Vanderbilt University Institutional Review Board
Informed Consent Document for Research

Principal Investigator: Paul A. Newhouse **Date: 01-04-17**
Study Title: *Nicotinic Treatment of Age-Related Cognitive Decline in Down Syndrome: An Open Label Pilot Trial*
Institution/Hospital: Vanderbilt University
IRB# 121759
This informed consent document applies to the Adult Participant and their Legal Guardian.

Name of the participant: _____ Age: _____
If you are a parent or legal guardian of a person who may take part in this study, permission from you is required. The assent (agreement) of your dependent may also be required; "we" means the doctors and other staff.

The following is given to you to tell you about this research study. Please read this form with care and ask any questions you may have about this study. Your questions will be answered. Also, you will be given a copy of this consent form.

You do not have to be in this research study. You can stop being in this study at any time. If we learn something new that may affect the risks or benefits of this study, you will be told so that you can decide whether or not you still want to be in this study.

1. What is the purpose of this study?

You are being asked to take part in this study because you may be developing memory loss. The purpose of this study is to test the safety and tolerability of a nicotine skin patch as a treatment for memory problems in adults with Down Syndrome. Studies have suggested that changes in memory, attention, and behavior that occur as people age may be a result of chemical changes in the brain. In persons with Down Syndrome, this decline may happen sooner than expected. We have found that nicotine can help older patients who have memory loss. This study is designed to test whether daily nicotine patch is safe, well tolerated, and whether nicotine treatment might improve memory, attention, and behavior in middle aged patients with Down Syndrome.

The total number of anticipated participants for this study is 15.

2. What will happen and how long will you be in the study?

SCREENING PROCEDURES:

If you agree to participate in the study, you will come in to the Vanderbilt Clinical Research Center to have a medical screening to see if you are right for the study. Screening will take about 2-3 hours and should take place over 1 day. We will have a doctor and nurse give you a checkup, to see if you're healthy to participate.

This will include:

- Physical exam, and urine pregnancy test for female participants
- Standard medical tests, including an electrocardiogram (ECG, or heart rate tracing), urinalysis, a blood sample (of about 2 teaspoons) for lab tests (complete blood count, electrolytes, etc), and tests for genes associated with risk for memory decline and other genes related to brain function.
- Memory and learning tests to evaluate how you're doing now
- Interview of you and your parent/guardian/caregiver.

If any test results are found at the screening day which we believe make you unable to participate in the study, we will explain these reasons to you, and if appropriate, refer you for further medical care.

EXPERIMENTAL PROCEDURES:

Baseline Day (Pre-Treatment Assessment): If you are approved to participate in the study, for your next study visit, you will be asked to come in for your first study visit day, which will last about 2 hours.

The Baseline Day will include:

- An interview about how you are feeling and performing your daily activities
- Tests of your memory, attention, and behavior
- Measurements of your heart rate, blood pressure, temperature, and breathing rate
- Brain Wave Tests (EEG/ERP)

One-Month Treatment Period: You will be given a supply of nicotine patches to be applied to your skin. We will ask you to put on the patch first thing in the morning every day, and remove it at bedtime. We will start you with a low dose (7mg), given for a few more hours each day. We will give you a schedule to gradually increase the length of time you wear the patch. You will increase the dose (to 14mg) after 2 weeks. We will schedule four (4) follow-up visits (Day 7, Day 14, Day 28, and Day 42) with both you and your parent/guardian, for more testing, and to check with you about any problems that may happen. We will ask you to call us if problems develop during this time or if your health changes.

Day 7 Assessment: This will be a short visit, to check how you're doing on nicotine patch treatment, and to document safety measures and any noticeable side-effects.

The Study Day will include:

- An interview about how you are feeling and performing your daily activities
- Vital sign measurements (heart rate, blood pressure, temperature, pulse and breathing rate)

Day 14/Day 28 Assessment: At the third and fourth visits, you will undergo a number of tests, some of which will be repeated from previous study days, see if you've noticed any changes relating to the drug, and to see if you are having any side-effects.

