Information letter with consent form for participation in scientific research for children ≥ 16 years of age on admission to the Princess Máxima Center

Dear ,

You are to be admitted to the Princess Máxima Center for Pediatric Oncology because there is suspicion of a form of cancer, or another condition that is treated in our hospital, for which, for example, treatment with chemotherapy or a stem cell transplant is required. We understand that this is a great shock for you.

The purpose of this letter is to ask you to take part in a medical scientific study. You decide for yourself whether you wish to take part. Before you make a decision, it is important that we explain what the study entails. Read this information carefully and discuss it with your parents, friends or family. There is also an independent person available who knows a great deal about this study.
Further information about participation in this kind of research can be found on the online page 'Medisch-wetenschappelijk onderzoek' (only available in Dutch). This page can be accessed via https://www.rijksoverheid.nl/onderwerpen/medisch-wetenschappelijk-onderzoek. Do you have any questions after reading the information? Then you are welcome to speak to the doctor treating you or to the research nurse.

Introduction
The Princess Máxima Center for Pediatric Oncology is both a hospital and a scientific research institute. Our scientific research is intended to improve the treatment of children with cancer and related conditions. We ask all children being treated in the Princess Máxima Center if they would like to take part in research in our hospital.

This information letter covers the following topics:
1. The biobank
2. The use of data collected in the course of care for scientific research.
3. Other information

Part 1: the BIOBANK
The official title of the biobank protocol in our hospital is: *"Prinses Máxima Centrum Biobank: establishing a biobank for extensive characterization of pediatric malignancies"*

What is a biobank?
For the Princess Máxima Center it is very important that bodily material, such as tumour tissue, blood, bone marrow, bodily fluids such as the cerebrospinal fluid, urine and/or cheek swabs of different groups of patients are collected for future medical scientific research. This material is stored in the laboratory. We call this a biobank. The stored material is preserved under standard conditions. Under these conditions, the material can be stored for a long time and can be used for future research.

What is the purpose of the biobank?
The purpose of the biobank is to collect and store bodily material from children being treated in the Princess Máxima Center and to make that material available for scientific research. This should hopefully enable us to improve the treatment of children in the future.

The bodily material may be collected when the diagnosis is first made, on subsequent appointments at the hospital and on other occasions during the treatment.

The Princess Máxima Center is a specialist hospital that uses new techniques for making diagnoses. To be sure of an accurate diagnosis, we always collect more than sufficient bodily material. Typically, not all of this material is used. The bodily material that remains is called residual material. We would like to store this residual material in the biobank.

Besides using this residual material, for some diseases we also wish to collect an extra sample of blood, bone marrow, urine or other bodily material. We will let you know if this applies to you. We always combine the collection of these extra samples with regular, planned sample taking. This means that you do not have to undergo any extra procedures.

During a biopsy or operation we sometimes also extract a small amount of extra (tumour) tissue. This will only be done if the doctor or surgeon carrying out the operation says it is safe to do so. If you have any questions about this, you can ask the doctor or surgeon who carries out the operation. For children with a brain tumour, we usually try to remove as much of the tumour as possible. Some of this brain tumour is then used to make a diagnosis and the rest of the tumour stored in the biobank. If only a piece of the tumour is removed (a biopsy) in order to make a diagnosis, the doctor will only remove the tissue that is necessary for optimum diagnosis and treatment.

Besides the extraction and collection of bodily material, we also wish to link bodily material to medical data about the disease and its treatment. The availability of this material in combination with medical data and laboratory results is very valuable for scientific research in the field of cancer and/or related conditions.

What kind of research do we perform with material from the biobank?
We are doing research into the causes of cancer in children or conditions related to it and into improving the treatment. We hope that this will lead to better diagnostics, new treatments, a better cure rate and fewer side effects. The bodily material will be studied in the future using various different techniques. For example, we can study cells under the microscope, and we can carry out measurements on different parts of cells, such as DNA and proteins, using other techniques. We also try to grow tumour cells in the laboratory, so that more material is made available for research. When we store or process material, we usually do not yet know which studies we will use it for. Every study that we (wish to) perform is referred to the scientific committee of the Princess Máxima Center. This is a committee that evaluates whether material and/or data from the biobank can be used.

