Patient information and informed consent to the participation in the ARPKD registry study ARegPKD

Initiator of the study:
Max C. Liebau, MD
Department of Pediatrics
University Hospital of Cologne
Kerpener Str. 62
50937 Koeln
Germany

Substitute:
Kathrin Burgmaier, MD
Department of Pediatrics
University Hospital of Cologne
Kerpener Str. 62
50937 Koeln
Germany

Dear patient,

Your doctor has made the diagnosis of "autosomal recessive polycystic kidney disease" (ARPKD) for you and has asked you to participate in our ARPKD patient registry study. With this form we want to give you information on why we undertake this registry and what participating would mean for you. Please take some time to read the following information carefully and please consult your doctor if you have any further questions.

What is known about ARPKD?
ARPKD is an inborn disease that progressively affects the kidneys and the liver. It is a rare but severe disorder. It makes the kidneys and the liver work less efficiently than in other children. ARPKD may present with different symptoms. Many patients are diagnosed during early childhood – or even prenatally – others during adolescence. There also is a major variability, even between affected siblings. ARPKD always affects the liver. In many patients renal cysts, fluid-filled cavities within the kidneys, occur. Other organs may also be involved.

ARPKD is a so-called recessive disorder, which means that the parents of the patients are usually healthy. Within the last 10-15 years some progress has been made in the understanding of the mechanisms leading to cystic kidneys. However, there is still no causative treatment for ARPKD. Data on long-term clinical courses and treatment response remain sparse.

While we progress in our search for curative treatment it is nonetheless critical for us to learn as much as possible about this rare and severe disorder in order to improve our understanding of the disease.

What are the goals of the ARPKD registry? Why is ARegPKD being conducted?
As a multinational registry, ARegPKD will give the possibility to collect ARPKD patient data from different centers all over the world (mainly across Europe). We want to identify e.g. symptoms and disease courses that point to the severe progression of ARPKD. Which different treatment approaches have been taken in other countries so far and which did show good results? Furthermore, we aim to look for the changes in your genetic material (your DNA) that lead to a mild or more severe course of ARPKD.

These questions can only be addressed in the setting of an international registry including patients from multiple centers. As ARPKD is a rare disease every single center has only limited experience with this disorder. We therefore want to collect the data from different center in a central registry. Patient data will be pseudonymously collected (see below) and our registry may give important information for future therapeutic studies on ARPKD. The registry is therefore being supported e.g. by the German Pediatric Nephrology Association (GPN).

Who can take part in the registry? How to register?
Only doctors can submit data to ARegPKD. You do not have to introduce data yourself. Every ARPKD patient, boy or girl, children and adults, can participate in ARegPKD.
Should other family members also be affected by the disease, we ask you to inform them about our registry.
However, your doctor can only include the data once you have given the written informed consent.

Who cannot take part in the registry?
Patients who have been diagnosed to suffer from a cystic kidney disease other than ARPKD may not participate.

How is ARegPKD being conducted? Which data are collected? Which examinations will be performed?
If you and your parents agree, medical staff at your corresponding hospital will include available clinical data e.g. on symptoms, ultrasound examinations, laboratory values, family history, renal and hepatic biopsies, and on performed genetic studies into the online data base. This data will be pseudonymous, meaning that your name and address will not be included. Your name will be replaced by an ID-code consisting of a code for the center and a personal ID (e.g. Harry Potter in Cologne → 01-13). Only your doctor will be able to link this ID data back to you. For this purpose your doctor will have a list, which will not be accessible for the coordinators of the registry. In exceptional cases, members of the study coordinating team will introduce medical data into the registry on site. Of course, these members are also subject to medical confidentiality.

From yearly follow-up examinations, data on your clinical course will be entered.

If you are already participating in a pediatric nephrological study, e.g. the 4C study (Cardiovascular Comorbidity in Children with Chronic Kidney Disease Study), specific data points can, if you agree, be transferred from the database of the study you are already participating in into the ARegPKD database. This is exclusively possible for data that has been obtained for the first study, e.g. your age, your height and growth or your laboratory values. Such a transferral of data facilitates the work of the registry, as these already existing datapoints do not need to be entered into a database for a second time. Obviously your data well be kept pseudonymized at all times. The data to be transferred can only be related to you by your corresponding medical staff.

In case of substantial changes of the scientific goal of ARegPKD, you will get additional information from ARegPKD through your corresponding doctor.

During the establishment of the project the initiators of ARegPKD were advised by the corresponding ethics committee. ARegPKD received a positive vote of the corresponding ethics committee.

Information on the handling of biological samples. How will biological samples be obtained? What will happen to these samples?

