Investigating Near-Threshold Perception During Anesthetic Sedation

NCT06403852

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UNIVERSITY OF MICHIGAN
CONSENT TO BE PART OF A RESEARCH STUDY

1. KEY INFORMATION ABOUT THE RESEARCHERS AND THIS STUDY

Study title: Investigating Near-Threshold Perception During Anesthetic Sedation

Company or agency sponsoring the study: National Institutes of Health (NIH)

Names, degrees, and affiliations of the principal investigator and study coordinator:

Principal Investigator: Zirui Huang, PhD, Department of Anesthesiology

Study Coordinators: Aaron Ellis, Department of Anesthesiology
Amy McKinney, MA, Department of Anesthesiology

1.1 Key Study Information

You may be eligible to take part in a research study. This form contains important information that will help you decide whether to join the study. Take the time to carefully review this information. You should talk to the researchers about the study and ask them any questions you have. You may also wish to talk to others such as your family, friends, or other doctors about joining this study. If you decide to join the study, you will be asked to sign this form before you can start study-related activities. Before you do, be sure you understand what the research study is about.

A research study is different from the regular medical care you receive from your doctor. Research studies hope to make discoveries and learn new information about diseases and how to treat them. You should consider the reasons why you might want to join a research study or why it is not the best decision for you at this time.

Research studies do not always offer the possibility of treating your disease or condition. Research studies also have different kinds of risks and risk levels, depending on the type of the study. You may also need to think about other requirements for being in the study. For example, some studies require you to travel to scheduled visits at the study site in Ann Arbor or elsewhere. This may require you to arrange travel, change work schedules, find childcare, or make other plans. In your decision to participate in this study, consider all these matters carefully.

This research is studying whether mental functions take place during different levels of anesthesia using a commonly used drug (propofol) while undergoing fMRI (functional Magnetic Resonance Imaging, or “brain imaging”), which shows areas in the brain involved in thinking at different depths of anesthesia.

Your health-related information including a urine drug test, urine pregnancy test, and fMRI will be collected for this research study.

There can be risks associated with joining any research study. The type of risk may impact whether you decide to join the study. For this study, some of these risks may include discomfort associated with being asked personal questions about your health history, discomfort from noise produced by the MRI machine, bruising at the site of IV insertion, and risks associated with receiving general anesthesia. More detailed information will be provided later in this document.

You may not receive any personal benefit from participating in this study.

We expect the amount of time you will participate in the study will be up to 4 hours for this one-time research visit.

You can decide not to be in this study. Participation in this study is completely voluntary. Even if you decide to join the study now, you are free to leave at any time if you change your mind.

More information about this study continues in Section 2 of this document.

2. PURPOSE OF THIS STUDY

2.1 Study purpose:

The purpose of this study is to see if mental functions take place during different levels of anesthesia using a commonly used drug (propofol) while undergoing fMRI (functional Magnetic Resonance Imaging, or "brain imaging"), which shows areas in the brain involved in thinking at different depths of anesthesia.

As a result of this study, we expect to gain a deeper understanding of mental function during different levels of anesthesia, and to evaluate if the use of ultrasonic brain stimulation accelerates return to consciousness.

Propofol is FDA approved for use in patients undergoing an anesthetic for medical treatment but is not approved for use in healthy volunteers.

3. WHO MAY PARTICIPATE IN THE STUDY

Taking part in this study is completely **voluntary**. You do not have to participate if you don't want to. You may also leave the study at any time. If you leave the study before it is finished, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled.

3.1 Who can take part in this study?

Inclusion Criteria:

- Healthy adults ages 18 – 40.
- Must have a body mass index (BMI) less than 30.
- Must be right-handed.
- Must be English speaking.
- Must be capable of giving written informed consent.

Exclusion Criteria:

- History of obstructive sleep apnea or any severe snoring history.
- Tattoos in the head or neck region and possibly from other body sites, based upon the judgment of the study coordinator or principal investigator.
- History of a difficult airway with a previous anesthetic.
- History of neurological disorders.
- Hypertension or other cardiovascular abnormalities.
- Pulmonary hypertension or other pulmonary abnormalities.
- Gastroesophageal reflux disease (GERD) or heartburn, or pancreatitis or a history of pancreatitis.
- History of significant head injury with loss of consciousness.
- Learning disability or other developmental disorder.

