NIEM II

NON INVASIVE ELECTROPHYSIOLOGICAL MONITORING

Subject information for participation in medical scientific research NIEM-II study

Data collection of monitoring of the condition of you and your child during delivery and the first six weeks after birth

Official title: Implementation of intrapartum non-invasive electrophysiological monitoring

Dear Madam,

We would like to ask you to participate in a medical study. You have received this information letter because you will give birth and might be able to participate in this study. Participation is voluntary and requires your written consent.

Before you decide whether you want to participate in this study, you will be given an explanation on what the study is about. You can read about the medical study in this information sheet, what it means for you, and what the pros and cons are of participating in the study. It is a lot of information. Please take time to read the information and determine whether you wish to participate? If you wish to participate, please fill out the form in Appendix C.

Ask your questions

You can take your decision based on the information in this information sheet. We also suggest that you do this:

- Put your questions to the healthcare professional and/or researcher who gave you this information.
- Talk to your partner, family or friends about this study.
- Read the information on https://www.government.nl/topics/medical-research.

1. General information

This study is initiated by Máxima MC (MMC) Veldhoven and is executed by doctors, midwives, nurses, medical students and researchers. For this study, a total of 2272 subjects are required. ZonMw and Máxima MC (location Veldhoven) are funding the research.

The Máxima MC Medical Research Ethics Committee (METC) have accessed and approved this study. The METC decided that our research falls under the Medical Research Involving Human Subjects Act (in Dutch: Wet Medisch-wetenschappelijk Onderzoek met Mensen), WMO). This means we are obligated to follow the rules laid out under this Act.

General information about how a medical scientific study is monitored can also be found on the website of the national government: https://www.government.nl/topics/medical-research.

2. Background of the study

When you give birth at the hospital the heartrate of the mother, the heartrate of the unborn child and the contractions are continuously recorded. In this way we monitor the condition of you and your child. This recording is called a cardiotocogram (CTG). The heartrate of you and your child and the contractions are recorded by two buttons on your belly. These are kept in place by two elastic bands around your waist (figure 1). The signal quality of these recordings can be low due to your movements or movements of the unborn child during delivery. Consequently, the buttons on your belly have to be repetitively repositioned during labour. To improve signal quality for measuring the heartrate of the unborn child, a small thread is attached to your child's head (scalp electrode) through the vagina after the membranes have ruptured (figure 2).

Figure 1. External conventional CTG monitoring with elastic bands.

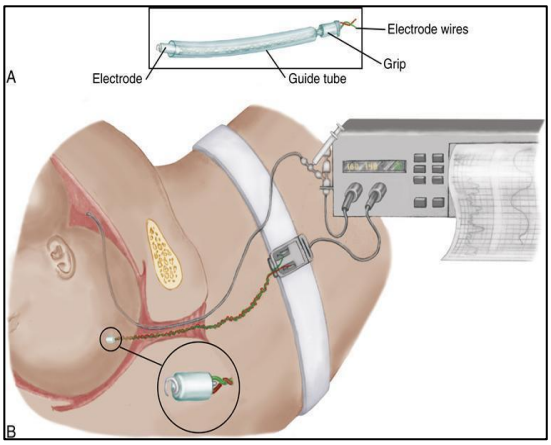

Figure 2. Internal measurement of the fetal heart rate of the unborn child by a scalp electrode.

<u>New method for monitoring the condition of the mother and the unborn child</u>

Recently, a new device to register the heartbeat of the mother, the heartbeat of the unborn child and uterine activity has been developed in collaboration with MMC. This is the Nemo Fetal Monitoring System (NFMS) (figure 3). This system monitors through single patch on the mother's belly. A transmitter on the patch wirelessly forwards the signal to the base station. Previous research has shown that the NFMS provides better registration of the heart of the unborn child and the uterine activity than the standard method with both bottoms (CTG). Because the patch is wireless, you can walk around during labour. Furthermore, using elastic bands and repositioning of the patch is not necessary.

Figure 3. The Nemo Fetal Monitoring System (NFMS). (© 2018, Nemo Healthcare B.V.)

