



**ChildrensHospitalLosAngeles**

*International Leader in Pediatrics*

Childrens Hospital Los Angeles  
**CONSENT/PERMISSION FOR CHILD TO PARTICIPATE IN RESEARCH**

**Treatment of Growth Hormone Deficiency in Children with  
 Optic Nerve Hypoplasia**

Subject's Name:	_____	
CHLA#:	_____	Birth Date: _____

**• INTRODUCTION**

Your child is asked to participate in a research study conducted by Dr. Mark Borchert from the Division of Ophthalmology and Dr. Mitch Geffner and Dr. Nina Ma from the Division of Endocrinology at Childrens Hospital Los Angeles. Your child is currently participating in Dr. Borchert's optic nerve hypoplasia (ONH) study. This research is sponsored by The Genentech Center for Clinical Research in Endocrinology. Your child has been asked to participate in this study because he or she has abnormal lab results suggest growth hormone deficiency. It is anticipated that 21 children will participate in this study. Participation in this study is completely voluntary. Please read the information below, and ask questions about anything you do not understand, before deciding whether or not to allow your child to participate.

**• PURPOSE OF THE STUDY**

The purpose of this study is to evaluate growth and development in children with optic nerve hypoplasia (ONH) that grow normally despite not producing enough growth hormone.

Hormone laboratory testing was performed on your child upon enrollment in Dr. Borchert's ONH study. Children diagnosed with ONH are at risk for hormone deficiencies, which is called hypopituitarism. We tested your child to check if he or she had any of the hormone deficiencies that are associated with hypopituitarism. At least one of the tests that were performed suggests that your child may have growth hormone deficiency.

Growth hormone cannot be measured in a single blood test, so we test the amount of other hormones that are responsible for carrying the growth hormone through the body. These hormones are called insulin-like growth factor-1 (IGF-I) and insulin-like growth factor binding protein – 3 (IGFBP-3). The amounts of these hormones are thought to represent how much of the growth hormone is in a child's body. If one or both of these are low, then growth hormone deficiency is suspected and a hormone doctor (endocrinologist) checks to see if the child is growing normally. Children that are not growing normally are tested further for growth hormone

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deficiency with a growth hormone stimulation test. With this test, we can confirm the presence of growth hormone deficiency. However, this testing is not usually done in children who are growing normally.

Through Dr. Borchert's study of children with ONH, it has been noted that a number of children with growth hormone deficiency do grow normally. It is unclear why they grow normally or if lack of growth hormone causes other developmental problems such as obesity or developmental delay. In order to examine obesity in children who are growth hormone deficient, we will measure lipid levels in your child.

In this study, we are evaluating growth outcomes in children with ONH that are growth hormone deficient and may or may not be growing normally. We will also evaluate the relationship of GH deficiency and other hormones on the development and the effect of growth hormone treatment on the natural history of obesity in children with ONH. Your child has been asked to participate in this study because his or her lab results for IGF-I and IGFBP-3 were below normal and/or he or she is not growing normally. Your child may or may not be growth hormone deficient, and we will determine this from a growth hormone stimulation test. The purpose of this study is to determine whether or not treatment with growth hormone benefits children with ONH who are growth hormone deficient but growing normally.

- **PROCEDURES**

If you allow your child to volunteer to participate in this study, the following will take place:

- 1) A growth hormone stimulation test to check the amount of growth hormone your child actually produces. The growth hormone stimulation test that will be used is the glucagon tolerance test. Your child will be admitted to the General Clinical Research Center of Childrens Hospital Los Angeles for approximately 4 hours to perform this test. The test will be in the morning, with no food or drink after midnight before the test.

Glucagon is a naturally occurring hormone that the body produces in response to low blood sugar. Glucagon stimulates the release of growth hormone and cortisol. Cortisol is a stress hormone that the body releases in response to stress. To perform the glucagon tolerance test, a small amount of glucagon will be injected into your child's skin (upper arm). The amount of glucagon will depend on your child's weight. For example, approximately ¼ tsp will be injected if your child weighs 25lbs and approximately ½ tsp will be injected if you child weighs 50lbs. One-half teaspoon of blood will then be removed from your child's vein 5 times over the course of 3 hours. An IV (a needle in a vein) will be maintained for blood withdrawals so that your child will require only one needle stick for blood withdrawal. The blood will be used to measure growth hormone and cortisol levels. If the results of this test are inconclusive or the test is not complete, your child will return for a second growth hormone stimulation test. The need for a repeat test very rarely occurs.

