VA Department of Veterans Affairs	VA RESEARCH CONSENT FORM
Version Date: May 2016	**Page: 1 of 10**
Subject Name:	**Informed Consent Date:**
Principal Investigator: Gregory Schilero, MD	**VAMC: James J Peters**
Title of Study: The Effects of an Oral Beta-2 Agonist on Respiratory Muscle Strength in SCI	

1. Purpose of study and how long it will last:

You are being asked to participate in a research study. The purpose of the study will be to determine if an oral beta-2 adrenergic agonist, sustained-release Albuterol (medication released for 12 hours), improves expiratory muscle strength and/or cough effectiveness in persons with tetraplegia and high paraplegia after sixteen (16) weeks of treatment. Sustained-release Albuterol is an FDA approved drug that treats the symptoms related to chronic obstructive pulmonary disease, and asthma. However, use of this drug in this study is considered experimental because persons with spinal cord injury (SCI) are not included in the FDA approved clinical population.

You are being asked to participate in this research because you are **ELIGIBLE**:

- male or female between the ages of 18 and 80
- have a chronic spinal cord injury (≥ 1 year since injury) (all ASIA levels)
- level of injury between C3-C8 (Tetraplegia) or T1-T6 (high level paraplegia)
- male with maximal inspiratory pressure (MIP) < 90 cmH2O (determined during screening)

  OR
- female with maximal inspiratory pressure (MIP) < 65 cmH2O (determined during screening)

You are **NOT ELIGIBLE** to participate if you have any of the following:

- history of asthma
- uncontrolled hypertension or cardiovascular disease
- use a beta-2 adrenergic agonists
- epilepsy or seizure disorder
- diabetes
- hyperthyroidism
- take corticosteroids
- take anti-depressants known as Monoamine Oxidase Inhibitors (MAOIs) (i.e. Marplan, Nardil, etc.) or tricyclic antidepressants (i.e. Floranil, Pamelo, etc.)
- hypersensitivity to albuterol or any of its' constituents
- are pregnant
- use or are suspected of using over-the counter supplements or prescribed medications with anabolic characteristics (promotes improvements to muscle mass and strength) including, but not limited to: creatine monohydrate, anabolic steroids (e.g., testosterone), growth hormone, and substances with similar actions or indications as those listed.

You will be one of approximately 24 subjects in the study which will require you to come to the VA Center of Excellence for the Medical Consequences of Spinal Cord Injury a minimum of three (3) times over the course of the eighteen (18) week study. Funds for conducting this research are provided by

the Department of Veterans Affairs Rehabilitation Research and Development Service Merit SPiRE award number B1910-P.

2. Description of the Study Including Procedures to be Used:

If you consent to participate in this research study, you will be asked to perform the procedures listed below. All procedures are done for research purposes only. If you consent to participate, you will be randomly assigned to receive either a sustained-release (medication released for 12 hours) albuterol tablet (8mg) or a placebo (non-active) pill. Regardless of which group you are in, you will be required to take a pill two (2) times per day for the duration of the study. Your involvement in the study will last 18 weeks. You will be tested in the research center on three (3) occasions; the onset of the study (baseline visit or week 0), after taking the medication for sixteen weeks (4 months) (Post vsit) and again 2 weeks after completion of the study drug (residual visit or week 18). The week 16 test will occur 2 to 7 days after you take the last dose of study drug. You will be one of approximately 24 individuals to participate in this study. On test days, you will be asked to perform the following: pulmonary function tests and lung volume assessments, respiratory muscle strength testing, and an ultrasound to determine the size and strength of your diaphragm. During the course of the study (4 months at home) you will be asked to complete the following: take pill daily, weekly home pulmonary function test, weekly symptom survey, and complete a bi-weekly phone interview with a member of the investigative team. The following table depicts these commitments:

Table 2: Procedures To Be Performed	**Baseline**	**Drug or Placebo**	**Post**	**Residual**
	Week: 0	**Week: 1-16**	**Week: 16**	**Week: 18**
Pulmonary Function Test and Lung Volumes	**X**		**X**	**X**
Respiratory Muscle Strength Testing	**X**		**X**	**X**
Diaphragmatic Ultrasound	**X**		**X**	**X**
Pulmonary Questionnaire	**X**		**X**	**X**
Take Daily Medication		**X**		
Weekly Home Pulmonary Function Test		**X**		
Weekly Self-Symptom Survey		**X**		
Bi-Weekly Phone Interview		**X**		

Pulmonary Function Test and Lung Volumes:

Pulmonary Function Test:

To determine how your lungs are working, a lung function test called spirometry will be completed. While seated in your wheelchair and after a mouth piece and nose clip are applied, you will be asked to breathe normally for 3 to 6 breaths. You will then be instructed to forcibly inhale until your lungs are

filled. After a brief pause, you will then be instructed to forcibly exhale the air in your lungs for at least 6 seconds. After a brief rest, we will repeat this maneuver a minimum of three and maximum of five times to ensure that we are obtaining consistent values.

