



**Study Title:** Identifying the CHARGE Gene in a Canadian Population

**Participant – Information and Consent  
Form 1 - Consenting on behalf of self**

**Investigators:** Kim Blake, MB, MRCP, FRCP(C), Paediatrician, Department of Pediatrics, IWK Health Centre

Mark Ludman, MD, FRCP(C), Medical Geneticist, Department of Pediatrics, IWK Health Centre

Jeremy Kirk, MB, MRCP, Paediatric Endocrinologist, Medical Head of the CHARGE/UK Family Support Group and advisor to Sense (UK Deafblind Charity) on CHARGE syndrome, Birmingham Children's Hospital, Manchester, UK

Isabel Smith, PhD, Psychologist, Departments of Pediatrics and Psychology, Dalhousie University/ IWK Health Centre

**Consultants:** Johane Robitaille, MD, FRCSC, Ophthalmologist, IWK Health Centre

Chitra Prasad, MD, FRCPC, FCCMG, Geneticist, Children's Hospital of Western Ontario

**Sponsor:** E. A. Baker Foundation, CNIB  
Serono Pharmaceuticals - granted £25,000 (\$57,000CAD) for genetic testing in UK

**Introduction**

We would like to invite you as an individual with CHARGE syndrome to participate in this genetic research study. You may have previously taken part in one or more clinical research studies concerning CHARGE syndrome, and you (or your parents) may have signed a consent form saying that you would be interested in being informed about future studies. You may also have contacted us directly because you are interested in participating in this study.

It is very important that you understand the purpose of the present study, how it may affect you, the risks and benefits of participating, and what you will be asked

to do, before you decide if you want to participate. This information and consent form is to help you make this decision. Participating in this study is entirely your choice, so you do not have to take part.

Questions are encouraged. If you have any questions that this form does not answer, either Dr. Blake or her research associates will be happy to give you more information.

### **Purpose of the Study**

Recently, there has been an important discovery in the genetics of CHARGE syndrome. Researchers in the Netherlands have found a large gene with defects that may be responsible for CHARGE syndrome in 75-80% of individuals with the disorder.

With blood samples from individuals with CHARGE syndrome such as you, it will be possible to compare genes to those identified in the Netherlands. By finding gene defects in our Canadian population, we will learn more about CHARGE syndrome and what causes this condition.

In one of the previous studies in which you may have participated, we identified clinical features of CHARGE syndrome. These are recorded in a database that identifies the individual with CHARGE syndrome by a code. Examples of information on clinical features are eyesight, hearing, heart problems, etc. If you did participate in this study, we will update this information over the phone with you (i.e., recent vision test results, recent heart surgeries). If you did not participate in this previous study, we will ask you about these clinical symptoms as part of the present study.

In the present study, we will also compare these clinical features with the gene defects. We may be able to answer the question, "Is there a relationship between the clinical problems such as heart defects that an individual with CHARGE syndrome has, and the specific gene defects that are present?"

### **Study Design**

Canadian individuals of all ages who have been identified as having CHARGE syndrome are invited to participate in this genetic study. This identification comes from one or more studies of CHARGE syndrome in Canada. We expect about ten participants with CHARGE syndrome at the IWK Health Centre in Halifax, and forty participants from other places in Canada.

If you did participate in the previous study mentioned above, clinical features such as hearing will be updated in the present study. You will also be asked new questions: 1) your place of birth, 2) the birthplace of both your parents 3) previous genetic testing, 4) the date of birth of both your parents, 5) date of CHARGE diagnosis, 6) heart anomalies, 7) scoliosis, 8) osteoporosis, 9)

mother's smoking, and use of alcohol, x-rays, and hair treatments during pregnancy, and 10) current province of residence.

If you did not participate in the previous study mentioned above, you will be asked about your clinical symptoms of CHARGE syndrome as part of the present study. We will request that you ask your physician to fill out a form, and from this, Dr. Blake will confirm whether the signs needed for a diagnosis of CHARGE syndrome are present. If the diagnosis is confirmed, you will be asked to provide blood samples. However, if the diagnosis is not confirmed, you will not be asked to provide a blood sample, and you will not be able to continue participating in the present study. Dr. Blake will call you to explain the diagnosis.

Blood samples will be taken from you and both of your parents (if possible). Dr. Blake or her research associates will tell you the best place to have the blood sample taken in your local area. The amount of blood needed will be approximately 20 cc (2-3 vials). Next, Dr. Blake or one of her assistants will arrange for the blood samples to be sent to the IWK Health Centre, where the analysis will begin, and then samples will be sent to a lab in the United Kingdom where the genes can be further studied.