3. Purpose of the study

The purpose of this study is to compare the number of interventions (instrumental vaginal deliveries, caesarean sections) of women monitored with the NFMS versus women monitored with the standard method (CTG). We think that the NFMS has the potential to reduce operative interventions due to a better registration of the heartbeat of the unborn child and the contractions. This may improve the health conditions for both mother and child. But we do not know the exact results. Hence we are conduction this study.

We will collect data from you and your child during labour up to six weeks after delivery. In addition, one and two years after the start of the study we ask 253 women to complete two questionnaires after delivery (with a maximum of 48 hours). The questionnaires are about the childbirth experience and about the experience with the NFMS.

We aim to include 2272 women who will be monitored with the NFMS. Data of these women will be compared with data from 2100 women monitored with standard care in the past and with another 253 women who will be monitored with standard care during this study.

4. What participation involves

You are eligible for participation if you meet the following criteria:

- Minimal age of 18 years old
- You are 37 to 42 weeks pregnant
- You have an indication for fetal monitoring during labour
- Your unborn child is in a vertex position

You are not able to participate in this study if:

- You have insufficient knowledge of Dutch or English language
- You are pregnant with multiple babies (twins, triplet)
- Your unborn child has a cardiac arrhythmia (detected and confirmed during pregnancy by ultrasound)
- You have a cardiac arrhythmia
- You have a skin condition in the area of the abdominal skin where we want to apply the patch
- You have a pacemaker
- It is already known that you will have a caesarean section or instrumental vaginal delivery, before participation in the study
- You participate in the study, but circumstances call for delivery of the baby by unplanned caesarean section before you are in active labour
- You are admitted to the hospital for a serious condition that happens when the body's immune system has an extreme response to an infection (sepsis)

Monitoring with the NFMS

You will be monitored with the NFMS during delivery until 1.5 hour after delivery. Before applying the patch on your belly, the skin is first cleaned with water and soap and then lightly scrubbed. This is necessary to ensure that the patch sticks well to optimise signal registration. The electrode patch is wireless, giving you complete freedom of movement.

Suppose the registration of the heartrate of the unborn child or the contractions with the new device is insufficient. In that case, the standard CTG will be used at your healthcare worker's judgment. This means that a fetal scalp electrode can be placed on your child's head for monitoring the baby's heart rate. Also, the contractions will be registered with the contraction button on your belly with an elastic band around your waist. The patch will stay on your belly up to 1.5 hour after delivery.

You can take a shower with the patch, but it is not possible to take a bath with the patch. In clinical care, most women do not take a bath during delivery (for example because they want an epidural or by other circumstances). If you definitely take a bath, the patch is first removed from your belly and the standard CTG is applied (as shown in figure 1 and 2). When you leave the bath, the standard CTG will be disconnected and the patch will be reapplied to your belly. It is also not possible to use a Transcutaneous Electro Neuro Stimulation (TENS) in combination with the patch. If you are using a TENS, the standard CTG method will be used. If you do not wish to use the TENS anymore, the standard CTG will be disconnected and the patch will be applied to your belly.

In case no NFMS is available for you, you will be monitored with standard CTG, standard of care. By signing the consent form in appendix C, you agree to collect, use and store data of you and the parents/ parent(s)/legal representative(s) agree to collect, use and store data of the child for (future) scientific research.

Differences in standard care

You will be monitored with the NFMS during delivery. After delivery, the patch will stay on the abdomen for 1.5 hour to be able to register the contractions of the womb. This may give us more insight in the birth of the placenta and the amount of blood loss.

In total 253 participants in this study will be randomly ask to complete two questionnaires after birth (with a maximum of 48 hours). The questionnaires are about your birth experience and your experience with the NFMS. The questionnaires are not part of standard of care and will take about 10 minutes. The questionnaires will be completed before you are going home.

