# PARENT/GUARDIAN INFORMATION AND INFORMED CONSENT

for the clinical trial:

**Initial treatment of idiopathic nephrotic syndrome in children with mycophenolate mofetil *vs.* prednisone: A randomized, open, controlled, multicenter trial (INTENT Study)**

**Trial code: INTENT-Studie**
**EudraCT No: 2014-001991-76**

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## Investigator: _____

Trial center:
**Address**
**Tel No.**
**Email**

EudraCT No. 2014-001991-76

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Dear parents, dear guardians,

Your child was diagnosed with nephrotic syndrome recently. The main distinguishing feature of this disorder is the loss of protein through the kidneys with the reduced protein levels in the blood leading to a swelling in the eyelids, the belly or the legs. The standard treatment of the German Society of Pediatric Nephrology (GPN) for nephrotic syndrome with prednisone was then initiated, and happily, it suppressed the protein excretion in your child.

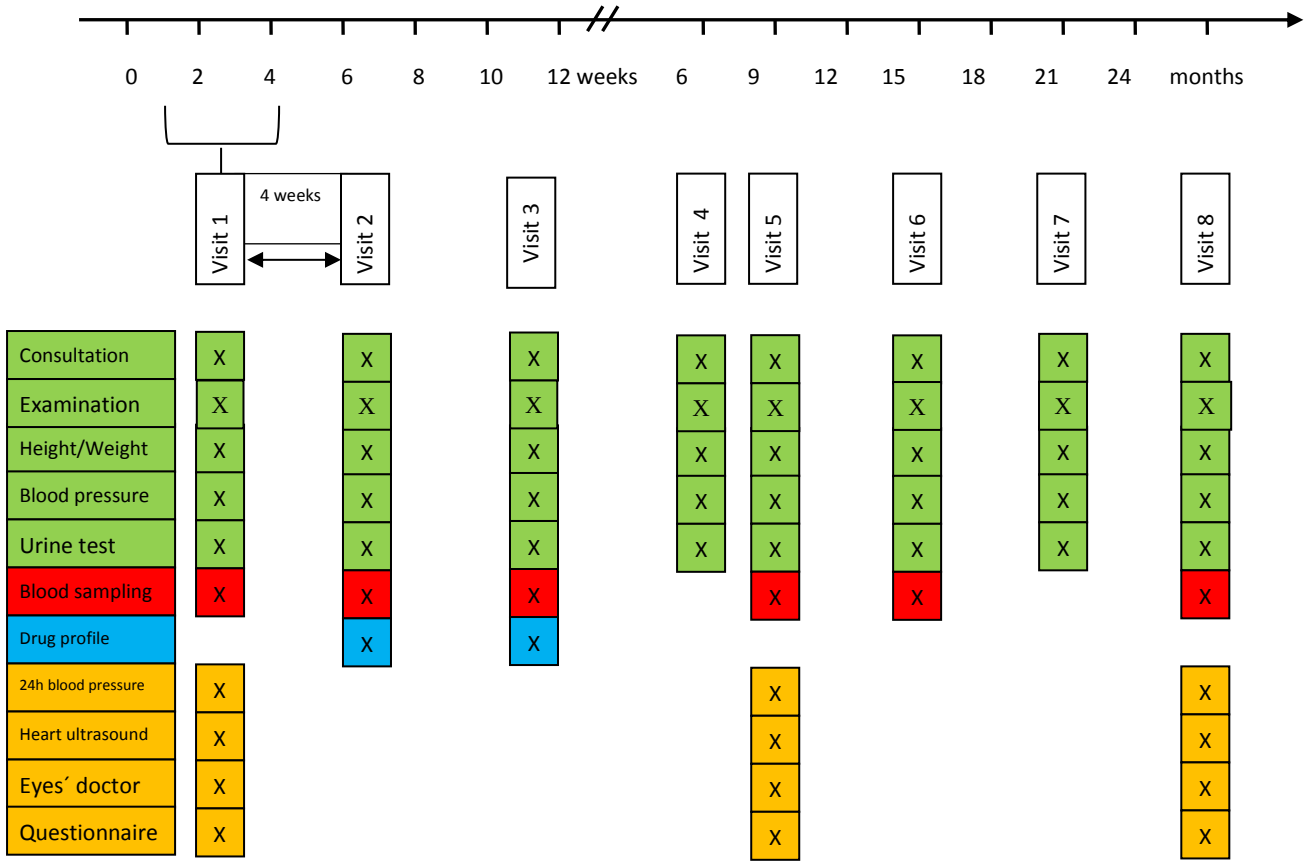
We would now like to ask you, whether you would be willing to let your child participate in the clinical trial described below.
Clinical trials allow us to acquire or extend findings on the effectiveness and tolerance of drugs. The clinical trial that we suggest you here has been – as prescribed by the law – assessed by the responsible ethics committee and approved and finally permitted by the responsible authority. This clinical trial will be conducted in some 45 German pediatric clinics; a total of about 400 children with nephrotic syndrome are proposed to participate. The trial is initiated and organized by the University Children's Hospital of Heidelberg, the Sponsor of this trial, and funded by the German Federal Ministry of Education and Research (BMBF). The Clinical Project Management is located in the University Children's Hospital of Cologne.
The participation of your child in this clinical trial is voluntary, meaning, your child will be included in this trial only upon your written consent and provided you have no objections to participating in a clinical trial. If your child does not want to participate in the clinical trial or wishes to discontinue it at some point, no disadvantages whatsoever will accrue to your child.
You have already been addressed on the proposed trial. The following text aims to elucidate the goals and the process for you. Then, an Investigator will conduct a consultation with you. Please do not hesitate to raise any issue that you are vague about. After that you will be provided with adequate time to take a decision on the participation of your child.

