University of Wisconsin-Madison Research Subject Information and Consent and Authorization Form

Title of Study: Quitting Using Intensive Treatment Study (QUITS)
Study Investigators: Timothy B. Baker, PhD, and James H. Stein, MD

INVITATION AND SUMMARY

You are invited to participate in a research study about whether long-term use of a quit smoking medication (varenicline/Chantix) and combining varenicline with nicotine patches help people quit smoking. You are invited because you are a smoker interested in quitting. Your participation is voluntary. About 1250 people will participate in this UW Center for Tobacco Research and Intervention (UW-CTRI) study.

If you are eligible and agree to participate, you will receive 3 months of a quit smoking medication called varenicline (Chantix) and 6 coaching sessions to help you quit smoking (3 in-person and 3 on the phone). About half of the people in the study will get active varenicline (Chantix) for 3 additional months (a total of 6 months) and the other half will receive a placebo pill for 3 additional months. Also, everyone will get patches for 6 months, but some people will get placebo patches for some or all of the 6 months. A placebo is a pill or patch with no medication. Varenicline and nicotine patches have both been approved by the Food and Drug Administration (FDA) but their combined use has not been approved by the FDA.

Everyone in the study will complete questionnaires and answer questions about their smoking, medication use, withdrawal symptoms, and emotions, including nightly questions for 32 nights (either by phone or email), and provide a blood sample for analysis of nicotine and cotinine (a nicotine by-product). You will have to come to the UW-CTRI office (either Madison or Milwaukee) for 4-6 study visits, each lasting about 1-2 hours and complete 8 study phone calls that will last about 25-45 minutes. Blood draws for Madison participants will occur at a separate site: the University of Wisconsin Hospital Outpatient Clinic (600 Highland Avenue, Madison).

The main risks of varenicline are nausea, disturbed sleep, and a possible worsening of pre-existing psychiatric conditions. The main risks of nicotine patches are skin irritation, insomnia, and vivid dreams.

There are other ways to get evidence-based quit smoking treatment, so you don't need to be in the study to get treatment. If you decide to join the study, you can change your mind or stop at any time. If you complete the study, we will pay you up to $310, and there will be no charge to you for any of the medicine, tests, or clinic visits. If you decide not to participate, any relationship you have with the University of Wisconsin-Madison (UW-Madison) or the University of Wisconsin Hospitals and Clinics (UWHC) will not be affected in any way.

More detailed information is on the following pages. If you have any questions, please call Principal Investigator Timothy B. Baker at (608) 262-8673 or the Project Director Megan Piper, PhD at (608) 265-5472.

WHAT ARE THE RESEARCHERS DOING IN THIS STUDY?
The purpose of this study is to investigate:

1. Are smokers more likely to quit if they get 6 months of active varenicline (Chantix) versus 3 months of varenicline and 3 months of placebo?

2. Are smokers more likely to quit if they get a combination of varenicline (Chantix) and nicotine patches compared to varenicline alone?

WHAT WILL HAPPEN IN THIS STUDY?
If you are eligible and decide to participate in this study, it will be randomly decided (like flipping a coin) which smoking treatment you will get. Everyone will get 6 months of patches and pills. You might get all placebo patches, 3 months of active and then 3 months of placebo patches or 6 months of active patches. You might get 3 months of active varenicline and then 3 months of placebo or 6 months of active varenicline.

A placebo patch is a patch with no active medication or nicotine in it. You will not know whether you have active or placebo patches and neither will the staff you work with during the study. These study medications are approved by the Food and Drug Administration (FDA), but they have not been approved to be used together. We will train you on how to use the study medications and ask about any changes in physical or mental health you may have from the medications. The quit smoking treatments will be provided at no cost to you. We ask you not to use any other quit smoking treatments while you are using the study medications.

All study participants will get quit smoking coaching during the visits 2 weeks before you quit and on your target quit day and 2 weeks after your quit day. You will also get quit smoking coaching during phone calls 1 week before your quit day, and 4 and 8 weeks after your quit day. Coaching will be audio recorded to provide feedback to the counselors.