When a blood sample is taken during a routine visit, we will take an additional blood sample on the same occasion. The amount of blood required for these analyses will be 5 to 30 ml. For small children we will reduce the amount to the minimum. During the course of the disease we will take 2-10 ml of blood once every year. This process will be repeated when blood is taken during a routine visit. Furthermore, urine (10-15ml) will be collected during a routine visit. The pseudonymized samples will be centrally stored in a laboratory at the Children's Hospital of the Hannover Medical School in Germany. If you agree the samples can be examined for genetic changes that might influence ARPKD. For this purpose, we want to analyze the genetic material of the tissue samples (the DNA) with novel high-resolution techniques for known changes associated with cystic kidney diseases but also want to look for changes that have not yet been described. If we find genetic changes known for ARPKD we can inform your doctor, if you wish so. In some countries the information changes will already be available for many patients.

The genetic analyses will be performed in cooperation with our partners. These are currently:

Dr. Bodo Beck
Institut für Humangenetik
Uniklinik Köln
Kerpener Straße 34
50931 Köln
Germany

Prof. Dr. Carsten Bergmann
Bioscientia Institut für Medizinische Diagnostik GmbH
Labor Ingelheim mit Zentrum für Humangenetik
Konrad-Adenauer-Straße 17
55218 Ingelheim
Germany

Prof. Dr. Klaus Zerres
Institut für Humangenetik
Uniklinik Aachen
Pauwelsstraße 30
52074 Aachen
Germany

If you, for medical reasons, need a kidney or a liver biopsy, or a biopsy of any other organ, we want to collect a small piece of the biopsy or of the affected kidney/liver, which will be removed by surgery, and store it for further molecular, genetic or immunological analyses and for further research on the disease and potential treatment options. With your approval, these samples can be obtained during the intervention without further harm and without impairment of the diagnostic possibilities. There will be no expansion of the intervention to obtain samples without a medical

indication. Furthermore, ARegPKD offers biopsy material being microscopically analyzed by an internationally recognized expert for ARPKD (a so-called reference histology assessment). The reference histology assessment will be performed by Prof. Dr. R. Büttner at the Institute of Pathology of the University Hospital of Cologne. The results will be communicated to your doctor. Remaining material, which will not be used for the analysis, will be stored at the site of the reference histology:

Prof. Dr. Reinhard Büttner
Institut für Pathologie
Uniklinik Köln
Kerpener Str. 62
50937 Köln
Germany

Within the ARPKD registry biological samples shall be collected and stored in a so-called "biobank", meaning blood samples (blood, plasm, serum), tissue samples of kidney and liver, potentially samples of biopsies from other tissues. From these, genetic material can be extracted, which will also be stored. After pseudonymization the samples will be kept at the Pediatric Research Centre of the Hannover Medical School (Hannover Unified Biobank), under the direction of Prof. Dr. T. Illig:

Prof. Dr. Thomas Illig
Pädiatrisches Forschungszentrum
Medizinische Hochschule Hannover
Carl-Neuberg-Str. 1
30625 Hannover
Germany

With your approval, the biological samples will only be used for scientific research on cystic kidney diseases. The results of genetic analyses will be saved separately from your personal data and cannot be related to yourself without the assistance of your doctor. Access to the pseudonymized samples and to the data required for analysis can be requested for scientific studies. The requesting centers have to send a written application to the steering committee (the scientific direction of the ARegPKD consortium, consisting of various experts for pediatric nephrology from different countries). The request can only submitted, after evaluation of a scientific study by an ethics committee. The steering committee will then decide on the request.

The samples will be stored in Hannover but may, under certain circumstances, be sent to other places (e.g. laboratories) and potentially to other countries. However, you have the right to ask for the elimination of your samples at all times. Data that has already been obtained will remain within the study even after the elimination of your samples, for as long as you agree.

As ARPKD is a rare and severe disease the samples are of very high scientific value. They will therefore not be eliminated after a certain time but will be stored indefinitely.

Will there be additional examinations or additional consultations required for ARegPKD?

No. Your doctor will introduce the data into the registry. There will be no additional examinations or hospital visits that would not be performed otherwise. Moreover, there will be no additional takings of blood samples.

Which risks result from ARegPKD?
ARegPKD is a registry study. Within ARegPKD, existing data will be collected. There will be no change of treatment or additional interventions for ARegPKD. During the blood takings of routine visits that your doctor would collect anyway, an additional small blood sample will be taken for ARegPKD.

How do you or your doctor profit from the participation? Are there any costs? Will you get any gratification?
Apart from the possibility to get your tissue material analyzed by a specialist and the potential possibility to obtain information about genetic changes that may have caused the disease, the participation in ARegPKD bears no further profit to you. Potentially, all ARPKD patients may profit from the results obtained within this registry study.
Registered centers will get information on ongoing clinical trials or novel therapeutic options quickly. There will be no costs for participants. Nor will there be any gratification.

