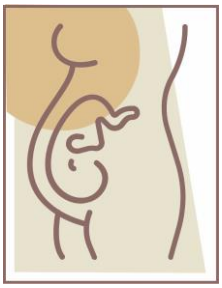
Subject information for participation in medical research



NIEM-O Study: A medical study on external monitoring of pregnant women during admission to the Obstetric High Care.

Official title: Non-Invasive electrophysiological monitoring at the obstetric high care

Introduction

Dear Madam,

With this letter, we would like to ask you to take part in a medical study. Participation is voluntary. You have received this letter because your doctor has admitted you to the Obstetric High Care (OHC) of Máxima MC (MMC). This information sheet contains information on the medical study, what it means for you, and what the pros and cons are from participating in the study. It is a lot of information. Please take the time to read the information and determine whether you wish to participate? If you wish to participate, please fill out the form in Appendix F.

Ask your questions

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

- Put your questions to the investigator who gave you this information.
- Talk to your partner, family or friends about this study.
- Read the information on www.rijksoverheid.nl/mensenonderzoek.
- Further information about participating in medical scientific research can be found in Appendix D - the enclosed brochure 'Medical scientific research'.

1. General information

MMC has set up this research project. Researchers, who can be doctors, interns and research nurses, carry out the research in MMC at the ward. For this study, 464 subjects who are admitted to the OHC of MMC are required. The medical ethics review committee from Máxima Medical Center has approved this study.

2. What is the purpose of the study?

The aim of this study is to improve care at the OHC and to promote the health of you and your child. Monitoring your child and you during the pregnancy contributes to this. Our research focusses on the way pregnant women are currently monitored. We will hereby collect data about the registration of the uterine activity, your and your child's heart rate during admission to the OHC, together with data about the outcome after delivery. For example, information about the need for a caesarean section, the birth weight of your child and admission to the pediatric ward after delivery. We will also send you two surveys about your experiences with the monitoring method.

3. What is the background of the study?

You are pregnant and your doctor wants to admit you, or has admitted you, to the OHC. During your hospital stay, the mother's heart rate, the heart rate of the unborn child and the activity of the uterine muscle (contractions) are recorded to keep a close eye on the condition of you and your child. This is called a cardiotocogram (CTG).

Current monitoring method ('standard treatment')

Depending on your reason for admission, a CTG will be made one to three times a day. Uterine activity (contractions) is recorded by placing a button on your abdomen that is held in place by elastic banding around your waist. Your child's heart rate is measured by placing another button on your abdomen that is held in place by a second elastic band around your waist. See Figure 1 for this monitoring method. This way of registering has been used as standard care for decades.

Figure 1. CTG monitoring with elastic banding

Figure 2. NFMS (Nemo Fetal Monitoring System)

New monitoring method (NFMS)

Recently, a new device to register the heartbeat of the unborn child, the mother and uterine activity has been developed in collaboration with MMC: the NFMS (Nemo Fetal Monitoring System), see Figure 2. This device uses a new technology that picks up electrical signals of the mother's heart, the baby's heart and the uterus. These signals are registered by a patch on the mother's abdomen. There is a transmitter on the patch that wirelessly transmits the signals to the base station. In recent years, the NFMS has extensively been studied. It turned out to be a safe alternative to the standard monitoring method. Previous research has also shown that this new monitoring method provides better registration in comparison to the standard monitoring method. It is also possible to wear the NFMS all day long. Leading, in contrast to the standard monitoring method, to the possibility of obtaining continuous data about your child's heart rate and uterine activity. By doing so, doctors monitor your condition and the condition of your child throughout the day.

For an overview of the comparison between the two monitoring methods, see Appendix B.

Since the NFMS registers data more accurately than the conventional CTG (the standard monitoring method), it can be used in place of the CTG during your admittance to the OHC.

The NFMS will thus be used to monitor both you and your child. To find out whether the NFMS also contributes to better outcomes for you and your child, your and your child's data are collected in this study. It is also valuable to compare your data to data of pregnant women who received the standard treatment. We want to collect data on a large scale. That is why we ask all women admitted to the OHC to participate in this study and for permission to use their data for scientific research.