Your child's thyroid hormone level will also be checked as part of the growth hormone stimulation test. However, if your child's previous thyroid test was close to being low, then the thyroid test will need be performed within two weeks of the growth hormone stimulation test. If your child's thyroid test comes back low, then the stimulation test

must be postponed until after an endocrinologist has evaluated your child for hypothyroidism (underactive thyroid).

- 2) If the results from this test show that your child is growth hormone deficient and he or she is not growing normally, your child will be treated with growth hormone according to standard clinical practice. If the results from this test show that your child is growth hormone deficient and is growing normally, your child will be directed to either 1) treatment with growth hormone or 2) no treatment with growth hormone. This is called randomization. Your child will have a 50/50 chance of being selected for either one (like flipping a coin). If your child is randomized to no treatment with growth hormone and he or she begins to have decline in growth, your child will be switched to treatment with growth hormone.
- 3) Your child will then be monitored every four months for three years or until your child is five years old, whichever is longer. An appointment will be scheduled for your child to return to the CHLA Endocrinology Clinic for a physical examination every four months. Your child will be measured for his or her height, weight, head size, and body fat for monitoring of growth. If your child is selected for treatment with growth hormone, s/he will also have laboratory testing during each follow-up examination to monitor his or her hormone levels and fasting lipids. Approximately 2 teaspoons of blood will need to be removed from your child's vein for this laboratory testing. If your child is already seeing a doctor in the Division of Endocrinology at CHLA, we will try to schedule these research study appointments for times when your child is going to see their doctor there. If your child is selected for no treatment with growth hormone, s/he will have laboratory testing only twice (once during the initial visit and once during the final visit) to monitor his or her fasting lipids. Approximately 1 teaspoon of blood will need to be removed from your child's vein for this laboratory testing.

Body fat will be measured by using a method called 'bioelectric impedance' to evaluate the amount of body fat in your child. Two thin wires will be attached to his/her hand and foot, one to his/her hand and the other to one of his/her feet. This method will send a small current from one wire to the other and give a result. It is completely painless and your child will only feel a slight tickle.

- 4) If your child is selected for treatment with growth hormone, this means your child will be given growth hormone to replace what he or she is missing. This requires that a parent give daily shots of growth hormone. Instructions will be provided on how to do this.

#### • **POTENTIAL RISKS AND DISCOMFORTS**

Occasionally the glucagon tolerance test causes nausea and vomiting. Rarely glucagon causes low blood sugar approximately 2 hours after its administration. Low blood sugar causes sweating, increased heart rate, and, if severe, may cause low blood pressure and seizures. Your child will be monitored throughout the course of the glucagon tolerance test for evidence of low blood sugar including occasional analysis of a few drops of blood from the intravenous line to insure that the blood sugar is normal. Low blood sugar will be treated appropriately with food, drink, or intravenous fluids.

If your child is selected for growth hormone treatment, he or she may experience discomfort from the growth hormone shots. Rarely, growth hormone can cause headaches due to increased pressure of the fluid surrounding the brain. If this occurs, growth hormone replacement will be

stopped. This results in complete reduction of the problem. Growth hormone therapy carries the theoretical risk of stimulating the growth of abnormal tissue such as tumors. This has not been known to occur in humans.

There may be additional risks to participation in this study that we do not know about and therefore cannot describe.

- **ANTICIPATED BENEFITS TO SUBJECTS**

Your child may benefit from early diagnosis of growth hormone deficiency and monitoring of growth to identify any fluctuations in growth that can be treated. Early treatment of growth hormone deficiency in patients with ONH may decrease the risk of obesity or delayed development. Of course, because growth hormone deficiency in ONH children that grow normally is not understood, no one can know in advance if it will be helpful in your child's particular case.

- **ANTICIPATED BENEFITS TO SOCIETY**

This study may help us understand the relationship between growth hormone deficiency and unexpected or unfavorable results such as obesity and developmental outcomes.

- **ALTERNATIVES TO PARTICIPATION**

You have the option of not participating (not having your child participate) in this study or withdrawing at any time. The test done for this study (e.g., the glucagon tolerance test (growth hormone)) may also be performed if you do not participate in this study at age four or if determined necessary by an endocrinologist. Growth hormone therapy is available outside of this study. The decision to start growth hormone therapy will be at the discretion of your child's endocrinologist.

