Penn
University of Pennsylvania

Institutional Review Board
3800 Spruce St., First Floor Suite 151
Philadelphia, PA 19104
Phone: 215-573-2540
(Federalwide Assurance # 00004028)

DATE: 14-Jun-2019
TO: Henry R Kranzler
CC: Pond, Timothy
Zindel, Leah

RE:
IRB PROTOCOL#: 820364
PROTOCOL TITLE: Placebo-controlled trial of bupropion for smoking cessation in pregnant women (PRIME)

SPONSOR: National Cancer Institute/NIH/DHHS
REVIEW BOARD: IRB #1

IRB AMENDMENT: NOTICE OF APPROVAL

Dear Dr. Kranzler,

The documents noted below, for the above-referenced protocol, were reviewed by the Institutional Review Board using the expedited procedure set forth in 45 CFR 46.110 and approved on 13-Jun-2019.

This study has been determined to pose greater than minimal risk to subjects. IRB approval for the study will expire on 10-Mar-2020.

The documents included with the application noted below are approved:
-HS-ERA Modification Submission, confirmation code: cjbgjcgd, submitted 06/07/2019
-Cover letter, Version 24, dated 6/7/2019
-Protocol, Version 24, dated 6/5/2019, tracked and clean
-Informed Consent form, Version 24, dated 6/7/2019, University of Pennsylvania subjects, tracked and clean
-Modification form, Version 24, dated 6/7//2019
-Cover letter, dated 6/13/2019 containing the list of documents for this submission
ONGOING REQUIREMENTS:

- You must obtain IRB review and approval under 45 CFR 46 if you make any changes to the protocol, consent form, or any other study documents subject to IRB review requirements. Implementation of any changes cannot occur until IRB approval has been given.
- Reportable event, such as serious adverse events, deviations, potential unanticipated problems, and reports of non-compliance must be reported to the IRB in accordance with Penn IRB SOP RR 404.
- When enrolling subjects at a site covered by the University of Pennsylvania's IRB, a copy of the IRB approved informed consent form with the IRB approved from/to stamp must be used unless a waiver of written documentation of consent has been granted.

UNIVERSITY OF PENNSYLVANIA

INFORMED CONSENT AND HIPAA AUTHORIZATION FORM

Protocol Title:	**Placebo-controlled trial of bupropion for smoking cessation in pregnant women**
Protocol Number:	820364
Principal Investigator:	Penn: Henry R. Kranzler, M.D. Treatment Research Center, 3535 Market St., Suite 500 Philadelphia, PA 19104 (215) 746-1943
Study Contact:	Penn: Leah Zindel, Study Coordinator (215) 746-1954
Emergency Contact:	Emergency Pager (215) 505-3799

Why am I being asked to volunteer?

You are being invited to participate in this study, **Placebo-controlled trial of bupropion for smoking cessation in pregnant women,** because you are pregnant and currently smoke cigarettes. The overall duration of the study is four and a half years, but your participation is expected to last only for six months from the time you first attempt to quit smoking. Approximately 360 women will be recruited for this study, with approximately 180 of them coming from the Hospital of the University of Pennsylvania (HUP) other UPenn facilities, or Thomas Jefferson University.

Your participation in this study is voluntary, which means that you can choose whether to participate or not. If you choose not to participate, there will be no loss of benefits to which you are otherwise entitled. Before you can make your decision, you will need to know what the study is about, the possible risks and benefits of being in this study, and what you will have to do in the study. The research team is going to talk to you about the research study, and they will give you this consent form to read. You may also want to discuss it with your family, friends, or doctor. You may find some of the medical language difficult to understand. Please ask the study doctor and/or the research team about this form. If you choose to participate, you will be asked to sign this form. You will have a chance to ask any questions that you may have before you sign this consent form. You will receive a copy of the signed consent form to keep.

It is important for pregnant smokers to quit smoking because it reduces both their risk for health problems and problems that their babies may experience. Bupropion is approved by the US Food and Drug Administration (FDA) for smoking cessation in people who are not pregnant, but there are no carefully controlled studies on the use of bupropion to help pregnant women quit smoking. Before being approved to help people quit smoking, bupropion was approved to treat depression. It has been used for that purpose in pregnant women, but has not been formally tested for that purpose.

Quitting smoking can be difficult for pregnant women. Although the best situation would be for pregnant women to quit smoking without the use of medications, bupropion may be helpful for pregnant women who cannot quit on their own.

