

# **Subject information for participation in medical scientific research**

## **The effect of discontinuing the use of acenocoumarol or phenprocoumon on the rate of degradation of elastic fibers in the body**

Dear Sir/Madam,

You are asked to take part in a medical-scientific study.

Participation is voluntary. Participation requires your written consent. You have received this letter, because shortly you will stop using your blood thinners (acenocoumarol or phenprocoumon) from the anticoagulation clinic. You may completely stop using blood thinners or you may switch to another type of blood thinners.

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 can also ask the independent expert, who is mentioned at the end of this document, for additional information. You may also discuss it with your partner, friends or family.

Additional information about participating in a study can be found in the enclosed general brochure on medical research.

### **1. General information**

This study is being carried out by the Canisius Wilhelmina Hospital (CWZ).

Medical Research Ethics Committee region Arnhem and Nijmegen has approved this study. General information about the assessment of research can be found in the general brochure on medical research.

### **2. Purpose of the study**

The department of pulmonary diseases of the Canisius Wilhelmina Hospital is investigating the influence of the blood thinners 'acenocoumarol' and 'phenprocoumon' on the degradation rate of elastic fibers in the body. Elastic fibers are important for the proper functioning of the lungs and blood vessels.

### 3. Background of the study

The lungs, blood vessels and skin largely consist of elastic fibers. In every person, there is a breakdown of these fibers throughout life. In healthy people elastin degradation takes place slowly and in people with COPD the degradation rate is increased. The rate of degradation can be measured by the determination of a particular substance in your blood ('desmosine'). This substance is found in everyone's blood, but the levels of desmosine are different in each person.

From previous studies, there are some indications that vitamin K protects the elastic fibers from degradation. So we expect that persons with a high vitamin K content in the body have a lower degradation rate of elastic fibers than people with a low vitamin K content. The blood thinners 'acenocoumarol' and 'phenprocoumon' inhibit vitamin K, thereby reducing the overall vitamin K content in the body. When you stop these blood thinners, vitamin K levels will increase again. We would like to investigate if the discontinuation of these blood thinners results in a lower degradation rate of elastic fibers. This has not been investigated before. It does not matter whether you have a pulmonary disease (such as COPD) or not.

### 4. What participation involves

If you participate, this includes the following:

#### Questionnaire

Using a short questionnaire, we would like to ask you some questions about the reason why you use blood thinners, the duration of anticoagulation treatment, smoking and the use of medicines. Filling in the questionnaire takes about five minutes. The questionnaire will be sent by mail.

#### Visits and measurements

This study requires that you will visit the Canisius Wilhelmina Hospital for drawing blood 2 times in a period of 6 months

- The first time is during one of the last of your regular visits of the anticoagulation clinic, when you still use blood thinners. At this moment, blood is already drawn to determine the thickness of the blood. Therefore, you do not have to visit the hospital an extra time and no additional needle stick has to take place. Two extra tubes of blood will be drawn. For this purpose you can visit the Canisius Wilhelmina Hospital on working days between 8 and 17 hours. It is also possible to visit some of the outer posts of the anticoagulation clinic, but only at the times you will find in the schedule below.
- The second visit is six months after discontinuation of the blood thinners (acenocoumarol or phenprocoumon). To remind you of this, you will receive a letter in about 6 months. We ask you to visit the anticoagulation clinic an additional time and one tube of blood will be drawn for the purpose of scientific research. You do not need to make an appointment, but you can

visit the CWZ on working days between 8 and 17 hours. It is also possible to visit some of the thrombosis posts for drawing the tube of blood, but only at the times you will find in the schedule below. If it is not possible for you to visit the CWZ or one of the outposts, blood can also be drawn at home. You can contact the researcher for this.

We use the extra tubes of blood to determine the degradation of elastic fibers in the laboratory. We also want to determine a particular gene (hereditary material), which provides information about the extent to which your body re-uses vitamin K.

Appendix C describes what tests will take place during each visit.

## **5. What is expected of you**

In order to carry out the study properly, it is important that you follow the study instructions.

The study instructions require that you:

- Visit the anticoagulation clinic after six months for drawing one tube of blood. You will receive a reminder for this visit.

It is important that you contact the investigator:

- if you start again with blood thinners (acenocoumarol or phenprocoumon)
- if you no longer want to participate in the study.
- if your contact details change.

## **6. Possible discomforts**

If you participate the study blood will be drawn one additional time. Drawing blood may be painful or cause some bruising.

In total, we will take 35ml of blood from you. This amount does not cause any problems in adults. To compare: a blood donation involves 500 ml of blood being taken each time.

## **7. Possible advantages and disadvantages**

It is important that you properly weigh up the possible benefits and disadvantages before you decide to join.

You will not personally benefit from participation in this study. Your participation may contribute to increased knowledge about the effects of blood thinners (acenocoumarol or phenprocoumon) on the degradation rate of elastic fibers in the body.

There are few disadvantages of participation in the study. There is an additional drawing of blood, which may be painful or cause some bruising.

Participation in the study also means that you have to visit the anticoagulation clinic of the CWZ one additional time. You are also invited to fill in one questionnaire, which will take approximately five minutes.

All these aspects have been described above under points 4, 5 and 6.

## **8. 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 to participate in the study. Participation is voluntary.

If you do participate in the study, you can always change your mind and decide to stop at any time during the study. You do not have to give a reason why you wish to withdraw, but you need to inform the investigator immediately.

The data collected until that time will still be used for the study. If you want, any bodily material collected can be destroyed.

