Patient information leaflet for adults

Efficacy, Safety and Tolerability of 0.08% PHMB eye drops in comparison with 0.02% PHMB + 0.1% propamidine eye drops in patients with *Acanthamoeba* keratitis

Official title:	*Randomized, Assessor-Masked, Active-Controlled, Phase 3 Study to Evaluate Efficacy, Safety and Tolerability of 0.08% Polyhexamethylene Biguanide (PHMB) Ophthalmic Solution in Comparison with 0.02% PHMB + 0.1% propamidine Combination Therapy in Subjects Affected by Acanthamoeba keratitis.*
Protocol number:	043/SI
Sponsor:	SIFI
Principal Investigator:	John KG Dart

Dear Patient OR Patient's Parent/Guardian,

If you are a parent/guardian of a minor patient legally incapable of giving consent and you are the one to provide the consent on behalf of the minor patient (your child), the word "you" in this consent refers to the child you are representing. If you are providing consent for a minor, your consent will be effective only if the minor gives his/her assent to participate (if capable to understand).

You are invited to take part in a Medical Research Study.

Participation is voluntary and requires your written consent. You have received this letter because you have been diagnosed with suspected *Acanthamoeba* keratitis (AK).

Before you decide whether you want to participate in this study it is important for you to understand why the research is being done and what it will involve. Please read this information carefully and ask the study doctor for an explanation if you have any questions. You may also discuss it with others, for example your treating ophthalmologist, partner, friends or family.

1. Background of the study

Acanthamoeba keratitis (AK) is a rare infectious eye disease that can become severe and seriously debilitating. The infection is caused by *Acanthamoeba* - a common protozoan present in soil, air and water.

85% of AK cases occur in contact lens wearers and the remaining cases after exposure to other sources of *Acanthamoeba* contamination. The incidence is low, with approximately 1 in every 100.000 contact lens users in the EU affected. However, for patients it is an often devastating ocular infection with a prolonged painful course, causing vision deterioration, and leading to blindness without proper treatment.

Symptoms vary from patient to patient, and often resemble other eye infections. The most commonly reported symptoms include eye redness, blurred vision, light sensitivity, eye

irritation, excessive tearing, and severe eye pain. *Acanthamoeba* keratitis can last for several months and over a year in about 25% of cases.

The trial drug PHMB (also known as polyhexanide and polyhexamethylene biguanide) was introduced in the early 1990's as an unlicensed eye drop for this disease because it was known to be effective against *Acanthamoeba.* Although it is not a licensed medicine it is widely used, in low concentrations, as a disinfectant in swimming pools, in cosmetics, and as a surface disinfectant for human use in surgery and wound cleaning.

This study is part of the European research project "Orphan Drug for Acanthamoeba Keratitis" (ODAK) that is led by SIFI, an Italian company specialized in eye care products. The ODAK project is partially funded by a grant from the European Commission. There is a lot of information about AK, and this project, on the ODAK website: http://www.odak-project.eu/en/

In this study, 130 AK patients from different European countries will participate.
A Medical Research Ethics Committee has approved this study.

2. Purpose of the study

There are no approved drugs worldwide for the treatment of AK (an approved drug is one that has been validated for use by the relevant authority of a government). Approval requires adequate information on safety and effect. However, drugs can be used without approval if there is no approved alternative. This is the current situation of the drugs used for AK.
Currently the most commonly used treatment for AK is the combination therapy of 0.02% PHMB with 0.1% propamidine taken as eye drops .

The purpose of this study is to investigate the safety and efficacy of AK treatment using 0.08% PHMB eye drops as a single therapy (known as monotherapy). As part of the ODAK development plan, PHMB 0.08% has been tested in the laboratory, on animals, and in one clinical trial with 90 healthy volunteers. It was proven to be safe and well-tolerated by both animals and healthy volunteers. Information regarding potential side effects is described at chapter 6: *Possible Side Effects and Discomforts,* of this document.

In this study, the efficacy and safety of 0.08% PHMB eye drops given as **monotherapy** will be compared to the efficacy and safety of the commonly used **combination therapy** of 0.02% PHMB with 0.1% propamidine eye drops.

3. What participation involves

Frequency of visits
The frequency of visits in this study will be the same as you may have with normal standards of care for this disease. However, your doctors might feel that they need to see you more often than the planned study visits to assess your response to treatment, which will require additional visits that are not part of the study.