4. What happens during the study?

How long will the study take?
Are you taking part in the study? This will take as long as your admittance to the OHC lasts. If you are readmitted, you will get the same monitor method (if the NFMS is available). You can choose to stop participating in the study at any time.

Step 1: Are you eligible to take part?
First, we want to know if you are eligible to participate. You may participate in the study if you meet the following criteria:

- You are at least 18 years old
- You are admitted to the OHC

Unfortunately, you will not be allowed to participate in the study if you:

- Have a multiple pregnancy (twins/triplets)
- Have a pacemaker
- Your medical history includes a serious skin disease that makes it impossible to apply the NFMS patch.
- Have insufficient knowledge of Dutch or English language
- You or your unborn child have arrhythmia or cardiac disease
- Are admitted for a serious condition that happens when the body's immune system has an extreme response to an infection (sepsis)

Step 2: The monitor method
If you participate in this study, you will receive the new monitoring method (NFMS). To compare the results with the standard monitoring method, we collect data from patients who have received the standard monitoring method in the past. In addition, a small part of the patients admitted to the OHC still receive the standard monitoring method. There are five NFMS available on the OHC. It is possible that no NFMS is available due to crowdedness. Your healthcare provider will let you know if no NFMS is available. Even if no NFMS is available, we would still like to collect your data.
You will then get the standard monitoring method. Your data will be used to compare with data of pregnant women who did receive the NFMS. You give consent by signing the enclosed form. If you don't want to participate in the research, you will receive the standard monitoring method.

*Step 3: Study and measurements*No extra visits to the hospital are needed for this study.
Measurements and data collection throughout the study are performed during your admission to the OHC. For an overview of the steps in this study, see Appendix C.

You will be monitored with the NFMS. The patch that is used is placed on the abdomen by the nurse. Before applying the patch, the skin is first cleaned with soap and water and then scrubbed lightly. This is necessary to ensure that the patch sticks properly. This results also in as little signal disturbance as possible. The NFMS remains in place and registers 24/7, i.e. all day and night. This gives your doctor insight into how you and your child are doing at all times. The NFMS is wireless so you can move around during registration. You can use the shower whilst the patch is attached. You cannot take a bath with the patch. The system with the patch has been tested and is safe. If the registration by means of the new device is unsatisfactory at any time during the registration, adjustments to the attachment of the patch will be made if possible. Sometimes it is necessary to place a new patch. Whenever registration doesn't improve, the system will be reverted to the standard system.

Surveys about your experiences

We will ask you to complete two digital questionnaires. The questions are about your experiences with the monitoring method. We will send both questionnaires to your email address immediately after you have been admitted to the OHC and agreed to participate in the study. The first questionnaire is about your health while using the monitor method. You complete this questionnaire on the first day after admission. The second questionnaire is about your experiences with the device. You complete this questionnaire on the day of your discharge from the hospital. It will take you approximately 3-5 minutes to complete the first questionnaire and approximately 5-10 minutes to complete the second questionnaire. Your experiences are of great importance for our research and will be included in the results of the research.

Additional ultrasound

In addition to this study, another study is looking into the potential prediction of preterm birth, using the NFMS data. The accuracy with which the NFMS can track your child's movements is another topic of this study. In order to see and record your child's movements, we will perform an ultrasound at the same time (only once). We need to conduct this ultrasound on the first 200 patients in order to fully investigate this. Your doctor or the researcher will let you know whether you will receive the additional ultrasound. The researcher will perform the ultrasound in your room, and it will last 45 minutes. Patients not included in this category will only get a standard ultrasound.

5. What agreements do we make with you?

We would like to make the following agreements with you:

- You should contact your caregiver/the investigator in these situations:
  - You experience skin irritation due to the patch
  - You no longer want to take part in the study.
  - Your telephone number, address or email address changes.
- With the NFMS, you are allowed to walk and take a shower during use of the patch. A bath is unfortunately not possible.

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

The NFMS has been approved and regarded safe for use in the hospital. Monitoring with the use of the patch on the abdomen is a very safe method and will not harm you or your child.