Genetic analysis and its possible consequences
Material from the biobank is also used for scientific research involving genetic analysis. We would like to inform you about genetic analysis and its potential consequences.

Genetic analysis: research on DNA
DNA is the material of heredity and is found in all cells of the body. DNA consists of small pieces that contain information about bodily characteristics, such as the colour of the eyes. We call these bits of DNA genes. If there are changes in the DNA in a body cell, cancer can occur. These changes are only present in the diseased cells and cause a tumour to grow, for example. DNA research can teach us a great deal about the causes of cancer and offers opportunities for new treatments.

To find out which DNA abnormalities occur in a tumour, we compare a person's DNA from diseased cells with the DNA of his or her healthy body cells. Healthy body cells can be obtained from blood, a smear of the cheek mucosa or a piece of skin, which can be taken during an operation, for example.

What do we do if we find something in the healthy cells that might be important to you?
It is possible that we discover a change in the DNA in healthy body cells that may be important for you or your family members. A change in healthy body cells can be accompanied by a predisposition to cancer or a predisposition to other conditions. We would like to explain more about this.

We know that about 10-15% of children with cancer have a genetic predisposition to cancer or other conditions, and in some of these cases other family members may also have a higher risk of this condition. If a genetic abnormality is discovered which has an impact on your medical care, we will always discuss this with you. We will then make an appointment for you with a doctor who is specialized in hereditary diseases; he or she will provide further explanation and guidance.

Knowledge about genetic predisposition can help to detect a condition at an early stage or sometimes even prevent it. However, it can also be stressful to know that there is an increased risk in the family. In addition, it could have consequences for taking out life or disability insurance.

By the way, if we do not find a congenital predisposition to an increased risk of developing conditions, this does not mean that it is not there. Knowledge about genetic predisposition is not yet complete. The detection of a congenital defect is not the aim of the genetic analysis of the tumour.
With regard to a genetic defect in healthy body cells that could be identified during the scientific research, you can indicate on the consent form whether or not you wish to be informed about it. Findings that are important for making decisions about medical care during the treatment of your condition, will always be discussed with you

Here at the Princess Máxima Center, scientific research is also carried out that specifically searches for (new) inherited causes of your condition. In such a case, we will first ask for your consent again. Therefore, this kind of research cannot take place with material from the biobank without you first being informed.

Rules for the management and use of the biobank
The rules for the management of the biobank are documented in a biobank regulation of the Princess Máxima Center. We will only use bodily material and data in the way described in this letter and in the regulation.

PART 2: THE USE OF DATA COLLECTED IN THE COURSE OF MEDICAL CARE

Data
By data collected in the course of medical care, we mean all medical data collected about a patient during the healthcare process from the time of diagnosis: the history of the condition, the results, the treatment and the possible side effects of the treatment. This includes answers to questionnaires on the KLIK portal for monitoring development and your quality of life. It can also include information collected in another treating hospital (e.g. shared care) linked with the Princess Máxima Center or in the UMCU, where parts of the treatment sometimes take place, information from your pharmacy or information from your treatment file provided to us by your general practitioner. This data can, if you give your consent to this, be used for scientific research and to improve the care and treatment of children with cancer and related conditions.

PART 3: OTHER INFORMATION

Who carries out research with your data and bodily material?
The (processed) bodily material and the data are used for scientific research by the Princess Máxima Center or other research institutes. Sometimes we work together with parties outside our hospital, such as international research institutes. In certain cases, we may grant commercial parties permission to use (processed) bodily material or data. We only do so if this use is in line with the mission of the Princess Máxima Center. We only enter into cooperation with others after careful consideration.

Confidentiality of your data and bodily material
To protect your privacy, your data and bodily material will be assigned a code. Your name and other data that can directly identify you will be stored separately. Only with the key to the code can data be traced back to you. The encryption key will be kept securely stored in our hospital. A trusted intermediary manages the codes. Therefore, if there is a reason to, we can trace the code back to you and contact you.
Your data and bodily material that, where applicable, is sent to other parties involved, will only contain the code and not your name or other information via which you can be identified. Also in reports and publications about research, your data cannot be traced back to you.