Screening
We will first evaluate your suitability to participate in this study. The study doctor will do an eye examination to confirm the AK diagnosis. This includes both the use of a special microscope to identify the amoeba, and also the collection of some tissue from the corneal surface. Cornea tissue collection and microscopy is optional if this has already been done

within 7 days prior to the screening visit, as part of your standard care. The study team will also measure your blood pressure and heartbeat and will do blood and urine tests. In addition, you will be asked to complete two questionnaires. The study doctor will further ask you about your medical history and the use of previous and current medication. Fertile women will have a pregnancy test.

Screening sometimes reveal findings that require further medical examination. We will always tell you about these findings. Further medical examination may be done by your GP or specialist.

Treatment
You will need to use the study medicines for a maximum of 12 months or until your AK is cured (whichever is earlier).

In this study, all patients will be equally divided in two treatment groups:

- Monotherapy: 0.08% PHMB (in a vial) and placebo* (in a bottle).
- Combination therapy: 0.02% PHMB (in a vial) and 0.1% propamidine (in a bottle).

*Placebo looks like the other treatment (propamidine) but contains no drug.

Which of these treatments you use will be determined by chance (like the flip of a coin). Neither you nor the study doctor will know which treatment you are receiving (masked study).

The daily dosing frequency will range and decrease over time from 16 drops to 4 drops, of each solution, during daytime. In **Appendix C:** *Overview of study procedures*, these dosing periods are described. This timeframe and dosing frequency are the same, or fewer than, the frequencies usually used for treating this disease.

Other medications, including steroid and antibiotic drops, and oral non-steroidal anti-inflammatory drugs, pain killers and sleeping tablets are permitted for use during the trial if needed.

If your condition deteriorates during the trial, to the point that you or your medical advisor think you should leave the trial, the treatment that you have been on will be revealed and you will have the option of continuing on one of the study treatments outside the trial. If you wish to use 0.08% PHMB drops you will be asked to continue with trial visits to allow us to collect safety data.

Visits and tests
What follows describes the examinations in general use for this disease, in specialist centres for treating eye infections. There are no additional investigations unique to this study.

The study visits will take place in a hospital participating in this trial; contact details can be found in **Appendix A**. You will visit the hospital every week in the first month, followed by additional monthly visits until the infection is cured. When you have finished treatment, you will be asked to visit the hospital after 1 month and 3 months for a follow up check. Each visit will take 1 to 2 hours.

The following will take place:

- Your blood pressure, pulse rate and body temperature will be measured during the screening visit.
- Corneal surface cells will be collected at the initial visit, and later if your condition deteriorates, to identify *Acanthamoeba*. You will receive local anaesthetic drops for this procedure which is painless. However, after the anaesthetic wears off, mild to severe pain can be experienced, the severity and duration of the pain varies.
- Your blood and urine will be tested to check for your general health status at the start and at the end of the study.
- If applicable, urine pregnancy tests will be done at every month, during the visits.
- You will be asked to complete two questionnaires about your general health status (EQ-5D) and your visual ability (VFQ-25) at every visit.
- Eye examinations will be performed at every visit.

Eye examinations
At each visit your vision will be measured by reading from a letter card and your eye pressure will be measured painlessly. Your doctor will use an instrument called a slit lamp microscope for a detailed eye examination. This instrument magnifies the different parts of the eye and uses a bright light. Pupil dilating drops may be used; these may cause blurred vision for up to 4 hours after the test.

A confocal microscope will be also be used initially, to identify Acanthamoeba in your cornea. Repeat examinations with this instrument may be recommended.

Appendix C describes which procedures take place at each visit.

4. What is expected of you

In order to carry out the study properly and for your own safety, it is important that you follow the study instructions.

The study instructions require that you:

- Administer the eye drops as directed.
- Do not participate in another medical study.
- Keep appointments for visits.
- Carry your participant card for the study with you. This card states that you are participating in this study. It also states who to contact in the event of an emergency. Show this card if you visit any other doctor or emergency department.

It is important that you contact the study doctor:

- Before you start using other medicines (even if they are homeopathic or natural remedies, vitamins and/or over-the-counter medicines).
- If you are admitted to hospital or are going for treatment there.
- If you suddenly develop any health problems.
- If you no longer want to participate in the study.
- If your contact details change.

