Subject information for parents/caretakers for participation in medical scientific research

Does your child also have an inguinal hernia on the other side?
A randomized study to study the necessity and cost-effectiveness of contralateral surgical exploration during inguinal hernia repair in children: contralateral exploration or not (HERNIIA study).

Dear Sir / Madam,

You receive this letter because your child* needs surgery to repair his/her inguinal hernia. We would like to ask you and your child to take part in a medical-scientific study. Participation is voluntary, and participation requires your written consent. Before you decide whether you want to participate in this study, you will be given an explanation about what the study involves. Please read this information carefully and ask the investigator for an explanation if you have any questions. You may also discuss it with your partner, friends or family.
Additional (general) information about participating in a study can be found on the website www.rijksoverheid.nl/mensenonderzoek.
* or the person you represent.

General information
This study is set up by Amsterdam University Medical Centers, location: VU University Medical Center in Amsterdam, The Netherlands. Among 400 children with an inguinal hernia from different countries will participate in this study. Medical Research Ethics Committee VU University Medical Center has approved this study.

Purpose of the study
Children with an inguinal hernia on one side often also have an inguinal hernia on the other side. This occurs in one out of ten children and cannot be seen from the outside. If an inguinal hernia also exists at the other side, a second surgery is necessary for its repair. Therefore, in many countries, at the time of hernia repair on one side, a second incision is made in the opposite groin to check whether a hernia is present. If a hernia is present, it can be repaired simultaneously. In seven out of eight children no hernia will be found and the incision was actually not necessary. In the Netherlands most surgeons do not make an incision on the opposite side to checker whether a hernia also exists on the opposite side. Consequently, one out of every eight children will need a second surgery at a later moment. It is not clear whether it is more beneficial to make an extra incision during the first surgery to explore whether there also is an inguinal hernia, or to perform a second operation at a later moment, and that is what we want to investigate.

Background of the study
Children with an inguinal hernia who are younger than six months old are most likely to have an inguinal hernia on the opposite side. The inguinal hernia will then be repaired in a second surgery. Additional risks and costs are associated with this operation. Sometimes, content of the inguinal hernia can get stuck. If that happens, children experience a lot of pain and in some cases emergency surgery is necessary. We want to investigate if it is necessary to make an extra incision in the opposite groin during the first surgery to explore whether there also is an inguinal hernia, or we should better wait and see.

What participation involves

Screening

We will first evaluate whether your child may participate. The surgeon/investigator will do a physical examination for diagnosis of the inguinal hernia. The investigator will also ask questions about the medical history of your child.

Treatment/surgery

All children will undergo the usual treatment for inguinal hernia. In one group (half of the children that participate in the study), a small incision will also be made in the opposite groin to check whether there also is a hernia. In the other group (other half of the children that participate in the study), no extra incision will be made. Study subjects will be completely randomly assigned to one of the groups.

Visits and tests

During ± 13 months, you and your child will visit the hospital three times. If your child does not participate in the trial, this will not be different. During these visits, the following will take place:

- During one visits we carry out a physical examination
- During one visit we will perform the operation

Furthermore, the researcher will give you a call four weeks and one year after the operation, and we would like to ask you to fill in questionnaires before and after the operation about the quality of life of you and your child. The questionnaires are available both on paper and online. You can complete them at home. It takes about 20 minutes to complete the questionnaires.

Other than standard care

If your child participates in this study, there will be no extra visits to the hospital compared to the usual care. Different from standard care are the questionnaires that we ask you to fill in prior to and after the operation.

What is expected of you

If your child participates in this study, he/she cannot participate in another medical study. It is important that you contact the investigator:

- If your child is admitted to a hospital or treated in a hospital, even for other conditions.
- If your child suddenly develops any health problems.
- If you no longer want your child to participate in the study.
- If your contact details change.

Wat are possible complications?

If we make an incision in both groins to search for inguinal hernia, complications can also occur in both groins. These complications are similar to the complications that can occur if we only operate on one side. Possible complications are similar to both sides. The following complications might occur, but not that often:

- Wound infection
- Recurrence of previously operated inguinal hernia
- Shrinking/complete disappearance of the testis (in boys)

What are possible advantages and disadvantages of participating in the study

Your child will not directly benefit or experience disadvantages from participation in this study. Participation of your child does contribute to increased knowledge about the best treatment strategy for children younger than six months of age with an inguinal hernia. This allows us to improve health care of children with inguinal hernias.

Disadvantages of participation in the study may be:

- Extra time and effort to complete the questionnaires;

In case an extra incision is made in the other groin:

- Potential complications of the incision and recovery of inguinal hernia repair if performed;

In case no extra incision is made in the other groin:

- A second surgery in case no extra incision is made to check for an inguinal hernia on the other side and after the first surgery a second hernia on the other side develops.