While taking part in this study you will be randomly assigned (like the flip of a coin) to receive bupropion or a placebo (a harmless, inactive substance) to help you quit smoking. Your chance of getting the bupropion or placebo is 50/50. This study is a double-blind study, meaning that neither the study staff nor you will know if you are getting the bupropion or the placebo. In addition to receiving the study medication, you will receive counseling on four occasions during your pregnancy and twice after the pregnancy to help you stop smoking or continue not to smoke. During the 10 weeks of treatment with bupropion or placebo, you will also receive a daily text message in the morning to remind you to take the medication and a text message in the evening to ask if you took the medication that day. You will also be offered the use of a cell phone with unlimited talk and text, but no data, to allow you to receive the text messages, participate in phone counseling sessions, and to contact study personnel during the study. There is no charge for this phone and you are not required to take it. You will be asked to return the phone to the study staff at the end of the study.

A note about the phones:

- The phones will be provided for the duration of the study, and will include unlimited domestic talk and text.
- International calls and text are not permitted.
- You will not be responsible for the cost of the phone if it is lost.
- The phones are to be returned if you withdraw from the study.
- The phones are to be returned at the end of the study, at which time the information contained on the phones will be electronically 'wiped.'
- The phones will be deactivated at the end of the study.

What is the purpose of this research study?

1. To determine whether bupropion is better than a placebo (a harmless, inactive substance) in helping pregnant women to quit smoking.

2. To evaluate the health effects of bupropion compared to placebo (a harmless, inactive substance) on pregnant women and their babies.

3. To evaluate the effects of bupropion compared to placebo (a harmless, inactive substance) on depressive symptoms and cigarette craving in pregnant women.

4. To examine whether your genotype (your unique DNA makeup) determines your bodily functioning and behavioral responses to bupropion. People may respond to bupropion in part based on differences in what they inherit from their parents. We will examine genes (made up of DNA) that are thought to be involved in the effects of bupropion. In addition, we plan to test genetic markers to identify genes that influence other behaviors and characteristics that we will ask you about and that are being measured as part of this research. We will also use your DNA to study differences in genes between groups of people, because these differences can help in understanding the role of genes in risk for different disorders among groups of people. Because the DNA analysis is a key part of the study, if you choose not to provide blood for a DNA sample, you may not be able to participate in the study.

How long will I be in the study? How many other people will be in the study?

You will be in the active phase of the study for 10 weeks and will have 3 follow-up visits: one about 24 weeks after you first attempt to quit smoking and one at 2 and at 6 weeks after your baby is born. Thus, the total time that you would be in the study is about 6 months. It is expected that, a total of 360 participants will participate in the study.

What am I being asked to do?

You are being asked to complete assessments in person and by phone and allow us to review your medical record and your baby's medical records after he or she is born. You will also be asked to give a blood sample (3 tubes, enough to fill 1.5 tablespoons), take a study medication for 10 weeks, set a date to quit smoking, and try to quit. Finally, you'll be asked to come back for 3 visits after the 10-week medication study. Overall, during the study, you'll be asked to attend a total of 10 visits, six of which will be in person and four will be done by telephone. The specific procedures are detailed below.

What procedures are involved with participation in this research study?

Visit A: Screening Visit: After you review this form and have all of your questions answered, you will be asked to sign the form. You will then be asked to provide the researchers with information to determine whether you are eligible to participate in the study. By signing this form, you also give us permission to review your medical record to obtain information on your medical history, smoking, and other substance use. Your signature on this form will also allow us to obtain information from your baby's medical record following delivery. We will use that information to see whether bupropion and smoking cessation reduce problems later in pregnancy and during delivery.

On this visit, you will be interviewed for about an hour at the clinic where you are receiving prenatal care. This interview will include questions about your medical and pregnancy history, and any mood or other symptoms that you may have. We will also ask you about any past or current use of alcohol, drugs, and cigarettes. During this visit, and all other in person visits, we will ask you to blow into an instrument that measures a chemical (carbon monoxide) that is in tobacco smoke.

If your date of delivery has not been estimated by ultrasound, we will ask you to have an ultrasound test to provide an accurate estimate of when your baby will be born.

If you are deemed eligible and decide to participate, we will also ask you to provide the names and contact information of people (trusted friends or family members) who may serve as additional contacts if we cannot locate you for safety or other study-related reasons. We will only tell them that you are in a study and that you gave us their names to help us contact you, if we are unable to reach you during the study.