- Allergic reactions to propofol.
- Allergic reactions to eggs or egg products.
- Allergic reactions to soybeans or soy products.
- Pregnant or nursing mothers.
- Contraindications to neuroimaging methods, including claustrophobia (inability to be in small, enclosed spaces).
- Inability or unwilling to fast, or withhold food and liquid intake, for 8 hours prior to your scheduled study visit.
- Inability or unwilling to have an adult accompany you to your study visit and to stay with you for 24 hours after your scheduled study visit.
- Unwilling to abstain from alcohol use for 24 hours prior to your scheduled study visit.
- History of drug use, or have a positive drug screen, or a current history of nicotine use.
- Participation in a clinical trial using an investigational drug or device within 30 days.
- Any impairment, activity, or situation that in the judgment of the study coordinator or Principal Investigators would prevent satisfactory completion of the study protocol.

3.2 How many people are expected to take part in this study?

A total of 36 participants are expected to participate in this study.

4. INFORMATION ABOUT STUDY PARTICIPATION

4.1 What will happen to me in this study?

You have already been screened and confirmed eligible for the study.

Pre-procedure preparation:

After signing this consent form, and in a private patient examination area, one of the anesthesiologists will perform a complete history and physical examination and medication history review.

We will confirm that you have had nothing to eat or drink for 8 hours prior to your study visit.

We will confirm you have not had any cold or flu symptoms for the past 14 days.

We will obtain a urine sample for a urine pregnancy test for females, and a urine drug screen for all participants. If there is any positive pregnancy or drug screen result, you will not be allowed to continue your participation in this study.

Next, you will be prepared for the fMRI machine. This preparation involves removing any metal from your body and clothing (i.e., jewelry, hairpins, pens, eyeglasses, body piercings, etc.). At this point we will ask you to change into the scrubs that we have on hand to prevent any interference with the fMRI procedure. Your belongings will be secured in these offices and made available after the study.

Procedure:

You will then have a small hollow tube called an intravenous (IV) line placed in a vein in your arm by an anesthesiologist. To help reduce the discomfort, the anesthesiologist will first numb your skin with a numbing medicine (lidocaine) before the IV needle is inserted.

Standard monitors will then be placed onto your body, which are used to measure and record vital signs such as blood pressure, pulse, and heart rate. You will be placed in the fMRI machine. A picture of your brain will be obtained with fMRI. This is not painful, but it is noisy. The noise is a series of beeps that the fMRI scanner generates. You may be in the fMRI scanner for up to 1.5 hours.

The IV anesthetic (propofol) will be given by an infusion pump. You will receive gradually increased doses of sedation until you reach the level of sedation required for the study. You will hear instructions during fMRI scanning, such as to squeeze a gripping device. You will be shown a series of images, repeated 10 times for each 30-minute session, and you will be asked to determine which category an image belongs to ("face" or "house") and if you recognize it from previous images ("Yes" or "No").

Post-Procedure:

After you have recovered sufficiently you will be allowed to leave with the adult who accompanied you to the visit. Recovery means you will be awake, fully responsive, able to walk, able to urinate, and no significant nausea or vomiting. **You will not be able to drive home from this visit and must have pre-arranged transportation from a trustworthy friend or family member (ie, not an Uber or other rideshare driver). While you may feel okay, keep in mind you may still have some effects of the sedation for up to 24 hours after the visit**. You will be provided with after care instructions, such as not driving for 24 hours after the procedure.

4.2 How much of my time will be needed to take part in this study?

You should plan to be at your scheduled study visit for up to 4 hours, which includes preparation and recovery time.

4.3 When will my participation in the study be over?

Your participation will be over after your study visit; we will continue to review your medical record for up to 30 days.

4.4 What will happen with my information and/or biospecimens used in this study?

With appropriate permissions, your fMRI data may also be shared with other researchers, here, around the world, and with companies. Your identifiable private information may be stripped of identifiers and used for future research studies or distributed to another researcher for future research studies without additional informed consent.