An extra ultrasound examination will be done during birth in a small group of participants . The ultrasound images are used to measure the thickness of the uterine wall during contractions. This will be combined with the NFMS contraction registration. It will only performed in women who have sufficient pain relief. The researcher will perform one or two ultrasound examinations at your delivery room, each lasting 20 minutes. The first ultrasound is done once sufficient pain relief is in place, and if possible, a second ultrasound when cervical dilation has increased with 2 cm. If you agree with the ultrasound examination, your doctor/midwife or the researcher will let you know whether you will receive the additional ultrasound.

The data collection from you and your child will continue for up to six weeks after delivery. You do not have to do any additional actions extra for this.

What if you do not participate in the study?

Suppose you do not participate in this study. In that case, we will monitor the heartbeats and contractions in the usual manner, the CTG with two elastic bands. Once the membranes have broken, a fetal scalp electrode can be placed for optimal recording of the fetal heart rate by the judgement of the healthcare provider. One button and elastic band is still positioned on your belly for monitoring the contractions. If you agree with data collection when you receive standard of care, data of you and your child will be used for (future) scientific research. By signing the consent form in appendix C, you agree to collect, use and store data of you and the parent(s)/legal representative(s) agree to collect, use and store data of the child for (future) scientific research.

5. What side effects, adverse effects or discomforts could you experience?

The NFMS is approved and considered safe for clinical use. However, the patch might cause a (mild) irritation on your skin. If the registration of the heartrate of the unborn child or the contractions with the NFMS is insufficient, a switch will be made to the standard CTG.

6. What are the pros and cons if you take part in the study?

It is important that you carefully consider the possible benefits and disadvantages before you decide to participate in this study. Think about this carefully and talk to other people about it.

Possible advantages of the NFMS are:

- The device is wireless, giving you complete freedom of movement. You can take any position you want during delivery.
- The device has a good signal quality, even in women with obesities.
- The device ensures that you do not have to wear straps around your waist. Previous research showed that patients prefer NFMS over CTG.
- No (repetitively) reposition of the patch necessary during labour.
- The patch is personal and hygienic.
- The patch lasts as long as the delivery takes.

Possible disadvantages of the NFMS are:

- Possible (mild) skin irritation through the patch. This will resolve by itself
- If the registration of the heartrate of the unborn child or the contractions with the NFMS is insufficient, a switch will be made to the standard CTG.
- If you are part of the small group in which the extra ultrasound will be performed, it will take 20 minutes of your time for one ultrasound or 40 minutes for two ultrasounds. The ultrasound will take place during your admission and will not interfere with your standard treatment.

Furthermore, by participating, you will help us to improve future care for women and their unborn child during the delivery.

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

It is up to you to decide if you wish to participate in the study. Participation is voluntary. If you do not want to participate, you will be treated with standard care during your delivery. You do not have to tell why you do not want to participate in this study.

If you do participate, you can withdraw from the investigation at any time, without giving any reason. However, we do ask you kindly to inform the researcher or healthcare professional. The data collected up to that point will be used for (future) research.

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

8. End of the study

Your participation in the study stops when:

- All data collection has been completed (until 6 weeks after delivery)
- You choose to quit
- The researcher/care provider considers it best for you to quit

The gynaecologist of Máxima MC, the government or the Medical Ethics Review Committee decides to stop the study.

The entire study ends when all measurements of the participants are collected. You will not be informed personally about the results of the study. After processing the data, the researcher will publish the results in scientific journals.

9. Usage and storage of your data

Your personal data and your child's data will be collected from the electronic patient file or questionnaires. Data such as your name, address, date of birth, data about you and your child during delivery, data about your health or the health of your child after delivery. The data collection from you and your child will continue for up to six weeks after delivery. The collection, use and storage of these data is required to answer the questions asked in this study and to be able to publish the results.

Missing information of you and your child will be requested by your practitioner, primary care physician, obstetrician or gynecologist, the child health center or the pediatrician to receive this information. We ask your permission for the request of your data and the permission of the parent(s)/legal representative(s) for the request of child's data

Confidentiality of your data

In order to protect your privacy and the privacy of your child, data is encoded. Your name and other information that can directly identify you and your child will be omitted. Data can only be traced back to you and your child with the key of the code. The key of the code remains safely stored in the local research institute. The only persons who have access to the key to this code are the investigators listed in appendix A. There will be no way to link data of you or your child personally in reports and publications.

