



Trial subject information for participation in medical-scientific trials

Additional oxygen for BPD

“Supplemental oxygen in children with bronchopulmonary dysplasia (BPD) following the neonatal intensive care period: the SOS BPD study”

Introduction

Dear Sir/Madam,

You are receiving this letter because your child has bronchopulmonary dysplasia (BPD) and requires supplemental oxygen. We kindly request that you allow your child to take part in a medical-scientific trial. Participation is on a voluntary basis. To take part, you will have to give us consent in writing.

Before you decide whether or not to take part in the trial, we will explain what exactly the trial entails. Please read this information through carefully and ask the researcher for further explanation if you have any questions. Alternatively, you can ask the independent expert, specified at the bottom of this letter, for additional information. You may also discuss it with your partner, friends or family.

Further information about participating in trials can be found on the website of the Rijksoverheid: www.rijksoverheid.nl/mensenonderzoek.

1. General information

This trial has been set up by paediatricians from the Sophia Children's Hospital (Rotterdam), the Emma Children's Hospital (Amsterdam) and the Beatrix Children's Hospital (Groningen) and is being conducted by paediatricians in different hospitals across the country.

This trial requires 198 children from the Netherlands who have BPD. The Erasmus MC medical ethics review committee has approved this trial. General information about reviewing trials can be found in the 'Medical-scientific trials' brochure.

2. Aim of the trial

The aim of this trial is to find out what the best lower saturation limit ('the oxygen content in the blood') is to withdraw supplemental oxygen from children with BPD. In this trial, we are comparing a lower limit of 90% with a lower limit of 95%. Or, is it better to keep the saturation higher or the same as 95% or is 90% just as good?



3. Background to the trial

Supplemental oxygen is the main treatment for children with BPD. However, it has never been investigated what a safe lower saturation limit is in children with BPD after the first few weeks of life, from week 36 of the pregnancy onwards. Both too much and too little oxygen can have serious consequences. Too little oxygen can lead to poorer increase in weight and thereby also poorer lung development and more lung complaints. Too little oxygen can also lead to a higher risk of cot death and be detrimental to development. Too much oxygen is also harmful to the lungs and brain, especially in premature children. Most hospitals observe a lower saturation limit of 90%; however, international guidelines advise 93-95%. But the higher the lower saturation limit should be, the longer children are given additional oxygen and the more frequently they will go home with it.

4. What participation entails

If you wish to allow your child to take part in the trial, we will follow your child's progress up to 1 year after the due date of the pregnancy.

When is your child able to participate?

Your child may take part in the trial from the moment that the pregnancy would have reached 36 weeks onwards. At that time, your child should still require supplemental oxygen, otherwise he or she will not be able to take part. The children participating in the trial are randomly distributed between 2 groups: in one group, we withdraw the supplemental oxygen at a lower limit of 90%; in the other group, at a lower limit of 95%. Fate decides in what group your child ends up; you and the physicians and researchers don't have any influence over this.

Visits and measurements

The trial will take 1 year to complete. During that year, you will visit the hospital twice, when your child is 6 and 12 months of age respectively. These are the standard visits that always take place after (extreme) prematurity, even if you aren't taking part in the trial. The visit will take around 1 hour. During each visit, we will weigh and measure your child and ask about lung complaints, hospital admissions and doctors' visits. Part of the standard treatment in some hospitals includes: a lung function test (by wearing a mask on the face), a CT scan, a sleep study and/or an ultrasound of the heart. The physician treating your child will tell you whether this happens in your hospital too. If your child takes part in the SOS BPD trial, the visit to the outpatients' clinic won't be any different or longer than it usually would be. We will, however, collect the data from the visits for the trial.

In addition to the standard outpatient visits, we will also ask you to answer a number of questions 3 times before the trial by means of a questionnaire sent to you via the internet. This will happen at the beginning of the study, when your child is 6 months old and when your child is 12 months old. The questionnaire will take around 20 minutes to complete. You will also receive a monthly e-mail asking whether your child has been ill, has been given any medication or has been admitted to hospital recently. You will also have the opportunity to make notes on a secure page on the trial website.



As long as your child is receiving supplemental oxygen, we will ask your physician or yourself (if your child is going home with oxygen) to actively withdraw the oxygen. Oxygen is usually withdrawn in consultation between you and the physician treating your child. For the trial, we will ask you or the physician treating your child to download the saturations from the saturation meter twice a week (or once a week if your child is at home with oxygen) and to e-mail the readings to the researchers. This will be explained to you if you decide to take part in the trial. If the downloaded data reveal that your child is exceeding the lower limit of 90 or 95% too frequently, we will ask the doctor or you to withdraw the oxygen faster. It may also become apparent that your child is falling under the lower limit just that bit too frequently, in which case we will ask you or your doctor to turn the oxygen level up.

Different to the usual care

The visits at 6 and 12 months are standard visits. At this age, all premature children are monitored in the neonatal centre, so these do not constitute additional visits. The questionnaires and the monthly e-mails are additional, however. What's more, the adjustments to your child's oxygen are also different: this happens using the data from the saturation meter which we will ask you to download.