If you are eligible for this study, the following things will happen:

Visit B: Baseline Visit: This in-person visit will be completed within 30 days of your screening visit and will last approximately 90 minutes. At the visit, we will measure your heart rate and ask you to complete seven questionnaires by telephone and in person. We will ask you to provide a blood sample (3 tubes, enough to fill 1.5 tablespoons) to be used to conduct genetic testing and to measure your body's ability to break down nicotine, which is contained in cigarettes.

You will then receive the first of six counseling sessions in the study. This first, "pre-quit" counseling session will last 30 minutes and will help to prepare you to quit smoking. With your permission, we will make an audio recording of this and all other counseling sessions that you receive during the study. These recordings will be deleted after they have been reviewed to ensure that study personnel have followed correct counseling procedures.

You will be given study medication at this visit and will be instructed to begin taking it the following morning. You will be asked to identify a **quit date** within a week of beginning the study medication. You will start the study medication by taking one capsule (150 mg/day or placebo, a harmless, inactive substance) each morning for the first 3 days and then one capsule each morning and each evening (150 mg twice daily) for the remainder of the 10-week study treatment period. At this visit, and at every visit while you are taking the study medication, you will be asked about any side effects

that you may have experienced from the study medication. We will also ask you to return all study medication that you have not taken and the study medication packaging.

At this visit, you will also be offered a cell phone (if you choose this option) to be used for the text messages, phone counseling visits and for reminder calls. You may not use the phone for international calls. At the end of the study, you will be expected to return the phone to study staff. The day after the Baseline Visit, you will begin to receive two daily text messages. The first message of the day (in the morning) will concern the expected development based on your baby's age, accompanied by a reminder to take your study medication. The second message of the day (in the evening), will ask you whether you took all of your study medication that day. You'll be asked to text back indicating that you received the message (in the morning) and whether you took the medication that day (in the evening). We will ask you which times you would like to receive the text messages each day.

Although the responses that you send us via text messages will help us to keep track of your participation, the inbox for our texting center is not monitored, so if you have any study-related questions or concerns, please call our study staff to speak with them directly, rather than texting them. Text messaging should not be used in emergency situations; for emergencies, you should instead call 911.

Visit C: Quit Date Visit: Your scheduled **quit date** visit will occur approximately one week after the baseline visit and will last approximately 45 minutes. During this visit, we will measure your heart rate and you will be asked to blow into an instrument that measures a chemical (carbon monoxide) that is in tobacco smoke. The study nurse or coordinator (trained and supervised by the nurse, psychologist, or physician) will collect any medication that you had not taken and the study medication packaging. You will receive a four-week supply of study medication and a study nurse or coordinator will ask you about any study medication side effects that you may have experienced since starting the study. You will also be asked to complete two questionnaires and will receive 20 minutes of "quit-day" counseling, which will help you to identify things that could cause you to return to smoking and to develop a plan to avoid tempting situations.

Visit D: Week 3: This visit will occur by telephone and will last approximately 25 minutes, during which time you will be asked to complete one questionnaire over the telephone. You will be asked about your cigarette use since the last visit and any medication side effects you may have experienced. You will also receive 10 minutes of counseling by phone to help you avoid smoking or, if you need to, set another quit date to try again to quit smoking.

Visit E: Week 5: This in-person visit will last approximately 30 minutes. You will be asked to complete two questionnaires and be interviewed about your cigarette use since the last visit. We will measure your heart rate and you will be asked to blow into an instrument that measures a chemical (carbon monoxide) that is in tobacco smoke. You will be asked to provide a blood sample (2 tubes, enough to fill 1 tablespoon) to be used to measure concentrations of study medication in your blood. The study nurse or coordinator (trained and supervised by the nurse, psychologist, or physician) will collect any medication that you have left and the study medication packaging. You will receive a five-week supply of study medication and a study nurse or coordinator will ask you about any study medication side effects that you may have experienced since starting the study and assess any changes to your mood. You will also receive 10 minutes of counseling to help you avoid smoking or, if needed, set another quit date to try quitting again.

Visit F: Week 7: This telephone visit will last approximately 15 minutes and you will be asked to complete one questionnaire. You will also be asked about your cigarette use since the last visit and any medication side effects you may have experienced.