Lung Volumes:
The total volume of air in your lungs will be assessed using the nitrogen washout technique. The nitrogen washout technique, which takes about five minutes to perform, will begin while you are seated in your wheelchair and after a mouth piece and nose-clips have been applied. You will then be asked to breathe room air as you normally do, into and out of the mouthpiece for 3 to 6 breaths. The air you exhale, which normally contains mostly of nitrogen, will be collected and analyzed by a machine called a metabolic cart. Once you have completed the 3 to 6 breaths you will be asked to take a slow deep breath in and to exhale until you feel that your lungs are empty, after which you will return to your normal breathing pattern. Following an additional 3 to 6 regular breaths, the metabolic cart will begin delivering 100% oxygen through the mouthpiece. You will continue to inhale 100% oxygen while taking normal breaths until oxygen is the only gas measurable in your exhaled air.

Respiratory Muscle Strength Testing:
You will be asked to swallow a small balloon attached to a tube connected to a computer. The balloon will be inserted by a study physician into one nostril after numbing medicine (4% lidocaine) has been applied to your nasal passages, throat, and to the balloon tube in order to make swallowing the balloon easier. Then, pressures at the mouth and around the balloon will be measured simultaneously by having you blow in and out as strongly as possible through a mouthpiece connected to a recording device. You will repeat these maneuvers a maximum of five times. You will then be asked to perform 5 to 10 cough maneuvers of varying intensities while pressure around the balloon is recorded.

Ultrasound of your Diaphragm:
Ultrasound will be performed while you are seated in your chair and breathing into a mouthpiece connected to a recording device. The ultrasound device will be placed on the side of your chest, about half-way up your ribcage, and you will be asked to inhale and exhale maximally for at least 5 breaths during which a continuous recording of ultrasound images will be obtained.

Study Drug or Placebo:
You will be randomly assigned (as in a coin flip) to receive either a sustained-release (medication released for 12 hours) albuterol tablet (4 mg/tablet per oral for the first week (7 days), then 8 mg/tablet the remaining 15 weeks, if no drug related adverse events occur during week 1) or an identically appearing placebo (non-active) pill. Regardless of which group you are in, you will be required to take one pill two (2) times per day (one in the morning and one at night) for the 16 weeks of the study. The

study drug/pill will be dispensed to you by the VA Research Pharmacy on your first visit and provided to you at no cost.

Weekly Home Pulmonary Function Test:
You will be provided with a small-automated handheld device which will be used to assess your pulmonary function on a weekly basis. You will perform three maneuvers to assess your expiratory muscle strength. To perform each maneuver, you will inhale until your lungs are filled, pause a moment and place the mouthpiece end of the device in your mouth and then forcibly exhale until your lungs are empty. The device will then prompt you to answer a few questions. The investigative team will provide a demonstration for you on how to use the device.

Weekly self-symptom survey:
You will be provided with a binder which contains a sheet of paper for each of the 12 weeks in the total study. Each sheet of paper will contain a short survey of questions designed to assess respiratory symptoms (questions related to how you are breathing). You will complete one survey per week for 12 weeks.

Bi-weekly phone interview:
A member of the investigative team will contact you over the phone on a biweekly basis to speak about any symptoms that you may be experiencing or have experienced since a previous discussion. The phone interview will only last a few minutes. Keep in mind that you are allowed to contact a member of the study team at any point should you have a question or emergency.

Pregnancy Test:
If you are female with child bearing potential you will be asked to complete a pregnancy test to ensure that you are not pregnant. You will have the choice to provide urine sample or a blood sample to complete this test. If you choose to give urine you will be asked to fill a urine sample cup which will be used to assess pregnancy. If you choose to give a blood sample, you will have a total of 5 ml (1 teaspoon) blood drawn from a vein inside your elbow to confirm that you are not pregnant. If the test shows that you are pregnant then you will be withdrawn from the study.