The Study Day will include:

- An interview about how you are feeling and performing your daily activities
- Tests of your memory, attention, and behavior
- Measurements of your heart rate, blood pressure, temperature, and breathing rate)
- Brain Wave Tests (EEG/ERP)

At the end of Study Day 28, you can remove the nicotine patch, and return any remaining patches and boxes to the study coordinator.

Day 42 Assessment: At the last visit, we will repeat the attention, memory and behavior testing and EEG/ERP from day 28, and a final safety assessment for any change since the end of the nicotine treatment.

3. Costs to you if you take part in this study:

There is **no cost** to you for taking part in this study. However, you/your parent/guardian/caregiver must still pay for any unrelated doctor's appointments and treatments that you normally would have. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you/your insurance.

4. Side effects and risks that you can expect if you take part in this study:

Nicotine and Patch Side Effects: As you may know, nicotine is the main component of cigarettes. Nicotine has many effects that have been well studied for many years. Possible side effects include increased heart rate and blood pressure, nausea, vomiting, dizziness, headaches, increased sweating, and occasionally shakes.

If you have serious heart disease, severe asthma, severe or active ulcer disease, untreated thyroid disease, epilepsy, or allergies to nicotine or similar drugs, you should not participate in this study.

In addition, nicotine patches can sometimes cause reddening or irritation of the skin where they are applied (17% of people using the patch). Diarrhea, sleepiness, stomachache, muscle pain, or joint pain are all side-effects that have sometimes been reported in patients using a nicotine patch.

You may be concerned about risks to your heart if you decide to participate. However, studies have not shown that nicotine replacement therapies (like nicotine patches) are associated with increased risk of heart disease or increased incidence of heart attacks.

There is no evidence that using nicotine patches would prompt a non-smoker to become cigarette smoker or to abuse nicotine products. The probability that participation in this study may prompt the subjects to begin to use nicotine products (like tobacco, cigarettes, cigars) is extremely low. There have been no cases reported in the medical literature of abuse by non-smokers of nicotine replacement products. We have given nicotine and nicotinic drugs over the years to several hundred non-smoking subjects including young and elderly normal volunteers, patients with Alzheimer's disease, and patients with Parkinson's disease. We have not had a single subject take up tobacco or nicotine use as a consequence of study participation.

Blood sampling: The blood draw may cause redness, slight discomfort, mild bruising, and possibility of infection. However this risk is low, as all blood samples will be taken by trained nursing staff.

Vital Sign Measurements: The sticky pads used to measure your heart rate and breathing rate may cause skin irritation in some people.

Electrocardiogram (ECG): To check your heart function, an electrocardiogram (ECG) will be done. This is a test that records the electrical activity of the heart. You will be asked to lie down and sticky patches will be put onto your chest. You will be asked to lie still. The sticky pads used for the ECG may cause skin irritation.

Electroencephalogram /Event Related Potential Test (EEG/ERP): To study patterns of your brain wave activity, you will have an EEG/ERP, or Brain Wave Test done. During this test, you will wear a snug cap that has small electrodes on it, which will record your brain waves from your scalp as you watch different sets of images on a computer screen. You will be asked to sit still and pay close attention to the computer screen.

Testing, Questionnaires, and Assessments: Some of the tests may be difficult or long, which may cause you to become tired or uncomfortable. You will be able to take breaks as needed, and we will do our best to make the process as smooth as possible.

5. Unforseeable risks of participation in this research study:

As with any research, there may be risks of participation or from the study medication that we cannot predict. If you experience any unpleasant effects during this study not mentioned in this consent form, please contact the study coordinator as soon as possible.

6. Payment in case the participant is injured because of this research study:

If Vanderbilt and the PI decide that you are injured as a **direct result** of being involved in this study, then your insurance will not have to pay for the cost of immediate (as in, when the injury happens) medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for the costs of any additional care (as in, followup treatments after the injury). There are no plans for Vanderbilt to give you money for the injury.

