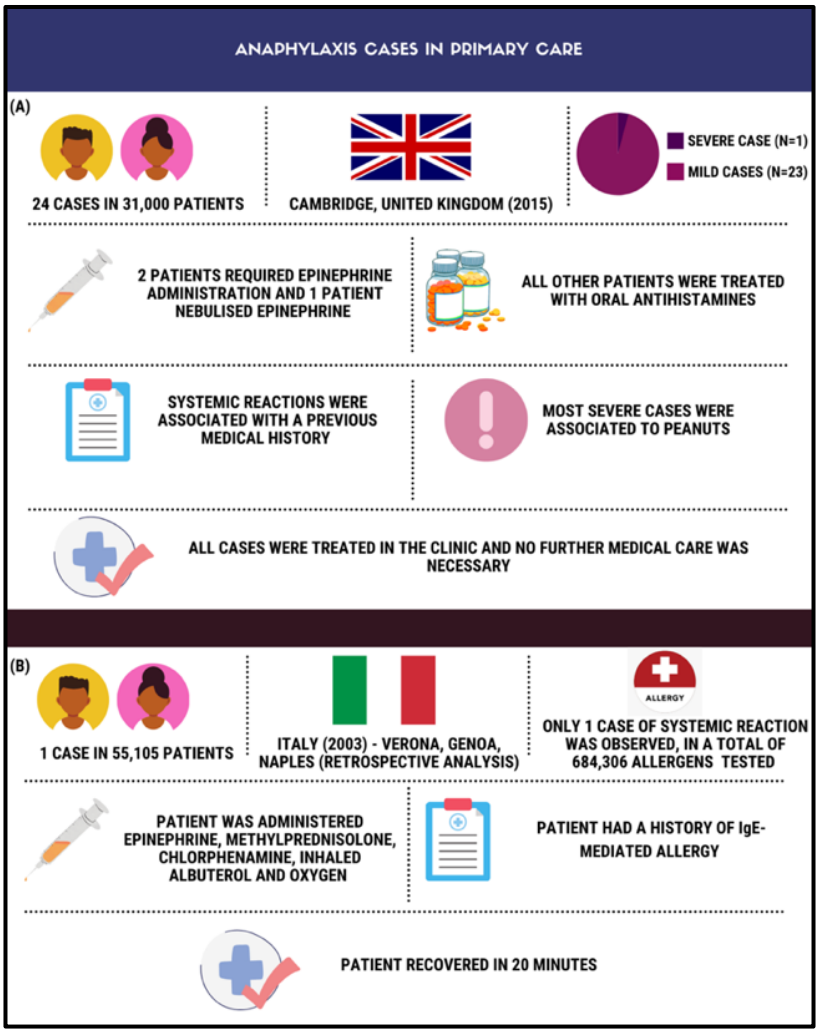
WHAT ARE THE ADVANTAGES OF MY CHILD TAKING PART?

The only tests of clinical significance to the child are the skin prick tests, which might for example inform a decision about the purchase of a pet. You will be informed about these results. The other tests won't be of clinical significance. The ultimate benefit will be in the future if we can show with a large intervention trial that measuring one or more of these biomarkers helps predict future wheezing exacerbations as well as guide treatment more efficiently, thus children stop receiving unnecessary medications. The benefit generated by this trial is to show that these markers can be measured in practice, and they are acceptable to the families.

WHAT ARE THE POSSIBLE DISADVANTAGES OR RISKS OF MY CHILD TAKING PART?

As mentioned before, this is an observational study with no new treatments to be prescribed by the research team. No risks are anticipated of the study procedures. A finger prick blood sample is used many times a day by millions of patients with diabetes of all ages for monitoring blood sugar levels. Skin prick tests have been routine for many years. There may be itching of the skin afterwards, and an antihistamine cream will be available if needed. In the highly unlikely event of a rare allergic reaction, appropriate treatment will be offered immediately.

RISK MANAGEMENT: All procedures (blood sampling through finger prick test, skin prick tests and FeNO collection) will be performed by trained research personnel and are of minimal risk. Skin prick tests are safe and have been used for many years, but adrenaline and antihistamines will be available while the study procedures are being performed, in case a child has a very rare allergic reaction (below).



WHAT HAPPENS WHEN THE STUDY STOPS?

When the study stops, we will analyse the data and the results will be published in a highly accredited medical journal. We will give you a feedback on the study's results as soon as they are published. In addition, after the study ends, you will be invited to a face-to-face focus group interview, or a one-to-one interview, or remotely through Microsoft Teams, depending on your availability. We will ask you to tell us what you think about the investigations and the conduct of the study. This will help us to design the future intervention study. Where possible a second independent researcher will sit as well in the focus groups discussion and interviews to ensure there is no bias. The conversations from the focus group and one-to-one interviews will be audio recorded, transcribed, and coded into themes. We will utilise an external company for transcribing the conversations called 1st Class. https://www.1stclass.uk.com/. We will also ask you to fill in a very short exit questionnaire to tell us what you think about biomarkers being used to guide children's therapy as well as your views on what you would like the future intervention study to be like. If this study is successful, it will lead to a new national randomized controlled trial of this approach in preschool children.

