A Multicenter Registry Study Examining the Efficacy of Specific Immunotherapy Guided by Component-Resolved Diagnosis for Dust Mite Allergens in Chinese Pediatric Patients With Rhinitis and/or Asthma (Explorer Study)

Informed Consent Form (For Minors Under 8 Years Old)

NCT: _____

Version: 1.0 Version Date: August 29, 2025

Research Institution	The Children's Hospital of Zhejiang University School of Medicine
Research Department	Pulmonology Department
Project Source	Investigator-Initiated Research

1. What am I being invited to?

You are being invited to take part in a clinical study. A clinical study helps us learn new things. In this study, we want to find out about the differences in how children with different patterns of house dust mite allergy respond to allergen immunotherapy after undergoing component-resolved diagnostics. We also want to see if it can help children with allergic rhinitis, with or without allergic asthma.

2. Why are we doing this study?

House dust mites are closely related to diseases like allergic rhinitis and allergic asthma. They mainly include Dermatophagoides pteronyssinus and Dermatophagoides farinae and are commonly found in places where people live. Allergic rhinitis often occurs together with other conditions like asthma and can seriously affect a child's quality of life.

Dust mites are made up of many different proteins, which are called "components." The rates of allergy to different dust mite components vary, and they can also differ across various regions in China. Component-resolved diagnostics is a more precise way to diagnose allergies. Allergen immunotherapy, also known as desensitization treatment, can reduce or even eliminate allergy symptoms, but it requires careful selection of children and long-term commitment.

In our earlier studies, we found that most children are allergic to several dust mite components at the same time. However, it is currently not clear whether children allergic to only certain components should receive specific immunotherapy. There is also a lack of nationwide data on the effectiveness and long-term follow-up of specific immunotherapy in children with dust mite allergy.

3. What will happen if I take part in the study?

This study will be carried out in 10 hospitals, and a total of 1,000 children with dust mite allergy are expected to take part. Our hospital plans to enroll 100 children.

If you join, you will be in the study for about 3 years, from the start to the end.

If you agree to take part, first please check the box in the right place on this form. Your father or mother (or parents) will sign another form. You can only be in the study if both you and your parents agree.

At the beginning of the study, this is what might happen: The doctor will ask your parents some questions about you and your health. You might feel a little bored. During the study, we will also need to take some blood: A doctor or nurse will use a needle to take some blood from your arm. It might hurt a little. You might get a small red dot or a bruise on your arm.

Remember to tell your parents and the doctor how you are feeling during the study, especially if you feel uncomfortable or scared. If you want to know more about any not-so-good feelings you might have, you can ask the doctor or your parents.

4. Will taking part in this study help me?

You might get better, or you might not. We cannot guarantee it. But by taking part, you might help other children who have the same condition as you.

5. Will taking part in this study affect my treatment?

No, taking part in this study will not affect your regular treatment.

6. Is it my choice to take part in this study?

Yes, whether or not you want to be in this study is up to you. No one will be upset, whether you choose to take part or not. If you don't want to, you don't have to. Even if you say yes now but change your mind later, you can still stop being in the study. Your doctor will still take care of you, even if you don't want to be in the study.

Informed Consent Signature Page

Subject's Print Name _____

☐ No, I do not wish to participate in this study

☐ Yes, I wish to participate in this study

Legal Guardian's Print Name_____

Relationship to Subject_____

Legal Guardian's Signature_____

Signature Date _____

Phone Number_____

(Only one legal guardian's signature is required for this study)

A Multicenter Registry Study Examining the Efficacy of Specific Immunotherapy Guided by Component-Resolved Diagnosis for Dust Mite Allergens in Chinese Pediatric Patients With Rhinitis and/or Asthma (Explorer Study)

Informed Consent Form (For Minors Aged 8 Years and Above)

NCT: _____

Version: 1.0 Version Date: August 29, 2025

Research Institution	The Children's Hospital of Zhejiang University School of Medicine
Research Department	Pulmonology Department
Project Source	Investigator-Initiated Research

We are inviting you to take part in a clinical study called: A Multicenter Registry Study on the Efficacy of Specific Immunotherapy Based on Component-Resolved Diagnostics for House Dust Mite Allergy in Chinese Children with Allergic Rhinitis With or Without Asthma. We are doing this study to learn more about certain things. We will explain the study below. Please take your time to understand it before you decide whether to join. If you have any questions or don't understand something, feel free to ask your study doctor, who will explain it to you carefully until you understand.