7. Positive effects that might result from this study:

a) The benefits to **science and humankind** that might result from your participation in this study:
You will be adding to our understanding of the effects of nicotine on the memory, attention and behavior of persons with Down Syndrome. This information will help us to decide whether long term nicotine treatment may improve memory, attention and behavior in middle aged persons with Down Syndrome. In other words, your participation may benefit the wider society.

b) The benefits that **you** might get from being in this study:
You may notice short-term benefits of nicotine therapy during the study. such as an improvement in your memory or attention performance; however you may also receive no noticeable benefit.

8. Other treatments you could get if you decide not to be in this study:

There are no accepted treatments for attention and memory decline in Down syndrome.

9. Payments for time spent taking part in this study or expenses:

Your parent/caregiver/guardian will be reimbursed (paid back) for their time, travel and trouble at $250 for the entire study (pro-rated at $50 per visit). You will be given a $50 Visa gift card as compensation (or payment) for your time and participation. However, if you do not pass the medical screening, we will be unable to offer compensation. We do not charge for medications, doctors' care or laboratory tests that are part of this study. We may ask you for your, Social Security number and address before you receive your payment for taking part in this study.

10. Reasons why the study doctor may take you out of this study:

- You are unable to follow the study procedures (attending all visits, remembering to wear patches daily)
- Your memory and attention problems get much worse
- You are unable to tolerate the medication
- You experience severe unpleasant side effects
- It is decided that this study is not in your best interests

If you are taken out of the study, you will be told the reason why.

11. What will happen if you decide to stop being in this study?

If you decide to stop being part of the study, call the study coordinator (see contact information below). Taking part in this study is completely voluntary, meaning you do not have to if you don't want to. Quitting the study will not affect your future care by Vanderbilt Hospital or future relationship with the University.

12. Who to call for any questions or in case you are injured:

If you have any questions about this research study or if you feel you have been hurt by being a part of this study, please feel free to contact us. You can call the principal investigator, **Paul Newhouse MD** at **615-936-0928** or the **study coordinator**, at **(615) 578-2955**.

For any other information about giving consent or your rights as a person in this study, to discuss problems, concerns, and questions, or to offer input, please feel free to call the Vanderbilt University Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

13. Confidentiality:

All data collected are given a subject number for your protection and privacy instead of using your name, and will be kept only on secure, password protected, networked computers in locked offices. Only research staff will have access to your information. All your materials will be labeled and coded with your subject identification number that is not linked in any way to your identifying information (like your address or phone number) for additional protection and confidentiality. This number will be used to identify your self-reported questionnaires, and computerized test data. A list linking names to identification numbers will be available only to authorized personnel and will be kept separately from patients' research charts. Only research personnel authorized by the Principal Investigator will have access to these records.

Vanderbilt may share your coded information with others or use it for other research projects not listed in this form. Vanderbilt will comply with any and all laws regarding the privacy of such information. There are no plans to pay you for the use or transfer of this de-identified information.

14. Authorization to Use/Disclose Protected Health Information:

All efforts, within reason, will be made to keep your protected health information (PHI) private. PHI is health information that has been gathered or kept by Vanderbilt as a result of your healthcare. This includes data gathered for research studies that can be traced back to you. Using or sharing ("disclosure") of such data must follow federal privacy rules. By signing the consent for this study, you are agreeing ("giving authorization") to the uses and likely sharing of your PHI. If you decide to be in this research study, you are also agreeing to let the study team use and share your PHI as described below.

As part of the study, we may share the results of your data and/or study-linked DNA samples to the following groups: people from the Federal Government Office for Human Research Protections, the Vanderbilt University Institutional Review Board, Vanderbilt's DNA Core Lab, and the Vanderbilt Kennedy Center. Federal privacy rules may not apply to these groups; but they have their own rules and codes to assure that all efforts, within reason, will be made to keep your PHI private.

The study results will be kept in your research record for at least six years after the study is finished. At that time, the research data that has not been put into your medical record will be kept for an unknown length of time. Any research data that has been put into your medical record will be kept for an unknown length of time.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact the study coordinator in writing and let us know that you withdraw your consent. Our mailing address is: **Department of Psychiatry, 1601 23rd Ave. S., Nashville, TN 37212.** At that time, we will stop getting any more data

about you. But, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

You have the right to see and copy the PHI we gather on you for as long as the study doctor or research site holds these data. To ensure the scientific quality of the research study, you will not be able to review some of the research data until after the research study is finished.