Information concerning data protection
Medical confidentiality and data protection regulations will be followed. Within the ARPKD registry personal data and medical findings will be collected, saved on a secure online server in a web-based data base before being analyzed. The electronic storage and analysis of data will be carried out pseudonymously, meaning that your name will be replaced by a patient ID consisting of an ID for the center and a personal ID (e.g. Harry Potter in Cologne → patient 01-13). Neither the exact date of birth nor your address will be entered. The month and year of birth will be saved. Your doctor will enter the data via a password-restricted area of an SSL-secured webpage into the database (SSL: Secure Sockets Layer, a protocol for encrypting information over the Internet). The database will be placed on a server, which will be maintained by the computer center of the University Hospital of Cologne and will be situated at the computer center of the University of Cologne. You have the right on information about the saved data and on correction of incorrectly processed data.
Transmission of data may only occur in a pseudonymized way to scientific institutions of the registry's direction and to their scientific cooperating partners. Of course everyone involved will treat these data confidentially. The transmission may also occur to cooperating partners in other countries. If data protection in these countries is not equal to the level of data protection in Germany, ARegPKD will try to maintain the level of data protection ensured in Germany.
In the case of publication of the results of this research project in scientific journals and at scientific meetings, the publication will not contain personal data that would allow inferences on your person. Furthermore, the results may be used commercially, e.g. they may be patented. You will not profit from a potential commercial benefit.
ARPKD is a rare disease meaning that international data collections like ARegPKD are difficult to organize and of high scientific value. Registry data will therefore not be deleted after a certain time frame as is usually done for other studies, but will be saved indefinitely.

The data will exclusively be employed for this study.

You have the right to request information (including free-of-charge provision of a copy) from the person in charge (see below) as to the personal data of your child that have been stored. You also have the right to demand data transfer, the correction of inappropriate data as well as the deletion of data or limitation of their processing. All data will be processed according to local regulations until a potential withdrawal from the study by the patient.
The person in charge of the personal data collected in the context of this study:
PD Dr. Max C. Liebau, Department of Pediatrics, University Hospital of Cologne, Kerpener Str. 62, 50937 Köln, Germany; Phone +49-(0)221-478-6831

The contact details of the Principal investigator´s data protection official in charge are as follows:
University Hospital of Cologne, Datenschutzbeauftragter der Universität zu Köln (Data Protection Official of the University of Cologne), Albertus-Magnus-Platz, 50923 Köln, phone: +49-(0)221 / 470-3872, e-Mail: dsb@verw.uni-koeln.de

The data protection supervisory authority in charge of the Principal Investigator is:
Landesbeauftragte für Datenschutz und Informationsfreiheit Nordrhein-Westfalen (Nordrhein-Westfalen State Commissioner for Data Protection and Freedom of Information)
Postfach 20 04 44
40102 Düsseldorf
Germany
Phone: +49-(0)211 38424-0
E-mail: poststelle@ldi.nrw.de
Internet: https://www.ldi.nrw.de

In case of concerns regarding data processing and compliance with data protection requirements, please contact the data protection official in your institution.
The contact details of the data protection official in charge at your corresponding facility are as follows:

Name of the data protection official _____

Address _____
Contact details _____

Furthermore, you have the right to lodge a complaint with the supervisory authority if you believe the processing of personal data pertaining to you to infringe the General Data Protection Regulation (GDPR).

The data protection supervisory authority in charge of your study facility is:

_____

_____

_____

_____

What happens if I want to retract my consent?
The participation in the study is completely voluntary. You can withdraw your participation in the study at any time without specification of reasons. There will be no negative consequences regarding your medical attendance. If you change your mind, please talk to your doctor.
By request, all data collected for the study will be deleted or anonymized (meaning this data cannot be linked to you in any way) and all remaining samples will be destroyed or handed over to you. If you decide to quit the study you can give your consent to the further storage of data or samples already collected.

Who is your contact person?
Your first contact person for this study is your corresponding doctor.

Local doctor:
Name:
_____
Institution:
_____
Phone:
_____

Further questions?
Please do not hesitate to contact us for further questions you may have.

Max Christoph Liebau, MD
Kathrin Burgmaier, MD

Klinik und Poliklinik für Kinder- und Jugendmedizin
Geb. 26, Uniklinik Köln
Kerpener Str. 62
50937 Köln
Germany
max.liebau@uk-koeln.de,
kathrin.burgmaier@uk-koeln.de
or kinderklinik-studiensekretariat@uk-koeln.de

Participation in ARegPKD

Consent

_____ _____

(patient name)

Please read the following sentences and statements carefully. Take your time for your decision. Please mark **"Yes"** or **"No"**. Your medical treatment will not be influenced by your decision in any way.

Have you read the explanations on this research (or has someone read it to you)?	□ Yes	□ No
Has someone explained the analyses to you?	□ Yes	□ No
Do you understand what this research is about?	□ Yes	□ No
Have you asked everything you wanted to ask?	□ Yes	□ No
Have you understood the answers to your questions?	□ Yes	□ No
Have you understood that you can quit the study at any time and that this is ok?	□ Yes	□ No
Do you agree to participate in this study?	□ Yes	□ No

If you answered any of the above questions or statements with „No" or if you do not want to participate, please do not sign with your name!

_____, _____ Patient: _____

(place) *(date)*

Name of informing doctor: _____

_____, _____ Doctor: _____

(place) *(date)*