International Platform for Childhood Interstitial Lung Diseases

European chILD Register and Biobank

chILD-EU

Patient Information and Declaration of Informed Consent for the Research Project "European chILD Register and Biobank" (chILD-EU register)

Patient >18 Years

Dear Patient,

You have been diagnosed with a childhood interstitial lung disease **(chILD)** or you belong to a group of patients with a lung disease or other disease that we would like to include in the European chILD Register and Biobank for the purpose of comparison to childhood interstitial lung disease. We would like to ask you to agree to take part in a proposed piece of research.

We explain the aims of that research and the procedure for it in the following Patient Information. Participation in the research is voluntary, that is, you will be included in this trial only if you declare your consent.

The doctor in charge of your case will have a detailed interview with you to inform you about the Research Project and the possible benefits and risks of your participation. **We would like you to read the following information** before the interview. You can already get a good general idea by doing so. Please ask your doctor if anything is unclear to you or if there is anything else you would like to know.

European chILD Register and Biobank,
Kids Lung Register Foundation (KLR e.V.)

Patient Information and Declaration of Informed Consent for the Research Project "European chILD Register and Biobank" (chILD-EU register)

Patient Information

Patient (last name, first name): _____

Date of birth: _____

Place of birth: _____

Summarized explanation of the project

In order to better research the natural course, risk factors, treatments and reasons for the development of childhood interstitial lung disease **(chILD)**, if you consent, we will centrally store and analyse details of your symptoms and quality of life, clinical data and also biological material collected from you. Our handling of your data and biological material in this regard is contractually regulated. As soon as a sufficient number of patients have been included in the register, the European chILD Register and Biobank management committee, in co-operation with an Ethics Board, will evaluate the data and publish them. Your data are secured by the mechanisms provided, i.e. the organization of the database and the handling of your biological material make it impossible for unauthorized persons to identify you. Our project is explained in detail in the following.

Who conducts the trial?

The **European chILD Register and Biobank (chILD-EU register),** held by the non-profit Kids Lung Register Foundation (KLR e.V.), conducts the clinical trial and consists of several European academic parties. The coordinator of this research association is Prof. Matthias Griese, who can be contacted at the following address:

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Germany

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Currently the European chILD Register and Biobank is managed by a number of parties and third-parties, working together in the chILD-EU Network. These include Prof. Andy **Bush**, Royal Brompton Hospital London, United Kingdom, Prof. Angelo **Barbato**, University of Padova, Prof. Annick **Clement**, Prof Jacques **de Blic**, Prof. Ralph **Epaud**, all three representing the University of Paris, National Reference Center for rare lung diseases, Gisela **Antony**, Philipps-University Marburg, Prof. Lutz **Goldbeck**, University of Ulm, Prof. Matthias **Griese**, University of Munich, Dr. Kai **Kronfeld**, Universitätsmedizin der Johannes

Gutenberg Universität Mainz, Dr. Nicolaus **Schwerk**, Hannover Medical School, Prof. Nural **Kiper**, Hacettepe University, Ihsan Dogramaci Childrens' Hospital, Ankara and Dr. Steve **Cunningham**, University of Edinburgh. This chILD-EU **register** management committee is supported in its work by an Ethics Board and a Data and Safety Monitoring Board headed by Prof. Peter Propping, University Clinic Bonn, Germany. The Boards advise the management committee of the chILD-EU **register** in all aspects of data protection, Ethical issues in genetic testing and performing register based clinical trials and all other relevant areas of ethics. Other physicians and scientists may also join the European chILD Register and Biobank, if their clinical experience qualifies them sufficiently. In that case, a written agreement between the Kids Lung Register Foundation (KLR e.V.) and the scientist on the spot regulates his/her rights and duties, especially with regard to data protection.
Further information, including information specifically for patients, and updated contact details are available on the association's website (www.childeu.net).

What this trial is about
First and foremost, the aim of the European chILD Register and Biobank, in which we are asking you to take part, is to characterize the natural course and treatment effects of various forms of childhood interstitial lung diseases as comprehensively as possible; in this case especially children with mono-genetically defined chILD, children with a lung biopsy for diagnosis of diffuse parenchymatous lung diseases (DPLD), also called childhood interstitial lung diseases (chILD), children with evidence for familial ILD and all patients with DPLDs related to the alveolar surfactant region will be included in the register.