**Why is this clinical trial conducted?**
The nephrotic syndrome in childhood is in more than 50% of the cases a chronic and remitting disorder (relapsing). The treatment at the initial occurrence of the disorder has been standardized for more than 20 years to be conducted with prednisone. This therapy involves among others such side effects as marked weight gain and mental changes (sadness, euphoria, depression) and might induce high blood pressure as well as blood sugar elevation.
The medication mycophenolate mofetil (CellCept®) is employed with success to stabilize the disorder in children with a frequently relapsing nephrotic syndrome or those whose nephrotic syndrome is prednisone-dependent. Mycophenolate mofetil is used in frequently relapsing nephrotic syndrome due to the lesser side effects compared to the long-term administration of prednisone.
The INTENT trial aims to find out whether the new therapy scheme is as good as the standard therapy without having to cause side effects to that extent.
If your child does not participate in the clinical trial or wishes to discontinue it at some point, it will be treated further with the prevailing standard therapy.

**Will my child take the new medication in any case?**
Mycophenolate mofetil (CellCept®) will be compared in the context of this clinical trial with prednisone, a medication already approved for the treatment of nephrotic syndrome. Your child has been taking prednisone since the beginning of the disorder up until the beginning of the trial. In case of participation, your child will either continue with that or switch to mycophenolate mofetil (CellCept®). Which of the two treatments your child will be administered, will be decided by chance (this procedure is called randomisation). The probability of taking mycophenolate mofetil (CellCept®) is 50%.

**How will the trial be conducted and what must we heed?**

Inclusion in the INTENT trial requires an elaborate medical history as well as a physical examination. Also required are blood pressure measurements and urine examinations.
A relapse of the nephrotic syndrome is ascertained through the recurrence of protein excretion in urine. That is why all children diagnosed with nephrotic syndrome are required to have their first morning urine examined with urine dipstick test every day and enter the findings in a log book. You will be provided with such a log book for your child upon participation in the trial. You are required to enter in this protocol the administration of the medication as well as possible infections and days of absence of your child from school.
The number of doctor's visits of a child with nephrotic syndrome depends on the course of the disorder, i.e. how many relapses your child experiences. If your child does not experience any relapses, regular examinations will be held in the first six months from the beginning of the disorder, and then every 6-12 months.
The INTENT trial is composed of two parts: In the first 12 weeks (calculated from the first prednisone administration upon diagnosis) your child will be given either the prevailing or the new medication for nephrotic syndrome. After that we observe over 2 years what effect the treatment will have. In this time, your child will have 8 appointments in the trial center, i.e. participation in the trial does not imply a higher number of doctor's appointments for your child.
The following outline depicts the distribution of the doctor's appointments in the course of the INTENT trial:




Throughout the trial, the appointments will involve not only consultations about the log book but also urine examination, blood sampling, long-term blood pressure measurement, ultrasound examination of the heart and eyes´ doctor examination. In addition, you and – depending on the age – your child will be handed a questionnaire, which will tell us how your child has been doing and how it feels.

It is possible that your child will have to be administered medication again and/or further after the first 12 weeks, as the nephrotic syndrome might recur during this time. Except in emergencies, your child may take these and possible other drugs (including over-the-counter medication) the Investigator is yet unaware of, only upon consultation with the Investigator. If your child receives a treatment from any other doctor, you must inform them of the participation of your child in the clinical trial. Likewise, the Investigator must be informed of each and every medical treatment that your child will receive from any other doctor in the course of the clinical trial. You will be handed a clinical trial ID for your child, which you will be expected to carry with you at all times.
You should store all medication your child has been given in the course of this clinical trial in safe custody so that they are out of the reach of children or other persons unable to assess the possible risks involved. Giving away to third parties is forbidden.

**Which personal benefits will my child derive from participation in the trial?**
When your child takes CelllCept®, it could possibly be subject to less side effects without compromising therapy success. However, given that the effectiveness of the trial preparation for this disorder is not scientifically proven yet, it is also possible that your child does not derive the desired benefit through its participation in this clinical trial. If your child undergoes the standard therapy, the treatment prospects are not expected to change through the participation in the trial versus non-participation.

**Which risks are associated with participation in the trial for my child?**
The treatment with mycophenolate mofetil (CellCept®) can lead to undesirable effects or complaints. The outlined undesirable effects and complaints are derived from the prescribing information and were collected in the context of drug administration following organ transplantations in children and adults, where the patients have taken other immunosuppressive drugs in addition. Considerably less undesirable side effects have been reported in the exclusive administration of mycophenolate mofetil (CellCept®) than in combination with other immunosuppressive substances within the continuous therapy of nephrotic syndromes.

<u>Mycophenolate mofetil (CellCept®) – Side effects</u>
The side effects depend on the duration of administration and the accompanying medication.
Very common (>10%)

- Infections such as sepsis (blood poisoning), gastrointestinal candidiasis (gastrointestinal tract fungal infection), urinary tract infection, herpes simplex (herpes infection), herpes zoster (shingles)
- Blood disorders: Leukocytopenia (decrease in the amount of white blood cells), thrombocytopenia (decrease in the amount of blood platelets), anemia
- Gastrointestinal tract: vomiting, stomach ache, diarrhea, nausea

Common (1-10%)

- Infections such as lung inflammation, influenza (flu), respiratory tract infection, respiratory tract candidiasis (respiratory tract fungal infection), gastroenteritis (infection of the digestive tract), candidiasis (fungal infection), bronchitis, pharyngitis (inflammation of the pharynx), sinusitis (inflammation of the sinuses), fungal dermatitis (skin fungus), candidal vulvovaginitis (vaginal thrush), cold
- Tumors: skin cancer, benign skin tumors
- Blood disorders: pancytopenia (decrease in the amount of red and white blood cells and blood platelets) , leukocytosis (increase in the amount of white blood cells),
- Metabolic and electrolytic disorders: acidosis (high acidity of the blood), hyperkalemia (elevated potassium levels in the blood), hypokalemia (reduced potassium levels in the blood), hyperglycemia (high blood sugar), hypomagnesemia (reduced magnesium levels in the blood), hypocalcemia (reduced calcium levels in the blood), hyperlipidemia (elevated