The patch can in some cases cause (mild) skin irritation. To prevent this, the patch will stay in place as long as possible. Sometimes it is necessary to reapply the patch or apply a new patch. This may be necessary, for example, if you experience skin irritation where the patch is applied, or if the patch no longer has good skin contact. If skin irritation does occur, report it to your caregiver or the researcher. Sometimes moving the patch or replacing it by a new one is sufficient, if this is unfortunately not the case, you will switch to the standard monitor method. The skin irritation will disappear on its own, no treatment is necessary.

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

Taking part in the study can have pros and cons. We will list them below. Think about this carefully and talk to other people about it.

Potential benefits of participating in the study may include:

- The NFMS is wireless and gives you more freedom of movement. You are also allowed to move during registration.
- With using the NFMS you do not have to wear belts around your waist. Previous research showed that women (during childbirth) liked the patch most compared to the transducers with banding.
- The NFMS provides continuous registration. The heart rate of your child, your heartrate and the uterine activity is continuously displayed in the doctors- and nurse's offices on screens. As a result, your doctor is able to monitor you and your child day and night.

Possible disadvantages of participating in the study may include:

- Possible (mild) skin irritation due to the patch
- If there is not enough signal coming through, it may be necessary to switch to the standard way of monitoring.
- If you are part of the group in which the extra ultrasound will be performed, it will take 45 minutes of your time. The ultrasound will take place during your admission and will not interfere with your standard treatment.

Don't want to participate?

You decide whether you want to participate in the study. Participation is voluntary. Don't want to participate? Then you get the standard monitor method. You don't have to say why you don't want to participate.

8. When does the study end?

The investigator will let you know if there is any new information about the study that is important to you. The investigator will then ask you if you want to continue to take part.

In these situations, the study will stop when:

- You have given birth (outcomes will be monitored until six weeks after giving birth)
- You do not have to be admitted anymore to the OHC at MMC

- You want to stop participating in the study yourself. You can stop at any time. Report this to your caregiver immediately. You do not have to explain why you want to stop. You will then get the standard monitoring method.
- One of the following authorities decides that the study should stop:
    - MMC,
    - The government, or
    - The Medical Ethics Review Committee assessing the study

What happens if you stop participating in the study?
The investigators use the data that have been collected up to the moment that you decide to stop participating in the study. The investigation is complete when all measurements of all participants are collected. You will not be personally informed about the results of the study. After processing the data, the investigator will publish the results of the study in scientific journals.

9. What happens after the study has ended?

You will not be personally informed about the results of the study. After processing the data, the investigator will publish the results of the study in scientific journals.

10. What will be done with your data?

Are you taking part in the study? Then you also give your consent to collect, use, store and if necessary share your encrypted data with other researcher within this research field. These researchers are those who are likewise interested in the findings of this research and are located inside the MMC, in the area, in the nation, or overseas. We also share a small amount of your data with Nemo B.V., in order to improve the quality of monitoring.

What data do we store?
Your personal data will be collected and stored for this research. Data such as your name, address, date of birth and data concerning your health and the delivery are collected. A number of data concerning your child are also collected and stored, such as gender, birthweight, Apgar scores, umbilical cord measurements, possible admission to the paediatric ward and general information about your child's health. The outcomes of your child's health will be collected until hospital discharge. When your child is discharged within the first four weeks after delivery, we will collect the data until four weeks after delivery.

Why do we collect, use, store and share your data?
We collect, use, store and share your data to answer the questions of this study, and to be able to publish the results. As a result, caregivers and researchers in the Netherlands and in the world have access to our knowledge and further research can possibly take place. Also performing the same research and thereby patient burden is prevented. We also collect data to improve the quality of monitoring.

How do we protect your privacy?
To protect your privacy, we give a code to your data. We only put this code on your data. We keep the key to the code in a safe place in the hospital.
When we process your data, we always use only that code. Even in reports and publications about the study, nobody will be able to see that it was about you.

Who can see your data?
In addition to the research team, some people can get access to your non-anonymised data at the research location. Including the data without a code. This is necessary to be able to check whether the study is being conducted in a good and reliable manner. Persons who have access to your data for review are: the committee that monitors the safety of the study, a monitor working for Máxima MC Veldhoven and national and supervisory authorities, for example, the Health and Youth Care Inspectorate. They will keep your data confidential. We ask you to give permission for this inspection.