We will generate a common European database and biobank, recruit and carefully characterize a cohort of chILD patients, determine the value of outcomes used for the patients, assess treatment variations used, and offer participation in randomized interventions with treatments. Thus, in the long run, this chILD-EU **register** will serve the improved understanding of the disease, including your own case, and will lead to the development of new and effective approaches to treatment. To achieve this goal, patients with other lung diseases (chronic bronchitis, localized lung abnormalities, pulmonary hypertension) and other diseases will be included in the chILD-EU **register**. For the detection of underlying genetic changes in cases of increased familial occurrence of chILD, genetic testing of patient's family members is planned. For that reason, family members will also be included in the chILD-EU **register**.

FOR PATIENTS WITH CHILDHOOD INTERSTITIAL LUNG DISEASE (chILD)

To achieve the described aim, we will not only use questionnaires to ask you detailed questions about your medical history and quality of life but also record the medical findings obtained in the course of routine diagnostic investigations in a structured way and store them in a treatment database managed centrally on our behalf. Since a number of major alternatives to the diagnoses of chILD exist, we would also like to have your own doctor's diagnosis confirmed by independent experts in an inter-disciplinary assessment procedure. To enable us to give a good description of the course of your disease, we will ask you questions not only once at the beginning, but several times during the course of the trial. In sub-studies we may want to approach you to directly enter data on symptoms and clinical course. Finally, we would like to store blood, pulmonary lavage fluid, urine, sputum, buccal swabs and/or tissue samples that have been collected from you either as part of routine medical procedures or specifically for research purposes, in a central biobank in Munich. Together with the stored clinical data, these biological materials will be used to discover new mechanisms in the development of the disease on a molecular level and they are an indispensable component in the development of new approaches to treatment. For future research projects it may be necessary that the cells of the biosamples are still capable of mitosis. Therefore we would like to immortalize some cells of the biosamples if applicable.

Amongst others, we will also perform genetic tests and gene expression studies on blood samples, with the aim of identifying the factors that permit a reliable diagnostic classification of the disease by means of a blood test. In addition, we wish to apply new genetic methods, especially where several cases of chILD exist within a family, to identify the genes responsible for triggering the disease.
It is certainly possible that in the above mentioned investigation of your biological material observations could be made that are of great importance to you and your relatives. For example, a gene mutation could be identified as the cause of your disease and it could certainly become possible to investigate your close relatives for its presence in the case of multiple occurrences of your disease within your family, although this would not of itself represent an improvement in the treatment options as such. However, the detection of certain gene mutations could be accompanied by the opportunity of developing targeted and hence better forms of treatment, a development from which you could possibly also benefit yourself. Finally, one or several factors permitting a reliable prognosis of the further course of your disease could become known. In such a case, the further course of your disease could be predicted more accurately, which would certainly be important in the case of an intended lung transplantation, for example, but might also be a strain on you, if the result was not very positive and treatment options were still lacking.
We hope to include at least 500 patients with your disease in the chILD-EU **register** in the next 3 years. The more patients agree to take part in this chILD-EU **register**, the more useful the evaluated data will be and the higher the chance of actually gaining a better understanding of your disease and, possibly, developing new methods of treatment.

What we are asking you to do
Subject to your agreement, after inclusion in the trial, we will ask you to do the following:

- complete a relatively extensive questionnaire, which will take about 1 hour to fill out and which will collect information about your previous history as well as about your quality of life that we consider relevant.
- give your treating as well as consenting physician permission to pass relevant clinical findings, that have been obtained before or simultaneously to your participation in the trial (results from the physical examination, blood tests, endoscopy of the airways, ultrasound scans, lung function tests, exercise tests, x-rays etc.), on to the Kids Lung Register Foundation (KLR e.V.), which holds the chILD-EU **register** and to send us images from high resolution computer tomography (HR-CT) scans.
- transfer ownership of samples that are collected during routine procedures by your treating physician and that are no longer needed for your further treatment to the Kids Lung Register Foundation (KLR e.V.). Among the samples collected during routine procedures that we would like to store centrally in our biobank are blood, urine, sputum, buccal swabs, the so-called pulmonary lavage fluid and/or tissue samples from lung biopsies, including wax blocks and lung transplants that are no longer needed.
- We also ask you to donate and transfer ownership of samples collected specifically for research purposes by the doctor who obtains your informed consent to the Kids Lung Register Foundation (KLR e.V.). Among the biological materials we are asking you to donate specifically for this research project are blood samples (about 30 ml). The blood samples will be taken at routine blood sample collections, so that an additional puncture of a vein is not necessary. These collections will be performed several times in the course of the trial.
  Your right to self-determination with regard to information remains unaffected by this transfer of ownership, i.e. if you wish to revoke your agreement to participate in this trial at any time, all biological materials collected from you will be effectively anonymized.
- After you have been included in the chILD-EU **register**, we will ask you at regular intervals (ideally every 3 months, but at least once a year) to complete another questionnaire, which will take about 15 minutes to answer and which will include questions about some of the topics