If you decide not to take part in this research study, it will not affect your treatment, payment or enrollment in any health plans or affect your ability to get benefits. You will get a copy of this form after it is signed.

STATEMENT OF STUDY PARTICIPANT

☐

I have read this consent form and the study has been explained to me verbally. All my questions have been answered, and I freely and voluntarily give consent to take part in this study.

_____
Name of Participant/Volunteer

_____ _____
Date Signature of Participant/Volunteer

_____
Name of Parent/Guardian

_____ _____
Date Signature of Parent/Guardian

Consent obtained by:

_____ _____
Date Signature

_____
Printed Name and Title

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Consent for Genetic Research

One purpose of this study is to look at certain genes (DNA) and how they affect your health and disease. Genes are the instruction manual for your body. The genes you get from your parents decide what you look like and how your body behaves. They can also tell us a person's risk for certain diseases and how they will respond to treatment. In particular, we are looking at the APOE gene, which is associated with Alzheimer's Disease, and similar kinds of cognitive decline in older persons and middle aged persons with Down Syndrome..

You are being asked to give a blood sample for genetic research. A single blood sample of 3 teaspoons will be drawn from a vein in your arm using a needle. This will take about 10-15 minutes of your time. What we learn about you from this sample will not be put in your health record. Your test results will not be shared with you or your doctor. No one else (like a relative, employer, or insurance company) will be given your test results.

Health insurance companies and group health plans may not use your genetic information when making decisions regarding your eligibility or premiums. Employers with 15 or more employees may not use genetic information when making a decision to hire, promote, or fire you or when setting the terms of your employment.

To prevent this, these samples will be given a code. Only the study staff will know the code. The name that belongs to the code will be kept in a locked file or in a computer with a password. Only authorized members of the lab will have access to your name. Your samples and information about you may be shared with others to use for research. To protect your privacy, we will not release your name. Your sample will be used to make DNA that will be kept for an unknown length of time (maybe years) for future research. The sample will be destroyed when it is no longer needed.

At any time, you may ask to have your sample destroyed. You should contact the study coordinator to have your sample destroyed and no longer used for research. We will not be able to destroy research data that has already been gathered using your sample. Also, if your identity was removed from the samples, we will not be able to locate and destroy them.

There will be no costs to you for any of the tests done on your samples.

Please check Yes or No to the questions below:

My blood sample may be used for gene research. ☐ Yes ☐ No

My blood sample may be stored/shared for future gene research for other health problems (such as cancer, heart disease, etc). ☐ Yes ☐ No

Participant's Name: _____ Date:_____

Parent/Guardian Signature: _____ Date: _____

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I, _____ [name of decision-maker/surrogate],
am the _____ [state relationship to participant]
of _____ [state participant's name].

I have read the informed consent document or it has been explained to me. I have had the opportunity to ask any questions and all of my questions have been answered. I have been informed that an investigational treatment may be administered to _____ [participant's name]. I believe receiving such treatment would be in the interests of _____ [participant's name] and is consistent with what he/she would have decided had he/she been able to do so.

Your decision to allow your family member/friend to participate in this research study is voluntary. You may choose not to allow his/her participation and he/she will receive alternative treatments without affecting his/her healthcare/services or other rights. You are also free to withdraw him/her from this study at any time. In the event new information becomes available that may affect the risks or benefits associated with this research study or your willingness to allow continued participation in this research study, you will be notified so that you can make an informed decision whether or not to continue your family member/friend's participation in this study.

Your family member/friend will periodically be re-evaluated for the capacity to give consent. If he/she is found to be capable, continued participation in this study would only occur with his/her consent.

_____ ___/___/___
Signature of Health Care Decision-Maker/Surrogate Date

_____ ___/___/___
Signature of Witness Date

_____ ___/___/___
Name and Signature of person obtaining consent Date