blood fat levels), hypophosphatemia (reduced phosphate levels in the blood), hyperuricemia (elevated uric acid levels in the blood), gout, anorexia
- Psyche: agitation, confusion, depression, anxiety, abnormal thinking, insomnia
- Nervous system: seizures, severe muscle tension, tremor (trembling), somnolence (drowsiness), Lambert-Eaton myasthenic syndrome (muscle weakness), dizziness, head ache, paresthesia (abnormal sensation), dysgeusia (distortion of the sense of taste)
- Heart and blood vessels: tachycardia (abnormally rapid heart rate), low or high blood pressure, vasodilatation (widening of the blood vessels)
- Lung: pleural effusion („water on the lungs“), dyspnea (breathlessness), cough
- Gastrointestinal tract: gastrointestinal bleeding, peritonitis (inflammation of the peritoneum), ileus (intestinal obstruction), colitis (inflammation of the large intestine), stomach ulcer, duodenal ulcer, gastritis, esophagitis (inflammation of the esophagus), stomatitis (inflammation of the mouth and lips), constipation, dyspepsia (indigestion), flatulence (bloating), belching
- Liver and bile: hepatitis, icterus (jaundice)
- Skin: skin tissue proliferation, exanthema (rash), acne, alopecia (hair loss)
- Joints: joint pain
- Kidney: renal failure
- General complaints: edema, fever, chills, pains, uneasiness, weakness
- Examinations: elevated levels of liver enzymes, elevated levels of creatinine in the blood, elevated levels of lactate dehydrogenase in the blood, elevated blood urea levels, elevated alkaline phosphatase levels in the blood, loss of weight

The prescribing information describes also uncommon (0,1-1%), rare (0,01-0,1%) and very rare (<0,01%) side effects.
Patients, who are treated with immunosuppressive medication and take a combination of drugs including CellCept®, are exposed to a higher risk of lymphoma (lymph node cancer) and other malignant tumors, particularly of the skin. Here the risk seems to hinge on the intensity and duration of immunosuppression rather than the administration of a specific medication.
In the INTENT trial the administration period of CellCept® is much shorter compared to cases following an organ transplantation, and the substance is employed in combination with other, immunosuppressive drugs only over a period of 14 days.
The risk of opportunistic infections (those caused by pathogens that do not infect a healthy host) increases likewise with the overall exposure to immunosuppressive drugs.
The following side effects have been observed following market launch:

- Gastrointestinal tract: gum proliferation (1-10%), inflammation of the large intestine (including CMV colitis) (1-10%), inflammation of the pancreas (1-10%)
- Immunosuppression-related disorders: severe, life-threatening infections, agranulocytosis (dramatically reduced white blood cells) (0,1-1%), hypogammaglobulinemia (too few antibodies in the blood)
- Lymphatic system and blood disorders
- Disorders of the respiratory tract and the chest area: pulmonary fibrosis (fatal in individual cases), bronchiectasis (permanent enlargement of parts of the airways of the lung)
- Hypersensitivity reactions, even allergic shock

For the sake of completeness, we should point out that the administration of CellCept® during pregnancy increases the risk of miscarriages and deformities. Therefore, particular precautions apply for sexually active women (normally no administration of CellCept® during pregnancy, highly effective contraception required, pregnancy test beforehand and no administration of CellCept® during the lactation period, too), as well as for sexually active men (condom usage during and 90 days after the completion of a therapy with CellCept®; also in sterilization, as CellCept® can pass into seminal fluid).

Prednisone - Side effects
The side effects depend on the duration of administration and the accompanying medication.