Access to your data
Some people and authorities may have access to all your data in our hospital, including to the unencrypted data. This is necessary in order to be able to check whether the study has been carried out properly and reliably. Individuals and authorities who receive access to your data for verification purposes are:

- the safety committee monitoring the study,
- a monitor hired by the research sponsor,
- national and international supervisory authorities, for example, the Inspectorate of Healthcare and Youth,
- the staff in the treatment team.

They will keep your information confidential. You will be asked to grant consent to this access. If you do not wish these persons to have access, none of your child's bodily material or data will be stored in the biobank.

Retention period for data and bodily material
Your data will be kept in our hospital for an indefinite period of time.

Withdrawal of consent
You can withdraw your consent to participation at any time. This applies to both the retention and the use for future research. The research data that has been collected up to the time that you withdraw your consent will still be used for research. Your bodily material will be destroyed after you have withdrawn your consent. If measurements have already been conducted using that bodily material, the results will still be used for research. If you wish all your data stored for the biobank to be deleted, you can request that this be done.

Transfer to countries outside the European Union (EU)
Sometimes we wish to send your encrypted data and bodily material to countries outside the EU, because we work together with researchers from those countries. In these countries, the EU rules for the protection of your personal data do not apply. However, your privacy will be protected in a similar way. This only happens if it is necessary for the study and the data is sufficiently protected by encryption.

More information about your rights with regard to the processing of your data
If you have any questions or complaints regarding the processing of your personal data, you can contact the Data Protection Officer of the Princess Máxima Center (fg@prinsesmaximacentrum.nl)
More information about your rights with regard to the processing of your personal data can be found on the website of the Data Protection Authority.

Registration of the study
Information about the biobank is also included in an overview of clinical trials, available at: www.trialregister.nl. This website does not contain any information that can be traced back to you as an individual. You can find this information under number NL7744.

What are the possible advantages and disadvantages of taking part?
Taking part does not directly benefit you. The research results will not be communicated back to you. However, the research results may help to improve care in the future. A possible disadvantage is that you experience discomfort when extra samples of bodily material are collected. However, we will always do this during a scheduled extraction which is necessary for routine care. The doctor or (research) nurse will inform you about this in advance.

Voluntary participation
If you decide to take part in the biobank and agree to the use of data collected in the course of medical care, we ask you to sign the accompanying consent form. The consent form will be centrally archived and stored in your file. If you decide not to take part, you do not need to do anything else. You do not have to sign anything. You do not have to explain why you do not want to take part. If you do take part, you are always free to change your mind and can withdraw your consent at any time, without having to give reasons. You can discuss this with your treating doctor. Your decision not to take part or to discontinue your participation in the biobank in the future, will not have any negative consequences for your treatment and will not impact the care and attention to which you are entitled in our hospital.

Duration of participation
Participation is for an indefinite period of time. The bodily material and medical data collected for the biobank and the use of the data collected in the course of medical care will be stored and used for research for an indefinite time period, or until you withdraw your consent.
If you withdraw your consent, this means that no new bodily material will be stored and no new medical data will be linked to your bodily material that is already stored. The use of the data collected in the course of medical care will also be discontinued if you inform the treating doctor accordingly.

In addition, you can choose from two options:

1) Once submitted, the bodily material and the medical data collected up to that point will remain available for scientific research as laid down in the consent form.

2) You ask for the material already collected to be destroyed and you ask that no more medical data be used for research with this biobank. If measurements have already been conducted using your bodily material, that data will still be used.

Are there costs involved or payment for taking part?
There are no additional costs or compensation for taking part in the biobank and for the use of data collected in the course of care.

Which medical ethics review committee has agreed to the biobank?
The medical ethics review committee of the Erasmus MC has approved the creation of the biobank.

Would you like to know more?
If you have any questions or complaints during the course of your treatment, you can always approach your treating doctor.

