VUMC Institutional Review Board
Informed Consent Document for Research

Study Title:	Metabolism-Informed Smoking Treatment (MIST)
Version #:	7
Version Date:	05-15-2024
PI:	Hilary Tindle, MD

Name of participant: _____ Date of Birth: _____

Part I. 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.

Key Information about this study:
The first section of this document contains some key points that the research team thought you would find important. The study is described in more detail after this section. If you do not understand something, please ask someone.

Vanderbilt University Medical Center (VUMC) is doing a research study called the **Metabolism Informed Smoking Treatment study (MIST**). It is being funded by the National Institutes of Health (NIH). The MIST study uses information on how fast the body breaks down nicotine in order to help people quit smoking. We will be enrolling about 1000 smokers at VUMC.

Quitting smoking can help prevent smoking-related diseases like cancer and heart disease and can help you live longer. After study enrollment you may receive a prescription for a 3 month supply of quit smoking medication to support a quit attempt. We will ask you to complete 5 surveys during this 12 month study. Study contacts can be completed over the phone and/or through the mail. You may be asked to come into our offices to complete a brief (5 minute) breath test around 6 months after joining the study. Additional details are below in the "**Procedures to be followed"** section below.

Detailed Information:
The rest of this document includes detailed information about this study (in addition to the information listed above).

You are being asked to take part in this study because you are a current smoker who is willing to consider taking FDA-approved medication to help you quit smoking and you may have insurance coverage for quit smoking medication.

You do not have to be in this research study. You may choose not to be in this study and get other treatments without changing your healthcare, services, or other rights. 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. Your medical record will

contain a note saying you are in a research study and may contain some research information about you. Anyone you authorize to receive your medical record will also get this information.

Good effects that might result from this study:
There are benefits to science and humankind that might result from this study. This study may help in the development of effective interventions to increase participation in evidence-based smoking cessation treatment. There may be no benefit to participation in this study. Participants in this study may benefit by being more efficiently connected to tobacco treatment resources. As a result, they may be helped to quit smoking; potential benefits to quitting smoking include:

- preventing smoking-related diseases like cancer and heart disease
- helping you live longer
- protecting your friends and family from secondhand smoke
- saving money that would be spent on cigarettes

Procedures to be followed:

- A blood sample is required for this study. This blood test measures how fast your body breaks down nicotine.
- Surveys are also part of this study at baseline and in follow up over 12 months.
- Your doctor will be told that you are in the study.
- You will receive automated phone calls followed by unencrypted email and/or text message (your choice) to help you quit smoking. You can request a callback from a tobacco coach.
- You will be assigned by random, like the flip of a coin, to either a **Usual Care** group or a **Precision Care** group.
    - If you are in the **Usual Care** group, you will use the stop smoking medication that you discussed with the Tobacco Treatment Counselor.
    - If you are in the **Precision Care** group, you will use the stop smoking medication that is recommended based on the results of your blood test.
    - After study enrollment, you will be given up to a 3-month supply of one or more of the following FDA-approved stop smoking medications:
        - Nicotine Replacement Therapy (such as patch, lozenge, or gum)
        - Varenicline (also called Chantix)
- If you report that you quit smoking at the 6 month survey, you will be asked to provide a saliva or breath sample to verify this.
- During this 12-month study we will monitor your use of stop-smoking medicine, any ER/hospital visits, and review your medical records for up to 10 years after study

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completion to monitor for long term outcomes.
- After completing this 12-month study, you may be invited to participate in future studies

- We will ask you to provide your social security number so we can verify your insurance, your doctor, pay you for your participation, and to search databases such as the Tennessee Hospital Discharge Data System, state vital records, and CMS (Centers for Medicare and Medicaid) databases for information about health care received outside of Vanderbilt.

Automated contacts and opportunity to connect with a tobacco coach: Our partner, TelASK Technologies, will help us contact you after study enrollment to offer additional support. During these calls you can ask for a callback from a tobacco coach who can answer your questions and help you to stay smoke-free. The coach can also help you to use your stop smoking medication correctly. The initial round of calls lasts 3 months. To set up these calls, we will send your name, contact information, gender (male/female/unknown), and date of study enrollment to TelASK. During call backs the tobacco coach may ask you about audio recording for quality. This will not affect your care and you can choose not to be recorded or stop the recording at any point.