Visit G: Endpoint visit: This in-person visit will last approximately 25 minutes. You will be asked to complete two questionnaires and about your cigarette use since the last visit. During the visit we will measure your heart rate and you will be asked to blow into an instrument that measures a chemical (carbon monoxide) that is in tobacco smoke. The study nurse or coordinator (trained and supervised

by the nurse, psychologist, or physician) will collect any medication that you had not taken and the study medication packaging. The study nurse or coordinator will ask you about any study medication side effects that you may have experienced since starting the study and assess any changes in your mood.

Visit H: Week 24 after the Quit Date: About six months after you started treatment, you will be contacted by telephone or by letter to remind you that your Week 24 visit is coming up. During this visit, which may be conducted by phone or in person, a research technician will complete one questionnaire with you and ask you about your cigarette use since the last visit. When the visit is in person, she will also ask for a carbon monoxide breath sample. If your Week 24 visit comes at about the same time that you deliver your baby, the study coordinator will see you in the hospital for this visit. If it comes at about the same time as your 6-week check-up with your doctor, the study coordinator will arrange for the visit to be on that day. Because the carbon monoxide breath sample is an important part of the study, the nurses at the hospital may ask for a breath sample at the time that you deliver and at the time of your office visit after the baby is delivered.

Visits I and J: 2 and 6 weeks after delivery: The last two sessions will be held by telephone after the birth of your baby. You will be asked to complete several questionnaires, similar to those completed previously. You will also receive 10 minutes of counseling over the phone.

What are the possible risks or discomforts?
Bupropion can cause two different kinds of risks: the risk to you (from the medication and from the blood sample collection) and the risk to your developing baby (from the medication).

What are the possible risks of bupropion to you?
Bupropion is an antidepressant medication that is also approved to help people quit smoking.

The Most Common Side Effects that you may experience are dry mouth (11%), insomnia (31%), and dizziness (8%).

Other Likely Side Effects (occurring in at least 1% of patients) include: runny nose; neck pain; loss of appetite; nausea and vomiting; rash; itching; dry skin; sweating; tremor; abdominal pain; constipation; agitation; muscle or joint pain; urinary frequency; sleepiness; abnormal thinking; bronchitis; hives; strange taste in the mouth; weakness; fever; headache; depression; irritability; and blurred or double vision.

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Unlikely Side Effects (occurring in less than 1% but greater than 0.1% of patients): include: bruising; swelling; back pain; chills; hernia; increased sensitivity to light; flushing; migraine; a drop in blood pressure on standing; heart pounding or racing; stroke; abnormal liver function; tooth grinding; trouble swallowing; increased stomach acid; inflammation of the lips, gums or tongue; jaundice; leg cramps and twitching; abnormal coordination; confusion, decreased interest in sex; decreased memory, a sense of feeling not yourself; rapid changes in mood; hostility; increased muscle tone; parkinsonism; decreased feeling or a tingling feeling in extremities; suicidal ideation; acne; difficulty focusing vision; dry eyes; excessive abnormal movement, over excitation; and an increased frequency or urge to urinate.

Rare but Potentially Serious Side Effects (occurring in less than 0.1% of patients) include: feeling ill; fainting; memory loss; feeling unreal; hypomania (increased activity level combined with a “high” mood and decreased need for sleep); loss of balance; and spasm of the airways. Bupropion has also been reported to cause seizures in rare instances. This has been reported in less than 0.1% of people taking the medication. You should not take bupropion if you have a history of seizure disorder (epilepsy) or if you ever had bulimia or anorexia nervosa, because Bupropion is more likely to cause seizures in people with these conditions.

Effects on Mood: When bupropion is used for quitting smoking, it can cause you to have serious mood changes. These include depression or mania (an extreme increase in mood and activity and a decreased need for sleep), hallucinations, paranoia, delusions, thoughts of killing someone, hostility, agitation, aggression, anxiety, and panic, as well as thinking about suicide, attempting suicide, and actually committing suicide. These effects may or may not be related to the stress of quitting cigarettes.

You should contact the study doctor immediately if you experience any of these symptoms: thoughts about suicide or dying, attempts to commit suicide, new or worse depression, new or worse anxiety, feeling very agitated or restless, panic attacks, trouble sleeping, new or worse irritability, acting aggressive, being angry, or violent, acting on dangerous impulses, an extreme increase in activity and talking or any other unusual changes in behavior or mood. We will also monitor you carefully for these symptoms.

What are the possible risks of bupropion to your developing baby?