### **Potential Harms**

The blood test may cause you some pain, and a bruise may form where the needle enters the skin. You may become distressed. However, EMLA cream (a kind of pain killer) can be put on the skin before the blood is taken so you do not feel as much pain. Dr. Blake or one of her associates can arrange with a personal contact in the laboratory you are visiting for the EMLA to be used if you decide to take part in this research study. If taking the blood is a burden, you could consider doing this at a time when you need a regular blood test or you are having an anaesthetic.

It is possible that receiving the genetic test results may affect you in a negative way. This means that you may not want to know the test results, so it is important to think about the different possible outcomes. For example, if the test is positive and shows that you carry the gene with the defects, this may affect such things as your insurance or your relationships. Therefore, you may choose (1) not to participate, or (2) participate and not receive the genetic information unless you request it at a later time. We are trying to anticipate all the possible outcomes so that you are properly informed. You may still have further questions before you are comfortable with participating in this research, and we will certainly answer those to the best of our knowledge.

### **Potential Benefits**

If a gene defect is found, this may benefit your immediate family (mother, father, brother, sister) by providing information about the cause of CHARGE syndrome.

This information may be helpful in family planning decisions for you in the future. Whether you are a patient of the IWK Health Centre, or from elsewhere in Canada, the research team will arrange for appropriate genetic counselling. Dr. Mark Ludman, who is the Head of the Medical Genetics department at the IWK Health Centre, will either provide counselling (in person or by telephone), or will arrange for counselling in your local area. The counselling will be offered before the blood sample is taken, as well as after the test results are known.

Also, if gene defects are found, and we find links between the gene and particular clinical features of CHARGE syndrome such as heart defects, this will help us better understand CHARGE syndrome and perhaps benefit other families in the future.

### **Alternatives to the Study**

Before you decide to participate in this study, you should know that you do not have to take part and have the blood test. Participation in this study is entirely your choice. Your decision whether to take part or not will have no effect on your present or future care at any hospital. You may decide not to participate. This would mean that your diagnosis would continue to be based on clinical features. This has been the way to diagnosis CHARGE syndrome until now. We still need to use the clinical features to diagnose CHARGE syndrome as the research suggests that 20% of individuals with a CHARGE syndrome diagnosis will not show the gene defect.

We do not want to disappoint individuals who have had testing and are negative for the CHARGE gene. Even if the gene shows no defect (it's normal), you certainly have CHARGE syndrome. However, a different gene may be involved and could possibly be discovered later. You may also indicate on the consent form whether you wish to be contacted about your blood sample being used in future testing, for example, if another gene is discovered. A genetic counsellor can explain all these issues further.

A genetic counsellor can also assist you with family planning decisions. Genetic counselling can be arranged even if you do not want to participate in this research. If your family does not have a genetic counsellor, counselling can be organised in your local area through your physician, or our research team can arrange counselling. So even if you do not wish to participate in this study, you may contact Dr. Blake at (902) 470-6499 to arrange for genetic counselling.

### **Withdrawal from Participation**

You may sign this consent, offer to participate, but you may decide at any time not to continue with the study. This may happen when you go for the blood tests. As mentioned above, this would not affect your present or future health care in any way.

The test results and the data on the clinical features will be kept at the IWK Health Centre for 25 years, under the supervision of Dr. Kim Blake. However, the blood and DNA samples will only be kept if you sign to give us permission to do so. If you do give us permission, the blood samples will be kept for 25 years at the IWK Health Centre under the supervision of Dr. Mark Ludman, Genetics, and Dr. Kim Blake, General Pediatrics. Samples sent to the UK will be kept for 25 years under the supervision of Dr. Jeremy Kirk. If you do not give us permission to keep the samples, they will be destroyed after the test. In order for the blood samples to be kept longer than 25 years, your permission will also be required. The blood and DNA samples, as well as the test results and data on the clinical features can be withdrawn and destroyed at any time if you desire.

During the twenty-five years in which the blood and DNA samples are stored at the IWK and in the UK, if there is any refrigerator failure resulting in damage to the samples, they will be destroyed. You will not be notified of this, should it happen.

### **Confidentiality**

Any information about you will be kept private. There will be no names used when the results are published. If the results of the study are published in the medical literature, they will not contain any information that could identify you as an individual.

Any information about you will be kept private. Only the research team will have access to your clinical details on the CHARGE syndrome database. However, in addition, the research records may be shown to the Research Office of the IWK Health Centre if they review the ethical aspects of our research. Study records (including test results) will be stored in a locked area and will be kept for a minimum of 25 years under the supervision of Dr. Kim Blake, as required by the IWK Health Centre Research Ethics Board.