- **FINANCIAL OBLIGATION**

This research study is funded by Genentech. Participants and their families are not responsible for any of the medical costs involved in this study and all exams are free of charge. Neither you nor your insurance company will be billed for your participation in this research. Growth hormone will be provided for the period of the study without charge. Further treatment with growth hormone beyond the duration of the study will be dependent on clinical need and availability of funds.

If your child needs to be examined for hypothyroidism, then he or she will be referred to an endocrinologist. This is not covered by the study and will need to be billed to your child's insurance.

- **PAYMENT FOR PARTICIPATION**

You will receive \$25 for each of your study visits (at least 10 visits total) to help with travel expenses for participation in the study.

• **EMERGENCY CARE AND COMPENSATION FOR INJURY**

If injury were to occur as a result of participating in this study the General Clinical Research Center (GCRC) will provide appropriate medical care. However, the duration and extent of any medical treatment will be determined by the GCRC Local Advisory Committee of the General Clinical Research Center. Additionally, Childrens Hospital Los Angeles and the physician investigators each maintain professional liability insurance to compensate patients for injuries caused by the fault of Hospital employees or physicians. The physicians are not employees or agents of the Hospital and are separately insured. If an injury is not caused by the fault of a Hospital employee or a physician, neither the Hospital nor the physicians provide reimbursement for treatment expenses or other compensation for the injury, and payment for care of such injury will be billed to you and/or your health benefit plan. You are not waiving any legal claims, rights or remedies because of your child's participation in this research study.

If you believe that physical injury has been suffered as a result of participation in this study, you should contact Dr. Mark S. Borchert at (323) 361-4510 or Dr. Mitch Geffner at (323) 361-7032. Treatment for such injury will be available under the same financial arrangement as treatment is usually provided.

• **PRIVACY AND CONFIDENTIALITY**

Members of the research team and, if appropriate, your physicians and nurses will know that your child is a research subject. All results will be kept confidential, but may be made available to you, and/or your child's physician if you wish. Authorized representatives of The Genentech Center for Clinical Research in Endocrinology, the CHLA Committee of Clinical Investigations, the General Clinical Research Center, the Food and Drug Administration and the Department of Health and Human Services may need to review records of individual subjects. As a result, they may see your name and your child's name; but they are bound by rules of confidentiality not to reveal your identity to others. No information about you, or provided by you during the research, will be disclosed to others without your written permission, except:

- if necessary to protect your child's rights or welfare (for example, if he or she is injured and need emergency care); or
- if required by law (i.e., child abuse, reports of certain infectious diseases).

When the results of the research are published or discussed in conferences, no information will be included that would reveal your child's identity.

Information gathered about your child through this study will be assigned a code and his or her name will be removed. Data will be stored in a locked location and will only be accessible by those mentioned above.

Because this study involves the diagnosis and possible treatment of a medical condition, a copy of this consent form will be placed in your child's medical record. This will allow the doctors that are caring for your child to obtain information about what medications or procedures your child is receiving in the study and treat him or her appropriately.

• **PARTICIPATION AND WITHDRAWAL**

Your child's participation in this research is VOLUNTARY. Your choice about whether or not to participate will have no affect on your child's care, services or benefits at Childrens Hospital Los Angeles. If you agree to participate, but later decide to remove your child from the study, you



may do so without affecting you or your child's rights to health care, services or other benefits at Childrens Hospital Los Angeles.

- **WITHDRAWAL OF PARTICIPATION BY THE INVESTIGATOR**

The investigator may withdraw your child from participating in this research if necessary to protect your child's health or if other situations arise that make it necessary to do so. If your child experiences any of the following side effects (excessive vomiting and seizures associated with low blood sugar) or becomes ill during the research, he or she may have to drop out, even if he or she would like to continue. The investigator, Dr. Mark Borchert, will make the decision and let you know if it is not possible for your child to continue. The decision may be made either to protect your child's health and safety, or because it is part of the research plan that people who develop certain conditions may not continue to participate.

If the results for the growth hormone stimulation tests show that your child produces enough growth hormone, you child will be withdrawn. If your child is randomized to no growth hormone treatment and demonstrates growth deceleration, he or she will be switched to growth hormone replacement and withdrawn.