During this study, something may be found by chance that is not important to the study, but may be important to you/your child. If this happens, it will be discussed with you. If you do not agree with this, your child may not participate in this study.

What if your child resists participation in the study

Your child or the person you represent may resist (refuse to cooperate) during the study. The investigator will then have to stop the study immediately. It is difficult to describe what exactly resistance is. Before the start of the study you will be given an explanation of what is considered resistance. The investigator will follow the Code of Conduct on resistance of minors.

If you do not want to participate or you want to stop participating in the study

It is up to you to decide whether or not your child will participate in the study. Participation is voluntary and you will have sufficient time (at least five days) to consider whether you and your child want to participate. If you do not want to participate, your child will be treated as usual for his/her inguinal hernia. The treating doctor then decides (in consultation with you) whether he/she will make an extra incision to check for an inguinal hernia on the opposite side or not.

If your child does participate in the study, you can always change your mind and decide to stop, at any time during the study. Your child will then be treated as usual. You do not have to explain the reason why, but you do need to tell the investigator immediately. The data collected until that time will still be used for the study.

If there is any new information about the study that is important for you, the investigator will update you. You will then be asked whether you still want to continue your participation.

End of the study

Your participation in the study stops when

- You have completed all the visits as described under ‘visits and tests’;
- You choose to stop;

- The investigator considers it best for you and your child to stop;
- The Medical Research Ethics Committee, the government or the hospital decides to stop the study.

The study is concluded once all the participants have completed the study. After processing the data, the investigator will inform you about the most important results of the study.

After this study, you may be contacted again for a follow-up study. Before we potentially ask you to participate you will of course first receive detailed information about participation in this follow-up study. You may refuse consent to potentially being contacted again.

Usage and storage of your data and data of your child
Your child's personal and medical data will be collected and used for this study. The collection, use and storage of your data is required to answer questions asked in this study and to publish the results. To protect the privacy of you and your child, data will be given a code. Your name and other information that can directly identify you, will be omitted. Data can only be tracked back to you with the encryption key. The encryption key remains safely stored in the local research institute. The data cannot be tracked back to you/your child in reports and publications about the study.

Data of you and your child
All data will remain confidential. Only the principal investigator, study coordinator and project leader know which code belongs to your child.

Some people can access the medical and personal data of your child. This is necessary to check whether the study is being conducted in a good and reliable manner. Persons who have access to your data for review are members of the study team, the committee that monitors the safety of the study, the controller/monitor which has been hired by the investigator, supervisory board of the hospital and the Healthcare and Youth Inspectorate. They will keep all data confidential. We ask you to consent to this access. Data will by kept at the Amsterdam UMC (Emma Children's Hospital AMC and VU Universitey Medical Center) for 15 years.

Registration of data if you do not want your child to participate
If you do not want your child to participate in this study, it would be very helpful for us to collect data about the treatment(s) your child receives for his/her inguinal hernia. Therefore, we would like to ask permission to request this information from the treating doctor once. In this way, we can learn about the follow-up period after inguinal hernia repair in children who do not participate in this study. After one year, one of the researchers will call you to ask how many inguinal hernia repair operations your child had in total. Registration of the data does not affect your child's treatment, and we do not ask you to do anything for this.

More information about your rights when processing data
For general information about your rights when processing your personal data, you can consult the website of the Dutch Data Protection Authority. If you have questions about your rights, please contact the person responsible for the processing of your personal data. For this study, that is: The Children Hospital, AON SS Antonio e Biagio e Cesare Arrigo (see Appendix A for contact details).

If you have questions or complaints about the processing of your personal data, we advise you to first contact the research location. You can also contact the Data Protection Officer of the institution (for contact details please see Appendix A) or the Dutch Data Protection Authority.

Registration of the study

A description of this clinical study will be available on https://clinicaltrials.gov/, as required by US law. This website does not contain any information that identify you or your child. After the study, a summary of the results may be placed on the website. You will find this study under HERNIIA trial.

Study subject insurance

Insurance has been taken out for everyone participating in this study. This insurance covers damage caused by the study. The insurance does not cover all damages. **Appendix B** contains more information about the insurance and the exclusions. It also tells you who to report damage to.

Will my GP and/or treating specialist be informed?

We will always send your GP and/or treating specialist a letter to let them know that you are participating in the study. Sometimes we may also request medical information from your GP/treating specialist. This is for your child's own safety. If you do not agree to this, your child cannot participate in this study.

Are there any costs/compensation for participation in this study?

Participation in this study is free of charge for you. Therefore, you will not receive any reimbursement and you will not be paid to participate in this study.