5. INFORMATION ABOUT STUDY RISKS AND BENEFITS

5.1 What risks will I face by taking part in the study? What will the researchers do to protect me against these risks?

The known or expected risks are:

Medical History Form: Though it is not experienced frequently, you may experience some discomfort associated with being asked personal questions about your health history. If you become distressed while completing questionnaires, we encourage you to seek clarification of any questions that you find to be unclear or troubling. Always remember that you have the option to stop participating at any time without any penalty to you.

Risks to pregnant or nursing women: The procedures that you are undertaking (MRI scanning, administration of propofol, ultrasound stimulation) in this study might affect a baby, before or after the baby is born. We do not know if MRI scanning and administration of propofol cause harm to a baby, so we do not want anyone who might

be pregnant to enter the study. You will be asked to have a urine pregnancy test to be sure you are not pregnant at the start of the study visit.

Neuroimaging with fMRI: *You may experience claustrophobia, or fear of tight places*. While inside the MRI, you may experience an acute panic attack due to claustrophobia. You will be pre-screened for fear of tight places. Once inside the magnet, you will be given a squeeze ball to signal the MRI operator if you are under acute distress.

You may experience some slight discomfort from noise produced by the MRI machine. You will be provided with foam earplugs. The primary risks known to occur from MRI are due to the magnet's ability to pull metal objects toward it. This pull can cause metal objects in the body (e.g., surgical clips or staples) to move and cause bleeding or disruption of surrounding tissue.

Metal objects carried or worn by a person (e.g., jewelry, hair clips, tools) can be pulled toward the magnet and, if free to fly, could strike an individual. The MRI can cause pacemakers or stimulators implanted in the body to malfunction. There is also a risk that metallic objects in or on the body may be heated by the radio frequency waves, possibly causing burns. Individuals will be screened for implanted metal objects and will be asked to remove all other metal objects. Women of childbearing potential will be screened for pregnancy with a urine pregnancy test immediately before they go into the scanner.

IV Line Placement: Having an IV line placed for this study may cause pain, minimal bruising at the site of insertion, or a small collection of blood (blood clot). We will use a small injection of lidocaine (numbing medicine) before we place the IV line to minimize pain during these procedures. We will additionally minimize these risks by ensuring that only an experienced provider inserts the IV line into your arm. General Anesthesia: The risks for receiving general anesthesia are airway obstruction (meaning some part of your body tissue is blocking your breathing tube) and aspiration of your stomach contents (meaning the contents of your stomach are brought up your throat and into your lungs). Airway obstruction is unlikely and is easily managed with a variety of techniques and devices by an experienced, board-certified anesthesiologist. To prevent aspiration of your stomach contents, we will ensure that you do not eat or drink anything 8 hours before the study.

Study Drug: Propofol is FDA approved for use in patients undergoing an anesthetic for medical treatment but is not approved for use in healthy volunteers.

The known side effects associated with **propofol**, which are infrequent, include: irregular heart rate (fast or slow), hypotension (low blood pressure), an increase in blood lipids, nausea, cough, slight burning or stinging around the IV needle, mild itching and skin rash, numbness or tingly feeling, confusion, agitation, anxiety, muscle pain, and discolored urine.

In extremely rare cases, inflammation of the pancreas, death, or overdose (too much drug) is possible.

Risks associated with propofol administration also can include possible allergic reaction to the drug, infection due to microbial contamination, slowing of your breathing which may require placement of a breathing tube or machine to assist breathing, or a decrease in blood pressure which may require giving a drug or IV fluids to increase your blood pressure.

We will minimize all risks by our initial screenings, asking inclusion/exclusion criteria questions, performing a complete history and physical, having you wear scrubs for MRI testing, performing pregnancy (female) tests, ensuring that you have fasted for at least 8 hours before the experiments, having standard monitoring equipment (which are used to measure and record vital signs such as blood pressure, pulse, and heart rate), and medications readily available if needed, and conducting all experiments in a UMHS anesthetizing location.

An adult will need to be with you as you will not be allowed to go home unsupervised. The study coordinator will call you the following day to ensure that you are feeling well and that you are not experiencing any side effects.

If you are experiencing a problem, the study coordinator will contact the clinicians who staff your study visit and appropriate actions will be taken. You should also feel free to contact the study team should you observe anything abnormal following your participation in the study.