PREGNANCY AND BREASTFEEDING

PHMB is widely used and approved for human use in several disinfectant solutions (for example, in surgery and for contact lenses). Because the effects of PHMB in eye drops on unborn babies, or a nursing infants, are not known any female who is pregnant or breastfeeding cannot be included in this study. Sufficient contraceptive precautions must be taken to prevent you becoming pregnant during the study.

If you are a female and become pregnant, or suspect that you have become pregnant while in the study, you must stop taking the study drugs and notify your study doctor immediately. Your study doctor will be asked to follow the outcome of your pregnancy.

Women of Childbearing Potential

Females of childbearing potential will have a urine pregnancy dipstick test taken to check for pregnancy every month. The results must be confirmed as negative (not pregnant) at the screening visit in order to be included for the study, and then negative at the monthly tests in order to continue study participation.

While using study drugs, and for 30 days after their last use, it is important to prevent pregnancy. All women who are able to become pregnant, and men or women who have not been sterilised (by hysterectomy, vasectomy, or bilateral tubal ligation), must EITHER choose from the methods of birth control listed below OR must completely avoid sexual intercourse, with a person of the opposite sex.

Recommended contraceptive methods are:

a. Intrauterine device (IUD) or intrauterine system in place for at least 3 months prior to first dose.
b. Subject and/or partner using a double-barrier method including, but not limited to, at least two of the following methods combined: male condom, female condom, diaphragm, cervical cap, and spermicide.
c. Partner has had a vasectomy ≥6 months prior to first dose.
d. Stable hormonal contraception (with approved oral, transdermal, or depot regimen) for at least 3 months prior to first dose.

Your Study Doctor or personal health care provider can discuss the benefits and disadvantages of these birth control options with you.

It is important that you use the same birth control method throughout the study and for at least 30 days following your last dose of PHMB.

<u>Women of non-childbearing potential are identified as follows:</u>

1. A female of uncertain child bearing potential may have a follicle stimulating hormone (FSH) serum test performed to confirm whether or they have the potential to get pregnant.

2. Pre-menopausal women must have undergone one of the following sterilization procedures at least 6 months prior to the first PHMB dose:
   a. hysterectomy
   b. bilateral oophorectomy
   c. bilateral tubal ligation
3. Postmenopausal women should have had no periods for at least 1 year prior to the first PHMB dose.

5. Possible side effects and discomforts

Based on previous observations in studies with PHMB, the potential side effects that can be expected are spotty erosions of the cornea and/or conjunctiva. This may give a sensation of stinging, or the feeling as if you have something in your eye. You may also get blurred vision and a red eye. In the previous volunteer study these symptoms disappeared a few days after starting treatment, or when the treatment was discontinued or. If these symptoms bother you (persist for more than a few minutes after the drops have been put in or are difficult to tolerate on application), contact the study doctor or study coordinator for advice.

The study medicine may also have side effects that are still unknown.

Comparator
The 0.02% PHMB + 0.1% propamidine combination therapy may also cause the same side effects. This combination has been the mainstay of treatment worldwide since the introduction of PHMB in 1992. Propamidine was introduced in 1985. The most common side effects are stinging, defects or erosion of the cornea surface and eye redness. These are not common at low dosing frequency during maintenance therapy (4 to 6 drops per day). Corneal inflammation has been reported with propamidine.

Cataract, iris thinning, poor vision, and corneal ulcers are all complications of AK. Some physicians have raised concerns that these complications may also be related to the treatment with PHMB and/or propamidine. However, there have been no signs of these complications in any of the toxicity studies carried out on PHMB before this trial. Propamidine has been licensed as an eye drop in many countries since the 1990's.

Blood tests
A blood test will be taken at the first and last study visit. This is a standard procedure that does not normally cause any problems. Taking blood may be painful or cause some bruising. During these 2 visits, we will take a total of 17 mL of blood from you. This amount does not cause any problems in adults. This is equivalent to 3 teaspoonfuls.

You can find more information about study treatment and procedures in **Appendix C**.

6. Possible advantages and disadvantages

It is important that you consider the possible benefits and disadvantages before you decide to participate. The study medication may treat your eye infection but this is not certain. Your disease may return or worsen at any time during this study.

Disadvantages of participation in the study may be:

- The time involved for you.
- Visits to the hospital
- The discomfort of the corneal scraping (collection of corneal cells) although this is a part of normal treatment for the disease.
- Instructions you need to follow.
- Using the study medicine according to strict procedures.
- Possible side effects.
- Possible discomforts of the tests or evaluations in the study (all normally carried out for treatment of this disease).