In total, over the course of a year, study participants will be asked to complete 3 more study visits that include coaching and questionnaires, 8 phone calls (3 with coaching) and nightly assessments for 32 days. Most study visits will last about 1 hour, with the exception of the next visit, which will last 1 and a half to 2 hours. The study assessments calls will last about 25-35 minutes. The 3 study calls that include both assessments and coaching will last about 45 minutes. The nightly brief questions will last about 3-4 minutes each night. In total, your participation could take about 9.5-10.5 hours.

For research purposes we will collect protected health information (PHI):
Protected health information, also called PHI, is information about your physical or mental health that includes your name or other information that can identify you, like your date of birth or medical record number. To do this study, we will use the following kinds of PHI:

- Your answers to questionnaires and interviews about your smoking and other tobacco use, demographics, emotional and physical health, your use of alcohol, your use of study medications, withdrawal symptoms, and your mood
- The names, addresses, and phone numbers of 3 people who will know how to contact you during your participation in this study. If we have been unable to get in touch with you (for example, if mail is returned or your phone is disconnected or no longer in use), we will ask these people how to contact you – we will not share anything about your participation in the study with these contacts.
- Your blood (up to 2 tablespoons) for analysis of nicotine and cotinine (a nicotine by-product)
- Audio recordings of your coaching sessions and interview questions
- Carbon monoxide breath tests

HOW IS BEING IN THIS STUDY DIFFERENT FROM REGULAR HEALTH CARE?
People wanting treatment to quit smoking from health care providers usually receive either brief coaching and a single prescription for medicine lasting 8-12 weeks or a referral for brief coaching and a starter package of medication from a telephone quitline. People in this study will have 6 coaching sessions and you will also receive at least 3 months and up to 6 months of 1 or 2 active medicines.

ARE THERE ANY RISKS?
The most common side effects associated with varenicline are nausea, insomnia or sleep disruption, vivid, strange, or unusual dreams, constipation, and gas. It is also important to note that some individuals may experience worsening of psychiatric conditions or symptoms such as anger, agitation, depression, or suicidal thoughts. Varenicline may be associated with a small, increased risk of certain heart problems in people with heart and blood vessel disease. Varenicline also may be associated with a small risk of new or worsening seizures. The most common side effects associated with nicotine patch include headache, skin irritation, difficulty sleeping and vivid dreams. Study staff will be checking your physical and mental health symptoms at every visit. You should notify study staff immediately and stop taking the study medication if you experience any significant emotional or heart-related symptoms, or a seizure. If you do report significant, unresolved emotional issues or thoughts of suicide, you will be asked to speak to a licensed psychologist or medical doctor who will evaluate your symptoms and help connect you to appropriate psychiatric services.

People who quit smoking may experience a number of unpleasant symptoms as part of the nicotine withdrawal syndrome. These symptoms may include the following: anger, frustration, irritability, craving for nicotine, anxiety, difficulty concentrating, restlessness, decreased heart rate, increased appetite or weight gain. In addition, smoking cessation

can increase the likelihood of depression in some individuals, and this is the reason we ask about depression and thoughts of hurting yourself during the study. Coaching received in the study may help you cope with symptoms such as these.
Drawing blood is associated with temporary pain at the needle insertion site. It can also be associated with bruising, fainting, or, in rare circumstances, a skin infection.

Some of the topics discussed in interviews or in questionnaires may cause temporary embarrassment or emotional discomfort for some people. If this happens to you, please let study staff know about your discomfort. You may choose not to answer any questions that make you uncomfortable. Another risk to taking part in the study is that your study information could be known to someone who is not involved in this study. If this happens, it could result in damage to your reputation, which could also affect your relationships with family and friends, affect your employment, or make it harder to get insurance or a job.

WILL BEING IN THIS STUDY HELP ME IN ANY WAY?
Both varenicline and the nicotine patch are FDA-approved smoking cessation treatments and have been shown to be more effective than placebo in helping people quit smoking. Quit smoking coaching has also been shown to help smokers quit. We don't know if being in this study will make it easier for you to quit smoking, but it may. All participants in this study will receive at least 3 months of free quit-smoking medication and 6 coaching sessions to help them quit smoking.

ARE THERE ANY COSTS?
The study medication (varenicline, nicotine patch), all clinic visits, lab procedures, and quit smoking coaching will be provided at no cost to you. All other costs related to basic expenses such as childcare will be your responsibility.

ARE THERE ANY ALTERNATIVES?