Do you have questions?

If you have any questions, please contact your child's treating doctor or the local researcher of The Emma Children's Hospital, Amsterdam UMC. If you would like any independent advice about participation in this study, you may content an independent doctor. She knows about the study but is not involved in it. If you have any complaints about the study, you may contact the complaint's committee at your hospital. All the relevant details can be found in **Appendix A:** Contact details.

Thank you for your attention.

Appendices to this information

A. *Contact details Emma Children's Hospital, Amsterdam UMC*
B. *Insurance information*
C. *Informed Consent Form(s) parents/caretakers*

Appendix A: contact details for The Emma Children's Hospital, Amsterdam UMC

Local investigator: Dr. J.P.M. Derikx, department of Pediatric Surgery, Emma Children's Hospital, Amsterdam UMC, Meibergdreef 9, 1105 AZ Amsterdam. E-mail: j.derikx@amc.uva.nl, Phone number: +3120 566 5693.
In case of emergency: Surgical resident (24 hours a day available) via phone number: +31205669111.

Independent expert: Drs. WG Leeuwenburgh-Pronk, department of Pediatrics, Emma Children's Hospital, Amsterdam UMC, Meibergdreef 9, 1105 AZ Amsterdam. E-mail: W.g.leeuwenburgh@amc.uva.nl, phone number: +3120 566 9111.

Complaints: E-mail: patientenvoorlichting@amc.nl or phone number: +31205663355.

Data Protection Officer of the institution: Data protection officer VUmc: privacy@vumc.nl.

Appendix B: Insurance Information

Insurance has been taken out by VU University Medical Center for everyone participating in this study. The insurance covers damage due to participation in the study. This applies to damage manifesting during the study or within four years of the end of your participation in the study. You must notify the insurance company about the damage within those four years. The insurance does not cover all damages. The damages that are not covered are listed briefly at the end of this text. This is set out in the Medical Research (Human Subjects) Compulsory Insurance Decree. This decree is available (in Dutch) on the 'Wettenbank' of the Dutch government (https://wetten.overheid.nl).

In the event of damage please contact the treating doctor or insurance company directly.

The insurance company for the study is (policy number: 624.529.204):
Name: Onderlinge Waarborgmaatschappij Centramed B.A.
Address: Postbus 7374, 2701 AJ Zoetermeer
Telephone number: +31703017070
E-mail: info@centramed.nl

The insurance offers a cover of €650,000 per study subject and €5,000,000 for the entire study (and €7,500,000 annually for all studies from the same sponsor).

The insurance policy does **not** cover the following damage:

- damage as a result of a risk that you were informed about in the written information. This does not apply if the risk occurs in a more severe form than envisaged, or if the risk was very unlikely to occur;
- damage to your health that would also have occurred if you had not participated in the study;
- damage resulting from not or not entirely following directions or instructions;
- damage to descendants as a result of a negative effect of the study on you or your descendants;
- damage as a result of an existing treatment method for research into existing methods of treatment.

Appendix C: Subject Consent Form parents/caretakers: does your child also have an inguinal hernia on the other side?

I have been asked to consent to the following person participating in this medical-scientific study:

Name of study subject (child): Date of birth: __ / __ / __

- I have read the subject information form. I was also able to ask questions. My questions have been answered to my satisfaction. I had enough time to decide whether to participate.
- I know that participation is voluntary. I know that I may decide at any time not to participate after all or to withdraw from the study. I do not need to give a reason for this.
- I give permission for my child's GP/treating specialist(s) to be informed that my child is participating in this study.
- I give permission for information to be requested from my child's GP/treating specialist (s).
- I give permission for the collection and use of my data to answer the research question in this study.
- I know that some people may have access to all my data to verify the study. These people are listed in this information sheet. I consent to the inspection by them.
- I give permission to transfer my data and my child's data to the Amsterdam UMC (Emma Children's Hospital AMC and VU Universitey Medical Center) and store it for 15 years.
- I □ **do**
  □ **do not**
  consent to being contacted again after this study for a follow-up study.
- I want to participate in this study.
- In case of sole parental authority, please state so below.

Name parent/caretaker: □ I have sole parental authority

Signature: Date: __ / __ / __

Name parent/caretaker:
Signature: Date: __ / __ / __

I hereby declare that I have fully informed this study subject about this study. If information comes to light during the course of the study that could affect the study subject's consent, I will inform parent(s)/caretaker(s) of this in a timely fashion.

Name of investigator (or his/her representative):
Signature: Date:__ / __ / __

Additional information was given by (if applicable):
Name: Job title:
Signature: Date:__ / __ / __

The study subject will receive the full information sheet, together with a signed copy of the consent form.

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