already asked at your initial inclusion in the trial as well as questions about your actual quality of life.

- To give your consent that your current treating physician who obtains your consent for this study will complete a questionnaire and send it to the Kids Lung Register Foundation (KLR e.V.), to describe the course of your disease as fully as possible. In addition medical letters or test results, which are effectively pseudonymized, will be transferred to the **chILD-EU register**.
- To give your consent for the doctor obtaining your informed consent to pass on any high resolution computer tomography scans performed in the meantime.

Benefits of participating in this trial

Participation in this trial does not involve any immediate benefits. However, you benefit from the start from the confirmation of your diagnosis by an independent team of experts, which involves a gain in certainty with regard to the prognosis of your disease. If the independent team of experts considers an alternative diagnosis likely, your own doctor will be informed. In addition, as a patient taking part in the **chILD-EU register**, you would automatically be informed of the opportunity to take part in clinical trials, if you fulfill the required inclusion criteria and wish to be informed. Finally, you would also possibly benefit, if you wish, from new knowledge about the origin of your disease. If important new knowledge of this kind was obtained during the trial, you would, after consultation of the Ethics Committee, be informed without delay and, in the case of any doubt, you would be offered the chance to have these factors investigated in your individual case. This would also apply to any results from genetic tests, if you consented to the performance of such tests and also want to be informed of these results. If relevant results are obtained in this area, the Ethics Committee, together with the management committee of the European chILD Register and Biobank, will decide how to inform you about these results and what accompanying services (e.g. genetic counselling) can be offered.

FOR PATIENTS WITH OTHER DISEASES

In contrast to patients with chILD, we will only collect limited relevant clinical data in your case. Also, if possible, we would like to centrally store (in Munich) biomaterials collected during either routine treatment (blood, pulmonary lavage fluid, urine, sputum, buccal swabs and/or tissue samples) or collected specifically for research purposes (blood samples only). We will perform genetic testing and gene expression studies on blood samples with the aim of determining the factors that allow for a conclusive diagnostic categorization of individual forms of chILD via blood tests. In combination with the stored clinical data this will serve the purpose of conclusive comparison of data from patients with chILD and patients with other diseases, based on a comparable scale of age and degree of disease affection.

FOR RELATIVES OF PATIENTS WITH chILD, WITH AND WITHOUT AN INCREASED FAMILIAL OCCURRENCE OF LUNG DISEASES

As it is expected that the majority of chILD cases are genetically determined, and for a secured identification of genetic factors responsible for the occurrence of these diseases in your family, we will either need a blood or oral mucosal sample from you. We also ask for the completion of a patient questionnaire, a clinical examination by one of our physicians and a lung function test. Your clinical data and biomaterials will be treated just like the ones from your family members.

FOR ALL PATIENTS

Participation in this trial/research project is voluntary. You can stop participating at any time, without giving reasons, without adverse effects to your medical care or your relationship with the doctor treating you. Conversely, however, you may be excluded from the trial if this is necessary for medical or organizational reasons.

At present we are not envisaging any time limit to participation in the chILD-EU **register**, since we wish to record all phases of the disease in the chILD-EU **register**.

Risks of participating in this trial

You will not incur any extra costs by taking part in this study. Most of the blood samples are intended to be collected in the context of routine diagnostic procedures, meaning that, apart from very few exceptions, no additional puncture of your vein should be necessary and you should not incur any additional risks in this way. If in an exceptional case a separate blood sample collection is necessary, small bruises could develop at the site where the vein was punctured to collect the blood samples. The total quantity of blood collected will not exceed 30-40 ml (~ a quarter of a small glass of water).