1. Why are we doing this study?

House dust mites are one of the most common indoor allergens worldwide. They are closely linked to allergic diseases like allergic rhinitis, allergic asthma, and atopic dermatitis. The main types are Dermatophagoides pteronyssinus and Dermatophagoides farinae, and they are found in many human living environments. Allergic rhinitis often occurs together with other conditions like asthma and can seriously affect a child's quality of life.

Dust mites are made up of many different proteins, which are called "components." Allergy rates to different dust mite components vary, and they can also differ across different regions in China. Component-resolved diagnostics is a more precise way to diagnose allergies. It can help tell the difference between co-sensitization and cross-sensitization, making the diagnosis more accurate. Allergen immunotherapy, also known as desensitization treatment, involves gradually exposing a child to the allergen to reduce or eliminate allergy symptoms. It is the only treatment that might change the natural course of allergic diseases, but it requires careful selection of patients and long-term commitment. It can greatly improve quality of life and reduce long-term problems.

In our earlier studies, we found that most children are allergic to several dust mite components at the same time. However, it is currently not clear whether children allergic only to certain specific components should receive specific immunotherapy. There is also a lack of nationwide data on how well specific immunotherapy works in children with dust mite allergy and what happens to them over the long term.

2. What do I need to do before joining the study?

If you agree to take part, you will need to sign this form before any study activities begin. Your father/mother/legal guardian (called your "guardian" from now on) will sign another form. You can only be in the study if both you and your guardian agree. You can talk with your guardian about the information the doctor gives you. If you reach the age of adulthood during the study, we will ask you to sign a consent form for adults. If the consent form is updated with a new version during the study, we will ask you to sign it again.

3. How will this study be done?

This study will be carried out in 10 hospitals, and a total of 1,000 people with dust mite allergy are expected to take part. Our hospital plans to enroll 100 participants.

If you join, you will be in the study for about 3 years, from the start to the end.

If you take part, here is what will happen:

1) After signing the consent form, we will take a blood sample (2 ml in a yellow-top tube). We will spin it in a centrifuge and keep the top layer (serum) frozen at -80° C. This will be used to test for allergen components. This will happen once a year, for a total of 4 blood draws. The blood samples will not be used for product development, shared with others, or given to outside groups.

2) An electronic data capture system will collect clinical data and information from your follow-up visits. We will not make any changes to your regular medical care.

4. Are there any discomforts or risks if I take part?

During the study, you might experience some things: You might feel tired or a bit embarrassed by the questions the doctor or nurse asks. When we take blood, the needle going into your arm might hurt a little. You might get a red mark, a bruise, or some soreness on your arm where the needle went in. There is a very small chance the spot could get infected.

You might have other feelings, too. If you feel uncomfortable at any time during the study, you must tell your parents or the doctor. You or your parents can call the doctor anytime.

5. Are there any benefits to taking part?

Taking part in this study might help identify which specific dust mite components you are allergic to. This might (or might not) be helpful for guiding immunotherapy. Also, the information from this study will help us learn important things about dust mite allergy, allergic rhinitis, and asthma. This could benefit other children with these conditions in the future.

6. Will taking part affect my treatment plan?

This part of the study is observational (a registry study). We are just collecting clinical data and information. We will not make any changes to your regular medical care, so there are no extra risks to your treatment.

7. Do I have to pay for anything if I take part?

The testing for allergen components in this study is free.

8. Will I get any compensation for taking part?

You will not receive any payment or compensation.

9. Do I have to join? Can I withdraw after joining?

Whether or not you join this study is your choice. If you choose not to join, no one will be upset with you. Your doctor or parents cannot force you to join if you don't want to.