- Lymphatic system and blood disorders: moderate leukocytosis (increase in white blood cells), lymphocytopenia (reduction of a subgroup of white blood cells), eosinopenia (reduction of a subgroup of white blood cells), polyglobulia (increase in red blood cells)
- Immune system disorders: weakening of the immune defense, masking of infections, exacerbation of latent infections (flare-up of dormant infections), allergic reactions
- Endocrine disorders (hormone disorders):
    - Adrenal suppression (suppression of the adrenal cortex) and induction of Cushing's syndrome (typical symptoms: „moon face", „buffalo hump" and fluid overload)
    - Inhibition of growth in children
    - Sex hormone disorders: amenorrhea (absence of ovulation and menstruation), impotence
- Metabolic and nutritional disorders: sodium retention with edema formation (reduced excretion of sodium and fluid accumulation), increased potassium excretion (caution: heart rhythm disorders), weight gain, impaired glucose tolerance (blood sugar metabolism disorders), diabetes mellitus (sugar diabetes), hypercholesterolemia and hypertriglyceridemia (increased blood fats), lipomatosis (accumulation of fat tissue)
- Psychiatric disorders: depressions, petulance, euphoria, escalated drive and appetite, psychoses, sleep disorders
- Nervous system disorders: Manifestation of a latent epilepsy (convulsion) and increased susceptibility to seizures in a manifest epilepsy, idiopathic intracranial hypertension (particularly in children) (increased pressure around the brain)
- Eye disorders: cataract, particularly with posterior subcapsular opacity, glaucoma, aggravation of the symptoms in corneal ulcer (corneal damage), facilitation of viral, bacterial and fungal inflammations of the eye. The systemic corticosteroid treatment causes an increased risk of a serous chorioretinopathy (inflammation of the eye ground)
- Heart disorders: hypertension (high blood pressure), increased arteriosclerosis and thrombosis risks
- Vascular disorders: vasculitis (blood vessel inflammation) (also as withdrawal syndrome after long-term therapy)
- Gastrointestinal tract disorders: gastrointestinal ulcer, gastrointestinal bleeding, pancreatitis (inflammation of the pancreas)
- Skin and subcutaneous tissue disorders: striae rubrae (stretch marks), atrophy (thin skin), spider veins (dilated cutaneous vessels), increased capillary fragility (increased vulnerability of cutaneous vessels), petechia and ecchymosis (subcutaneous bleeding), hypertrichosis (excessive body hair), steroid acne (acne due to prednisone), delayed wound healing, rosacea-like (perioral) dermatitis (rash around the mouth), changes in skin pigmentation (complexion), hypersensitivity reactions, e.g. drug exanthema (rash)
- Skeletal muscle, connective tissue and bone disorders: muscle atrophy (muscle wasting) and muscle weakness, osteoporosis (dose-dependent, also possible in short-term administration), bone infarction (cellular death of bone components without inflammation) (humeral and femoral heads).

Furthermore, trial-related measures taken in the context of this clinical trial can pose risks or lead to complaints. These specifically concern infliction through blood sampling: The sampling involves the intubation of a cannula, through which the blood can flow in the blood tube. Risks associated with blood sampling and the intravenous cannula include bruises at the puncture site, where the needle or the cannula is inserted in the vein. Sometimes, a minor bleeding lasting a few minutes might occur when the needle is pulled out. Rare occurrences: mispuncture injuring nerves or arteries, dizziness,

nausea, faint, swelling at the puncture site, localized infections, as well as a possible infection, which might just spread to the entire body. Standard precautions are taken to avert these complications (safe storage, disinfection…).
The amount of blood gathered per sampling is about 10 ml (equivalent of 2 teaspoons roughly). Throughout the 6 sampling sessions required by the trial over 2 years, it will add up to a total of some 60 ml (equivalent of 4-6 tablespoons). If your child is in the group taking CellCept®, then 2 ml of blood (= ½ teaspoon) will be gathered additionally at each sampling session in visits 2 and 3, amounting to about 1 more teaspoon.

Please advise the personnel at the trial facility of *all* complaints, disorders or injuries that appear in the course of the clinical trial. If these seem to be severe, advise the personnel of the trial facility immediately, by telephone if necessary.

**Which other treatment options are there outside of the trial?**
Patients that do not participate in the trial will be treated as per the standard therapy of the German Society of Pediatric Nephrology (GPN).

**Who may not participate in this clinical trial?**
Your child may not participate in this clinical if it is already participating in any other clinical trial or research project, or if they have done so recently.

**Does participation in the trial imply additional costs for us?**
The participation of your child in this clinical trial implies no additional costs for you whatsoever.