Because of the side effects of the medications, you may feel sleepy or not yourself for up to 24 hours. Do not engage in any activity that requires alertness or coordination during your 24-hour recovery period. This includes driving; operating heavy machinery; using power tools; cooking; climbing; riding a bicycle; or rollerblading/skating. Do not make important or complex decisions or sign legal documents. Do not drink alcoholic beverages. It is recommended that you remain in the company of a family member, friend, or attendant for the next 24 hours.

Additionally, there may be a risk of loss to confidentiality or privacy. See Section 9 of this document for more information on how the study team will protect your confidentiality and privacy as with any research study, there may be additional risks that are unknown or unexpected.

As with any research study, there may be additional risks that are unknown or unexpected.

5.2 What happens if I get hurt, become sick, or have other problems as a result of this research?

The researchers have taken steps to minimize the risks of this study. Even so, you may still have problems or side effects, even when the researchers are careful to avoid them. Please tell the researchers listed in Section 10 about any injuries, side effects, or other problems that you have during this study. You should also tell your regular doctors.

5.3 If I take part in this study, can I also participate in other studies?

Being in more than one research study at the same time, or even at different times, may increase the risks to you. It may also affect the results of the studies. You should not take part in more than one study without approval from the researchers involved in each study.

5.4 How could I benefit if I take part in this study? How could others benefit?

You may not receive any personal benefits from being in this study. As a result of this study, we expect to gain a deeper understanding of mental function during different levels of anesthesia, and to evaluate if the use of ultrasonic brain stimulation accelerates return to consciousness.

5.5 Will the researchers tell me if they learn of new information that could change my willingness to stay in this study?

Yes, the researchers will tell you if they learn of important new information that may change your willingness to stay in this study. If new information is provided to you after you have joined the study, it is possible that you may be asked to sign a new consent form that includes the new information.

6. ALTERNATIVES TO PARTICIPATING IN THE STUDY

6.1 If I decide not to take part in this study, what other options do I have?

Participation in this study is completely voluntary. You do not have to participate as this is a volunteer-based study.

7. ENDING THE STUDY

7.1 If I want to stop participating in the study, what should I do?

You are free to leave the study at any time. If you leave the study before it is finished, there will be no penalty to you. You will not lose any benefits to which you may otherwise be entitled. If you choose to tell the researchers why you are leaving the study, your reasons for leaving may be kept as part of the study record. If you decide to leave the study before it is finished, please tell one of the persons listed in Section 10 "Contact Information".

7.2 Could there be any harm to me if I decide to leave the study before it is finished?

No.

7.3 Could the researchers take me out of the study even if I want to continue to participate?

Yes. There are many reasons why the researchers may need to end your participation in the study. Some examples are:

- The researcher believes that it is not in your best interest to stay in the study.
- You become ineligible to participate.
- Your condition changes and you need treatment that is not allowed while you are taking part in the study.
- You do not follow instructions from the researchers.
- The study is suspended or canceled.

8. FINANCIAL INFORMATION

8.1 Who will pay for the costs of the study? Will I or my health plan be billed for any costs of the study?

The study will pay for research-related items or services that are provided only because you are in the study. This includes the drug and pregnancy test for screening, and the one-time MRI visit with propofol administration. You should not receive a bill for any of the services you receive. If you receive a bill, please contact the study coordinator listed in Section 10.1.

The study team has given you instructions about this research study. It is important that you follow these instructions carefully. If you get sick, have a medical complication, or are injured because of your being in the study, call Dr. Tarnal immediately at 734-936-4000 and ask to "page Dr. Tarnal". The doctor will either treat you or send you to another doctor for treatment.

If you are injured or in the event of a medical emergency, dial 911 or visit your nearest Emergency Room. If you believe the study has made you sick or caused you injury, contact one of the people listed in section 10 of this document (Contact Information). If taking part in the study makes you sick or causes you injury, you or your insurance provider will be billed for all costs of treatment as the study does not provide compensation for sickness or injury caused by the study. It is possible that your insurance will not cover these costs.

By signing this form, you do not give up your right to seek payment if you are harmed because of being in this study.