If you say yes now but change your mind later, you can stop being in the study at any time. Just tell your doctor or your parents/guardian whenever you want to stop. Your doctor will still take care of you, even if you don't want to be in the study.

10. Could I be asked to leave the study?

The study doctor might decide that you need to leave the study if:

You do not follow the study team's instructions (poor compliance).

The study doctor thinks continuing could be harmful to you.

The study is stopped by the Ethics Committee or a regulatory authority.

11. Will my privacy be protected if I take part?

All your study documents will use a code number instead of your name. Any public reports about the study results will not include your personal information.

All data and the code linking it to you will be kept securely by the researchers' institution (the Children's Hospital, Zhejiang University School of Medicine). Study data will be kept for at least 10 years.

During the study, if any new information or medical findings related to your health become available, we will contact you and your parents/guardian promptly. For example, we might suggest some tests based on this new information.

The information and data from your participation might be used in other approved scientific research in the future. You have the right to say no to your data being used again for other research. This will not affect your rights in any way, and you can still continue in this study.

12. What will happen to any leftover biological samples?

After testing your blood samples, if there is any leftover serum, we would like to keep it. These samples might be used for other approved scientific research at our institution. You have the right to refuse to let us keep your leftover samples. Even if you agree now, you can change your mind later. This will not affect your rights in any way, and you can still continue in this study.

13. Who should I contact if I have questions about the study or my rights?

You can ask questions about this study anytime. You can call the doctor, who will answer all your questions. If you have a study-related injury or any questions, please contact:

Phone: 86+13397813805

If you have questions about your rights as a research participant, you can contact the Ethics Committee:

Name: Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine

Address: 3333 Binsheng Road, Binjiang District, Hangzhou, Zhejiang Province, China

Phone: 0571-86670076

Informed Consent Signature Page

I have read and understood the information in this informed consent form, have been given the opportunity to ask questions, and am satisfied with the answers provided. I voluntarily agree to participate in this study.

Subject's Print Name _____

Subject Signature _____

Signature Date _____

Legal Guardian's Print Name_____

Relationship to Subject_____

Legal Guardian's Signature_____

Signature Date _____

Phone Number_____

(Only one legal guardian's signature is required for this study)

A Multicenter Registry Study Examining the Efficacy of Specific Immunotherapy Guided by Component-Resolved Diagnosis for Dust Mite Allergens in Chinese Pediatric Patients With Rhinitis and/or Asthma (Explorer Study)

Informed Consent Form (For Parents/Guardians)

NCT: _____

Version: 1.0 Version Date: August 29, 2025

Research Institution	The Children's Hospital of Zhejiang University School of Medicine
Research Department	Pulmonology Department
Project Source	Investigator-Initiated Research

Dear Parent or Legal Guardian, Your child is being invited to participate in a research study: A Multicenter Registry Study on the Efficacy of Specific Immunotherapy Based on Component-Resolved Diagnostics for House Dust Mite Allergy in Chinese Children with Allergic Rhinitis With or Without Asthma. Whether or not your child participates in this study is entirely voluntary. This informed consent form provides important information about the study. Please read it carefully before deciding whether to allow your child to participate. If you have any questions or anything is unclear, please ask the study doctor, and the research team will answer all your questions.

This study is being conducted by Children's Hospital, Zhejiang University School of Medicine. This study has been reviewed and approved by the Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine.

1. Why is this study being conducted?

House dust mites (HDM) are one of the most common indoor allergens worldwide. They are closely linked to allergic diseases such as allergic rhinitis (AR), allergic asthma (AA), and atopic dermatitis. The main types are Dermatophagoides pteronyssinus and Dermatophagoides farinae, and they are widely found in human living environments. AR is one of the most common allergic diseases in children, with a global prevalence of approximately 10%-40% (reaching up to 50% in some regions), and it often coexists with other conditions like asthma. Asthma is the most common chronic inflammatory airway disease globally, affecting about 10-15% of children. AA is the most common subtype of childhood asthma (accounting for 80% of cases) and significantly impacts children's quality of life.