3. Description of any Procedures that may Result in Discomfort or Inconvenience

Respiratory Muscle Strength Testing:
There will be a slight discomfort or inconvenience associated with measurement of mouth pressures. The nasal catheter does not cause discomfort. The swallowing of the stomach balloon tube passed through a nostril may result in mild, transient discomfort and may cause gagging, coughing and nose and throat irritation. There is a small chance that the balloon catheter could cause injury to your esophagus (swallowing tube) or to the nostril. A pulmonary doctor will be present during the entire

study and will assist with insertion of the balloon tube. If you are unable to swallow the balloon tube the study will be terminated.

Study drug or placebo:
There will be no discomfort associated with taking the pill. You may experience the following potential side-effects including but not limited to (all are mild and resolve quickly upon drug discontinuation):

- Tremors
- Muscle cramps and/or musculoskeletal pain
- Insomnia
- Nervousness
- Headache
- Tachycardia
- Palpitations
- Nausea and vomiting

Pregnancy Test (Blood Collection):
You understand that a routine blood sample will be drawn from a vein inside your elbow and this can be associated with mild discomfort due to the blood draw. The risks of a blood draw include the possibility of a bruise or infection at the site of skin puncture, temporary faintness and rarely, actual fainting (a temporary loss of consciousness due to reflex swelling of blood vessels that results in a rapid fall in blood pressure).

"Since this research may have unknown effects on an unborn child and should not be done during pregnancy, it is necessary for a pregnancy test to be done first. To your knowledge you are not pregnant at the present time. You also agree to avoid becoming pregnant (use contraceptives, take precautions against becoming pregnant, etc.) during this study."

4. Expected Risks of Study:

Respiratory muscle strength testing:
There may be some discomfort while the stomach balloon is being swallowed. Discomfort will be minimized by use of a topical anesthetic agent. Performing maximal mouth pressures does not present any serious risks, however you may experience lightheadedness after inhaling and exhaling as strongly as possible.

Study drug or placebo:
You may experience the following potential side-effects including but not limited to (all are mild and resolve quickly upon drug discontinuation):

- Tremors

- Muscle cramps and/or musculoskeletal pain
- Insomnia
- Nervousness
- Headache
- Tachycardia
- Palpitations
- Nausea and vomiting

Blood Collection:
The risks of blood draw include the possibility of a bruise or infection at the site of skin puncture, temporary faintness and rarely temporary loss of consciousness due to vasomotor instability (i.e., the blood vessels reflexively swell resulting in a fall in blood pressure which is commonly called "vasovagal episode").

There also may be risks and discomforts that cannot be foreseen.

5. Expected Benefits of the Study:

There are possible benefits by taking part in this study such as gains in your pulmonary function and expiratory muscle strength. There may be no direct benefit to you from this study. But, any information we get from this study will help others.

6. Other Treatments Available:

This is a research study; your participation is voluntary. Should you desire additional treatment options, you should contact your primary physician to discuss.

7. Use of Research Results:

We (I) will let you and your physician know of any significant new findings made during this study which may affect your willingness to participate in this study. All research material generated from this study will remain in the possession of Gregory Schilero, MD and his study team at the JJP VAMC.

Your research records will be maintained according to the requirements of the JJP VAMC as follows:
Data Collection, Storage, and Transfer:

- Your coded electronic data will be collected on VA computers that are not connected to the internet.
- Your coded electronic data without your name, or other identifying information, will be stored on secured networks, behind electronic security systems, in access-restricted folders.
- Hard copies of your data will be stored in a locked file cabinet behind 2 locked doors.

Access to the research materials generated from the study will be restricted to Gregory Schilero, MD and his study team. Your medical records will be maintained according to this medical center's requirements and all research investigator files will be destroyed six years after the end of the fiscal year when the research project has been completed per Records Schedule DAA-0015-2015-004-0032, Section 7.6 Research Investigator Files. If results of this study are reported in medical journals or at meetings, you will not be identified by name, by recognizable photograph, or by any other means without your specific consent. No information by which you can be identified will be released or published unless required by law. In order to comply with federal regulations, research records identifying you may be reviewed by the following:

Authorized representatives of the JJPVAMC (e.g. Institutional Review Board, Research Compliance Officer) and VA, including the Office of Research Oversight (ORO), Federal Agencies such as the Government Accounting Office (GAO), VA Office of Inspector General (OIG), and Office for Human Research Protections (OHRP) may have access to your research records. If this research involves articles regulated by the FDA, the FDA may choose to inspect and copy research records that identify individual research subjects.