- **HOW TO OBTAIN INFORMATION**

In the event of a research-related injury or if your child experiences side effects, please immediately contact the investigator listed below.

Daytime, Monday through Friday, 8:00 A.M. through 4:30 P.M. you may call Dr. Mark Borchert at (323) 361-4510 or Dr. Mitch Geffner at (323) 361-7032. You may also contact Cassandra Fink, M.P.H. for any questions relating to your child's participation in this study. She may be reached at (323) 361-2267, Monday through Friday, 8:00 A.M. through 4:30 P.M.

Evenings, nights, weekends or holidays you may call the hospital number 323/660-2450 and ask for the Division of Ophthalmology Service doctor on-call.

If your questions are not an emergency, you can obtain better information by calling Dr. Mark Borchert, Monday through Friday, 8:00 a.m. through 4:30 p.m., than by calling Division of Ophthalmology on call service after hours.

- **FINANCIAL INTEREST OF THE INVESTIGATOR**

Funding for this research study is provided by Genentech. The funding is used to support the activities of the Division of Ophthalmology and Department of Diabetes, Metabolism, and Endocrinology and to reimburse both areas for the costs of the study personnel. Compensation is *based* upon the number of research subjects enrolled. If your physician is an investigator for this study, s/he is interested in both your healthcare and the conduct of this research. You are not under any obligation to participate in a research study conducted by your doctor.

- **RIGHTS OF RESEARCH SUBJECTS**

You may withdraw your permission for your child's participation at any time and discontinue participation without penalty. You are not waiving any legal claims, rights or remedies because of your child's participation in this research study. If you have questions regarding your child's rights as a research subject, you may contact the CHLA Office for Human Subjects Protections at 323/361-2265.

As a participant in a GCRC sponsored study you have the right to speak with the Research Subject Advocate for the GCRC. Dr. Alan B. Lewis or a member of his staff is available to discuss the study with you privately and answer any questions you may have prior to enrolling in the study or at any time during or following completion of the study. The discussion will remain confidential. Dr. Lewis and his staff can be reached at 323/669-2265.

**SIGNATURE OF LEGAL REPRESENTATIVE**

Your signature(s) below indicate

- You have read this document and understand its meaning;
- You have had a chance to ask questions and have had these questions answered to your satisfaction;
- You consent to your child’s participation in this research study; and
- You will be given a copy of the signed permission form and of the *Experimental Subject’s Bill of Rights*.

\_\_\_\_\_  
Name of Subject

\_\_\_\_\_  
Name(s) of Parent(s)/Guardian

\_\_\_\_\_

\_\_\_\_\_  
Signature of Parent (Guardian)

\_\_\_\_\_  
Date

\_\_\_\_\_  
Signature of Parent (Guardian)

\_\_\_\_\_  
Date

**SIGNATURE OF INVESTIGATOR**

I have explained the research to the subject’s parent(s)/guardian and answered all of his or her questions. I believe that he or she understands the information described in this document and freely gives permission for his or her child to participate.

\_\_\_\_\_  
Name of Investigator

\_\_\_\_\_  
Signature of Investigator

\_\_\_\_\_  
Date (must be the same date as subject’s)

**SIGNATURE OF WITNESS**

My signature as witness certified that the parent(s)/guardian signed this permission form in my presence as his or her voluntary act and deed.

\_\_\_\_\_  
Name of Witness

\_\_\_\_\_  
Signature of Witness

\_\_\_\_\_  
Date (must be the same date as subject’s)



**SIGNATURE OF INTERPRETER**

\_\_\_\_\_  
Name of Interpreter

\_\_\_\_\_  
Signature of Interpreter and Date (must be the same date as subject's)

*Please check appropriate box and sign below.*

Investigator's Statement of Certification for Subjects less than Seven Years of Age (Assent)

The undersigned investigator, Dr. Mark Borchert or Dr. Mitchell Geffner, hereby certifies that he or she has discussed the information contained in the study consent to the subject, including any risks that may reasonably be expected to occur. The undersigned further certifies that the subject was encouraged to ask questions, that all questions were answered, and that assent was obtained.

Assent was not obtained for a subject under 18 years of age. *(Please state the reason. Examples include: child is an infant; child is comatose; child lacks cognitive abilities to understand the information.)*

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

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

Signature \_\_\_\_\_