**Is my child insured throughout the trial?**
German Medicines Act prescribes that all participants of a clinical trial of a drug are insured. According to the enclosed general terms and conditions of the insurance company, "the ceiling of the insurer's liabilities" is set as 500.000 € per insured person. The maximum liability for all insurance claims as to the insured clinical trial is set as 5.000.000 €.

If you suspect that the participation in the clinical trial has damaged your child's health or intensified a pre-existing suffering, you must directly advise the insurer

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|---|---|
| **Name and Address of the Insurance**: | Zurich Insurance plc, 53287 Bonn |
| **Telefon**: | 0228 268 2650 |
| **Fax**: | 0228 268 6666 |
| Insurance policy number: | 801.520.894.139 |

right away of this situation, countenanced by the Investigator of your child if need be, to secure the indemnity of your child. When you are countenanced by the Investigator, you will receive a copy of the notification. If you notify the insurer directly, please remember to inform the Investigator as well.

In clarifying the cause or the scope of a damage, you must cooperate and do everything to avert and alleviate the damage.

For the duration of the clinical trial your child may receive any other medical treatment only upon consultation with the Investigator, except in emergencies. You must immediately inform the Investigator of an emergency treatment undergone.

**Will new findings be disclosed to us during the clinical trial?**

You will be informed of the new findings, which have been acquired within the scope of this clinical trial and might influence your decision as to the further participation of your child in the trial. You will then have the opportunity on that basis to together think over your decision to participate further in this clinical trial.

**Who decides if our child discontinues the clinical trial?**
You may terminate the participation of your child or withdraw your consent to the INTENT trial anytime without having to state any reasons, and without disadvantaging your child in its medical treatment.
Under certain circumstances, it is also possible that the Investigator or the Sponsor decides to abort the participation in the clinical trial, without your being able to influence the decision. The reasons for that could be for instance:

- Continuation of the participation in the clinical trial is medically untenable.
- The complete clinical trial will be aborted.
- There appear such side effects of the medication (prednisone, CellCept®) that do not fade in spite of a reduced dosage.
- Protocol violation through lessened administration
    - Dosage reduction of more than 50%
    - Administration break of more than 3 days

In case you decide to withdraw your child from the clinical trial, or the participation is aborted for another reason than stated, it is important for the safety of your child, that it undergoes a recommended closing check-up. The Investigator will brief you on how and where further treatment will be conducted.

**What happens to the data of my child?**
The duty of medical confidentiality and the data protection regulations will be adhered to. During the clinical trial medical findings and personal information will be collected and written down in the personal file of your child or stored electronically at the trial facility. Provided it is necessary for the proper conduct and surveillance of the INTENT trial (e.g. assessment of side effects, urine determination on suspicion of relapse…), health data available at the attending doctors will be collected and accessed. Data essential for the clinical trial will further be stored, analyzed and, if necessary, communicated to the Clinical Project Management, University Hospital Cologne, Clinic and Polyclinic for Pediatric and Adolescent Medicine, Kerpener Str. 62, 50937 Cologne, to the Institute of Medical Biometry and Informatics (IMBI), Marsilius-Arkaden, Turm West, Im Neuenheimer Feld 130.3, 69120 Heidelberg, to the Center for Child and Adolescent Medicine, Im Neuenheimer Feld 430, 69120 Heidelberg, to the Coordinating Center for Clinical Trials at the University Hospital Heidelberg, Im Neuenheimer Feld 130.3, 69120 Heidelberg, and to the Data Safety Monitoring Board in pseudonymised form.

The blood samples (serum) will be sent in pseudonymised form in the context of the clinical trial to the following center and stored there until analysis:
Central Laboratory / TDM MPA, University of Cologne, Institute of Pharmacology, Gleuelerstr. 24, 50931 Cologne.

Pseudonymization refers to processing personal data in such a way that they cannot be matched with a specific person involved without recourse to additional information (“key”). This additional information is stored separately and subject to technical and organizational measures which ensure that the personal data cannot be associated with an identified or identifiable natural person.