HDM are complex mixtures composed of various proteins, referred to as "components." As of 2025, the WHO/IUIS has officially named 39 HDM allergen components. Based on sensitization rates, many studies classify them into major, intermediate, and minor components. Major components are strongly correlated with clinical symptoms (e.g., asthma, rhinitis) and are primary targets for specific immunotherapy (AIT). Intermediate components have lower sensitization rates but may become major sensitizers in specific populations or regions; they can potentially exacerbate allergic symptoms, and some are associated with cross-reactivity. Minor components are often cross-reactive proteins rather than direct causes of allergy symptoms, or they only sensitize individuals in specific populations. The sensitization characteristics of different HDM components vary significantly across different geographical regions in China.

Component-resolved diagnostics (CRD) is a more precise allergy diagnostic method. It uses natural or recombinant single-component allergens to identify the specific molecules causing the allergy. By detecting specific IgE (sIgE) antibodies against individual allergen components, CRD helps distinguish between genuine sensitization and cross-reactivity, such as differentiating co-sensitization from cross-sensitization, thereby improving diagnostic accuracy.

Allergen immunotherapy (AIT), also known as desensitization therapy, is a causative treatment for allergic diseases. It works by gradually exposing the child to the allergen, inducing immune tolerance, thereby reducing or eliminating allergic symptoms. AIT is indicated for patients with clearly identified and unavoidable allergens (e.g., HDM, pollen), those with poor symptom control on pharmacotherapy or requiring long-term medication, and those unwilling to use long-term medication. AIT is currently the only treatment with the potential to alter the natural course of allergic diseases, but it requires careful selection of indications and long-term adherence. Prior to initiating AIT, the causative allergen must be clearly identified through skin prick tests (SPT) or sIgE testing. When indications are met, AIT can significantly enhance quality of life and reduce long-term complications.

In preliminary studies, our group found that most children are sensitized to multiple HDM components simultaneously, including not only major components but also intermediate and minor ones. Current guidelines do not provide clear recommendations on whether AIT should be administered to children sensitized exclusively to intermediate and minor components. Furthermore, there is a lack of national data on the efficacy and long-term follow-up outcomes of AIT in children with HDM allergy.

2. What needs to be done before participating in the study?

If you and your child decide to participate, we will ask you to sign this informed consent form before any study-related activities begin. If a new version of the consent form is generated during the study, we will ask you to sign it again.

3. How will this study be conducted?

This study will be carried out in 10 hospitals, with a total of 1,000 HDM-positive participants expected to enroll. Our site plans to enroll 100 participants.

Your child's participation, from start to finish, will last approximately 3 years.

If your child takes part, the following will occur:

1) After signing the consent form, a blood sample (2 mL in a yellow-top tube) will be collected. The sample will be centrifuged, and the upper serum layer will be stored at -80° C for allergen component testing. This will occur once per year, for a total of 4 blood draws. The collected blood samples will not be used for product development, shared with third parties, or provided outside the study.

2) Clinical data and information from your child's subsequent follow-up visits will be collected using an electronic data capture (EDC) system. No modifications will be made to routine diagnostic or treatment procedures.

4. Are there any discomforts or risks associated with participating? Are there protective measures?

This is an observational study. It only involves collecting clinical data and information without modifying routine diagnostic or treatment procedures. Therefore, it poses no additional risks related to examinations or treatment for the participant.

Risks of Biological Sample Collection: Blood collection may cause pain, local bruising, bleeding, local infection, or other physiological discomfort. Procedures will be performed by professional nurses strictly following standard operating protocols.

5. What are the potential benefits of participating?

Participation in this study may help identify the specific component sensitization profile of your child's HDM allergy. This may (or may not) be helpful in guiding decisions regarding HDM immunotherapy. Furthermore, the information obtained from this study will contribute valuable knowledge regarding diseases associated with HDM allergy, such as AR and asthma, potentially benefiting children suffering from these conditions in the future.

6. Will participating affect my child's treatment plan?

This subsequent part of the study is observational (a registry study). We will collect clinical data and information without modifying any routine diagnostic or treatment procedures. Therefore, it poses no additional risks related to your child's treatment.