Your data and samples are secured

The place responsible for processing your data is the Kids Lung Register Foundation (KLR e.V.), of which the coordinator of the European chILD Network, Prof. M. Griese, University of Munich, is currently the chairman (for contact details, see above). You can find out where the current site of data-processing is at any time by visiting the consortium's website (www.childeu.net).

For reasons of data protection, your medical data and your identifying data (in particular your name, address and complete date of birth) will be stored separately at two different sites so it is not possible to identify you on the basis of the medical data:

- The above-listed medically relevant data, i.e. your previous history, medical findings, treatment methods, treatment results, quality of life data, prescribed drugs and sample data are stored in a central treatment database in pseudonymized form (i.e., your identifying data, in particular, your name and address, are replaced by a code number). It is not possible to identify you on the basis of the pseudonym alone. This central treatment database is managed on our behalf by a private computing centre, regularly audited by the Central Information Office at the Philipps-University Marburg. We guarantee that the computing centre maintains an appropriate standard of data protection and data security.
- Your identifying data and your code number are stored separately from these medical data at the University of Mainz. These personal data (contact details) will be treated as confidential. Your contact details are needed so that we can contact you at a later time, if necessary, and inform you about relevant results from the assessment by the independent team of experts or from the investigations performed by this research association, and about the chance to participate in other clinical trials (if you agree).

Only a limited number of people have access to your data. These people are bound by a duty of confidentiality. The data are protected against unauthorized access and may be used only for the research project. Only a small, authorized group of employees have access to your contact details stored in Giessen and these people have access only if this has been decided by a vote of the Ethics Committee led by an independent expert (see above) in agreement with the management committee of the European chILD-Register and Biobank. Your contact details will not be passed on to any other place or third party at any time.

For quality assurance, monitors can be permitted access to the data for a limited period; a decision by the management committee of the register is necessary for this. These persons are bound by a duty of confidentiality.
The blood, pulmonary lavage and/or tissue samples, that is, the biological materials taken from you, will be collected centrally at the University of Munich and used in the scientific investigations planned within this research association. The samples taken from you will also be stored and processed centrally in pseudonymized form, that is, under a code number. The data concerning these samples will be stored in the central treatment database under the code number.
To investigate certain scientific questions, it may be necessary to pass on your biological materials - as well as your clinical data - to others. In that case, too, they will be passed on only in pseudonymized form. The management committee of the chILD-EU **register** decides about such passing on of clinical data or biological materials for scientific purposes, after consulting the Ethics Board of the chILD-EU.
The long-term conservation of your data and biomaterials in the chILD-EU **register** will be ensured by the non-profit Kids Lung Register Foundation (KLR e.V.) as responsible body, even after the funding of the chILD-EU network project has ended. After the chILD-EU project has ended, decisions regarding necessary procedures and organizational activities for the operation of the chILD-EU **register** will be taken by the board of the KLR e.V. which is elected by the annual general meeting of members.
You can request information about your stored data at any time. You have the right to have incorrect data corrected. You have the right to revoke your consent to the processing of your personal data or to have your personal data deleted at any time, unless the provisions of the law conflict with such a request.
If you withdraw from the trial, or if the research project is stopped, no further data or biological materials will be collected from you. All data and biological materials already existing will be effectively anonymized by irreversible deletion of the personal datasets. This means that after that, it will no longer be possible to connect these data and biological materials with you.
The results from the trial will be published without personal reference to you.

The academic participants in Paris, France already run a national register on the diseases worked on in the chILD-EU **register** project. In this case the transfer from the French register into the chILD-EU **register** of the above-listed medically relevant data, i.e. your previous history, medical findings, treatment methods, treatment results, quality of life data, prescribed drugs and sample data at start and collected over time, may be organized by electronic data transfer, i.e. not by directly entering the data into the chILD-EU **register**. The biomaterials collected or parts of them may also be transferred to the European chILD Register and Biobank for the purposes listed above.

Declaration of Informed Consent

Patient (last name, first name): _____

Date of birth: _____

Place of birth: _____

(The original Declaration of Informed Consent is kept by the Investigator; the patient receives a copy of the Declaration of Informed Consent. The patient keeps the Patient Information.)