For how long do we store your data and body material?
We store your data in the hospital for 15 years

May we use your data for other research?
After this study, your data may also be important for other scientific research in the field of monitoring pregnant women. For this purpose, your data will be stored in the hospital for 15 years. You give permission by signing the consent. Do you not give permission? You'll get the same care.

Share your data with other researchers
In order to make it possible to publish the results of this research in certain scientific journals and to give other researchers the opportunity to carry out further research, it is necessary to make anonymized data available. There will be no way to link data to you personally. You consent to the exchange of this data when signing the consent form.

Share your data with Nemo B.V.
In order to improve the quality of monitoring, Nemo B.V. studies the relationship between certain data (like duration of pregnancy) and the quality of monitoring. Therefore, it is necessary to share coded data with them. There will be no way to link data to you personally. You consent to the exchange of this data when signing a specific consent section on the consent form.

What happens if there are accidental discoveries?
It is possible that during the study we discover something that is important for your health or the health of your child. In that case, the investigator will contact your caregiver. You will then discuss what needs to be done with your doctor or specialist. With the form, you give consent to inform your doctor or specialist.

Can you take back your consent for the use of your data?
You can take back your consent for the use of your data at any time. This applies both to the use in this study and to the use in other medical research. But please note: if you take back your consent,

and the investigators have already collected data for research, they are still allowed to use this information

Do you want to know more about your privacy?

- Do you want to know more about your rights when processing personal data? Visit www.autoriteitpersoonsgegevens.nl.
- Do you have questions about your rights? Or do you have a complaint about the processing of your personal data? Please contact the person who is responsible for processing your personal data. For the present, this is:
    - MMC. See Appendix A for contact details, and website.
- If you have any complaints about the processing of your personal data, we recommend that you first discuss them with the research team. You can also contact the Data Protection Officer of MMC. Or you can submit a complaint to the Dutch Data Protection Authority.

11. Will you receive compensation if you participate in the study?

Participation in this study will not cost you anything. Neither will you get any compensation if you take part in this study.

12. Are you insured during the study?

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 D. It also says who you can report damage to.

13. Exchange of information

The researcher will contact your main practitioner to request your medical information if your main practitioner does not work at MMC. This is required to gather all of your data, even if you were monitored at another hospital, are (temporarily) admitted to MMC and will return to your original hospital. This includes, for example, the date of delivery, the start of your child and your health up to 4 weeks after your delivery. You consent to the exchange of this data.

14. Do you have any questions?

You can ask questions about the study to your caregiver or the research team. Would you like to get advice from someone who is independent from the study? Then contact Dr. L. Bok paediatrician at MMC. He knows a lot about the study, but is not a part of this study. Do you have a complaint? Discuss it with the investigator or the doctor who is treating you. If you prefer not to do so, please visit the complaints officer of MMC. Appendix A tells you where to find this.

15. How do you give consent for the study?

You can first think carefully about this study. You have at least an hour to do this, and you can use more time if necessary. Then you tell the investigator if you understand the information and if you want to take part or not. If you want to participate, fill out the consent form that is included. You and the investigator will both get a signed version of this consent form.

16. Appendices to this information

A. Contact details
B. Comparison between the monitoring methods
C. Flow chart study
D. Leaflet ‘Medical scientific research’
E. Information about the insurance
F. Consent form(s)

Appendix A: contact details for the MMC

Investigators:
Drs. N.D. de Klerk, medical researcher gynaecology/obstetrics, Máxima MC Veldhoven
Ir. I. de Vries, researcher, Máxima MC Veldhoven
Dr. J. van Laar, gynaecologist-perinatologist, Máxima MC Veldhoven
Dr. M. van der Ven, technical physician, Máxima MC Veldhoven
Dr. A.F Fransen, gynaecologist, Máxima MC Veldhoven
Dr. H.J. Niemarkt, pediatrician, Máxima MC Veldhoven
Dr. Ir. R. Vullings, engineer
Prof. Dr. S.G. Oei, gynaecologist-perinatologist, Maxima MC Veldhoven
Telefoon: 040-8888384
Email: niemo.studie@mmc.nl