All these aspects and additional details have been described above under points 2, 3 and 4.

7. 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 completely voluntary.

If you do not want to participate, you will be treated as is usual for your eye infection. The study doctor can tell you more about the various treatment options that exist and the benefits and risks associated with them.

If you do participate in the study, you can always change your mind and decide to stop, at any time during the study. You will then be treated as normal for your eye infection. You do not have to say why you are stopping, but you do need to tell the study doctor immediately so your doctor can start with an alternative treatment. The study doctor will ask if you are willing to undergo a final study visit. The data collected until that time will still be used for the study.

If there is any new information about the study that is important for you, the study doctor will let you know. If you want to continue participating in the study, after any new information becomes available, you will need to sign an updated informed consent form.

8. End of the study

Your participation in the study stops when:

- You have completed all the visits as described in **Appendix C**.
- You choose to stop.
- You become pregnant.
- The infection responds poorly to treatment.
- You have been treated for the maximum period of 1 year after start of the study treatment.
- The study doctor considers it best for you to stop.
- The Medical Research Ethics Committee, the government or SIFI, as Sponsor of the clinical study, decide to stop the study.

The study is concluded once all the participants have completed the study. Participants who have not been cured after the maximum treatment period of 1 year will be offered the best clinically available treatment, which may include PHMB 0.08% drops. The study doctor will discuss the options for further medical care with you.

After the last visit of the last patient, all data will be reviewed and analysed, and, the study doctor will inform you about the most important results of the study. The study doctor will also tell you which treatment you received. If you do not want this to happen, please tell the study doctor. He/she will only tell you if you wish to know.

9. Usage and storage of your corneal tissue, blood samples and data

For this study it is necessary to collect and use your corneal tissue, blood samples and your medical and personal data. These tissues are used for routine tests and are destroyed on completion of the tests. Each study subject will receive a code that will be linked to the results

of these investigations. Your name will be deleted and your data is anonymized using an identification code (ID). Only your year of birth will be reported.

Your data under the GDPR (General Data Protection Regulation)
SIFI is the sponsor for this study based in Italy. SIFI will be using information from you and your medical records in order to undertake this study and will act as the data controller for this study. This means that SIFI is responsible for looking after your information and using it properly. SIFI will keep identifiable information about you for 15 years after the study has finished.

Your rights to access, change or move your information are limited, as SIFI needs to manage your information in specific ways in order for the research to be reliable and accurate. If you withdraw from the study, SIFI will keep the information about you that SIFI has already obtained. To safeguard your rights, SIFI will use the minimum personally-identifiable information possible.

Moorfields Eye Hospital will collect information from you and your medical records for this research study in accordance with our instructions.

Moorfields Eye Hospital will keep your name, NHS number and contact details confidential and will not pass this information to SIFI. Moorfields Eye Hospital will use this information as needed, to contact you about the research study, and make sure that relevant information about the study is recorded for your care, and to oversee the quality of the study. Certain individuals from SIFI and regulatory organisations may look at your medical and research records to check the accuracy of the research study. SIFI will only receive information without any identifying information. The people who analyse the information will not be able to identify you and will not be able to find out your name, NHS number or contact details.

Moorfields Eye Hospital will keep identifiable information about you from this study for 15 years after the study has finished.

You can find out more about how we use your information at https://www.moorfields.nhs.uk/content/how-we-use-your-information and/or by contacting the Data Protection Officer ('DPO') from the Information Governance Department of Moorfields Eye Hospital at 020 7253 3411 or moorfields.ig@nhs.net.

Your corneal tissue
Your corneal tissue will be collected by corneal scraping for diagnostic purposes only and destroyed after the test is complete.

A description of this clinical study will be available on www.clinicaltrialsregister.eu. This website does not contain any information that can identify you. A summary of the results may be placed on the website. You will have access to this website. You will find this study under **EudraCT number:** 2016-001823-30.

10. Study subject insurance

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

11. Will my treating physician be informed if I participate?

We will send your GP or ophthalmologist a letter to let them know that you are participating in the study. This is for your own safety. If you do not agree to this, you cannot participate in this study.

12. Costs of the study

The treatment for the study and all study procedures are free of charge for you. You will not be paid for your participation in this study. You will receive an expense allowance (for public transport travel costs) for your participation in this study.