5. What is expected of you?

Participation in the trial means:

- That we will ask you and your doctor to observe the agreed saturation limit
- That we will ask you to keep a note of any admissions, doctors' visits and complaints in an online diary
- That in some hospitals, an additional test will be conducted: a lung function test which involves wearing a mask on the face.

6. Potential detrimental effects

This trial is being conducted because we don't know what's best for children with BPD: a lower limit of 90% or of 95%. Most hospitals currently maintain a lower limit of 90%. The benefit of this is that children are able to stop taking oxygen more quickly and don't go home with oxygen as frequently. The disadvantage could be that children and their lungs don't grow as well. Too low a volume of oxygen could also affect development. The advantage of a lower limit of 95% is that we expect children to grow better and therefore develop more healthy lung tissue. The disadvantage is that children are given additional oxygen for longer and will go home with it more frequently. Too much oxygen can also be harmful to the lungs.

7. Potential advantages and disadvantages



It is important that you weigh up the potential advantages and disadvantages carefully before deciding to take part. A higher lower limit for the oxygen may cause growth/lung growth to improve, but this isn't guaranteed.

Disadvantages of participating in the trial are: potential detrimental effects on the trial measurements.

Participation in the trial also means:

- the child may have to use oxygen at home for longer
- that you will have agreements (in relation to the lower oxygen limit, in particular) that you will have to observe.

It is important that you weigh up the potential advantages and disadvantages carefully before deciding to take part.

8. Your child's resistance

Your child could be resistant (refuse to cooperate) during the trial, in which case, the researcher would have to stop the trial straight away. It is difficult to describe exactly what resistance is. Before the start of the trial, we will discuss with you what is understood by resistance. The researcher will abide by the Code of Conduct for the Resistance of Under-Aged Patients.

9. If you do not wish to participate in or wish to stop the trial

It is up to you whether your child takes part in the trial. Participation is entirely voluntary in nature.

If you do not want your child to take part, your child will be treated for BPD in the usual manner. That means that the doctor treating your child will decide the lower saturation limit with you.

If you do decide to participate, you can change your mind at any time and stop, even during the trial. Once again, your child will be treated the usual way without having to state your reasons for doing so. However, you will need to report this to the researcher straight away. The data that has been collected up to that moment will be used for the trial.

If there is new information about the trial that is important for you, please allow the researcher to tell you. You will then be asked whether you wish to continue to take part.

10. End of the trial

Your child's participation in the trial will stop once:

- all visits are over
- you yourself decide to stop
- the researcher or your child's doctor thinks it's better if your child stops



- the authorities or the assessing medical ethics review committee decides to stop the trial.

The entire trial is over once all participants have finished.

After processing all the data, the researcher will notify you of the main results of the trial.

Because the entire trial takes three-and-a-half years to complete, it can take a while before you can expect the results.

11. Use and retention of your child's data

For this trial, it is necessary to collect and use medical and personal data relating to your child. This is necessary to answer the questions asked in this trial and to publish the results.

Confidentiality of your child's data

To protect your child's privacy, each trial subject is given a code which is stated on the data. The name and other personal data that could be used to identify your child are omitted. The researcher is the only person who knows your child's code. The key for the code remains with the researcher. Even in reports about the trial, only that code is used.

Access to the data

Some people may view your child's medical and personal data to verify whether the trial has been conducted properly and reliably. General information about this can be found in the 'Medical-scientific trials' brochure.

People who are able to view your data are: the research team, the safety committee monitoring the trial, an auditor who has been brought in by the researchers of the trial and the Dutch Health Care Inspectorate. They will keep your data confidential. When you sign the consent form, you are consenting to the collection, retention and viewing of your medical and personal data.

Data retention period

The researcher will retain your child's data for a period of 15 years in accordance with the statutory retention period.

Withdrawing consent

You can withdraw your consent to the use of personal data again at any time. This applies both to this trial and to its retention and use for any future trials. Trial data collected up to the moment you withdraw your consent will then still be used in the research.

Further information about your rights when processing data

For general information about your rights when processing your personal data, you may consult the Dutch Data Protection Authority's website (www.autoriteitpersoonsgegevens.nl).



If you have any questions about your rights, please contact the data controller responsible for the processing of your personal data, See enclosure A for contact details.

If you have any questions or complaints about the processing of your personal data, we advise contacting the trial location in the first instance. You may also contact the Data Protection Officer at the Erasmus MC or the Dutch Data Protection Authority.

Registration of the clinical trial

This trial also appears in a list of medical-scientific trials, namely the trial register (www.trialregister.nl; trial code 7347). This website doesn't contain any information that can be traced back to your child. However, the website may show a summary of the results. General information about registering trials can be found in the 'Medical-scientific trials' brochure.

12. Insurance for trial subjects

Appropriate insurance will be taken out for everyone who decides to enter this trial. The insurance covers damage caused by the trial. It does not cover all damage. **Enclosure B** contains further information about the insurance, including who you can report damage to.

13. Notifying the GP and/or treating specialist

We always send your child's GP and/or treating paediatrician a letter to tell them that your child is taking part in the trial. This is for your child's own safety. If you do not agree to this, your child will not be able to take part in this trial. The GP or paediatrician will also receive a letter concerning the 6 and 12-month visits. This is also the norm even if your child is not taking part in the trial.