Clinical Trials:

Because this research involves articles regulated by the FDA, the FDA may choose to inspect and copy medical or research records that identify individual research subjects. A description of this clinical trial will be available on http://www.ClinicalTrials.gov, as required by U.S. Law. This website will not include a summary of the results. You can search this website at any time.

8. Special Circumstances:

If you are a patient, a copy of this consent form will be placed in your medical record.

9. Compensation and/or Treatment in the Event of Injury:

The VA must provide necessary medical treatment to a research subject injured by participation in a research project approved by a VA R&D Committee and conducted under the supervision of one or more VA employees. Further information about compensation and medical treatment may be obtained from the medical administration service at this VA medical center.

10. Voluntary Participation:

You are not required to take part in this study; your participation is entirely voluntary you can refuse to participate in this study or withdraw your participation in this study after you consent without penalty or loss of VA or other benefits to which you are entitled.

11. Termination of Participation:

You are not required to take part in this study; your participation is entirely voluntary you can refuse to participate in this study or withdraw your participation in this study after you consent without penalty or loss of VA or other benefits to which you are entitled. You may be withdrawn from participation by the investigative team without your consent if you are unable to complete the study requirements in a timely manner, or if the investigators have reasonable cause.

12. Costs and Reimbursements:

As a veteran or non- veteran, you will not be charged for any treatments or procedures that are part of this study. For veterans who are required to pay co-payments for medical care and services provided by VA, these co-payments will continue to apply for medical care and services provided by VA that are not part of this study. You will receive $300 for completing the 16 week study and an additional $75 dollars for the third and final visit at week 18. For completing the study in its entirety you will receive a total $375. Payment will be in the form of an electronic deposit check approximately 6-8 weeks following study completion due to the administrative processing time.

13. Contact Person(s):

To obtain answers to questions about the research, report or seek treatment for a research-related injury, or to voice concerns or complaints about the research contact **Gregory Schilero, M.D.** at the following:

- During the Day: **Gregory Schilero, MD 718-584-9000, ext. 6701**
- After Hours: **Gregory Schilero, MD, cell (914-374-0811)**

To voice concerns or complaints about the research from someone outside of the research team, contact the following: I understand that should I wish to discuss my participation in this study with any other doctor or layperson, I can contact **Mary Sano, Ph.D**. ACOS-R&D Program by requesting an appointment at **(718) 741-4228** hospital extension 4228, first floor in the research building, room **1F-01** If I have questions, concerns and/or complaints concerning the research study, I can ask one of the researchers listed above or contact **Dr. Sano.** Medical problems during the course of the study should be addressed to the investigator at the phone listed above. If I have problems, concerns, and questions about the research and research subject's rights, I can contact Dr. Sano, who is not affiliated with this research study, to obtain information or to offer input.

RESEARCH SUBJECTS' RIGHTS: I have read or have had read to me all of the above.
Dr. Schilero or his delegate has explained the study to me and answered all of my questions. I have been told of the risks or discomforts and possible benefits of the study. I have been told of other choices of treatment available to me.

I understand that I do not have to take part in this study, and my refusal to participate will involve no penalty or loss of rights to which I am entitled. I may withdraw from this study at any time without penalty or loss of VA or other benefits to which I am entitled.

The results of this study may be published, but my records will not be revealed unless required by law. This study has been explained to me. I have had a chance to ask questions. I voluntarily consent to participate in this study. I will receive a signed copy of this consent form.

Subject Signature	Date	Time

Person Obtaining Informed Consent (Print Name) (Investigator or Delegate as indicated on Assurance Page)	Signature of Person Obtaining Informed Consent	Date

VERBAL CONSENT IF THE PARTICIPANT LACKS UPPER LIMB FUNCTION TO COMFORTABLY WRITE

_____ is unable to sign the consent form due to impaired arm function. I certify that I have carefully explained the purpose and nature of this research to him/her in appropriate language and he/she has had an opportunity to discuss it with me in detail. I have answered all of his/her questions and he/she has consented to participate in this research. I, therefore, am signing the consent form to document that he/she has given his/her consent to participate in this research study.

Person Obtaining Consent:

Name: _____

Signature: _____

Date: _____

Witness Name: _____

Signature: _____

Date: _____