13. Any questions?

If you have any questions, please contact the study doctor or the study co-ordinator.
If you have any complaints, you may contact the [complaints' officer/committee at your hospital/institution/other]. All the relevant details can be found in **Appendix A**: *Contact details*.

Thank you for your attention.

14. Appendices to this information

A. Contact details for Moorfields Eye Hospital, City Road Branch
B. Insurance information
C. Overview of study procedures
D. Informed Consent Form

Appendix A: contact details for Moorfields Eye Hospital, City Road Branch

The study will be conducted at:
Moorfields Eye Hospital, 162 City Road, London EC1V 2PD
Telephone: 020 7253 3411

About the Research project and your participation: if you have any questions before or during the research, about the details of the research project and how these affect you, you can call the doctor or nurse at the following number:

Principal Investigator:
Name: John Dart
Tel: 020 7566 2320 09.00-17.00 Monday to Friday
Email: j.dart@ucl.ac.uk

Study Nurse:
Elaina Reid
Tel: 07718 669373
Email: Elaina.Reid@moorfields.nhs.uk

Independent medical expert (not participating in the study)
Richard Wormald
Tel: 020 7566 2256
Email: Richard.Wormald@moorfields.nhs.uk

Data Protection Officer ('DPO')
Information Governance Department of Moorfields Eye Hospital
Tel: 020 7253 3411
Email: moorfields.ig@nhs.net

Complaints:
Patient advice and liaison service (PALS)
Tel: 020 7566 2324/2325
Email: pals@moorfields.nhs.uk

For urgent medical problems (caused by a flare up of the disease): contacts are detailed here. Please do not contact your General Practitioner, who will not be able to help. Please state that you are an *Acanthamoeba* keratitis study patient.

From 09.00 to 17.00 hours, 7 days a week: the Corneal and External Disease Fellow "On call" at Moorfields Eye Hospital, City Road Branch, EC1V 2PD. Tel: 020 7253 3411

Outside these hours: call, or attend, the Accident and Emergency Department at Moorfields Eye Hospital, City Road Branch, EC1V 2PD (open 24 hours). Tel: 020 7253 3411

Appendix B: Insurance Information

Insurance has been taken out by sponsor for everyone participating in this study. The insurance covers damage due to participation in the study. This applies to damage manifesting during the study or within four years of the end of the study. You must notify the insurance company about the damage within those four years.

The insurance does not cover all damages. The damages that are not covered are listed briefly at the end of this text. This is set out in the Medical Research (Human Subjects) Compulsory Insurance Decree.

In the event of damage please contact the insurance company [or claims adjustor] directly. Let the study doctor know if you think that your participation in this study has caused damage to you. The study doctor will inform you whether you can get medical care for your problem and how you can get this. If you feel that you have been injured, please contact the study coordinator on phone number 0207 566 2821.

The insurance company for the study is:	
Name:	HDI Global SE –
UK Address:	10 Fenchurch Street London EC3M 3BE United Kingdom
Telephone number:	+44 (0)20 7696 80999
Policy number:	390-01164225-14000

The insurance offers a cover of GBP 3,000,000 for the entire study.

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

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

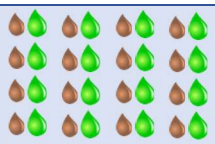
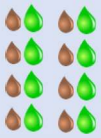
Appendix C: Study Treatment & Procedures

Intensive treatment schedule used for the first 19 days and for the treatment of any relapse of disease.

- **Days 0 to 5:** 1 drop of each solution every hour (16 times/day) during daytime
- **Days 6 to 12:** 1 drop of each solution every 2 hours (8 times/day) during daytime
- **Days 13 to 19:** 1 drop of each solution every 3 hours (6 times/day) during daytime
- **Days 20 to resolution:** 1 drop of each solution for 4 times during daytime

Eye drops are administered directly from the vial or bottle into the eye. Instructions how to apply the eye drops correctly are given by the doctor and/or nurse prior to start of the first application and thereafter at each hospital visit.

