I, __________________________ hereby request testing for one or more of the biochemical tests indicated below to be performed in my muscle biopsy.

I understand that biological samples of muscle tissue will be provided for this testing by me or my relative as follows:

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<table>
<thead>
<tr>
<th>Name of Individual to be Tested</th>
<th>Date of Birth</th>
<th>Relationship</th>
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</thead>
</table>

Please circle the **individual test(s) or profile** for which you are providing consent:

**Glycogen Storage Disease Profile**
- Acid & neutral maltase
- Phosphorylase
- Phosphorylase b kinase
- Phosphofructokinase

**Mitochondrial Myopathy Profile**
- NADH dehydrogenase
- NADH cytochrome c reductase
- Succinate dehydrogenase
- Succinate cytochrome c reductase
- Cytochrome c oxidase
- Citrate synthase

**Modified Mitochondrial Myopathy Profile**
- Succinate dehydrogenase
- Cytochrome c oxidase
- Citrate synthase

**Myoglobinuria Profile**
- Phosphorylase
- Phosphorylase b kinase
- Phosphofructokinase
- Phosphoglycerate kinase
- Phosphoglycerate mutase
- Lactate dehydrogenase
- Carnitine palmitoyltransferase
- Citrate synthase
1. Description of the Diseases Evaluated by Profiles

General: The purpose of all profile testing is to identify specific deficiencies in the enzymes analyzed that are known to cause certain metabolic muscle diseases as described below.

(a) Glycogen Storage Disease Profile:

Description of Disease: The diseases detected by this profile include the following:

1) Acid and Neutral Maltase deficiency (Pompe disease; Glycogen Storage Disease Type II; autosomal recessive inheritance): This disorder has progressive infantile and adult onset subtypes. Infants typically present with pronounced hypotonia (muscle weakness) and severe cardiomegaly (enlarged heart). Other signs include frequent respiratory infections, failure to reach motor milestones, and difficulty feeding. Children and adults show much greater heterogeneity (differences in clinical features). The most common clinical manifestations are progressive muscle weakness and respiratory insufficiency, ultimately leading to loss of ambulation and the need for ventilation support. Heart involvement is rare in this patient population.

2) Myophosphorylase deficiency (McArdle Disease; Glycogen Storage Disease Type V; autosomal recessive inheritance): This is a disorder that prevents the body from converting glycogen (a source of complex sugar) to energy. The disorder is characterized by pain and cramps with physical exertion with onset any time in childhood through adulthood. Symptoms occur when the enzyme, myophosphorylase, is absent or greatly diminished in muscle tissue of an individual who has inherited 2 mutations or alterations in the PYGM gene causing this enzyme deficiency.

3) Phosphorylase b kinase deficiency (Glycogen Storage Disease IX; X-linked inheritance): Onset can be in childhood or adult life. Symptoms include exercise intolerance, muscle cramps, muscle glycogen accumulation, and in some patients, progressive muscle weakness. Glycogen storage occurs in muscle due to the absence of phosphorylase b kinase due to a mutation in the PHKA1 gene causing the enzyme deficiency.

4) Phosphofructokinase deficiency (Glycogen Storage Disease Type VII; autosomal recessive inheritance): The disorder is characterized by exercise intolerance, muscle weakness, muscle cramps with exertion, and glycogen storage in muscle. Symptoms occur when the enzyme is absent or greatly diminished in muscle tissue of an individual who has inherited 2 mutations or alterations in the PFKM gene causing this enzyme deficiency.

Description of the test procedure and meaning of test results: The enzymes evaluated in this profile all have in common the ability to digest stored glycogen in muscle as a source of energy. When the enzymes are defective or absent, glycogen begins to accumulate in muscle. The test for each enzyme involves preparation of a muscle homogenate (grinding of a small piece of frozen muscle biopsy in a solution using a motor driven pestle) and the use of a spectrophotometer to measure the ability of each enzyme to utilize glycogen as an energy source. A positive test result suggests a likely diagnosis of the disease represented by the test. A negative test result may or may not rule out a specific diagnosis, however, additional testing may improve the diagnostic capability of the overall test procedure.

