Informed Consent for Participation in a Research Study

GW IRB# NCR234775

Title of Research Study: ***Genome Wide Association Study of Patients with Muscle-Specific Kinase Myasthenia Gravis***
Investigator: ***Henry Kaminski, MD***

Key Information:

The purpose of this form is to provide you (as the parent of a prospective research study participant information that may affect your decision as to whether or not to let your child participate in this research study. Read the information below and ask the research team any questions you might have during the consent process before deciding to give your permission for your child to take part. If you decide to let your child be involved in this study, this form will be used to record your permission.

What is the purpose, procedures, and duration of this study?

This study is part of the Rare Diseases Clinical Research Network (RDCRN), an initiative of the National Institutes of Health (NIH) to advance medical research on rare diseases. A long-term goal of the network is to improve diagnosis and treatment of rare disease conditions.

The purpose of this study is to understand and identify the variations in genes associated with MuSK myasthenia gravis. We propose to collect saliva samples from 1,000 subjects with MuSK myasthenia and perform a genome wide association study, an approach to find genetic markers associated with a particular disease. This study is done in collaboration with the National Institutes of Health. The expected duration for this study is a one-time submission of saliva sample.

What are the reasons you might choose for your child to volunteer for this study?

There is no direct benefit to your child for providing one-time saliva sample for this research project. Research conducted using your child's sample will help to better understand causes for MuSK myasthenia and ultimately provide insight for targeted treatment.

What are the reasons you might not choose for your child to volunteer for this study?

There are no physical risks associated with this study. However, there is a potential risk of loss of confidentiality. Research staff will make every effort to keep your child's information confidential. Information from this research project will be maintained in a secure GW MFA server at the George Washington University under the supervision of Dr. Henry Kaminski. If results of this research study are reported in journals or at scientific meetings, the people who participated in this study will not be named or identified.

Does my child have to take part in this study?

Your child does not have to take part in this research. Your child may decline to participate or to withdraw from participation at any time. You can agree to allow your child to take part and later change your mind. If you and your child choose not to take part or choose to stop taking part at any time, there will be no penalty or loss of benefits to which your child is otherwise entitled.

Detailed Consent Form:

Why is your child being invited to take part in a research study?

We invite your child to take part in a research study because they have muscle specific kinase (MuSK) myasthenia gravis.

What should I know about a research study?

- Someone will explain this research study to you. You may ask all the questions you want before you decide whether to allow your child to participate or not.
- Participation is voluntary; whether or not your child takes part is up to you and your child.
- You and your child can agree to take part and later change your mind.
- Your decision not to allow your child to take part or to stop your child's participation will not be held against you or your child.
- Your decision will not affect the medical care your child receives. If you decide not to allow your child to take part, they can still continue to receive medical care.
- You may take this document home to read or to discuss with your family members or doctor before deciding for your child to take part in this research study.

Why is this research being done?

This first ever study aims to collect saliva samples for DNA analysis from 1000 patients with muscle specific antibody positive myasthenia gravis. These DNA samples are then used in development of a genome-wide association study (GWAS).

Genome-wide association studies (GWAS) would likely allow us to identify genes associated with a MUSK myasthenia. GWAS has been used in other forms of MG to understand the disease better, but never in MUSK MG. Knowing genes that put patients at risk will tell us more about how the disease may start and then potentially better ways to identify people at risk and treat the disease.

How long will my child be in the study?

The expected duration is to provide a one-time saliva sample.

How many people will take part in this research study?

We expect about 1000 people will take part in the entire study.

What happens if I agree for my child to be in this research?

If you agree for your child to be in this research, you will need to contact the study team to learn more about the study. You will undergo informed consent process to sign consent form for your child provided with confirmation of your child's MuSK myasthenia gravis diagnosis. With your supervision, your child will then provide saliva sample in person or through mail to be returned back to George Washington University.

- **Saliva Collection Procedure:**

Step 1: Remove the collection funnel and tube from the pack. Next, twist to close the collection funnel on to the tube gently.
Step 2: Spit saliva into funnel and repeat until saliva liquid (not foam) reaches fill line.
Step 3: Untwist the collection funnel and replace the tube cap tightly. Discard the funnel.
Step 4: Shake the tightly closed tube a few times to mix the saliva with the solution.

Note: Saliva collection may seem simple, but does take time and effort to fill the small container to the fill line. The liquid part of the saliva needs to be at the fill line and bubbles do not count. This process often takes several minutes to produce enough saliva and people with a dry mouth may take longer.

What other choices does my child have besides taking part in the research?

Instead of being in this research study, the choices may include participating in other research studies available to your child and/or continuing their standard of care to which they would otherwise be entitled.

What happens if I agree for my child to be in research, but later change my mind?

You or your child may refuse to participate or you may want to discontinue your child's participation at any time without penalty or loss of benefits to which your child would otherwise be entitled.

Is there any way being in this study could be bad for my child?