The date the blood samples are drawn will be recorded in the database with the data on the clinical features. The blood samples at the IWK Health Centre and the DNA samples in the UK will be identified by a code and will have "Individual with CHARGE" and 'male' or 'female' marked on them. All three samples belonging to an individual with CHARGE syndrome, and his/her parents, will have the same code. However, the code will include "IC" for the individual with CHARGE syndrome, "PM" for the father, and "PF" for the mother. The blood and DNA samples will be anonymous, so this means that the only people who will know the names will be Dr. Blake and her research assistants. Any other people involved will only see a code, and not a name.

## **Costs and Reimbursement**

We will pay for the drawing of the blood samples, the shipment of samples, the laboratory costs, and the genetic testing. We unfortunately cannot pay costs for your travel or inconvenience.

## **Research Rights**

Your signature on this form will show that you have understood the information about the research study. Agreeing to participate in this study does not mean that you give up your rights. If you become sick or injured because of participating in this study, necessary medical treatment will be available to you at no cost to you.

By signing this form, you are not giving up any of your rights, and you are not changing the responsibilities of the investigators, or of other people involved.

If you have any questions at any time during or after the study about these rights, or about research in general, and you would like another opinion, you may contact the Research Office at the IWK Health Centre at (902) 470-8765, Monday to Friday between 9 a.m. and 5 p.m. (Atlantic Time).

## **Contact Person**

If you have any questions or concerns following your enrolment in the study, you may contact Dr. Kim Blake (paediatrician) at (902) 470-6499, or Dr. Mark Ludman (medical geneticist) at (902) 470-8754.

## **Communication of Results**

Analysis of genes from the individual with CHARGE syndrome and both parents in the laboratories at the IWK Health Centre and in the UK may take a few weeks.

The information that we give you on a named basis about you will be totally private for you. As soon as the results are known, Dr. Blake or another member of the research team will call you to ask you if you wish to know your individual test results. This information will be about the gene defects, and will only be available verbally because we are only beginning to understand the genetic aspects of CHARGE syndrome. If you wish, you will later be provided with a written summary of the general study results when the study is finished. This information will include a group summary of any links found between the gene defects and the clinical problems. If you wish to know more population results for the individuals with CHARGE syndrome, or if you do not wish to know any results now, but do at a later time, you may contact Dr. Blake.

If genetic results are found that do not relate to the present study (for example, information about your mother and/or father's genes), these results will not be available. Also, none of the results will be used for any commercial purpose.



**Study title: Identifying the CHARGE Gene in a Canadian Population:**

Participant ID: \_\_\_\_\_ Participant INITIALS: \_\_\_\_\_

**Participant (Individual with CHARGE syndrome) Consent**

I have read or had read to me this information and the authorization form. I have had the chance to ask questions that have been answered to my satisfaction before signing my name. I understand the nature of the study and I understand the potential risks. I understand that I have the right to withdraw from the study at any time without affecting my care in any way. I have received a copy of the Information and Authorization Form for future reference. I freely agree to participate in this research study.

\_\_\_\_\_  
Name of Participant – **Your name, Individual with CHARGE syndrome** (Print)

\_\_\_\_\_  
Signature of Participant – **You, Individual with CHARGE syndrome**

Date: \_\_\_\_\_ Time: \_\_\_\_\_

**STATEMENT BY PERSON PROVIDING INFORMATION ON STUDY**

I have explained the nature and demands of the research study and judge that the individual with CHARGE syndrome named above understands the nature of the study.

Name (Print) \_\_\_\_\_ Position \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

**STATEMENT BY PERSON OBTAINING CONSENT**

I have explained the nature of the consent process to the person authorized and judge that they understand that participation is voluntary and that they may withdraw at any time from participating.

Name (Print) \_\_\_\_\_ Position \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_



**If further gene testing becomes available, I consent to be contacted about my blood and DNA samples being used for further tests related to CHARGE syndrome. I understand that all samples will be anonymous, and only Dr. Blake and her research team will have access to my name.**

Name - **You, Individual with CHARGE syndrome** (Print) \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_

**I consent for my blood and DNA samples to be kept for twenty-five years for possible further tests about CHARGE syndrome (of which I will be informed and give my consent before my samples are used). I understand that all stored samples will be anonymous, and only Dr. Blake and her research team will have access to my name.**

Name - **You, Individual with CHARGE syndrome** (Print) \_\_\_\_\_

Signature: \_\_\_\_\_ Date: \_\_\_\_\_ Time: \_\_\_\_\_