Surveys: You will be asked to complete a baseline survey which could take about 20 minutes to finish. During the study you will be contacted at 1, 3, 6, and 12 months after study enrollment by unencrypted email, text message, or phone (your choice) to complete a survey about your smoking and medication usage. Costs for data, texts, and minutes are not paid by the study. Your telephone/wireless carrier's standard charges may apply. If we are not able to reach you by email/text/phone, we may mail the surveys to you.

Confirming smoke free status: If you have quit smoking at the 6--month follow-up survey and you are not using nicotine replacement therapy at that time, we will ask you to complete a saliva sample which tests for nicotine levels in your saliva. If you are using nicotine replacement medicine at that time, we will ask you to complete a breath test instead of the saliva test. This breath test measures the amount of carbon monoxide in your lungs. If you have an upcoming appointment/hospitalization, study staff may also attempt to meet you in person. In case you are not able to come in person to our clinic, there is an option to do the breath test and/or the saliva test from home. The iCO™ personal Smokerlyzer® is a device that can be attached to your smart device and activated via an app. The results of the breath test are then sent to the study team. The saliva test is a small kit that you can complete at home and return by mail. All tests used to confirm smoke free status are collected only for the proposed research project, and only study staff will have access to these data.

Possible side effects and risks that you may experience if you take part in this study:

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Blood draw: You are being asked to have your blood drawn. Risks of a blood draw are minimal and could include pain, allergic reaction, infection, or bleeding at the needle stick site. Rarely, we may be able to use stored blood. Finally, if the first test result is not valid, a new sample of blood may be needed.

Symptoms that may go along with quitting smoking (unrelated to medications): The process of quitting smoking can be associated with many potential side effects including irritability, difficulty concentrating, changes in mood or behavior, and difficulty sleeping. These symptoms are known to occur whether people use medication or not. In other words, these symptoms occur even in people taking placebo (sugar pill) while they are quitting smoking. People who have conditions such as depression or anxiety may tend to experience more symptoms when quitting smoking. It is important to remember that anyone is capable of quitting smoking, regardless of their health conditions. If during the study you have any thoughts about suicide, immediately call 911 or go to the emergency room and ask them to contact your primary care doctor. When you are able, please contact study staff 615-701-MIST (6478).

This study is intended for women who are **not pregnant or breastfeeding because some of the medications to quit smoking should not be used during pregnancy or breastfeeding.** During the study if you become pregnant or are breastfeeding, please notify your Primary care provider (PCP) and study staff.
Possible side effects with stop smoking medications: Study staff have determined that you are medically eligible to receive these medications. Please notify your primary physician and the research team if you experience side effects of a medication. Study staff will call you to monitor the side effects. Dr. Hilary Tindle, the Primary Investigator, can be reached at 615-701-MIST (6478).

- **Nicotine Replacement Therapy (NRT):**
  Nicotine replacement therapy has been available for over two decades and is sold over the counter. Possible side effects of the patch include skin irritation or itching, which is commonly managed by rotating patch sites and/or applying an over-the-counter corticosteroid cream (such as 1% hydrocortisone), and trouble sleeping. Mouth, throat and nose irritation, heartburn, or hiccups may occur among people who use nicotine gum and lozenge. Many of the side effects of the lozenge or gum can be avoided by correct use of the medication. For the nicotine nasal spray and inhaler the most common side effects can include mouth/throat irritation, coughing, runny nose, and watery eyes. In rare cases dizziness, headache, nausea, and rapid heartbeat can occur. Severe and/or life-threatening side effects include allergic reactions, such as swelling of your throat and tongue, chest pain, a fast and abnormal heartbeat and inability to think

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clearly or logically.

- **Varenicline** (also called Chantix):
  Common side effects of varenicline include nausea, sleep disturbance and vivid dreams, gastrointestinal symptoms, and vomiting. Individuals with pre-existing psychiatric conditions may experience symptoms such as behavioral changes, agitation, depressed mood, and suicidal behavior during the process of quitting smoking with and without varenicline treatment. In a large FDA-mandated trial (EAGLES, Lancet 2016) varenicline was found to be safe and effective in patients with and without pre-existing psychiatric conditions. Women who are pregnant or breastfeeding should not use varenicline.