You do not have to participate in this study to get help with quitting smoking. If you decide not to participate in this study, you can get help from your primary care provider at your health clinic. Also, you can receive help from the Wisconsin Tobacco Quit Line by calling the toll-free number 1-800-QUIT-NOW (1-800-784-8669).

WILL I BE PAID FOR MY PARTICIPATING IN THE STUDY?
You will receive up to $310 for participating in this study. You will receive $20 for completing today's Orientation, $20 for completing the next visit (Visit 1), $10 for completing follow-up calls at Weeks 4, 8, 11, 17 and 39 (a total of $50), $50 for completing 80% of the nightly assessments, $25 for completing between 60 and 79% of the nightly calls, $20 for completing the call at Week 23, and $60 for completing the call at Week 52. If you are asked to attend the 23-week visit, you will receive an additional $40 for completing it. If you are asked to attend the 52-week visit, you will receive an additional $50 for completing it. Payment occurs at Visit 1, Week 4, Week 23, and Week 52 time points.

WHAT HAPPENS IF I GET SICK OR INJURED AS A RESULT OF THIS STUDY?
In the event that you are physically injured as a result of participating in this research, emergency care **assistance** will be available. However, you will be responsible for the charges for the emergency care. Here are some other things you need to know if you get sick or are injured because of this research:

- If the sickness or injury requires medical care, the costs for the care will be billed to you or your insurance, just like any other medical costs.
- Your health insurance company may or may not pay for this care.
- No other compensation (such as lost wages or damages) is usually available.
- UW-Madison and UW Health do not have a program to pay you if you get sick or are injured because of this study.
- By signing this consent form and taking part in this study, you are not giving up any legal rights you may have. You keep your legal rights to seek payment for care required because of a sickness or injury resulting from this study.

There is no commitment to provide any compensation for research-related injury. You should realize, however, that you have not released this institution from liability for negligence. Please contact the Project Director Megan E. Piper, PhD at 608-265-5472 if you are injured or for further information.

DO I HAVE TO BE IN THIS STUDY? WHAT IF I SAY YES AND CHANGE MY MIND LATER?
No, you do not have to be in this study. Taking part in research is voluntary. This means that you decide if you want to be in the study. If you decide now to take part, you can choose to leave the study at any time. If you do decide to participate, you may change your mind at any time without penalty or loss of benefits that you had prior to the study. If you decide to leave the study, we will tell you how to leave the study safely. Information that was already collected may still be used and shared with others, but the researchers will no longer be able to collect NEW information about you. In addition, the Principal Investigator can end your study participation if there are serious violations of the study protocol or procedures by you that put you at risk. You will be told of any new and significant findings that may affect your willingness to continue. Your decision of whether or not to participate in this study will not affect the quality of your medical care at this institution.

If you decide not to be in the study, you can contact your regular health care provider or we can provide you with information on services available through the Wisconsin Tobacco Quit Line.

HOW WILL THE RESEARCHERS KEEP MY INFORMATION CONFIDENTIAL?
We have strict rules to protect your personal information and protected health information (PHI). We will limit who has access to your health information, your name, address, phone number, and other information that can identify you. We will also store this information securely. We may publish and present what we learn from this study, but none of this information will identify you directly without your permission.

However, we cannot promise complete confidentiality. Federal or state laws may permit or require us to show information to university or government officials responsible for monitoring this study. This includes access to your study and lab records so that study monitors, auditors, the Institutional Review Board and regulatory authorities can verify study procedures and/or data. These groups will maintain your confidentiality. By signing this consent form, you are authorizing this access to your records.

WHO AT UW-MADISON CAN USE MY INFORMATION?

- UW-Madison regulatory and research oversight boards and offices
- Accounting and billing personnel at the UW-Madison

WHO OUTSIDE THE UW-MADISON WILL RECEIVE MY INFORMATION?

- The National Heart, Lung and Blood Institute (the study sponsor) **and the** U.S. Office for Human Research Protections
- Serious adverse events that occur during participant medication use or within 28 days after medication use will be reported to Pfizer, Inc. along with information about the participant and the event.
- Serious adverse events associated with use of the varenicline or nicotine patch will be reported to the Food and Drug Administration and the drug manufacturer
- A description of this clinical trial will be available on *http://www.ClinicalTrials.gov*, as required by U.S. Law. This Web site will not include information that can identify you. At most, the Web site will include a summary of the results. You can search this Web site at any time.