The use of bupropion for quitting smoking in pregnant women has not been well studied. There is a risk that bupropion could adversely affect your baby. Bupropion is classified by the FDA as "Pregnancy Category C," meaning that although animal studies have shown an adverse effect on the developing fetus, there are no well-controlled studies in humans, and the potential benefits of use during pregnancy may outweigh the risks.

Bupropion given to rats and rabbits at doses between 30 and 100 times those to be used in this study showed no clear evidence of birth defects. A slightly increased incidence of birth defects and skeletal variations were observed in rabbits. Decreased fetal weights were seen at 10 times the doses that will be used in this study. In another study, rats given bupropion at oral doses of up to 70 times the dose to be used in this study throughout pregnancy and lactation produced offspring showing no apparent birth defects.

No study has specifically tested bupropion for the treatment of either depression or quitting smoking in pregnant women. One study looked at the medical records of more than 7,000 women who took antidepressants during pregnancy. The review showed no greater risk for birth defects among the more than 1,000 women who took bupropion during the first trimester than women who took other antidepressants during the first trimester or who took bupropion during the second or third trimesters. In another study that reviewed the medical records of women who took medication during pregnancy, there was an increased risk of cardiac malformations among women who took bupropion during the first trimester (three months) of pregnancy. To lessen any risk to your developing baby, we will not begin treatment until after the first trimester of pregnancy.

Are there risks associated with taking the placebo medication?

Each placebo capsule contains 120 mg of calcium, which taken twice a day as part of the study, is less than the equivalent of the calcium contained in a single glass of milk. Your obstetrician may have recommended a calcium supplement as well. Therefore, if you plan to take a calcium supplement in addition to what is prescribed by your obstetrician, please discuss it with the study staff, as too much calcium could cause a problem with your kidneys.

What are the possible risks of a blood draw?

There will most likely be some mild discomfort from the blood draw. Some people develop a bruise at the needle site; some people report dizziness after the blood is drawn, which can cause fainting; and, some people develop minor infections. To prevent you from falling, you will be seated at the time blood is drawn and will be permitted to lie down if you feel faint. To prevent infection, the area where the needle is to be inserted will be wiped with a disinfectant before and after the needle is inserted. Only sterile needles will be used. The puncture site will be covered with a bandage. Sometimes we may not be able to draw blood at the first visit. We will try again at the Week 5 visit. If we still cannot get blood at that visit, we will not keep trying. We will obtain DNA from your saliva instead.

Risks Related to Genetic (DNA) Testing:
The principal risk of genetic testing is breach of confidentiality, with sensitive information concerning your genetic risk for disease becoming known. Such information, if available to you, could cause distress and if available to health or life insurers could adversely affect your access to insurance or its benefits.

A recent federal law, called the Genetic Information Non-Discrimination Act (GINA), helps reduce the risk from health insurance or employment discrimination. The law does not include other types of misuse by life insurance or long term care insurance. If you want to learn more about the GINA law, you can find the information on the internet or ask our study staff. Our study staff will provide you with a GINA law handout, which includes an internet web link.

Variation in some genes is known to be directly related to risk for certain illnesses, and other genes we may study in your DNA may be shown at some point in the future to be related to illness. Certain genetic research may reveal that you are at risk for certain diseases or that you are a carrier of a genetic disorder. This could mean that you or members of your extended family may have an increased likelihood of developing the disorder, or may be carriers.

Safeguards To Be Taken: To guard against these risks, you will not be provided with genetic test results and your confidentiality will be closely protected. All study information will be kept in a research record that is separate from your medical record and not available to insurance companies. We will not make any of our genetic findings available to you, nor will we add them to your medical record. (If you want to know your risk for genetic diseases, we will refer you to a genetic counselor.) We hope that this will prevent any information that could cause you trouble in the future from becoming known to anyone other than the scientists working on this study. While we cannot foresee situations where we would be forced to reveal potentially sensitive information about you (despite our efforts to maintain confidentiality), or where people who should not have this information could obtain it, it is possible that presently unforeseen situations may arise where this could happen.

Privacy concerns with text messages: The primary privacy concern with using text messages in a health context is that the messages can be intercepted by someone other than the person for whom they were intended. The text messages are not encrypted and may be read or accessed by others on your phone.