(b) Mitochondrial Myopathy Profile:

Description of Disease: Mitochondrial diseases result from failure in the function of the mitochondria, specialized compartments or organelles present in every cell of the body except red blood cells. Mitochondria create more than 90% of the energy needed by the body to sustain life and support growth. When they fail to function properly, less and less energy is generated within the cell. Diseases of the mitochondria appear to cause the most damage to cells of the brain, heart, liver, skeletal muscles, kidney and the endocrine and respiratory systems. In other words,
they can affect multiple organ systems in the body either individually or in combinations. These disorders can occur in all ages. They are evaluated in our laboratory by measuring the activities of 6 mitochondrial enzymes in muscle that can contribute to mitochondrial disease. The enzymes are Complex I (NADH dehydrogenase), Complex I-III (NADH cytochrome c reductase), Complex II (succinate dehydrogenase), Complex II-III (succinate cytochrome c reductase), Complex IV (cytochrome c oxidase) and citrate synthase, a marker for mitochondrial content in muscle. Mitochondrial diseases can follow autosomal recessive, dominant or X-linked modes of inheritance or maternal (also known as mitochondrial or cytoplasmic inheritance) inheritance.

Description of the test procedure and meaning of test results: The enzymes evaluated in this profile all are involved in the production of energy in mitochondria. When the enzymes are defective or absent, mitochondrial function begins to fail either partially or completely. The test for each enzyme involves preparation of a muscle homogenate (grinding of a small piece of frozen muscle biopsy in a solution using a motor driven pestle) and the use of a spectrophotometer to measure the ability of each enzyme to utilize a particular substrate in the production of energy. A positive test result suggests a likely diagnosis of the disease represented by the test. A negative test result may or may not rule out a specific diagnosis, however, additional testing may improve the diagnostic capability of the overall test procedure.

(c) Modified Mitochondrial Myopathy Profile
This profile is provided as an abbreviated mitochondrial myopathy profile to accommodate a small muscle sample that is inadequate for performance of the entire mitochondrial profile. Those enzymes with the greatest potential of providing diagnostic information is chosen for this profile from the main Mitochondrial Myopathy Profile.

(d) Myoglobinuria Profile
Description of Disease: The diseases diagnosed by enzymes analyzed in this profile all have certain features in common: muscle pain or cramps with or without weakness; muscle breakdown (rhabdomyolysis) leading to the release from muscle of a coca cola-colored substance called myoglobin into the blood stream and urine; myoglobin is an indicator of muscle damage that can be life-threatening. Most of these disorders are triggered by an environmental factor such as exertion, exposure to extremes in temperature, dehydration, viral infection, anesthesia, or certain other drugs such as statins.

The first three enzymes of this profile have already been described as part of the Glycogen Storage Disease Profile above.

1) Phosphoglycerate kinase deficiency: This is a disorder that prevents the body from converting glycogen to energy. The disorder is characterized by pain and cramps with physical exertion with onset any time in childhood through adulthood. Symptoms occur when the enzyme is absent or greatly diminished in muscle tissue of an individual who has inherited 2 mutations or alterations in the PGK1 gene causing this enzyme deficiency. The disorder is X-linked therefore occurring in affected males.

2) Phosphoglycerate mutase deficiency (Glycogen Storage Disease X): This is a disorder that prevents the body from converting glycogen to energy. The disorder is characterized by pain and cramps with physical exertion with onset any time in childhood through adulthood. Symptoms occur when the enzyme is absent or greatly diminished in muscle tissue of an individual who has inherited 2 mutations or alterations in the PGAM2 gene causing this enzyme deficiency. The disorder is autosomal recessively inherited.
3) Lactate dehydrogenase deficiency (Glycogen Storage Disease XI): This disorder is characterized by muscle cramps, pain, exercise intolerance, muscle rigidity, stiffness and rhabdomyolysis with myoglobinuria. It is inherited by an autosomal recessive mode when 2 mutations are present in the LDHA gene.