To further help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, we cannot be forced (for example by court order or subpoena) to disclose information that may identify you in any federal, state, local, civil, criminal, legislative, administrative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except to prevent serious harm to you or others, and as explained below. You should understand that a Certificate of Confidentiality does not prevent you, or a member of your family, from voluntarily releasing information about yourself, or your involvement in this study. If an insurer or employer learns about your participation, and obtains your consent to receive research information, then we may not use the Certificate of Confidentiality to withhold this information. This means that you and your family must also actively protect your own privacy.

You should understand that we will, in all cases, take the necessary action, including reporting to authorities, to prevent serious harm to yourself, children, or others. For example, in the case of child abuse or neglect or suicide.

A Certificate of Confidentiality does not represent an endorsement of the research study by the Department of Health and Human Services or the National Institutes of Health.

WILL INFORMATION FROM THIS STUDY GO IN MY MEDICAL RECORD?

- For Milwaukee Site participants: None of the information we collect for this study will be put in your medical record.
- For Madison Site participants: Your Nicotine/Cotinine lab results are sent only to the study team. However, if your medical record is connected to UWHealth, you and your doctor may be able to see that you are enrolled in a UW-QUITS study as well as see the results of your Nicotine/Cotinine labs. No other information we collect for this study would be in your medical record.

As required by the study sponsor, after the conclusion of the study, ALL information that can identify you will be removed from the health information collected in this study. At that time, it is no longer PHI and this authorization will no longer limit how the remaining information can be used. This means the information without anything that identifies you could be used or shared for reasons other than the ones described in this form (for example, use by a researcher from another university).

WHAT IF I HAVE QUESTIONS?

Please take as much time as you need to think over whether or not you wish to participate. If you have any questions about this study at any time, contact the Project Director Megan E. Piper, PhD at 608-265-5472.

If you have any questions about your rights as a research subject or complaints about the research study that you could not resolve with the study team, contact the UWHC Patient Relations Representative at 608-263-8009. The Patient Relations Representatives work with research subjects to address concerns about research participation and assist in resolving problems.

Authorization to participate in the research study and permission to use and/or disclose my health information:

I have read the information in this consent and authorization form, reviewed any questions, voluntarily agree to participate in this study and give authorization for the information I provide to be used by the study. I have received a copy of this consent and authorization form.

_____

Printed name of Participant

_____ _____

Signature of Participant **Date**

_____

Printed name of Person Obtaining Consent

_____ _____

Signature of Person Obtaining Consent **Date**

ADDITIONAL INFORMATION AND PERMISSION RELATED TO THE GENETIC RESEARCH COMPONENT

PURPOSE

The researchers are seeking your permission to use a portion of the blood sample provided for genetic analysis. Genetic analysis is when researchers look to see how inherited factors may be related to specific outcomes, such as quitting smoking or response to treatment. The genetic analyses, which may focus on specific genes or include analyses of all of your genes, will examine how genetic factors influence treatment success. Your DNA will be stored until all genetic analyses are completed.

ARE THERE ANY BENEFITS TO ME?

There is no direct benefit to you from the genetic research. The results of genetic tests will not be useful for your health care, and the results will not be shared with you or your doctor. Your decision whether or not to participate will not affect your compensation from the study.

ARE THERE ANY SIDE EFFECTS OR RISKS TO ME?

No additional blood draw is required for this study component. The main risk for genetic testing is to your confidentiality. The information obtained while you are in this study will remain confidential to the extent allowable by law. The results of this study may be used for medical or scientific publications, but you will not be identified personally in any such reports. Samples and genetic information may be sent to other laboratories for testing, but will be identified only with an ID number. This ID number will only be linked to your identity in one secure file that can be accessed by only the database administrator and the Principal Investigator. Neither you nor anyone else (such as your insurance company) will be able to obtain the results of any genetic test performed on your sample. We will store genetics samples for future analyses, but again, they will not be associated with your identity except via the separate ID number. If we conduct a genome wide association study (GWAS) which looks at all of the genome not just specific genes, approximately 5 years after the collection of all of the DNA samples in this study, we are required to submit the genetic results to the federal (U.S. government) genetic database. Your genetic data will be submitted using the DNA-specific identifier, which is only linked to your identity in a file that only the UW Biotechnology Center staff, the QUITS data administrator and the QUITS principal investigator can access. It is important to note that not all the risks of genetics research are known at this time.