We will use the following methods to reduce the risk of your text messages being misused:

- You will be asked to approve your participation in the text messaging. To confirm your willingness to participate in the text messaging, you will be asked to respond to a text message confirming that you want to participate and confirming your phone number.
- We will also address with you how you may adjust the settings on your phone to limit information shown in text message alerts, and how you may delete private messages after they are read and/or sent. We store all information that identifies you, on a server in a manner that is compliant with legal requirements for confidentiality and privacy. Information transmitted through text messaging may be stored by your cell phone service provider in accordance with *its* privacy policy.

What if new information becomes available about the study?
During the course of this study, we may find more information that could be important to you. This includes information that, once learned, might cause you to change your mind about being in the study. We will notify you as soon as possible if such information becomes available.

What are the possible benefits of the study?
1. The counseling, text message reminders, and study medication may help you quit smoking.

2. Quitting smoking may improve your health and the health of your unborn child.

3. The knowledge obtained from this study may benefit other health care providers or pregnant smokers who decide whether to use bupropion to quit smoking during pregnancy.

4. You may not have any benefit while taking part in this study.

What other choices do I have if I do not participate in the study?

1. You can try to quit smoking on your own, without the use of bupropion or placebo.

2. You can receive care from your health care provider to quit smoking.

3. You may choose not to participate and not receive smoking cessation treatment.

Will I be paid for being in this study?

You will be paid for your travel and time, and for returning your study medication packagings, as described below. You will also be offered the use of a cell phone with coverage for text and talk, if you choose this option, at no cost to you. At the end of the treatment period, you are expected to return the phone to study staff. You will be paid $20 when you return the phone. Payments will be made to you with a Greenphire ClinCard. A Greenphire ClinCard is a reloadable, prepaid card that may be used for in-store purchases (by selecting either the "credit" or "debit" option), online purchases, in an ATM to get cash, and for cash advances at a bank (though there are fees associated with ATM withdrawals or bank cash advances). The study doctor or other staff member will tell you more about when you will get paid and provide you with an information sheet about how to use the Greenphire ClinCard. Funds added to the card should be available immediately, however in some cases it may take up to 1 business day. If you lose the card, please contact our study staff immediately. The study coordinator can cancel the original card and reissue a new card to you.

Visit		Time Spent	Travel Costs	Return Medication Pack(s)& Phone	Total for Visit
Visit A: Screening (IP)		$10	$15		**$25**
Visit B: Baseline (IP/T)		$60	$15		**$75**
Visit C: Week 1 (IP)		$35	$15	$1	**$51**
Visit D: Week 3 (T)		$10			**$10**
Visit E: Week 5 (IP)		$35	$15	$4	**$54**
Visit F: Week 7 (T)		$10			**$10**
Visit G: Week 10 (IP)		$30	$15	$5	**$50**
Visit H: Week 24	Phone or In-person	$45 $45	$0 or $15		**$45** **Or** **$60**
Visit I: 2 Weeks postpartum (T)		$10			**$10**
Visit J: 6 Weeks postpartum (T)		$10		Return Phone: $20	**$30**
Total payment for full participation		**$255**	**$75 or $90**	**$30**	**$360 or $375**

The maximum amount that you will be paid is $375 for full participation, including an in-person visit at Week 24 and returning all of your medication packagings. If you are scheduled for a telephone visit at Week 24, the maximum that you will be paid for full participation is $360. The amount that you actually receive will be based upon the assessments that you complete and number of study medication packagings you return. **You will also receive a baby gift of a box of 42 size 2 diapers and a tub of 40 baby wipes at the Week 10 or Week 24 visit (approximate value of $15.00 for both).** Please note that if you receive more than $600.00 compensation in one year for participation in research studies at the University of Pennsylvania, you must provide an Individual Tax Identification Number or Social Security Number for tax purposes.

Will I have to pay for anything?
There will be no cost to you for any of the study procedures. However, as part of this study you will receive and send text messages, and receive phone counseling. If you opt out of receiving a cell phone, standard text and voice messaging rates will apply as billed to you by your cell phone service provider.

When is the study over? Can I leave the study before it ends?
This study is expected to end after all participants have completed all visits, and all information has been collected. This study may also be stopped at any time without your consent because:

- The Principal Investigator believes that it is necessary for your health or safety or that of your unborn baby. Such an action would not require your consent, but you will be informed if such a decision is made and the reason for this decision.
- You have not followed study instructions.
- The National Cancer Institute (which is sponsoring the study), the study Principal Investigator, or the Food and Drug Administration (FDA) has decided to stop the study.

If you decide to participate, you are free to leave the study at anytime. Withdrawal will not interfere with your future care.