4) Carnitine palmitoyltransferase (CPT) II deficiency: This is a disorder of lipid (fat) metabolism preventing the body from converting lipids to energy and is characterized by pain and cramps with physical exertion, during periods without food (fasting), exposure to extremes in temperature, or during viral infection. Symptoms occur when the enzyme, CPT II, is absent or greatly diminished in muscle tissue of an individual who has inherited 2 mutations or alterations in the CPT2 gene (genetic material known as DNA) causing this enzyme deficiency.

**Description of the test procedure and meaning of test results:** The enzymes evaluated in this profile all are involved in the production or utilization of energy in muscle. The test for each enzyme involves preparation of a muscle homogenate (grinding of a small piece of frozen muscle biopsy in a solution using a motor driven pestle) and the use of a spectrophotometer to measure the ability of each enzyme to utilize a particular substrate in the production or utilization of energy. A positive test result suggests a likely diagnosis of the disease represented by the test. A negative test result may or may not rule out a specific diagnosis, however, additional testing may improve the diagnostic capability of the overall test procedure.

2. Limitations of Testing

Testing for the diagnosis of one or more of the disorders above involves the use of specialized procedures that will analyze your muscle biopsy specimen. Unless specifically indicated, this test is not part of a research protocol and is being used for clinical purposes. The testing is very accurate and sensitive for the diagnosis of each disorder with detection ranging from 80 to 95% of cases, depending on the disorder, with clear clinical and other laboratory evidence for the specified disease. The test report will state the level accuracy with which each disorder has been ruled out or diagnosed and whether or not further testing will be necessary to confirm or refute the diagnosis.

2. Cost of Testing

You will ultimately be responsible for payment of fees related to this testing. In most cases, health insurance companies will reimburse for all or a portion of the related costs.

3. Confidentiality

Specialized testing and the interpretation of the results are complex. The information obtained from this test will be provided to your physician who will then inform you of the results either directly or through a genetic counselor. It will be your physician’s obligation to provide you with any genetic counseling pertaining to the results and potential consequences of these test results. To the extent required by law, all of the records, findings, and results of this testing are considered and shall remain confidential and shall not be disclosed to anyone without your written consent. In addition, the results can only be released by law to (a) insurance companies and other third party payers, such as Medicaid if necessary for the payment of services to you and (b) to any person to whom a court orders disclosure under limited circumstances set forth by law.

4. Use of Your Specimen After Testing is Completed

Once your test results are completed, additional testing may or may not be performed on your specimen depending on which option you choose below. **PLEASE SELECT ONLY ONE OF THE FOLLOWING OPTIONS:**

(a) My muscle specimen will be destroyed within 60 days of testing.  ____________________________

Initials
(b) An aliquot of my specimen may be stored as long as deemed necessary for general research purposes with the retention of my name on the sample. I understand that the Robert Guthrie Biochemical & Molecular Genetics Laboratory is not performing a banking service by retaining my specimen. I consent to future contact for any and all purposes related to further diagnostic studies performed including the provision of general information about the findings; information about specific testing of my sample that may benefit me or my family members in relation to my choices regarding preventive or clinical care; and I understand there is no additional risk to me for consenting to future contact and complete confidentiality will continue to be maintained. The potential benefits of further clinical studies of my sample may provide additional information that impacts favorably on my future health care.

OR

(c) An aliquot of my specimen may be stored as long as deemed necessary for additional research studies, however, all identifiers, including my name, must be removed before initiating the research studies. I understand that information about specific testing of my sample will not be available because the sample will not be individually identifiable.

I further understand that participation in biochemical genetic testing is completely voluntary and I have had the opportunity to have all of my associated questions answered by my physician or a genetic counselor. I also may withdraw my consent in writing for any and all testing at this time.

Signature: 
Name (Print): 
Witnessed by: 
Date: 

Physician's/Counselor's Statement: I attest to the fact that I have explained biochemical genetic testing to this individual. I have addressed the limitation of the testing as outlined above, and have answered any questions posed by the individual regarding the testing. I request that the above indicated genetic testing be performed.

Signature: 
Name (print): 
Date: 

Please Print the name, address and phone number of all physicians to whom you authorize the release of test results. Any further disclosure of test results to person or organizations not listed below will require further informed consent at a later date.

Name of Licensed Physician  Address  Telephone Number