The risks and discomforts associated with participation in this study are not greater than those ordinarily encountered in daily life or during the performance or routine physical or psychological examinations or tests.

What happens to my child's information collected for the research?

Limited demographic data (name, DOB, sex at birth, race, ethnicity) and clinical data (medical history and family history), will be collected by the George Washington University research team under supervision of Henry Kaminski, MD. This limited data of your child will be stored in a primary research database at the RDCRN Data Management and Coordinating Center (DMCC) at the Cincinnati Children's Hospital designated by the National Institutes of Health. Your child will be assigned a subject identifier as part of the study and a code number called a Global Unique Identifier (GUID) using an NIH GUID system. The GUID is a unique code made up of letters and numbers that allows researchers to share data from other studies in which your child has participated without letting others know who your child is. A GUID does not contain direct identifiers, and your child cannot be identified using only the GUID. To generate the GUID, we will ask you and/or your child for your child's full date of birth (day, month, year), first name at birth, last name at birth, middle name at birth (if applicable), city/municipality of birth, country of birth.

We would like to make your child's data, without direct personal identifiers, available for other research studies that may be done in the future. The deidentified data/samples collected from this study will be shared and stored indefinitely at the NIH lab of Dr Traynor. Any of your child's personal identifiable information will not appear in the federal data repository or this study clinical research database with exception of e-

consent option maintained by the RDCRN DMCC which includes your child's name and contact information. This information will be stored to document electronic consenting process and to contact study team if you or your child have any questions. A code link with your child's name and other identifying information will be kept in a secure, password protected file under GW MFA servers maintained by GW research team under supervision of Dr. Henry Kaminski

Our goal is to make more research possible to learn about health and disease. The NIH and the data management center uses several layers of protection for the clinical data stored there. It meets all of the local and federal security requirements for research datacenters. The NIH may make your child data, without direct personal identifiers, available for other research studies in the future. Future research may be about similar diseases or conditions to this study, but could also be about unrelated diseases, conditions, or other aspects of health. Researchers who want access to your child's data will have to tell the NIH, through a data access request and application process, about the research they want to do. They will have to do ethics training and have IRB approval to do the research. They will have to sign a legal agreement stating they will not try to find out about child.

To the extent allowed by law, we limit your child's personal information to people who have to review it. We cannot promise complete secrecy. The IRB and other representatives of this organization may inspect and copy your child's information. Others include the National Institutes of Health whom we are collaborating with in this research project.

To help us protect your child's privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify your child in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. The researchers will use the Certificate to resist any demands for information that would identify your child. The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you, your child, a member of your family from voluntarily releasing information about your child or their involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information. The Certificate of

Confidentiality will not be used to prevent disclosure to state or local authorities for reasons such as child abuse and neglect, or harm to self or others.

Electronic Consent (eConsent) option

If you or your child choose to use the electronic consent option instead of paper option, you will be directed to a website and database administered by the Data Management and Coordinating Center (DMCC) at the Cincinnati Children's Hospital. You or your child will be asked to enter name and contact information into the electronic website. This information will be stored to document the electronic consenting process and to contact you or your child if you indicate you or your child have any questions. All of the study information will be stored and maintained securely by the Data Management and Coordinating Center (DMCC) at the Cincinnati Children's Hospital and vendors they use for secure storage. Linkages with other data sources will be performed without revealing your child's identity to authorized researchers. We will not give out your child's name or any other information that could directly identify your child to other researchers.

Sample for Genetic Testing

Dr. Traynor at the National Institute of Aging at the NIH will perform genetic analysis or genetic testing on your child's sample. Genetic research is a research that studies genes, including gene characteristics and gene versions that are transmitted by parents to children. Genetic research may include looking at information, such as personal appearance and biochemistry, gene sequences, genetic landmarks, individual and family medical histories, reactions to medications and responses to treatment. Genetic research raises certain questions about informing you of any results. Possible risks of knowing results include: anxiety; other psychological distress; and the possibility of insurance and job discrimination. A possible risk of not knowing includes being unaware of the need for treatment. These risks can change depending on the results of the research and whether there is a treatment or cure for a particular disease.

Sometimes patients have been required to furnish information from genetic testing for health insurance, life insurance, and/or a job. A Federal law, the Genetic Information Nondiscrimination Act of 2008 (GINA), generally makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to discriminate against your child based on your child's genetic information.

Furthermore, Investigators in this study may try to re-contact you in regards to your child in the future. If you are re-contacted and want to know what the investigators have learned about your child's samples, you should understand the following:

- The information may be too limited to give you particular details or consequences;
- Your child may be determined to carry a gene for a particular disease that can be treated;
- Your child may be determined to carry a gene for a particular disease for which there is no current treatment;
- Your child may carry a gene for a disease and might consider informing relatives that they, too, might carry the gene.

*May we contact you about future studies that may be of interest for your child?
____ Yes ____ No

How will my child's privacy and health information be protected?