If you have any questions or remarks, you can also contact:

- Your pediatric oncologist, who can be reached via the secretariat of the Princess Máxima Center on telephone number 06 50 00 65 70

- The research nurses, who can be reached via telephone number: 06 25 71 05 24 or by email to: researchnurses@prinsesmaximacentrum.nl

If you are unsure about whether or not to participate, you can consult an independent doctor who is not personally involved in the biobank but who is an expert in this area.

- The independent doctor Dr. W. Kollen can be reached on the following telephone number: 06-50 00 61 15.

If, before or during your treatment, you have questions about the biobank that you would rather not ask your doctor or the nurses, you are also welcome to contact the independent doctor.
If, after carefully considering all the information, you decide to take part in future scientific medical research, we ask you to sign and date the consent form, together with your treating doctor.

Be sure to take the time to discuss this information and do not hesitate to consult your treating doctor if you have any questions. If you decide to take part, you will receive a copy of this document, after you and your treating doctor have both signed to confirm your participation.

If you are not satisfied, you can contact the Patient Service department. Patient Service is a department of the Princess Máxima Center and the UMC Utrecht. Well-trained staff with knowledge of the care process in both institutions will support you in dealing with your complaint. The Patient Service department is there to provide assistance and information about the options for complaint handling, but can also mediate in case of a complaint. The main objective of mediation is to find a mutually acceptable solution to the problem as soon as possible. For more information and to access the complaint form, please go to: https://www.prinsesmaximacentrum.nl/nl/over-ons/rechten-en-plichten.

The Patient Service department can be contacted by telephone from Monday to Friday from 8.30h to 12.00h and from 13.00h to 17.00h via telephone number 088 75 588 50 or 088 75 562 08. You can also obtain the complaint form from there.

The postal address is:
Prinses Máxima Centrum/UMC Utrecht
Klachtenbemiddeling huispostnummer D01.343
Antwoordnummer 8419
3500 VW Utrecht
www.prinsesmaximacentrum.nl

With best regards,

On behalf of the pediatric oncologists and research nurses of the Princess Máxima Center.

Consent form for child ≥ 16 years of age on admission to Princess Máxima Center

I have been asked to give my consent for participation in future scientific research in the Princess Máxima Center comprising the use of data collected in the course of medical care, including data from the KLIK portal and the shared centres, and in the biobank, with *official title: "Prinses Máxima Centrum Biobank, establishing a biobank for extensive characterization of pediatric malignancies"*

Name: _____Date of birth: ___ / ___ / ___

I have read the information letter. I have had the opportunity to ask any further questions. My questions have been answered sufficiently. I have had ample time to decide if I would like to take part.

I know that participation is completely voluntary. I know I can decide not to take part at any time. I do not have to give a reason for that.

I consent to the storage of my extracted bodily material in the biobank of the Princess Máxima Center, for an indefinite period of time.

I consent to the use of my encrypted residual material for future scientific research.

I consent to the extraction of a small amount of extra tissue or extra biopsy from me and to the use of this for future scientific research.

I consent to the collection of extra samples of blood, urine or other bodily material from me and to the use of this for future scientific research.

I consent to the use of my data collected in the course of medical care (medical data) for future scientific research.

I choose **to be/not to be (*)** informed of any findings of scientific research on the DNA of healthy body cells (genetic predisposition to diseases).

I consent to allow some individuals and authorities approved and trusted by the Princess Máxima Center to access all my data. This is necessary to be able to check whether the biobank procedure has been carried out properly and reliably.

I consent to the transfer of my encrypted and anonymized data and bodily material to other countries, including countries outside the EU.

After signing the consent form, I will receive a copy of the signed page.

Signature: …… Date of signature: __ / __ / ____

Doctor:

I hereby declare that I have informed the aforementioned person about the biobank of the Princess Máxima Center and about the use of data collected in the course of medical care.

If during scientific research information becomes available that could affect the consent of the person, I will inform him or her in good time.

Name of doctor: ……..

Signature: ..... Date of signature: __ / __ / ____

*Delete as appropriate.