8.2 Will I be paid or given anything for taking part in this study?

You will be paid a total of $200 for completing the visit.

If you choose to stop participating before it is finished, your compensation will be pro-rated at $25 per hour of participation.

This will be paid to you via a check that will be mailed to you after your completion of the study visit. You should expect to receive your payment within 7-10 days of your completed visit.

8.3 Who could profit or financially benefit from the study results?

It is unlikely that anyone will profit or financially benefit from the study results.

Research can lead to new discoveries, such as new tests, drugs, or devices. Researchers, their organizations, and other entities, including companies, may potentially benefit from the use of the data or discoveries. You will not have rights to these discoveries or any proceeds from them.

9. CONFIDENTIALITY OF SUBJECT RECORDS AND AUTHORIZATION TO RELEASE YOUR PROTECTED HEALTH INFORMATION

The information below describes how the confidentiality of your research records will be protected in this study, and any sub-studies described in this document.

9.1 How will the researchers protect my information?

All measures will be taken to protect your privacy. All your information will be stored on password protected computer files and only members of the research team will have access to this information. In addition, your information will not be linked directly to your name but rather indirectly by a random number scheme. The study team will have access to the key which allows your name to be determined from the random number that was assigned to you. Also, all members of the research team are trained and certified in human subjects' privacy.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. The researchers with this Certificate may not disclose or use information, documents, or biospecimens that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other action, suit, or proceeding, or be used as evidence, for example, if there is a court subpoena, unless you have consented for this use. Information, documents, or biospecimens protected by this Certificate cannot be disclosed to anyone else who is not connected with the research except, if there is a federal, state, or local law that requires disclosure (such as to report child abuse or communicable diseases but not for federal, state, or local civil, criminal, administrative, legislative, or other proceedings, see below); if you have consented to the disclosure, including for your medical treatment; or if it is used for other scientific research, as allowed by federal regulations protecting research subjects.

The Certificate cannot be used to refuse a request for information from personnel of the United States federal or state government agency sponsoring the project that is needed for auditing or program evaluation by the National Institutes of Health which is funding this project or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA). You should understand that a Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself or your involvement in this research. If you want your research information released to an insurer, medical care provider, or any other person not connected with the research, you must provide consent to allow the researchers to release it.

The Certificate of Confidentiality will not be used to prevent disclosure as required by federal, state, or local law such as child abuse and neglect, or harm to self or others.

The Certificate of Confidentiality will not be used to prevent disclosure for any purpose you have consented to in this informed consent document.

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

9.2 What protected health information (PHI) about me could be seen by the researchers or by other people? Why? Who might see it?

Signing this form gives the researchers your permission to obtain, use, and share information about you for this study, and is required for you to take part in the study.

Medical information and billing records are protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA). This type of information is called protected health information (PHI). PHI about you may be obtained from any hospital, doctor, and other health care provider involved in your care, including:

- Hospital/doctor's office records, including test results (X-rays, blood tests, urine tests, etc.)
- Billing information
- Demographic information
- Personal identifiers

There are many reasons why information about you may be used or seen by the researchers or others during or after this study. Examples include:

- The researchers may need the information to make sure you can take part in the study.
- The researchers may need the information to check your test results or look for side effects.
- University, Food and Drug Administration (FDA) and/or other government officials, auditors, and/or the IRB may need the information to make sure that the study is done in a safe and proper manner.
- Study sponsors or funders, or safety monitors or committees, may need the information to:
    - Make sure the study is done safely and properly
    - Learn more about side effects ○ Analyze the

    results of the study
- Insurance companies or other organizations may need the information to pay your medical bills or other costs of your participation in the study.
- The researchers may need to use the information to create a databank of information about your condition or its treatment.
- Information about your study participation may be included in your regular UMHS medical record.
- If you receive any payments for taking part in this study, the University of Michigan finance department will need your name and address for tax reporting purposes. In a calendar year if: 1) your payments total greater than $400 for this study or 2) if you receive payments of greater than $400 for being in more than one study, the University of Michigan finance department will also require your Social Security Number for tax reporting purposes. If you do not wish to provide your Social Security Number, you may continue to participate in research studies, but you will not be able to receive payment for the remainder of the

calendar year.Federal or State law may require the study team to give information to government agencies. For example, to prevent harm to you or others, or for public health reasons.