The Genetic Information Nondiscrimination Act of 2008 is a Federal law that is supposed to prevent health insurance companies and employers from discriminating against people based on genetic information. There are some limits to this law: 1) It does not apply to businesses that employ fewer than 15 people. So, if you work somewhere with fewer than 15 employees, your employer could fire you or make other decisions about employment using genetic information. 2) Regardless of where you work, it does not apply to life insurance, disability insurance, or long-term care insurance. This means that if you had an abnormal genetic test result, and that result

became known, then you could be denied or pay higher rates for life insurance, disability insurance, or long-term care insurance.

WHO WILL USE MY HEALTH INFORMATION IN THE GENETIC COMPONENT?
The following groups will need to use information about you for this study (your age, sex, race, tobacco dependence):

- **The UW Biotechnology Center (DNA extraction**):
  The people at UW who receive your information may need to share information with others outside of UW for the research study. They will not receive personal identifying information. In addition to DNA samples, they will receive information regarding your age, sex, race, tobacco dependence and physical and mental health.

The people outside of UW who will receive your information are:

- **Washington University at St. Louis (Genetic analysis laboratory):**
  The researchers at UW who receive your information plan to share the same information as is shared with Washington University for the genetic analyses.
- **The National Institutes of Health GWAS repository**:
  This is a national project designed to analyze DNA information from a large number of people across the country in order to better analyze diseases such as tobacco dependence

HOW WILL MY INFORMATION BE PROTECTED IN THE GENETIC COMPONENT?
Your information will be entered directly into a password-protected computer and encrypted (coded in a way that only people with security clearance can see it). Information will then be stored on a secure computer in a locked room. Any information transmitted outside the UW will be transferred in a secure manner with no identifiable information transmitted to these entities.

IS MY PERMISSION TO PARTICIPATE IN THE GENETIC COMPONENT VOLUNTARY?
Your permission is voluntary. You do not have to sign this Authorization form and you may refuse to do so. This will not affect your ability to participate in the rest of the study.

HOW LONG WILL MY PERMISSION LAST?
This Authorization does not have an end date. You can end this Authorization at any time, however, by withdrawing your permission in writing. Beginning on the date your permission ends, no new health information will be used. Any health information that was shared before you withdrew your permission will continue to be used. After this Authorization ends, you can no longer actively take part in this DNA research bank. Withdrawal of your permission should be made in writing to Megan Piper,1930 Monroe St. Suite 200, Madison, WI 53711.

Authorization to Use and/or Share Health Information for the Genetic Component

Certification: I have read this Authorization form describing how my health information will be used and shared for storage in a DNA research bank for this study. I have had a chance to ask questions about the use of my health information and I have received answers to my questions. I agree to the use of my health information and I agree to the use and/or sharing of my health information for storage in the DNA research bank for this genetic study.

_____ _____

Signature of Participant **Date**

or

_____ I do not wish to participate in the genetic component
(Participant Initials)

VOLUNTARY STATEMENT OF INTENT TO AVOID PREGNANCY

According to the FDA and the manufacturers of varenicline and the nicotine patch, these medications should not be used by pregnant women. The risks of these medications to an unborn child are not fully known. We ask female study participants who are able to get pregnant or who believe that it is possible to get pregnant to agree to the statement below about avoiding pregnancy while taking study medication. Women who are menopausal and have not have a menstrual period in more than one year are not required to sign. Male participants are not required to sign this statement.

I, _____ (print name), agree to attempt to avoid pregnancy while I am taking study medication. I will continue to employ medically acceptable means to avoid pregnancy that have been approved by study staff. These methods include abstinence from sex with men, condoms, diaphragm, birth control pills, injectable contraceptive (e.g., Depo-Provera), contraceptive implant (e.g., Implanon), IUD, hysterectomy, tubal ligation, sterilization, vasectomy, or being more than 2 years post-menopausal. I will immediately contact study staff if pregnancy is suspected. I am aware that I may decline to sign this statement and my refusal to sign will have no effect on my further relationship with the University of Wisconsin; however, I cannot participate in this research study.

_____ _____

Signature of Participant **Date**