Expired carbon monoxide test and saliva cotinine test: There are no known serious adverse effects from these tests. The expired carbon monoxide test may sometimes cause people to feel mildly short of breath or cause cough during the test.

Payments for your time spent taking part in this study: You can be reimbursed up to $280 for full participation in this study. Here is a breakdown.

- $10 - screening blood test
- $40 - completed baseline survey
- $20 each for completed surveys at months 1, 3, 6, and 12
- $100 for sample given for a saliva or breath test at 6 months.
  - Plus, up to $50 additional for travel for in-person testing.

Your social security number is needed to provide you with a study payment card.

Costs to you if you take part in this study:

If you agree to take part in this research study, you and/or your insurance will not have to pay for the tests and treatments that are being done only for research. However, you are still responsible for paying for the usual care you would normally receive for the treatment of your illness. This includes treatments and tests you would need even if you were not in this study. These costs will be billed to you and/or your insurance.

You have the right to ask what it may cost you to take part in this study. If you would like assistance, financial counseling is available through the Vanderbilt Financial Assistance Program. The study staff can help you contact this program. You have the right to contact your insurance company to discuss the costs of your routine care (non-research) further before choosing to be in the study. You may choose

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not to be in this study if your insurance does not pay for your routine care (non-research) costs and your doctor will discuss other treatment plans with you.

Payment in case you are injured because of this research study:
If it is determined by Vanderbilt and the Investigator that an injury occurred as a direct result of the tests or treatments that are done for research, then you and/or your insurance will not have to pay for the cost of immediate medical care provided **at Vanderbilt** to treat the injury.

There are no plans for Vanderbilt to pay for any injury caused by the usual care you would normally receive for treating your illness or the costs of any additional care. There are no plans for Vanderbilt to give you money for the injury.

Who to call for any questions or in case you are injured:
If you should have any questions about this research study or if you feel you have been hurt by being a part of this study, please contact the Principal Investigator, Dr. Hilary Tindle, at 615-701-MIST (6478).

For additional 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 VUMC Institutional Review Board Office at (615) 322-2918 or toll free at (866) 224-8273.

Reasons why the study doctor may take you out of this study:
Under some situations the study physician may remove you from the study, for example, if your blood test was invalid.

What will happen if you decide to stop being in this study?
If you decide to stop being a part of the study, you must tell the study doctor, Dr. Hilary Tindle, in writing. Her mailing address is 2525 West End Avenue, Suite 450, Vanderbilt University Medical Center, Nashville, TN 37203. Deciding to not be part of the study will not change your regular medical care in any way.

Clinical Trials Registry:
A description of this clinical trial will be available on www.clinicaltrials.gov, as required by U.S. Law. This Web site will not include information that can identify you. At most, the website will include a summary of the results. You can search this Web site at any time.

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Information on Confidentiality, Authorization to Use/Disclose Protected Health Information, and Agreement to Participate in Study.

Confidentiality:

Vanderbilt may share your information, without identifiers, to others or use it for other research projects not listed in this form. Vanderbilt, Dr. Tindle and her staff 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.

All efforts, within reason, will be made to keep your personal information in your research record confidential. Total confidentiality cannot be guaranteed. To prevent a breach of confidentiality, these measurements and test results will be given a code and only the study staff will know the code. The name that belongs to the code will be kept in a locked file cabinet or on a computer with a password. Only Dr. Tindle and the research team will have access to your name. Your measurements and clinic data may be used indefinitely, and they may also be shared with other research groups; but they will be destroyed when no longer needed.

This study has support from the National Institutes of Health (NIH). Your study information is protected by a Certificate of Confidentiality. This Certificate allows us, in some cases, to refuse to give out your information even if requested using legal means.

It does not protect information that we have to report by law, such as child abuse or some infectious diseases. The Certificate does not prevent us from disclosing your information if we learn of possible harm to yourself or others, or if you need medical help.

Disclosures that you consent to in this document are not protected. This includes putting research data in the medical record or sharing research data for this study or future research. Disclosures that you make yourself are also not protected.