The Health Insurance Portability and Accountability Act (HIPAA) requires that researchers and health care providers protect the privacy of information that identifies your child and relates to your child's past, present and future physical and mental health or conditions, or the provision of health care. If you agree for your child to participate in this research, protected health information will be used and shared with others for purposes of the study.

Below is more detailed information about how your child's health information will be shared and protected. By signing this form, you are allowing the people and groups that are listed in the next paragraphs to use your child's health information for this research study. Your child's information will only be used or shared as explained in this authorization form.

Protected health information that may be used and released (disclosed) in this study includes
information such as:

• This consent form
• Demographic information (like your child's name, date of birth, etc.)
• Information about your child's medical history from your child's medical records and your child's doctor's

office
• Laboratory results obtained on specimens collected from your child (your child's saliva sample);
• Interviews with your child conducted by members of the Research Team
• Other data created or collected during this study

Only members of the GW research team may obtain your child's individual protected health information from hospitals, clinics, health care providers, and health plans that provide health care to you as part of the eligibility and recruitment process performed at GW. GW research team will recruit and assign your child's saliva sample with a study designated identification number. Your child's sample will be stored in Ross Hall at GW School of Medicine and Health Sciences under supervision of principal investigator, Dr. Henry Kaminski. Only your child's de-identified saliva sample, without any information that identifies your child will be shipped to Bryan Traynor, MD laboratory of Neurogenetics at the NIH for processing.

By signing this form, you allow the use, sharing, copying, and release of your child's protected health information in connection with this study by:

- The members of the GW research team
- Other healthcare providers such as labs which are part of the study
- Institutional officials who are responsible for compliance

If you decide to allow your child to take part in this study, your consent for this study will not expire unless you cancel (revoke) it. The information collected during your child's participation will be kept indefinitely. You can always cancel this Authorization by writing to the study doctor. If you cancel Authorization, your child will also be removed from the study. However, standard medical care and any other benefits to which your child are otherwise entitled will not be affected. Canceling your Authorization for your child only affects the uses and sharing of your child's information *after* the study doctor gets your written request. Information gathered before then may need to be used and given to others. Once your child's health information has been disclosed to others outside of the medical practice, the information may no longer be covered by the federal regulation that protects privacy of health information. You can also refuse to sign this consent/Authorization for your child not to be part of the study. You can also tell us you want your child to leave the study at any time without canceling the Authorization. By signing this consent form, you give us the permission to use and/or share your child's health information as stated above. Finally, you should understand that the study doctor

is not prevented from taking steps, including reporting to authorities, to prevent serious harm to yourself, your child or others.

Are there any costs for participating in this research?

There are no costs for participating in this research study.

Are there any compensation for participating in this research?

If you agree for your child to take part in this research study, we will provide $20 gift card for your child's time and effort. You or your child will be paid in the form gift card of choice (VISA gift card, or Amazon e-gift card). Please note if you or your child choose physical card, payment will be processed through GW's forte system, the university's preferred payment option for study participants. Your consent to use this system will need to be obtained in separate consent form.

What else is there to know?

A federal law, called the Genetic Information Nondiscrimination Act (GINA), generally makes it illegal for health insurance companies, group health plans, and most employers to discriminate against your child based on your child's genetic information. This law generally offers the following protections:

- Health insurance companies and employer-based group health plans may not request your child's genetic information that we get from this research.
- Health insurance companies and employer-based group health plans may not use your child's genetic information when making decisions regarding your child's eligibility or premiums.
- Employers with 15 or more employees may not use your child's genetic information that we get from this research when making a decision to hire, promote, or fire your child or when setting the terms of your child's employment.
- All health insurance companies and group health plans must follow this law. All employers with 15 or more employees must follow this law as of November 21, 2009. The protections offered by GINA apply regardless of when the research that obtained the genetic information was conducted, even if prior to the effective date.

Be aware that this law does not protect your child against discrimination on the basis of your child's genetic information by companies that sell life insurance, disability insurance, or long-term care insurance.

If you have any questions, concerns or complaints about the study, contact the study team, listed below:

	Study Doctor	Study Coordinator
Name:	Henry Kaminski, MD	Helen Girma
Address:	2150 Pennsylvania Ave NW 7th Floor Washington DC 20037	2150 Pennsylvania Ave NW 7th Floor Washington DC 20037
Telephone number:	202-741-2710	202-677-6205
Email address:	hkaminski@mfa.gwu.edu	hgirma@mfa.gwu.edu

If you have any questions, concerns or complaints about your child's rights as a research participant and the research, The Office of Human Research of George Washington University, at telephone number (202) 994-2715, can provide further information.

Signature Block for Adult

By signing below, you agree that the above information has been explained to you and you have had the opportunity to ask questions. You understand that you may ask questions about any aspect of this research for your child during the course of the study and in the future. Your signature below documents your permission for your child to take part in this research.

_____

Printed name of Parent(s) or Legal Guardian

_____ _____

Signature of Parent(s) or Legal Guardian Date

_____ _____

Signature of person obtaining consent Date