Dosing frequency per day is also shown in the following schedule:

Period	Days 0 to 5	Days 6 to 12	Days 13 to 19	Days 20 to resolution
Instructions	16 times per day; 1 drop of each solution every hour (32 drops in total)	8 times per day; 1 drop of each solution every 2hours (16 drops in total)	6 times per day; 1 drop of each solution every 3 hours (12 drops in total)	4 times per day; 1 drop of each solution (8 drops in total)
Drops per day = placebo or 0,1% propamidine = 0,02% or 0,08% PHMB				

STUDY PROCEDURES

Visit 1 – from two days before to the day of the randomization:

- Signing the consent form
- Discussion about your personal information, including medical history, and previous and current medication usage
- Measurement of blood pressure, heartbeat and body temperature.
- Blood draw (8.5 mL)
- Urinalysis
- Urine Pregnancy test (women of childbearing age only)
- Eye examination, including:
  - Examination with special microscope
  - Collection of cornea tissue
- Discussion about side effects

Visit 2 – Day 0 (day of randomization - may be combined with visit 1):

- Completing of two questionnaires (EQ-5D and VFQ25)
- Assigning study treatment (randomization).
- Dispensing and administration of study medicine at the hospital
- Eye tests
- Photography of affected cornea
- Discussion about side effects and current medication

Visit 3 – Day 7

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Administration of study medicine at the hospital
- Eye tests

Visit 4 – Day 14

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Administration of study medicine at the hospital
- Eye tests
- If applicable; start introduction of adjunction medication

Visit 5 – Day 21

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Administration of study medicine at the hospital
- Eye tests

Visit 6 – Day 30

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Dispensing and administration of study medicine at the hospital
- Eye tests
- Photography of affected cornea
- Urine Pregnancy test

Visit 7, 8, 9 etc – from Day 60 and every month thereafter until 30 days after the end of treatment

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Dispensing and administration of study medicine at the hospital
- Eye tests
- Urine Pregnancy test

Additional visits that may be necessary if a relapse occurs between these visits

- Completing of two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Dispensing and administration of study medicine at the hospital
- Eye tests
- Collection of corneal tissue
- Urine Pregnancy test

End of Study Visit - 90 Days after end of treatment OR Early Termination of study due to poor response

- Completing two questionnaires (EQ-5D and VFQ25)
- Discussion about side effects and current medication
- Eye tests
- Photography of affected cornea
- Urine pregnancy test
- Blood draw (8.5 mL)
- Urinalysis

Appendix D: Informed Consent Form

Efficacy, Safety and Tolerability of 0.08% PHMB eye drops in comparison with 0.02% PHMB + 0.1% propamidine eye drops in patients with Acanthamoeba keratitis

	Patient initials
1. I have read the subject information form and I understand the information. I was also given the opportunity to ask further questions. My questions have been answered to my satisfaction. I had enough time to decide whether to participate.	
2. I know that my 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.	
3. I give permission for my GP to be informed about my participation in this study.	
4. I know that some people can access my data. These people are listed in this information sheet.	
5. I consent to my data and corneal tissue being used in the way and for the purpose stated in the information sheet (see also section *9. Usage and storage of your corneal tissue, blood samples and data* of this information sheet).	
6. I consent to my data being stored for 15 years at the study doctor's site.	
7. I consent to my data being stored for a minimum of 15years at the sponsor of the study. This is study data without my name.	
8. For women of childbearing age: I know that I must not become pregnant during the study.	
9. For women of childbearing age: the study doctor has discussed the most suitable contraceptives for me and/or my partner with me.	
10. I agree to my data being forwarded to countries outside the European Union not governed by European guidelines for personal data protection. This must, however, be essential for the study. The data must be shared in encoded form without stating my name.	
11. I want to participate in this study.	

Subject number:

_____	_____	____ / ____ / _____
Name of adult patient OR parent/guardian	Signature of adult patient OR parent/guardian	Date

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Person who has obtained the consent

I have explained to the patient the terms of the present Information and Consent form and I have answered all questions.

_____	_____	____ / ____ / _____
Name of person who obtained the consent	Signature of person who obtained the consent	Date

Statement of the Investigator (study doctor)
I attest that the terms of this information and consent form were explained to the subject and all questions have been answered. The subject has been clearly informed about the possibility to withdraw participation without any prejudice. I commit myself along with the research team to respect what was agreed, according to the statements on this information and consent form, and I will provide a signed and dated copy to the patient prior to participation in the study.

If information comes to light during the course of the study that could affect the patient's consent, I will inform him/her of this in a timely fashion.

_____	_____	____ / ____ / _____
Name of Investigator	Signature of Investigator	Date

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