Breach of confidentiality: Your medical records will be reviewed, and relevant medical information will be collected and stored in a secure electronic database at Vanderbilt University Medical Center. This data will be password protected and only select research team members will have access to the password. However, despite these protections it is possible that this database could be compromised, and a breach of confidentiality could occur.

Privacy:

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Any samples and information about you may be made available to others to use for research. To protect your privacy, we will not release your name. You may not receive any benefit as a result of the tests done on your samples. These tests may help us, or other researchers learn more about causes, risks, and treatments around smoking or how to prevent this and other health problems.

Your samples may be used to make new products or tests. These may have value and may be developed and owned by the study staff, Vanderbilt University, and/or others. If this happens, there are no plans to provide money to you. At any time, you may ask to have your sample destroyed; however, 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.

Study Results: Results will be published in a peer reviewed medical journal and will not be made otherwise available to participants of the study.

Authorization to Use/Disclose Protected Health Information
What information is being collected, used, or shared?
To do this research, we will need to collect, use, and share your private health information. By signing this document, you agree that your health care providers (including both Vanderbilt University Medical Center and others) may release your private health information to us, and that we may use any and all of your information that the study team believes it needs to conduct the study. Your private information may include things learned from the procedures described in this consent form, as well as information from your medical record (which may include information such as HIV status, drug, alcohol or STD treatment, genetic test results, or mental health treatment).

Who will see, use or share the information?
The people who may request, receive or use your private health information include the researchers and their staff. Additionally, we may share your information with other people at Vanderbilt (Ingram Cancer Center Data Safety Monitoring Committee), for example if needed for your clinical care or study oversight. By signing this form, you give permission to the research team to share your information with others outside of Vanderbilt University Medical Center. This may include the sponsor of the study (National Institutes of Health) and its agents or contractors, outside providers, study safety monitors, government agencies, other sites in the study, data managers and other agents and contractors used by the study team. We try to make sure that everyone who sees your information keeps it confidential, but we cannot guarantee that your information will not be shared with others. If your information is disclosed by your health care providers or the research team to others, federal and state confidentiality laws may no longer protect it.

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Do you have to sign this Authorization?
You do not have to sign this Authorization, but if you do not, you may not join the study.

How long will your information be used or shared?
Your authorization for the collection, use, and sharing of your information does not expire. Additionally, you agree that your information may be used for similar or related future research studies.

What if you change your mind?
You may change your mind and cancel this authorization at any time. If you cancel, you must contact the Principal Investigator in writing to let her know by using the contact information provided in this consent form. Your cancellation will not affect information already collected in the study, or information that has already been shared with others before you cancelled your authorization.

Unless told otherwise, your consent to use or share your PHI does not expire. If you change your mind, we ask that you contact Dr. Tindle in writing and let her know that you withdraw your consent. Her mailing address is 2525 West End Avenue Suite 450, Nashville, TN 37203. At that time, we will stop getting any more data about you. However, the health data we stored before you withdrew your consent may still be used for reporting and research quality.

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 BY PERSON AGREEING TO BE IN THIS STUDY

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

_____ _____
Date Patient/Volunteer Signature

Consent obtained by RA:

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Date and Time: _____

Signature of RA obtaining consent: _____

Printed Name and Title: _____

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Part 2. Consent for Genetic Research

The purpose of this study is to look at genes (DNA) and how they affect 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.

You are being asked to give a blood and/or saliva (spit) sample for genetic research. **In most cases, this blood sample can be part of the same blood draw from Part I.** 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, boss, or insurance company) will be given your test results.

A single blood sample up to 15 ml (3 teaspoons) will be drawn from a vein in your arm using a needle. This will take about 5 minutes of your time.

A saliva sample of approximately 2 ml (about half a teaspoon) may be collected using a tube you will spit into if a blood sample cannot be obtained. Most people take between 2 and 5 minutes to provide a saliva sample.

Blood samples – You may feel bothered or pained from the needle stick. You may have a bruise, or the site may get infected. It is rare, but some people faint.

One risk of giving samples for this research may be the release of your name that could link you to the stored samples and/or the results of the tests run on your samples. This may cause problems with insurance or getting a job.

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 cabinet or on a computer with a password. Only study staff will have access to your name.

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 your genetic information that comes from this research when deciding to hire, promote, or fire you or when setting the terms of your employment.