14. No payment for participating

The additional tests and treatment for the trial won't cost you anything. You will not receive payment for taking part in this trial.



15. Any questions?

If you have any questions, please contact the trial team. For independent advice about taking part in this trial, please contact the independent doctor, Dr P.J.F.M. Merkus. He knows a great deal about this trial, but doesn't have anything to do with the trial.

In the event of complaints, please contact the complaints officer at your hospital. All information can be found in **Enclosure A**: Contact details.

16. Signing of consent form

Once you have had sufficient thinking time, you will be asked to decide about your child's participation in this trial. If you decide to take part and give consent, please confirm this in writing using the enclosed informed consent form. By giving written consent, you confirm that you have understood the information and agree to take part in the clinical trial.

The signatures page will be retained by the doctor treating your child. You will receive a copy of this consent form.

Thank you for taking the time to read this letter.



Enclosures to this information

- A. Contact details
- B. Information about insurance
- C. Consent form



Enclosure A: contact details for *name hospital*

Researcher at *name hospital*:

Local principle investigator.

Telephone number: xxxxx. E-mail: xxxxxx

Coordinating researcher:

Ms S.J.A. Balink, research physician at Erasmus MC - Sophia Children's Hospital.

Telephone number: +31 (0)6 500 33994. E-mail: sosbpd@erasmusmc.nl.

Independent doctor:

Dr P.J.F.M. Merkus, paediatric pulmonologist, Amalia Children's Hospital, Radboud UMC

Nijmegen. Telephone number: +31 (0)24 361 4430. E-mail: Peter.Merkus@radboudumc.nl

Complaints:

Hospital format

Data Protection Officer:

Hospital format



Enclosure B: information about insurance

Erasmus MC has taken out insurance for everyone taking part in this trial. The insurance covers damage caused as a result of taking part in the trial. This applies to damage caused during the trial or within four years of the end of the trial. Claims must be submitted to the insurer within this four-year period.

This insurance policy does not cover all damage. You will find a brief outline of the exceptions below.

The full version of these provisions are included in the Compulsory Insurance for Medical Research Involving Human Subjects Decree, which can be consulted at www.ccmo.nl, the website of the Central Committee on Research Involving Human Subjects (go to 'Bibliotheek' and select 'Wet- en regelgeving').

In case of damage, submit your claim directly to the insurer.

The insurer for this clinical trial is:

Name:	CNA Insurance Company Limited
Address:	Polarisavenue 140, 2134 JX Hoofddorp
Telephone number:	+31 (0)23 303 6004
E-mail:	Esther.vanherk@cnaeurope.com
Policy number:	10.220.695
Contact person:	Ms Esther Van Herk

The insurance offers coverage of €650,000 per trial subject and €5,000,000 for the entire trial and €7,500,000 per year for all trials conducted by the Erasmus MC.

The following damage is **not** covered by the insurance policy:

- damage caused by a risk of which you were informed in the written information. This does not apply if the materialisation of the risk is more severe than foreseen or if materialisation of the risk was highly unlikely.
- damage to your health that would also have materialised if you had not entered the clinical trial;
- damage as a result of failure to follow directions or instructions or failure to follow these in full;
- damage to your descendants caused by an adverse effect of the trial on you or your descendants;
- damage caused by an existing treatment method in the case of research into existing treatment methods.



Enclosure C: Consent form for parents or guardians

Additional oxygen for BPD

I have been asked to give my consent to my child's participation in this medical-scientific trial:

Name of child:

Date of birth: __ / __ / __

- I have read the information letter for parents/guardians. I was also able to ask questions. My questions have been answered satisfactorily. I had enough time to decide whether or not to enter my child in the trial.
- I know that participation is voluntary. I also know that I may decide to withdraw my child from the trial at any time, without having to state any reasons for doing so.
- I give my consent to the GP/paediatrician treating my child being informed that my child is taking part in this trial.
- I give my consent to the requesting of information from the paediatrician treating my child concerning my child's hospital admissions.
- I am aware that some people are able to view my child's data. The people in question are specified in this information letter.
- I give my consent to the use of the data in the manner and for the purposes stated in the information letter.
- I give my consent to my child's data being retained at the trial location for a period of 15 years after this trial has finished.
- I give my consent to the use of my e-mail address, only for this trial.
- I **do***
 do not
give my consent to my child being contacted again about a follow-up trial once this trial has ended.
- I agree to my child taking part in this clinical trial.

Name of parent/guardian 1:

Signature:

Date: __ / __ / __

E-mail address:

Name of parent/guardian 2:

Signature:

Date: __ / __ / __

E-mail address:



I hereby declare that I have notified in full the above-mentioned person/persons about the named trial.

If any information were to emerge during the trial that could affect the parent's or guardian's consent, I shall notify him/her in due time.

Clinical researcher's name (or his/her representative):

Signature:

Date: __ / __ / __

Additional information has been provided by:

Name:

Position:

Signature

Date: __ / __ / __

* Place a cross next to that which is applicable.