The data will exclusively be employed for this clinical trial.
You have the right to request information from the person in charge (see below) as to the personal data of your child that have been stored. Also, you have the right to demand the correction of inappropriate data as well as the deletion of data or limitation of their processing.

**The person in charge of the personal data collected in the context of this clinical trial:**
Prof. Dr. med. Burkhard Tönshoff, Center for Child and Adolescent Medicine, Im Neuenheimer Feld 430, 69120 Heidelberg.

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 trial facility are as follows:**

Name of the data protection official _____

Address _____

Contact details _____

The contact details of the Sponsor's data protection official in charge are as follows:
Heidelberg University Hospital, Data Protection Official, Im Neuenheimer Feld 672, 69120 Heidelberg, Datenschutz@med.uni-heidelberg.de

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 trial facility is:**

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The data protection supervisory authority in charge of the Sponsor is:
Landesbeauftragter für Datenschutz und Informationsfreiheit Baden-Württemberg (LfDI BW);
(Baden-Württemberg State Commissioner for Data Protection and Freedom of Information)
Postfach 102932; 70025 Stuttgart;
Tel.: 0711/6155410;
Fax: 0711/615541-15;
Email: poststelle@lfdi.bwl.de
Internet: http://www.baden-wuerttemberg.datenschutz.de

The data is secured against unauthorized access. A decryption is possible only under prerequisites the law prescribes.
The Medicines Act covers further terms of reference on the required extent of the Consent in the data collection and use. **Particulars, especially of the withdrawal option are available in the Informed Consent attached to this Patient Information.**

**What happens to the blood and urine samples of my child and the imaging recordings?**

The blood and urine samples and the imaging recordings will exclusively be employed for this clinical trial. Possible residual materials will be shredded at the end of the trial.

**Who should I contact for further inquiries?**

**Consultations at the trial facility**
You have at all times the opportunity to consult further with the Investigator stated on page 1 or any other Investigator as well as the Clinical Project Management.

**Contact point**
In addition, for general inquiries about clinical trials there exists a contact point of the responsible higher federal authority (the EudraCT No. of the INTENT trial is: 2014-001991-76). Participants in clinical trials, their legal representative or proxy can appeal to this contact point:

**Bundesinstitut für Arzneimittel and Medizinprodukte**
**(German Institute for Drugs and Medical Devices)**
Clinical trials / Inspections department
Kurt-Georg-Kiesinger-Allee 3
**53175 Bonn**

Telephone: 0228 / 207-4318 Fax: 0228 / 207-4355
Email: klinpruefung@bfarm.de

## INFORMED CONSENT

for the clinical trial:

**Initial treatment of idiopathic nephrotic syndrome in children with mycophenolate mofetil *vs.* prednisone: A randomized, open, controlled, multicenter trial (INTENT Study)**

**Trial code: INTENT-Studie**
**EudraCT-No: 2014-001991-76**


**Principal Investigator**
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Fax: 0221 478 5835
Lutz.Weber@uk-koeln.de
Marcus.Benz@uk-koeln.de
Rasmus.Ehren@uk-koeln.de


**Investigator:** _____

Trial center:

**Address**

**Tel No.**

**Email**

**Informed Consent**

.....
Name of the patient in block letters

Date of birth .....

.....
Name of the 1. guardian in block letters

.....
Name of the 2. guardian in block letters

I am/ We have been informed through a personal consultation with the Investigator

.....
Name of the doctor

articulately and extensively about the trial medication and comparative therapy as well as the substance, significance, risks and implications of the clinical trial. I/We have also read and understood the text of the Parent/Guardian Information and the privacy statement attached. I/We have had the opportunity to consult the Investigator about the implementation of the clinical trial. All of my/our questions have been satisfactorily answered.

The opportunity to document further questions on the part of the parents/guardian, patient or other aspects of the consultation:

I/We had sufficient time to decide.

I am / We are aware that I/we can withdraw the consent to participation in the trial anytime without having to state any reasons (in words or writing), and without disadvantaging my child in their medical treatment.