The information sheet I received gave me a general idea about the clinical trial.

On _____(date) at _____ (time), Dr._____, who can be contacted under Tel. No._____ had a detailed interview with me.

The topics of the interview were, in particular,
□ more details on content and practical procedure of the trial, especially
_____

□ the question to what extent benefits, risks or stresses can be expected, especially_____

□ questions about data protection and insurance cover and advice of my right to revoke my consent at any time.

I had the opportunity to ask questions. These questions have been answered satisfactorily and in full. I have received the written Patient Information on the abovementioned trial/research project and have been given a copy of my signed Declaration of Informed Consent. I have read and understood both documents. I was given sufficient time to think in peace and quiet and decide whether to participate. I do not have any further questions at present.

I hereby declare that I am taking part in the above-mentioned trial/the abovementioned research project. I have been advised that my participation in the trial/research project is voluntary, that I do not incur any disadvantages by refusing to participate and that I have the right to stop my participation at any time, without giving reasons.

I agree to the collection, storage, processing and transmission of information on my health and biological materials within the context of the trial "European chILD Register and Biobank" described in the Patient Information.

I also agree that authorized employees of the domestic and foreign supervisory authorities and of the sponsor may have access to my personal data in the course of their duties for monitoring purposes. These persons are bound by a duty of confidentiality. I have been informed of my data protection rights. Due to the rarity of the disease I agree to the non-limited storage time.

_____, the_____ _____

<Place> <Date> <Patient>

I hereby expressly declare that I transfer all rights of ownership of all biological materials previously collected by the doctors treating me, …… (names) and, further, all rights of ownership of the biological materials to be collected in the future by the doctor obtaining my informed consent for this trial to the Kids Lung Register Foundation (KLR e.V.) which holds the European chILD Register and Biobank.
Yes ( ) No ( )

Further I agree to the immortalization of cells from the biological materials obtained from me.
Yes ( ) No ( )

Irrespective of my basic participation in the trial, I agree to the performance of genetic tests on the biological materials obtained from me.
Yes ( ) No ( )

I agree that the results of previous and in the future conducted diagnostic tests including genetic analyses are made available to the register.
Yes ( ) No ( )

I hereby expressly declare my wish to be informed in a suitable way about knowledge obtained from any new and relevant genetic tests of my biological materials.
Yes ( ) No ( )

I hereby expressly declare my wish to be informed about clinical trials investigating the safety and/or efficacy of certain drugs, for which I could, in principle, be considered, on the basis of the status of my disease.
Yes ( ) No ( )

I also wish to be informed about new knowledge obtained in the context of the research activities of the European chILD Register and Biobank, if these have been obtained from my biological materials and permit conclusions about the further course of my disease.
Yes ( ) No ( )

I agree that pseudonymized data and biosamples obtained from me are transferred to university and non-commercial research institutions for research purposes in case of consent of the management committee and the Ethics Board of the chILD-EU register.
Yes ( ) No ( )

I agree that pseudonymized data and biosamples obtained from me are transferred to industrial research institutions for research purposes in case of consent of the management committee and the Ethics Board of the chILD-EU register.
Yes ( ) No ( )

I agree that data and biological materials obtained from me are kept in the register in the event of death
Yes ( ) No ( )
In case of allowing further storage of the data and biological materials it should be done
as currently pseudonymized ( ) anonymized ( )
(Where anonymized means that research results can not be traced back to the patient and therefore possibly important information for other family members can not be communicated.)

_____, the_____ _____
<Place> <Date> <Patient>

_____, the_____ _____
<Place> <Date> <Informing physician>

For relatives:

I agree that data concerning the medical history and biological materials (blood samples or buccal swab) from me are collected for research purposes and stored and that genetic tests are performed using theses biological materials.
Yes ( ) No ( )

I would like to be informed about the results of the genetic tests through the informing doctor.
Yes ( ) No ( )

I have the right to stop my participation in the chILD-EU register at any time, without giving reasons. On demand all data and biological samples collected up to then need to anonymized or deleted.

_____, the_____ _____

<Place> <Date> <Relative>

_____, the_____ ____ _____

<Place> <Date> <Informing physician>