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

## **9. End of the study**

Your participation in the study stops when

- you have completed all the visits as described under point 4
- you choose to stop
- the investigator considers it best for you to stop

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.

## **10. Usage and storage of your data and bodily material**

For this study it is necessary to collect and use your bodily material (blood samples) and medical and personal data. Each study subject will receive a code that will be marked on the

blood samples and the data. Your name and other personal data that could directly identify you will then be deleted.

### **Your data**

All your data will remain confidential. The investigators are the only people who will know which code you have. The key to the code will stay with the investigator. In the reports about the study only this code will be used.

Some people may access your medical and personal data. This is to check whether the study has been conducted in a good and reliable manner. General information about this can be found in the general brochure on medical research.

People who may access your data are the study team and the Healthcare Inspectorate. They will keep your data a secret. If you sign the consent form, you consent to your medical and personal data being collected, stored and accessed.

The investigator will store your data for 15 years.

### **Your bodily material**

Of the blood samples, a part is stored in the laboratory of the Canisius Wilhelmina Hospital.

### **Future use of data and/or bodily material**

We will not keep your blood samples. After we have determined the degradation rate of elastic fibers and the levels of vitamin K, we will destroy the blood samples.

This study is listed in a clinical trial registry called Clinical Trials ([HYPERLINK "http://www.ClinicalTrials.gov"](http://www.ClinicalTrials.gov)}), as required by the US law. This website does not contain any information that can identify you. The website may contain a summary of the results. You can find this study under (...)

## **11. Study subject insurance**

This study is not associated with any risks for you. The medical ethics committee region Arnhem-Nijmegen has therefore decided that the Canisius Wilhelmina Hospital does not need to take out additional insurance.

## **12. No compensation for participation**

The extra collections of blood samples for the study are free of charge for you. You will not be paid for your participation in this study. However, you will receive a fee for your (extra) travel expenses

## **13. Any questions?**

If you have any questions, please contact mrs. L. Bloem-de Vries, MD, physician of the anticoagulation clinic, or mr. R. Janssen, MD, PhD, pulmonologist in the Canisius Wilhelmina Hospital. If you would like any independent advice about participation in this study, you may contact mr. S. Simons, MD, PhD. He knows about the study but is not involved in it.

If you have any complaints, you may contact the complaints' committee at the Canisius Wilhelmina Hospital. All the relevant details can be found in **Appendix A**: Contact details.

## **14. 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 give permission, we will ask you to confirm this in writing on the appended consent form. By your written permission you indicate that you have understood the information and consent to participation in the study. The signature sheet is kept by the investigator. You will get a copy or a second copy of this consent form.

Thank you for your attention.

## **16. Appendices to this information**

- A. Contact details
- B. Overview/description of study procedures
- C. Informed Consent Form
- D. Medical Scientific Research Brochure. General Information for Study Subjects (version September 9, 2014)

## **Appendix A: contact details**

During office hours you can contact:

### **Principal investigators:**

Mr. R. Janssen, MD, PhD, pulmonologist  
Canisius Wilhelmina Hospital, department of pulmonary diseases  
Phone: +31 (0)24 3658755.

Mrs. L. Bloem -de Vries, MD, physician and head of Committee Anticoagulation  
INR Anticoagulation Clinic – Canisius Wilhelmina Hospital  
Phone: +31 (0)24 365 5173

### **Independent doctor:**

Mr. S. Simons, MD, PhD, pulmonologist  
Gelre Ziekenhuizen, department of Respiratory Medicine  
Phone: +31 ( { HYPERLINK "tel:%2B31555818412" \t "\_blank" } )

You can contact Mr. Simons, MD, PhD, for information and advice regarding this study. He is not involved in the conduct of the investigation.

### **Complaints Board:**

All CWZ employees are committed to providing you with good professional care. Still, you may be dissatisfied with something.

You can contact the customer service in a variety of ways:

E-mail: [customer.service@cwz.nl](mailto:customer.service@cwz.nl)

Phone: +31 (0) 24 365 73 00

Postal: Response Number 90, 6500 WL Nijmegen

Available from Monday to Friday from 9:00 to 13:00

### **Hospital Address:**

Canisius Wilhelmina Hospital  
Weg door Jonkerbos 100  
6532 SZ Nijmegen  
Phone: +31 (0) 24 365 76 57

## **Appendix B – Overview of tests**

If you participate in the research, this will include the following:

1. You will receive a short questionnaire by mail within a month. Filling in this questionnaire takes about 5 minutes. You can return this questionnaire to us by mail.
2. During one of the the last visits to the anticoagulation clinic, two extra tubes of blood will be taken. At this moment, blood is already drawn to determine the thickness of your blood. Therefore, you do not need to visit the anticoagulation clinic an additional time and no additional needle stick has to take place.
3. Half a year after stopping acenocoumarol or phenprocoumon, we ask you to visit the anticoagulation clinic once for drawing one tube of blood. This blood sample is used for the purpose of scientific research.

## Appendix C: Subject Consent Form

The effect of stopping acenocoumarol or phenprocoumon on the rate of degradation of elastic fibers in the body

- 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 know that some people can access my data. These people are listed in this information sheet.
- I consent to my data and blood samples being used in the way and for the purpose stated in the information sheet
- I consent to my data being stored at the research location for another 15 years after this study.
- I  **do**  
 **do not** consent to being contacted again after this study for a follow-up study
- I want to participate in this study.

Name of study subject:

Signature:

Date: \_\_ / \_\_ / \_\_

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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 him/her of this in a timely fashion.

Name of investigator (or his/her representative):

Signature:

Date: \_\_ / \_\_ / \_\_

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\* Delete as appropriate.