Information letter with consent form for participation in scientific research for parent(s)/guardians(s) on admission of their child to the Princess Máxima Center.

Dear parent(s)/guardian(s),

Your child is to be admitted to the Princess Máxima Center for Pediatric Oncology because there is a 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 allow your child to take part in a medical scientific study. You and your child must decide together about your child's participation in the study. Before you and your child make a decision, you will be given an explanation of what the study entails. Read this information carefully and discuss it with your partner, 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). You can access this page via https://www.rijksoverheid.nl/onderwerpen/medisch-wetenschappelijk-onderzoek. Do you or your child still have questions after reading the information? If so, you can contact your child's doctor or the research nurse. You and your child (over 12 years of age) must decide together whether your child will take part or not.

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 parents/guardians of children being treated in the Princess Máxima Center if they would like their child to participate 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 your child. We always combine the collection of these extra samples with regular, planned sample taking. This means that your child does 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 could be important to you and your child?
It is possible that we discover a change in DNA of healthy body cells that may be of interest to you, your child or family members. A change in healthy body cells can be accompanied by a predisposition to cancer or a predisposition to other conditions. We will gladly inform you further 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 found that affects the medical care of your child, we will always discuss it with you. We will then make an appointment for you with a doctor who specializes in inherited conditions for 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.

It is also important to note that if we do not find a genetic predisposition for an increased risk of developing diseases in your child, this does not mean that it is not there. Knowledge about genetic predisposition is not yet complete. The detection of a genetic abnormality is not the aim of the genetic analysis of the tumour.

With regard to a genetic abnormality in healthy body cells that could be determined during the scientific research, you can indicate on the consent form whether or not you want to be informed about it. Findings that are important in making medical choices at the time of treatment for your child's 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 child's condition. In such a case, we will first ask for your permission again. Such research cannot take place on material from the biobank without you first being informed about it.

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 your or your child's questionnaires from the KLIK portal for monitoring your child's development and 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 child's pharmacy or information from you child's treatment file provided to us by your child's 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 will do research with your child's 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 child's data and bodily material
To protect your child's privacy, your child's data and bodily material are encrypted. The name and other data that can directly identify your child are stored separately. Only with the encryption key can data be traced back to your child. 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 your child and contact you and your child.
The data and bodily material sent to any other parties involved only contain the code, but not the name or other data by which your child can be identified. In reports and publications about research, the data cannot be traced back to your child either.

Access to your child's data
Some individuals and institutions may have access to all of your child's 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 child's 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.
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Retention period of your child's data and bodily material
Your child's data will be kept in our hospital for an indefinite period of time.

Withdrawal of consent
You can withdraw your consent for your child's 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 child's bodily material will be destroyed after your consent has been withdrawn. If measurements have already been conducted using that bodily material, the results will still be used for research. If you wish all your child's 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 want to transfer your child's encrypted data and bodily material to countries outside the EU, because we work with researchers from those countries. In these countries, the EU rules for the protection of your child's personal data do not apply. However, your child's privacy will be protected at an equivalent level. This only happens if it is necessary for the study and the data are sufficiently protected by encryption.

Further information on your rights in the context of processing your child's data
If you have any questions or complaints about the processing of your child's personal data, please 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 child's 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 your child as a person. You can find this information under number NL7744.

What are the possible advantages and disadvantages of taking part?
Taking part does not directly benefit your child. The study results will not be communicated back to you and your child. However, the research results may help to improve care in the future. A possible disadvantage is that your child experiences discomfort when extra samples of bodily material are taken. However, we will always combine this with scheduled sample taking that is necessary for routine care. The doctor or (examining) nurse will inform you and your child about this in advance.

Voluntary participation
If agree to your child's participation in the biobank and to the use of your child's data collected in the course of medical care, we ask you to sign the accompanying consent form. Children who are 12 years of age or older will also receive their own information letter and consent form, which they must sign themselves. The consent forms are archived centrally and included in your child's file. If you decide that your child will not take part, you do not have to do anything else. You do not have to sign anything. You do not have to say why you do not want to take part. If your child does take part, you and your child can always change your mind and withdraw your consent at any time without giving reasons. You can discuss this with your child's doctor. Your decision not to allow your child to take part or to terminate your child's future participation in the biobank will not adversely affect the further treatment and will not affect the care and attention to which your child is 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 or your child withdraw your consent.
If you or your child 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 data collected in the course of medical care will also be stopped if you or your child indicates this to your doctor.

In addition, you can choose from two options:

1) Once submitted, your child's bodily material and the medical data collected up to that point will remain available for scientific research as stated in the consent form.

2) You request the destruction of the material already collected from your child and that no more medical data be used for research with this biobank. If any measurements have been made using that bodily material, that data will still be used.

Are there any costs or payment if your child takes 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 ethical 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 child's treatment, you can always approach your child's treating doctor.

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

- Your child's pediatric oncologist, who can be reached through the Princess Máxima Center secretariat, on telephone number 06 50 00 65 70
- The research nurses, who 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 your child should take part, 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 child's treatment, you have questions about the biobank that you would rather not ask your child's doctor or the nurses, you are also welcome to contact the independent doctor.

If, after carefully considering all the information, you decide to consent to your child's participation in future scientific medical research, we ask you to sign and date the consent form, together with your child's treating doctor.

Please take the time you need to discuss this information and do not hesitate to consult your child's doctor if you have any questions. If you decide to consent to your child's participation, you will receive a copy of this document, after you and your child's treating doctor have both signed to confirm participation.

If you are not satisfied, please contact the Patient Service Department. The 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 possibilities of complaint handling, but can also mediate in the 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 get the complaints 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 parents/guardians on admission to the Princess Máxima Center

I have been asked to give my consent for the participation of my child 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 centers, and in the biobank, with official title: *"Prinses Máxima Centrum Biobank, establishing a biobank for extensive characterization of pediatric malignancies"*

Name of child: _____ Date of birth: ___ / ___ / ___

I have read the information letter for parents/guardians. I have had the opportunity to ask any further questions. My questions have been answered sufficiently. I have had ample time to decide if my child should take part.

I know that participation is completely voluntary. I know I can decide at any time to stop my child's participation. I do not have to give a reason for that.

I consent to my child's collected bodily material being stored indefinitely in the Princess Máxima Center's biobank.

I consent to the use of my child's anonymized residual material for future scientific research.

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

I consent to the extraction of extra blood, urine or other bodily material from my child and to its use for future scientific research.

I consent to the use of my child's 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 child's 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 child's 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.

Parents/guardians:

Name of parent/guardian**: ……

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

Name of parent/guardian**: ……

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

Doctor:

I hereby declare that I have informed the aforementioned person/persons 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 parents/guardians, I will inform him or her in good time.

Name of Doctor: ……..

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

*Delete as appropriate.
**If the child is under 16 years of age, the parents exercising custody or the guardian will sign this form. Children from 12 to 15 years of age who are able to make decisions independently (legally competent) must also sign the consent form for children and adolescents.