Who can see or use my information? How will my personal information be protected?

We will do our best to ensure that the personal information that we collect on you and your baby will be kept private in your research record. However, we cannot guarantee total privacy. The personal information that we collect may be given out if required by law. If information from this study is published or presented at scientific meetings, your name and other personal information will not be used. The Food and Drug Administration (FDA) may review your research records.

How will confidentiality be maintained and my privacy be protected?
We will identify your research records only by a code number. The code number will not be based on any information that could be used to identify you (for example, social security number, initials, birth date, etc.). The master list linking names to code numbers will be kept separate from the research data. All research information will be kept in locked files at all times.

The research team will make every effort to keep all the information you provide during the study strictly confidential, as required by law. The Institutional Review Board (IRB) at the University of Pennsylvania is responsible to protect the rights and welfare of research volunteers like you. The IRB has access to study information. Any documents you sign, where you can be identified by name, will be kept in a double-locked location. These documents will be kept confidential. All the documents will be destroyed when the study is over (though federal regulations require that this be done no less than three years after the study is formally closed).

Upon completion of the study, the DNA blood sample will be kept in storage indefinitely to permit complete analysis of the sample. However, the sample will forever be separated from your identity. There will be no way, not even through codes, to link the sample back to you. These de-identified

samples may be shared with other researchers and used in other projects, but will not be identified as having come from you.

If you choose to withdraw from the study after your DNA sample has been obtained, we will destroy all records in our research files connecting your identity with your sample(s). In this way, the samples could only be studied anonymously from this point forward.

What information about me may be collected, used or shared with others?
The following personal health information will be collected, used for research and may be disclosed or released during your involvement with this research study:

- Name
- Address
- Telephone number
- Email address
- Social Security Number
- Date of Birth
- Photo Identification
- Medical record number
- Audio-recordings, if you agree to have your counseling sessions taped

There is the possibility, if treatment is provided for study-related issues, that an electronic medical record (EMR) may be created for you. An Electronic Medical Record (EMR) is an electronic version of the record of your care within a health system. An EMR is simply a computerized version of a paper medical record.

If you are receiving care or have received care within the University of Pennsylvania Health System (UPHS) (outpatient or inpatient), results of these research-related procedures (i.e. laboratory tests, imaging studies and clinical procedures) may be placed in your existing EMR maintained by UPHS.

Once placed in your EMR, these results are accessible to appropriate UPHS workforce members that are not part of the research team. Information within your EMR may also be shared with others who are determined by UPHS to be appropriate to have access to your EMR (e.g., health insurance company, disability provider, etc).

A description of this clinical trial will be available on http://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.

Why is my information being used?
The research team will use your contact information to contact you during the study. Other information and the results of tests and procedures will be used to:

- do the research
- oversee the research
- to see whether the research was done right

Who may use and share information about me?
The following individuals may use or share your information for this research study:

- Dr. Kranzler and the study team at Penn that collects and reviews data for this study. The study team is located at two locations at the University of Pennsylvania in Philadelphia, PA 19104: the Treatment Research Center, 3535 Market Street Suite 500 (Dr. Kranzler) and the Department of Obstetrics and Gynecology, 2000 Courtyard, Hospital of the University of Pennsylvania, 3400 Spruce St. (Dr. Srinivas).
- Dr. Hand and the study team at Jefferson that collects and reviews data for the study. The study team is located at MATER 1233 Locust Street, 4th floor, Philadelphia, PA 19107.
- Kevin Lynch, Ph.D. and staff from University of Pennsylvania's Data Management Unit.

- The University of Pennsylvania Institutional Review Boards (The committees charged with overseeing research on human subjects) and the University of Pennsylvania Office of Regulatory Affairs
- The University of Pennsylvania Office of Human Research (the office that monitors research studies)
- Authorized individuals in the University of Pennsylvania School of Medicine who may monitor the research activities and findings, to protect the safety and welfare of all participants.

Who, outside of the School of Medicine, might receive my information?
The following individuals or organizations may receive your information from this research study:

- The Office of Human Research Protections, which is the government agency that oversees research with humans
- The University of Pennsylvania Institutional Review Boards (The committees charged with overseeing research on human subjects) and the University of Pennsylvania Office of Regulatory Affairs.
- Philadelphia Department of Public Health Institutional Review Board
- The Food and Drug Administration, which is the government agency that oversees the use of medications
- The National Cancer Institute
- Rachel Tyndale, Ph.D. University of Toronto, will analyze blood samples.
- Brenda Curtis, Ph.D., MSPH
- Greenphire ClinCard for processing study payments
- StudyCue, LLC (operating as Sense Health) which is the web service that will provide text messaging services

Once your personal health information is disclosed to others outside the School of Medicine, it may no longer be covered by federal privacy protection regulations.