WILL MY CHILD'S DETAILS AND INFORMATION BE CONFIDENTIAL?

Yes. All your child's details and information will be kept anonymised and confidential. Please note that your child will not be identified in any report or publication.

WHAT WILL HAPPEN TO THE RESULTS OF THE STUDY?

The results will be presented at national and international medical conferences. They will also be published in a medical journal so that other doctors worldwide can learn from this study. Your child will not be identified in any report/publication.

PARTICIPANT DATA AND INFORMATION

Imperial College London is the sponsor for this study and will act as the data controller for this study. This means that we are responsible for looking after your information and using it properly. Imperial College London will keep your personal data for:

- 10 years after the study has finished in relation to data subject consent forms.
- 10 years after the study has completed in relation to primary research data.

We will need to use information from you as well as your child and his/her GP contact details and medical history for this research project. This information will include your child's full name, initials, date of birth, gender, ethnicity, medical history, your child's GP contact details as well as, your contact details (telephone number, email) and your smoking history.

People will use this information to do the research or to check your records to make sure that the research is being done properly. People who do not need to know who you are will not be able to see your name or contact details. Your data will have a code number instead. We will keep all information about you safe and secure. Once we have finished the study, we will keep some of the data so we can check the results. We will write our reports in a way that no-one can work out that you took part in the study.

WHAT ARE YOUR CHOICES ABOUT HOW YOUR INFORMATION IS USED?

You can stop being part of the study at any time, without giving a reason, but we will keep information about you that we already have. We need to manage your records in specific ways for the research to be reliable. This means that we won't be able to let you see or change the data we hold about you. If you agree to take part in this study, you will have the option to take part in future research using your data saved from this study.

WHERE CAN I FIND OUT MORE ABOUT HOW MY CHILD'S INFORMATION IS USED?

You can find out more about how we use your information

- at www.hra.nhs.uk/information-about-patients/
- by asking one of the research team
- by sending an email to [Imperial College email], or
- by ringing us on [phone number].

LEGAL BASIS

As a university we use personally identifiable information to conduct research to improve healthcare, and services. As a publicly funded organisation, we have to ensure that it is in the public interest when we use personally identifiable information from people who have agreed to take part in research. This means that when you agree to take part in a research study, we will use your data in the ways needed to conduct and analyse the research study. Health and care research should serve the public interest, which means that we have to demonstrate that our research serves the interests of society as a whole. We do this by following the UK Policy Framework for Health and Social Care Research

WHAT IF SOMETHING GOES WRONG?

If your child is harmed by taking part in this research project, there is no-fault compensation cover in place. If your child is harmed due to someone's negligence, then you may have grounds for a legal action. The sponsor holds negligent and non-negligent harm insurance policies to cover any claims. Regardless of this, if you wish to complain, or have any concerns about any aspect of the way you have been treated during the course of this study then you should immediately inform the Investigator (Professor Andrew Bush, email: a.bush@imperial.ac.uk). The normal National Health Service complaints mechanisms are also available to you.

COMPLAINT

If you wish to raise a complaint on how we have handled your personal data, please contact Imperial College London's Data Protection Officer via:

- **email** at dpo@imperial.ac.uk
- via **telephone** on 0207594 3502
- via **post** at Imperial College London, Data Protection Officer, Faculty Building Level 4, London SW7 2AZ.

If you are not satisfied with our response or believe we are processing your personal data in a way that is not lawful you can complain to the Information Commissioner's Office (ICO). The ICO does recommend that you seek to resolve matters with the data controller (us) first before involving the regulator.

WHO IS ORGANISING AND FUNDING THE RESEARCH?

The Asthma UK Centre for Applied Research (AUKCAR) is the funder for this study. Imperial College London will act as the main Sponsor for this study. Delegated responsibilities will be assigned to the NHS trusts taking part in this study. Your doctor will **not** be paid for including you in this study.

STUDY REVIEWAL

The study documents are reviewed by the Health Research Authority (HRA) which includes Research Ethics Committee (REC).

CONTACT FOR FURTHER INFORMATION

Please contact Andreas Perikleous, PhD student researcher:

- **Telephone:** 07865521654
- **Email:** tailor01@imperial.ac.uk

Or alternatively in the John Radcliffe Hospital at 0300 304 7777, asking for Mr. Andreas Perikleous.

Thank you so much for considering taking part to this study. Please **note** that a copy of the patient information sheet will be given to you, should you decide to let your child take part. The signed consent form will be sent automatically to your email when submitted.