**Privacy:**

I am / We are aware, that in the context of this clinical trial, personal data, particularly medical findings as to my/our child are to be collected, stored and analyzed. The employment of the data on their health is to comply with statutory stipulations and requires under Article 6 (1) (a) of the General Data Protection Regulation the voluntary submission of the following Informed Consent prior to participation in the clinical trial, meaning, without the following Consent, my/our child may not participate in the clinical trial.

1. I/We consent that in the context of this clinical trial, personal data, particularly health data and data pertaining to my/our child will be collected and recorded for purposes described in the information document in hard copy as well as electronically at the Institute of Medical Biometry and Informatics (IMBI), Heidelberg University. Where required, the collected data may be communicated in pseudonymised (encrypted) form:
   a) to the Clinical Project Management University Hospital Cologne, Clinic and Polyclinic for Pediatric and Adolescent Medicine, Kerpener Str. 62, 50937 Cologne, to the Coordinating Center for Clinical Trials (KKS) at the University Hospital Heidelberg, Im Neuenheimer Feld 130.3, 69120 Heidelberg, to the Institute of Medical Biometry and Informatics (IMBI), Marsilius-Arkaden, Turm West, Im Neuenheimer Feld 130.3, 69120 Heidelberg, to the Center for Child and Adolescent Medicine, Im Neuenheimer Feld 430, 69120 Heidelberg, and to the Data Safety Monitoring Board,
   b) in case of an application for approval: to the applicant and the authority responsible for the approval (German Federal Institute for Drugs and Medical Devices),
   c) in case of undesirable incidents: to the Clinical Project Management, the Coordinating Center for Clinical Trials (KKS) at the University Hospital Heidelberg, the Sponsor, the responsible ethics committee and the responsible higher federal authority (German Federal Institute for Drugs and Medical Devices), as well as the European Database by the latter.

2. I/we further consent that commissioners authorized by the Sponsor and sworn to secrecy and the responsible surveillance authority have access to the personal data, particularly health data made available by the Investigator, provided it is necessary for the inspection of the proper conduct of the trial. For this measure, I/we release the Investigator from the duty of medical confidentiality.

3. The Consent for the collection and processing of the personal data of my/our child, particularly those pertaining to my health, is irrevocable. I / We have already been informed that my/our child can end their participation in the clinical trial anytime. In case of such a revocation of my/our consent for participation in the trial, I/we consent that the data filed up to that point may be employed further on, provided it is required to
   a) ascertain the effects of the drugs to be tested,
   b) ensure that the interests of my/our child worth protecting are not impaired,
   c) meet the requirement of submitting complete documents for approval.

4. I/We consent that my/our child's data be stored for at least ten years upon conclusion or abortion of the trial, as stipulated by the regulations on the clinical trial of drugs. After that, the personal data will be deleted, but for any operation of law.

5. I am / We are informed of the following statutory provision: If I/we withdraw my/our consent for my/our child to participate in the trial, all authorities that have stored the personal data of my/our child, health data in particular, must verify without delay to what extent the data stored is required for the purposes stated in No. 3 a) to c).

Data no longer required is to be deleted immediately.

6. I/We consent that health data available at the attending doctors will be collected and accessed, provided it is necessary for the proper conduct and surveillance of the INTENT trial (e.g. assessment of side effects, urine determination on suspicion of relapse…)
In this regard, I/we release these doctors from the duty of medical confidentiality. *(If not favored, please cross out.)*

7. I/We consent that the pediatrician / family doctor of my/our child

.....
Name

be informed of the participation of my/our child in the clinical trial (if not favored, please cross out).

**I/We consent that my/our child participates in the abovementioned clinical trial voluntarily.**

I/we have received a copy of the Patient Information and Consent. The trial center keeps another copy.

.....
Name of the patient in block letters

.....
Name of the 1. guardian in block letters

..... .....
Date Signature of the 1. guardian

.....
Name of the 2. guardian in block letters

..... .....
Date Signature of the 2. guardian

I have conducted the consultation and obtained the consent of the guardian of the patient.

.....
Name of the Investigator in block letters

..... .....
Date Signature of the consulting **Investigator**