7. What if my child is injured as a result of participating in the study?

If your child experiences an injury or an adverse event during the study or related to medication/treatment, please contact the study doctor. Your child will receive timely medical care. For any injury determined to have a causal relationship with this study, the Children's Hospital, Zhejiang University School of Medicine, and the relevant participating institutions will cover the medical expenses and provide appropriate financial compensation in accordance with relevant national laws and regulations.

Even after signing this informed consent form, you retain all your legal rights.

8. Are there any costs for participating in this study?

The allergen component testing in this study is free of charge. You will not need to pay for it.

9. Will there be any compensation for participating?

You will not receive any payment or compensation.

10. Is participation mandatory? Can I withdraw after agreeing to participate?

No, participation in this study is entirely voluntary. You may refuse to allow your child to participate.

You may also withdraw your child from the study at any time. Withdrawing will not result in any penalty, discrimination, or retaliation, nor will it affect your child's future medical care or rights. If you wish to withdraw your child from the study, please inform us. We will ensure that your child ends their participation in the safest manner possible.

11. Under what circumstances might my child be asked to leave the study?

The study doctor has the right to decide that your child should be withdrawn from the study under the following circumstances:

You or your child do not follow the study team's instructions (poor compliance).

The study doctor determines that continuing the study could cause unnecessary harm.

The study is terminated by the Ethics Committee or a regulatory authority.

12. What happens if new information becomes available during the study?

During the study, if any new information arises that might affect your child's willingness to continue participating, the study doctor will inform you and your child promptly. You will be given adequate time to consider whether you wish for your child to continue in the study.

13. Will my child's information be protected if they participate?

All study-related documents for your child will be identified by a code number, not by name. Any public reports on the results of this study will not disclose any personal information about you or your child.

All data and the linking code will be stored securely by the researchers' institution. Study data will be retained for at least 10 years. Your child's medical records related to this study may be reviewed by the researchers, the Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine, and government regulatory authorities.

The information and data generated from your child's participation in this study may be used in other approved scientific research in the future. You have the right to refuse the secondary use of this information/data. This will not affect your child's rights in any way, nor will it affect your child's continued participation in this study.

14. What will happen to any remaining biological samples?

After testing your child's blood samples, if there is any remaining sample, we would like to continue storing it. These samples may be used for other approved scientific research at our institution. You have the right to refuse the storage of remaining samples. If you agree to storage initially, you may withdraw this consent at any time. This will not affect your child's rights in any way, nor will it affect your child's continued participation in this study.

15. Who should I contact if I have questions about the study?

You may ask questions about any aspect of the study that you do not understand. The project team will answer all your questions. If you feel your questions have not been fully answered, or you do not understand the answers provided, please continue asking until you are satisfied.

Contact Information:

Phone: 86+13397813805

If you have questions about your child's rights as a research participant, or wish to report any concerns or complaints about the study process, you may contact the Ethics Committee:

Name: Medical Ethics Committee of the Children's Hospital, Zhejiang University School of Medicine

Address: 3333 Binsheng Road, Binjiang District, Hangzhou, Zhejiang Province, China

Phone: 0571-86670076

Informed Consent Signature Page

I have read and understood the information in this informed consent form. I have had the opportunity to ask questions, and I am satisfied with the answers provided by the study doctor. I have been given sufficient time and opportunity to consider the details of the study and decide whether to participate.

I voluntarily consent to my child's participation in this study.

Signing this informed consent form does not constitute a waiver of any of my legal rights.

I authorize the research staff, the Ethics Committee, and government regulatory authorities to access my child's medical records related to this study.

I ☐agree / ☐disagree to the use of my child's information and data from this study in future research.

I ☐agree / ☐disagree to the storage and use of my child's remaining biological samples from this study in future research.

Subject's Print Name _____

Signature Date _____

Legal Guardian's Print Name_____

Relationship to Subject_____

Legal Guardian's Signature_____

Signature Date _____

Phone Number_____

(Only one legal guardian's signature is required for this study)