Access to your data for verification

Some people may have access to all of your data and your child's data at the local research institute, also to the data without code. This is necessary in order to check whether the study has been carried out properly and reliably. Persons who have access to your data for inspection are the committee that monitors the security of the investigation, an independent inspector hired by the investigator (for this study: Clinical Trial Center Maastricht) or national and international supervisory authorities, for example, the Health and Youth Care Inspectorate. They will keep your data confidential. We ask you and the legal representative(s) of the child to give permission for this inspection.

Data of the heart rate of the unborn child and the contractions of the uterus measured with the NFMS are provided in a secure environment with Nemo Healthcare® (the company that developed the NFMS) to answer research questions. Nemo Healthcare® does not have access to direct data traceable to you.

Retention period of your data

Your data must be kept for 15 years at the research location (Máxima MC, location Veldhoven). You consent to this.

Storage and use of data for other research
The data collected in this study may also be of importance for other scientific research in the field of fetal monitoring during delivery. Scientific information such as publications and anonymous data is available for everyone. To this end, your data will be stored for 15 years. You can indicate on the consent form whether or not you agree with this. If you do not agree with this, you can still participate in the current study.

Sharing your data with Nemo Healthcare B.V.
To improve the quality of monitoring, Nemo Healthcare B.V. is investigating the relationship between certain medical data and the quality of the recordings. You can provide separate consent for the exchange of this data in the consent form.

Information about unexpected findings
Data collected during this study will be analysed after the study has already ended. Therefore, unexpected findings in the data will no longer be relevant for your health and/or the health of your child at that time and will not be fed back for this reason.

Withdrawing consent
You can withdraw your consent to use your personal data and the data of your child at any time. This applies to this study and also to use and storage for future research. However, the study data collected until you withdraw your consent will still be used in the study.

More information about your rights when processing data
For general information about your rights when processing your personal data, please consult the website of the Dutch Data Protection Authority. If you have any questions about your rights, please contact the Data Protection Officer of the MMC. See Appendix A for contact details and website.

If you have questions or complaints about the processing of your personal data, we advise you to first contact the coordination researcher. You can also contact the Data Protection Officer of the MMC. See appendix A for contact details, or the Dutch Data Protection Authority.

10. Insurance
Insurance has been taken out for everyone who takes part in this study. The insurance pays for damage caused by the study. But not for all damage. You can find more information about this insurance and any exceptions in Appendix B. It also says who you can report damage to.

11. No financial compensation for participation
Participating in this study, will not give additional costs for you. Because your participation in this study is entirely voluntary, you will not be given money or gifts to take part in this research.

12. Do you have any questions?

If you have any questions, please contact the coordinating investigator. For independent advice on participating in this research, you can contact the independent expert. He knows a lot about the study, but has no association with the study. All details can be found in Appendix A: Contact details.
If you have any complaints about the study, you can discuss this with the investigator or your threating specialist. If you prefer not to, you can contact the complaints mediator of the MMC. All details can be found in Appendix A: Contact details.

13. Signing the consent form

When you have had sufficient time for reflection, you will be asked to decide on participation in this study. If you want to participate, we kindly ask you to confirm this by signing the consent form, attached in appendix C. If you sign this form, you indicate that you have understood the information about participation in the study and agree the terms. Both you and the investigator will receive a signed copy of the consent form.

Thank you for your attention.

14. Appendices

A. Contact details

B. Information about the insurance

C. Informed Consent Form

Appendix A: Contact details

Investigators:
Dr. J.O.E.H. van Laar, gynaecologist-perinatologist, Máxima MC Veldhoven
Dr.ir. M.B. van der Hout-van der Jagt, Technical University of Eindhoven, Máxima MC Veldhoven
Drs. A. van Barschot, researcher, department of gynaecology and obstetrics, Máxima MC Veldhoven
Telephone: 040-888 83 84
Email: NIEMIIstudie@mmc.nl

Independent expert:
Dr. K.P. Dijkman, pediatrician, Máxima MC Veldhoven
Telephone: 040-888 93 50
Email: k.dijkman@mmc.nl