The Principal Investigator or study staff will inform you if there are any additions to the list above during your active participation in the trial. Any additions will be subject to University of Pennsylvania procedures developed to protect your privacy.

FINANCIAL DISCLOSURE
Dr. Schnoll, a co-investigator on this research study, has served as a consultant to Glaxo Smith Kline and Pfizer, companies that manufacture medications for nicotine dependence. Both companies are not involved with this study. If you would like more information, please ask the researchers or the study coordinator.

How long may the School of Medicine use or disclose my personal health information?
Your authorization for use of your personal health information for this specific study does not expire. Your information may be held in a research database. However, the School of Medicine may not re-use or re-disclose information collected in this study for a purpose other than this study unless:

- You have given written authorization
- The University of Pennsylvania's Institutional Review Board grants permission
- As permitted by law

Can I change my mind about giving permission for use of my information?

Yes, you may withdraw or take away your permission to use and disclose your health information at any time. You can do this by sending written notice to the Principal Investigator of the study. If you withdraw your permission, you will not be able to stay in this study.

What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study.

You will be given a copy of this Research Subject HIPAA Authorization describing your confidentiality and privacy rights for this study.

By signing this document you are permitting the School of Medicine to use and disclose personal health information collected about you and your baby for research purposes as described above.

What happens if I am injured from being in the study?

If you experience an emergency, please call 911 or go to your nearest emergency room. If during the study, you have a medical problem that is not an emergency you may first contact the Principal Investigator: Dr. Kranzler (Penn) or Dr. Hand (Jefferson), whose numbers are listed on page one of this form.

For participants at Penn: If it is after hours, and you cannot reach Dr. Kranzler, you will need to speak to the TRC study doctor on call. To do so, please dial the 24-Hour Emergency Beeper at (215) 505-3799. The phone will ring once, and you will hear several beeps followed by no sound. Then, dial your full phone number, including area code, and hang up the phone. The study doctor will receive your page and call you back at the number you entered. If you are not contacted promptly, please try again. The study doctor on call will evaluate the problem and, if needed, contact the obstetrics doctor on call.

There are no plans for the University of Pennsylvania to pay you or give you other compensation for the injury. You do not give up your legal rights by signing this form.

If you think you have been injured as a result of taking part in this research study, tell the person in charge of the research study as soon as possible. The researcher's name and phone number are listed on the first page of this consent form.

Who can I call with questions, complaints or if I'm concerned about my rights as a research subject?

If you have questions, concerns or complaints regarding your participation in this research study or if you have any questions about your rights as a research subject, you should speak with the Principal Investigator listed on page one of this form. If a member of the research team cannot be reached or you want to talk to someone other than those working on the study, you may contact the Office of Regulatory Affairs with any question, concerns or complaints at the University of Pennsylvania by calling (215) 898-2614.

For more information about the Jefferson Institutional Review Board or Jefferson's Human Research Protection Program, please visit their website at http://www.jefferson.edu/human_research/irb/index.cfm, or for questions about your rights as a research participant at Jefferson: Thomas Jefferson University, 1015 Chestnut St. Suite 1100 Philadelphia PA 19107; Phone (215)–503-8966.

When you sign this form, you are agreeing to take part in this research study. This means that you have read the consent form, your questions have been answered, and you have decided to volunteer. Your signature also means that you are permitting the University of Pennsylvania to use your personal health information collected about you for research purposes within our institution. You are also allowing the University of Pennsylvania to disclose that personal health information to outside organizations or people involved with the operations of this study.

A copy of this consent form will be given to you.

Agreeing to receive a cell phone is not a requirement to participate in the study. Please initial your decision:

Yes, I agree to receive a cell phone: _____

No, I do not agree to receive a cell phone: _____

Agreeing to audio recording is not a requirement to participate in the study. Please initial your decision:

Yes, you agree that we can record your counseling sessions: _____

No, you do not agree that we can record your counseling sessions: _____

_____	_____	
Name of Subject (Please Print)	Signature of Subject	Date

_____	_____	
Name of Person Obtaining Consent (Please Print)	Signature	Date