Independent expert:
Dr. L. Bok, pediatrician, Máxima Medical Center Veldhoven
Email: L.bok@mmc.nl
Phone (office): 040 8888270

Complaints:
If you have any complaints about the study you may contact the complaint officer of Máxima MC Veldhoven.
Telephone: (040) 8889481
Email: klachtenfunctionaris@mmc.nl
Department for quality and safety

Data Protection Officer:
If you have questions and/or comment regarding the processing of your personal data within Máxima MC, you can contact the data protection officer.
Telephone: (040) 8888366
Email: gegevensbescherming@mmc.nl
Website: https://www.mmc.nl/privacy

Appendix B: Comparison between the monitoring methods

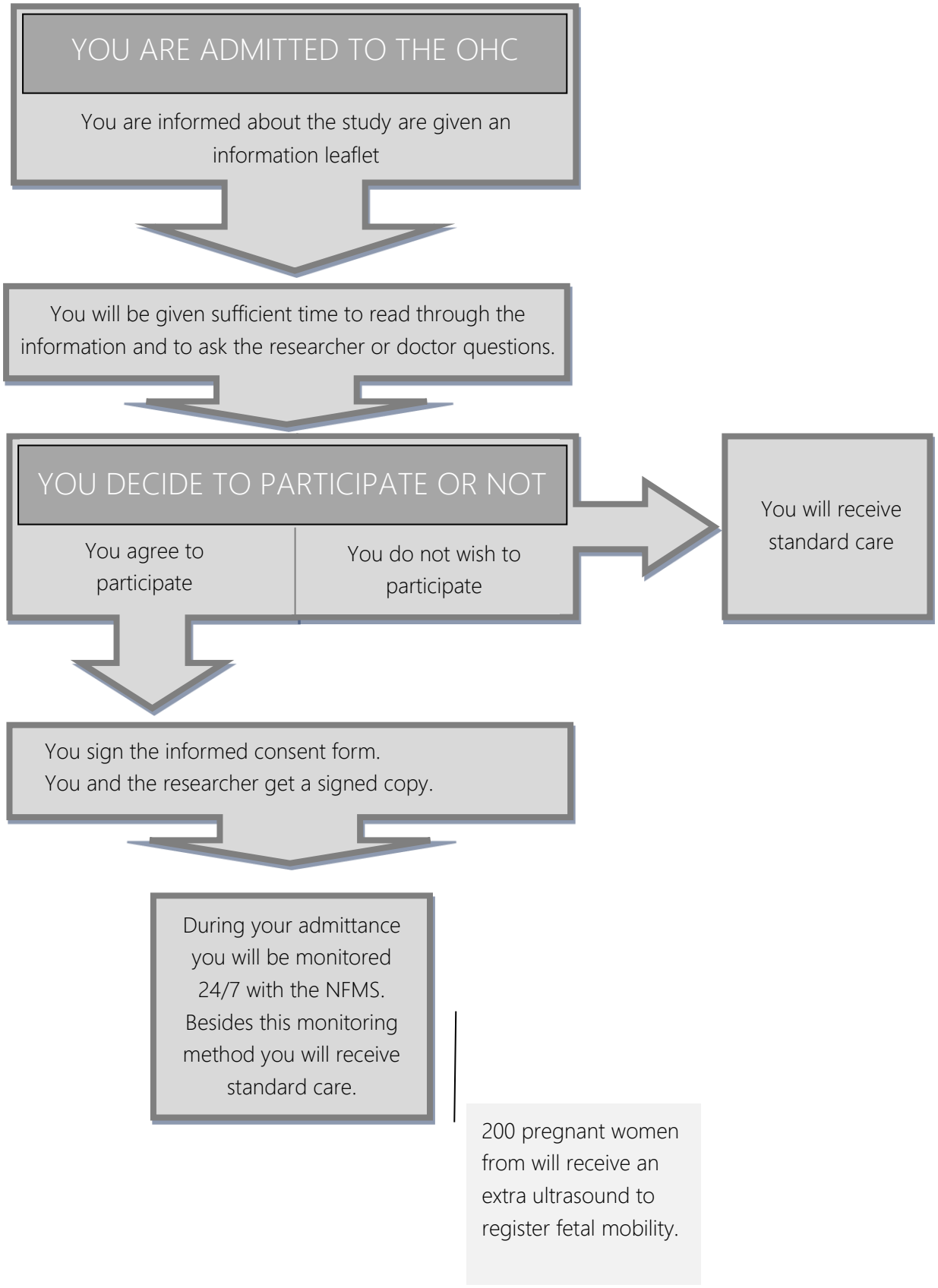
	Standard method	NFMS (new method)
Components	- Two elastic banding - Two transducers - Base - Wiring	- Base - Link - Patch
How long is the registration?	Once up to three times a day. Every registration takes around 45 minutes.	Continuous, all day and night.
How much can you move around?	You are not allowed to move around/walk during registration.	You are allowed to move and walk during registration
Are you allowed to move yourself in the room?	No, you can not/are not allowed to move around without assistance	Yes, you can even shower with the patch
Benefits	Shorter duration of registration, in between these moments no appliances are attached.	- You can move around - It is wireless - Continuous monitoring
Cons	- You can not move during registration - Elastic banding can be experienced as uncomfortable - Unguarded moments between the registration moments	- Mild skin irritation may occur - If the signal does not come through properly, it can be decided to switch to the standard way of monitoring
Reliable registration of the heartrate of your baby[1]	82,5%	99,9%
Accuracy registration of heartrate of your baby[1]	73%	95,7%