The results of this study could be published in an article, but would not include any information that would let others know who you are.

9.3 What happens to information about me after the study is over or if I cancel my permission to use my PHI?

As a rule, the researchers will not continue to use or disclose information about you, but will keep it secure until it is destroyed. Sometimes, it may be necessary for information about you to continue to be used or disclosed, even after you have canceled your permission or the study is over.

Examples of reasons for this include:

- To avoid losing study results that have already included your information
- To provide limited information for research, education, or other activities. (This information would not include your name, social security number, or anything else that could let others know who you are.)
- To help University and government officials make sure that the study was conducted properly

As long as your information is kept within the University of Michigan Health System, it is protected by the Health System's privacy policies. For more information about these policies, ask for a copy of the University of Michigan "Notice of Privacy Practices". This information is also available on the web at http://www.uofmhealth.org/patient+and+visitor+guide/hipaa. Note that once your information has been shared with others as described under Question 9.2, it may no longer be protected by the privacy regulations of the federal Health Insurance Portability and Accountability Act of 1996 (HIPAA).

9.4 When does my permission to use my PHI expire?

Your permission expires at the end of the study, unless you cancel it sooner. You may cancel your permission at any time by writing to the researchers listed in Section 10 "Contact Information" (below). If you withdraw your permission, you may no longer be eligible to participate in this study.

10. CONTACT INFORMATION

10.1 Who can I contact about this study?

Please contact the researchers listed below to:

- Obtain more information about the study
- Ask a question about the study procedures or treatments Talk about study-related costs to you or your health plan
- Report an illness, injury, or other problem (you may also need to tell your regular doctors)
- Leave the study before it is finished
- Express a concern about the study

Principal Investigator:	Zirui Huang, PhD
Mailing Address:	1500 East Medical Center Drive, University Hospital 1H247
Telephone:	(734) 647-8129
Study Coordinator:	Aaron Ellis

Mailing Address: 1500 East Medical Center Drive, University Hospital 1H247
Telephone: (734) 936-3701
Email: aaronel@med.umich.edu

You may also express a question or concern about a study by contacting the Institutional Review Board listed below:

University of Michigan Medical School Institutional Review Board (IRBMED)
2800 Plymouth Road, Building 520, Room 3214
Ann Arbor, MI 48109-2800
Telephone: 734-763-4768
Fax: 734-763-1234 e-mail:
irbmed@umich.edu

If you are concerned about a possible violation of your privacy or concerned about a study you may contact the University of Michigan Health System Compliance Help Line at 1-866-990-0111.

When you call or write about a concern, please provide as much information as possible, including the name of the researcher, the IRBMED number (at the top of this form), and details about the problem. This will help University officials to look into your concern. When reporting a concern, you do not have to give your name unless you want to.

11. RECORD OF INFORMATION PROVIDED

11.1 What documents will be given to me?

Your signature in the next section means that you have received a copy of the following document:

- ☐ This "Consent to be Part of a Research Study" document. (*Note: In addition to the copy you receive, copies of this document will be stored in a separate confidential research file and may be entered into your regular University of Michigan medical record.*

12. SIGNATURES

Consent to Participate in the Research Study

I understand the information printed on this form. I have discussed this study, its risks and potential benefits, and my other choices with the study coordinator. My questions so far have been answered. I understand that if I have more questions or concerns about the study or my participation as a research subject, I may contact one of the people listed in Section 10 (above). I understand that I will receive a copy of this form at the time I sign it and later upon request. I understand that if my ability to consent or assent for myself changes, either I or my legal representative may be asked to re-consent prior to my continued participation in this study.

Print Legal Name: _____

Signature: _____

Date of Signature (mm/dd/yy): _____

Principal Investigator or Designee

I have provided this participant and/or his/her legally authorized representative(s) with information about this study that I believe to be accurate and complete. The participant and/or his/her legally authorized representative(s) indicated that he or she understands the nature of the study, including risks and benefits of participating.

Printed Legal Name: _____

Title: _____

Signature: _____

Date of Signature (mm/dd/yy): _____