Complaints:
If you have any complaints about the study, please contact the complaints mediator.
Telephone: 040-888 94 81
Email: klachtbemiddeling@mmc.nl
Department for quality and safety

Officer data protection:
If you have any questions and/or comments with regard to the processing of your personal details within MMC, you can contact the officer data protection.
Telephone: 040-888 83 66
Email: gegevensbescherming@mmc.nl
Website: https://www.mmc.nl/privacy

Appendix B: information about the insurance

The Máxima MC has taken out insurance for everyone who takes part in the study. The insurance pays for the damage you have suffered because you participated in the study. This concerns damage you suffer during the study or within 4 years after you participated in the study. You must report damage to the insurer within 4 years.

Have you suffered damage as a result of the study? Please report this to this insurer:

The insurer of the study is:
Name insurer: Lloyd's Insurance Company S.A.
Address: Bastion Tower, Marsveldplein 5, 1050 Brussel, België
Policy number: MCIEEA23030

The claims representative of the study is:
Name: Ralph van Helden
Address: Beursplein 37, 3001 DD Rotterdam
E-mail: ralph.vanhelder@lloyds.com
Telephone number: + 31(0)102052110

The insurance pays a maximum of €650.000 per person, a maximum of €5.000.000 for the entire study, and a maximum of €7.500.000 per year for all studies by the same sponsor.

Please note that insurance does **not** cover the following damage:

- Damage due to a risk about which we have given you information in this sheet, unless:
    - The risk turned out to be greater than previously thought.
    - Or if the risk was very unlikely.
- Damage to your health that would also have happened if you had not taken part in the study.
- Damage that happens because you did not follow directions or instructions or did not follow them properly.
- Damage caused by a treatment method that already exists. Or by research into a treatment method that already exists.

These provisions can be found in the 'Besluit verplichte verzekering bij medisch-wetenschappelijk onderzoek met mensen 2015' (Medical Research (Human Subjects) Compulsory Insurance Decree 2015'). This decision can be found in the Government Law Gazette (https://wetten.overheid.nl)

Appendix C: Subject Consent Form [Patient]

Data collection of electrophysiological monitoring of the condition of mother and child during delivery and the first weeks after delivery

Implementation intrapartum non-invasive electrophysiological monitoring

The information regarding the child is valid for the parent(s)/legal representative(s) of the child.

- I have read the information letter. I was also able to ask questions. My questions have been sufficiently answered. I have had enough time to decide if I want to join this study.
- I know participation is voluntary. I also know that I can decide at any time not to participate or to stop participating without giving a reason.
- I know that I will be monitored with standard of care, CTG monitoring in case no NFMS is available and that my data and data of my child will be used in this study.
- I give permission for researchers to collect and use my personal and medical data and the data of my child from the electronic patient file or questionnaires for the purpose of answering the research question in this study.
- I give permission for researchers to request medical information from me and/or my child after delivery from my practitioner, primary care physician, obstetrician, gynaecologist, child health center or pediatrician to answer the research question of this study.
- I know that in order to monitor the study, some people may have access to all my data. These people are listed in this information letter. I consent to such access by these people.
- I give permission to keep my data stored for 15 years at the research location.
- Please fill in everything in the grey boxes:

Authority child:

☐ Both parents / legal representatives declare to sign the consent form.

☐ Parent 1 / legal representative 1 declares sole parental authority over the child.

Subject / parent 1 / legal representative 1:

– I want to participate in this study.

– I consent to the collection and use of my child's data for the study as described in the information letter.