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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.
Your samples, genotypes or other laboratory measures obtained from your sample, and information from your medical record and from this study may be shared with others to use for research. To protect your privacy, we will not release your name or other personal information that could identify you.

You will not receive any benefit as a result of the tests done on your samples. These tests may help us learn more about the causes, risks, treatments, or how to prevent this and other health problems.

Giving samples for research is your free choice and you may be in the study even if you do not want your samples used or stored for gene research.

At any time, you may ask to have your sample destroyed. You should contact study staff at 615-936-6668 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. You will not be paid for the use of your samples.

Information about you (medical record and study related, also known as phenotype data) and information derived from your blood/saliva sample (also known as genotypes) may be submitted in coded form to a controlled access government health research database for broad sharing for future gene research on health and disease with other Universities, non-profit institutes, for-profit companies, and government institutes.

We will not share any personal identifiers when sharing information about you or your blood/tissue sample. The genetic information derived from your blood/saliva sample will not be placed into your medical record, and the results of the genetic analysis will not be shared with you.

Donating your data may involve a loss of privacy, but information about you will be handled as confidentially as possible. Study data will be physically and electronically secured. As with any use of electronic means to store data, there is a risk of breach of data security. Genetic information that results from this study does not have medical or treatment importance at this time. However, there

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is a risk that information about taking part in a genetic study may influence insurance companies and/or employers regarding your health.

Taking part in a genetic study may also have a negative impact or unintended consequences on family or other relationships. It is possible that future research could one day help people of the same race, ethnicity, or sex as you. However, it is also possible through these kinds of studies that genetic traits might come to be associated with your group. In some cases, this could reinforce harmful stereotypes.

There will be no direct benefit to you from allowing your data to be kept and used for future research. However, we hope we will learn something that will contribute to the advancement of science and understanding of health and disease.

If the data or any new products, tests or discoveries that result from this research have potential commercial value, you will not share in any financial benefits. If you decide later that you do not want your information to be used for future research, you can notify the investigator in writing at: Dr. Hilary Tindle, Vanderbilt University Medical Center, 2525 West End, Suite 450, Nashville, TN 37203, and any remaining data will be destroyed. However, we cannot retract any data that has been shared with other researchers.

Please check Yes or No to the questions below:

My blood/saliva sample may be used for gene research in this study.

☐ Yes ☐ No

My blood/saliva sample may be stored/shared for future gene research at VUMC.

☐ Yes ☐ No

My blood/saliva sample may be stored/shared for future gene research for other health problems (such as cancer, heart disease, etc.).

☐ Yes ☐ No

Patient/Volunteer Name:
Date: _____

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Part 3. Additional 12-month quit test

Confirming smoke free status: If you have quit smoking at the 12-month follow-up survey and you are not using nicotine replacement therapy at that time, we will ask you to complete a saliva sample which tests for nicotine levels in your saliva. If you are using nicotine replacement medicine at that time, we will ask you to complete a breath test instead of the saliva test. This breath test measures the amount of carbon monoxide in your lungs. If you have an upcoming appointment/hospitalization, study staff may also attempt to meet you in person. In case you are not able to come in person to our clinic, there is an option to do the breath test and/or the saliva test from home. The iCO™ personal Smokerlyzer® is a device that can be attached to your smart device and activated via an app. The results of the breath test are then sent to the study team. The saliva test is a small kit that you can complete at home and return by mail. All tests used to confirm smoke free status are collected only for the proposed research project, and only study staff will have access to these data.

Possible side effects and risks of expired carbon monoxide test and saliva cotinine test: There are no known serious adverse effects from these tests. The expired carbon monoxide test may sometimes cause people to feel mildly short of breath or cause cough during the test.

Payments for your time spent taking part in this additional quit test: You can be reimbursed up to $150 for completing the quit test. Here is a breakdown.

- $100 for sample given for a saliva or breath test at 12-months.
  - Plus, up to $50 additional for travel for in-person testing.

STATEMENT BY PERSON AGREEING TO ADDITIONAL SAMPLE

I have read this additional consent section, and the research procedure has been explained to me verbally. All my questions have been answered, and I freely and voluntarily choose to take part in this additional sample collection.

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Consent obtained by:

Date and Time: _____

Signature of staff obtaining consent: _____

Printed Name and Title: _____