Figure 1. CTG monitoring with elastic banding. The 'Standard Method'.

Figure 2. NFMS (Nemo Fetal Monitoring System). The 'New Method'.

[1] Vullings R, van Laar, Judith O. E. H. Non-invasive Fetal Electrocardiography for Intrapartum Cardiotocography. Front Pediatr 2020;8:599049

Appendix C: Flowchart study



Appendix D: Leaflet Medical Scientific Research

Appendix E: 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 the researchers (contactdata can be found in *Appendix A)* and 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: MCIEEA23029

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. But this does not apply if the risk turned out to be greater than we 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 F: Informed consent form – subject

Belonging to the NIEMO-study: A medical study on external monitoring of pregnant women during admission to the Obstetric High Care.

- I have read the information sheet. I was able to ask questions. My questions have been answered well enough. I had enough time to decide if I wanted to take part.
- I know that taking part is voluntary. I also know that at any time I can decide not to take part in the study. Or to stop taking part. I do not have to explain why.
- I give the investigator consent to inform and contact specialist (s) who treats me that I am taking part in this study and to retrieve my and my child's data after birth, that are requisite for the research.
- I give consent to give my doctor or specialist information about accidental discoveries made during the study that are important for my health.
- I give consent to collect and use my data. The investigators only do this to answer the question of this study.
- I know that some people will be able to see all of my data to review the study. These people are mentioned in this information sheet. I give consent to let them see my data for this review.
- I give consent to collect my data, when no NFMS is available or I don't want to receive the NFMS, and I receive standard treatment

- Please tick yes or no in the table below.

I give consent to share my coded with other researchers	Yes☐	No☐
I give consent to store my data to use for other research, as stated in the information sheet.	Yes☐	No☐
I give consent to ask me after this study if I want to participate in a follow-up study.	Yes☐	No☐
I give consent to share some of my coded data with Nemo B.V. in order to improve quality of monitoring	Yes☐	No☐

- I want to take part in this study.

My name is (subject): ……..
Signature: …… Date : __/__/__

If there is another (authoritative) parent, legal representative(s) or guardian besides you (the mother), we also ask that person to give separate permission for the collection of your child's data after birth

Is there is another (authoritative) parent, legal representative(s) or guardian besides you?

□ Yes
□ No

If you answered YES, they must sign below for permission. If that person does not give permission, we are not allowed to collect your child's data.

The name of the other (authoritative) parent, legal representative(s) or guardian is:
……..

Signature: …… Date: __ / __ / __

I declare that I have fully informed this subject about the study mentioned.

If any information becomes known during the study that could influence the subject's consent, I will let this subject know in good time.

Investigator name (or their representative): .....
Signature:…… Date: __/__/__

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