Name subject (initials, first and last name):_____

_____

Date of birth: _____/_____/_____

Signature:_____ **Date:** _____/_____/_____

Additional consent:

I give permission to use the NFMS to monitor the condition of me and my unborn child during labour and for monitoring the uterus activity up to 1.5 hour after childbirth.	☐ Yes	☐ No
I give consent to contact me again after this study for a follow-up study.	☐ Yes	☐ No
I give consent for the collection and use of my data and data of my child for comparable studies in the future, and to share data anonymously with other researchers.	☐ Yes	☐ No
I give permission to share my monitoring record and some of my coded data with Nemo Healthcare B.V. in order to improve the quality of the monitoring.	☐ Yes	☐ No
I give consent for an additional ultrasound during labour.	☐ Yes	☐ No

In case there is another (authoritative) parent, legal representative, or guardian besides you (the mother), we also request that this person provide separate consent for the collection of your child's data. This consent includes agreement with any additional permissions selected beforehand that concern the collection, use, or sharing of your child's data.

Parent 2 / legal representative 2 (if applicable):

- I give consent to the collection and use of my child's data for the study as described in the information letter and agree to the additional permissions selected beforehand that concern the collection, use, or sharing of my child's data.

Name parent 2 / legal representative 2:_____

Signature:_____ **Date:** _____/_____/_____

---------- **Fill in below by the researcher (or her representative)** ----------

- I hereby declare that I have fully informed the participant 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 her of this in a timely fashion.

Name of investigator (or her representative):_____

Signature:_____ **Date:** _____/_____/_____

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

Appendix C: Subject Consent Form [Researcher]

Data collection of electrophysiological monitoring of the condition of mother and child during delivery and the first weeks after delivery

Implementation intrapartum non-invasive electrophysiological monitoring

The information regarding the child is valid for the parent(s)/legal representative(s) of the child.

- I have read the information letter. I was also able to ask questions. My questions have been sufficiently answered. I have had enough time to decide if I want to join this study.
- I know participation is voluntary. I also know that I can decide at any time not to participate or to stop participating without giving a reason.
- I know that I will be monitored with standard of care, CTG monitoring in case no NFMS is available and that my data and data of my child will be used in this study.
- I give permission for researchers to collect and use my personal and medical data and the data of my child from the electronic patient file or questionnaires for the purpose of answering the research question in this study.
- I give permission for researchers to request medical information from me and/or my child after delivery from my practitioner, primary care physician, obstetrician, gynaecologist, child health center or pediatrician to answer the research question of this study.
- I know that in order to monitor the study, some people may have access to all my data. These people are listed in this information letter. I consent to such access by these people.
- I give permission to keep my data stored for 15 years at the research location.
- Please fill in everything in the grey boxes:

Authority child:

☐ Both parents / legal representatives declare to sign the consent form.

☐ Parent 1 / legal representative 1 declares sole parental authority over the child.

Subject / parent 1 / legal representative 1:

– I want to participate in this study.

– I consent to the collection and use of my child's data for the study as described in the information letter.

Name subject (initials, first and last name):_____

_____

Date of birth: _____/_____/_____

Signature:_____ **Date:** _____/_____/_____

Additional consent:

I give permission to use the NFMS to monitor the condition of me and my unborn child during labour and for monitoring the uterus activity up to 1.5 hour after childbirth.	☐ Yes	☐ No
I give consent to contact me again after this study for a follow-up study.	☐ Yes	☐ No
I give consent for the collection and use of my data and data of my child for comparable studies in the future, and to share data anonymously with other researchers.	☐ Yes	☐ No
I give permission to share my monitoring record and some of my coded data with Nemo Healthcare B.V. in order to improve the quality of the monitoring.	☐ Yes	☐ No
I give consent for an additional ultrasound during labour.	☐ Yes	☐ No

In case there is another (authoritative) parent, legal representative, or guardian besides you (the mother), we also request that this person provide separate consent for the collection of your child's data. This consent includes agreement with any additional permissions selected beforehand that concern the collection, use, or sharing of your child's data.

Parent 2 / legal representative 2 (if applicable):

- I give consent to the collection and use of my child's data for the study as described in the information letter and agree to the additional permissions selected beforehand that concern the collection, use, or sharing of my child's data.

Name parent 2 / legal representative 2:_____

Signature:_____ **Date:** _____/_____/_____

---------- **Fill in below by the researcher (or her representative)** ----------

- I hereby declare that I have fully informed the participant 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 her of this in a timely fashion.

Name of investigator (or her representative):_____

Signature: _____ **Date:** __ / __ / __

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