INFORMED CONSENT FORM- INITIAL CONSENT AND HIPAA AUTHORIZATION

For use with participants with capacity to consent only

For use with cohort 3 only

TITLE: METH-OD: A PHASE 2A STUDY OF IXT-M200 IN PATIENTS WITH TOXICITY FROM METHAMPHETAMINE OVERDOSE

PROTOCOL NO.: M200C-2101
WCG IRB Protocol # 20210895

SPONSOR: InterveXion Therapeutics, LLC

INVESTIGATOR: Name
Address
City, State Zip
Country

STUDY RELATED PHONE NUMBER(S): Phone Number
Phone Number (24 hours)
[24 hour number is required]

Taking part in this research is voluntary. You may decide not to participate, or you may leave the study at any time. Your decision will not result in any penalty or loss of benefits to which you are otherwise entitled.

If you have any questions, concerns, or complaints or think this research has hurt you, talk to the research team at the phone number(s) listed in this document.

In this consent form “you” generally refers to the research subject.

You are invited to take part in a research study because you have mild to moderate toxicity (undesirable or harmful effect of a drug) from a methamphetamine overdose. Your participation is voluntary and requires your written consent. If you decide not to take part in this study, you can continue with your current medical care.

Participating in a research study is not the same as getting regular medical care. The goal of a research study is to collect information about a medical treatment; the goal of regular medical care is to improve your health. Being in this study does not replace your regular medical care, but you may have additional evaluations or changes in your treatments during the study.

InterveXion Therapeutics, LLC is sponsoring this study. The study is being funded by the National Institute on Drug Abuse (NIDA), with grant number U01 DA053043, who appreciates your involvement in the study. Your study doctor will be paid for his or her work in this study.

The study will take place at approximately 5 centers in the United States with about 24 people with mild to moderate toxicity from a methamphetamine overdose participating.

The study has been reviewed by an Institutional Review Board (IRB). An IRB is a group of scientists and non-scientists who review the ethics of research. The goal of the IRB is to protect the rights and welfare of study subjects.

Before agreeing to be in this study, it is important that you read and understand this form. It describes the goal, procedures, benefits, risks, discomforts, and precautions of the study. It also describes different procedures that are available to you and your right to withdraw from the study at any time. Please read this information carefully and ask the study doctor or study staff for an explanation if you have any questions.

If you choose to participate in this study, you will be asked to read and sign this initial consent document. You will receive a copy of this signed and dated form to keep.

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

Why is this study being done?

InterveXion Therapeutics, LLC has begun a study of an investigational drug (also known as the “study drug”) called IXT-m200 as a possible treatment for mild to moderate methamphetamine toxicity. An investigational drug is one that has not been approved by regulatory agencies, such as the United States (US) Food and Drug Administration (FDA), European Union (EU) European Medicines Agency (EMA), or others.

The goal of this study is to learn how well different doses of the study drug work and how safe the study drug is in participants with a methamphetamine overdose.

The study has enrolled enough participants dosed with IXT-m200, but still needs additional participants who are given treatment-as-usual for comparison.

How long will my participation in this study last?

You will be in this study for approximately 28 days. You will be treated in the emergency department, then asked to return for a check-up 2 days later and again after 4 weeks.

What will happen during this study?

The study is divided into 3 periods: a screening period, a treatment period, and a follow-up period. During each study period, you will have 1 or more visits with your study doctor. You will need to stay in the emergency department initially for at least 2 hours after receiving the study drug. How long you stay in the emergency department will depend on the treatment you get and how you respond to the treatment. It is expected you will be ready to leave in a few hours, but it may be 8 hours or more before you are ready to leave the emergency department. It is also possible that you will be admitted to the hospital as an inpatient after your emergency department treatment. All other visits should not take more than 1 to 2 hours.

Before any study-related tests and procedures can be done, you will be asked to read and sign this informed consent form. The goal of the screening period is to determine whether you meet the requirements to take part in this study. If you do not meet the requirements, the study doctor will explain why and will discuss other treatment options with you.

If the study doctor determines that you meet all of the requirements to be in the study, you will be assigned to receive the following treatments:

- treatment as usual, which will be up to 4 mg of lorazepam (Ativan), up to 5 mg of haloperidol (Haldol), or a combination of both.

You will receive up to 4 mg of lorazepam by IV and/or up to 5 mg of haloperidol by intramuscular injection (injection into a muscle) into your arm or buttocks or by IV. Lorazepam and haloperidol are drugs commonly used to treat methamphetamine toxicity symptoms.

Description of the procedures and tests

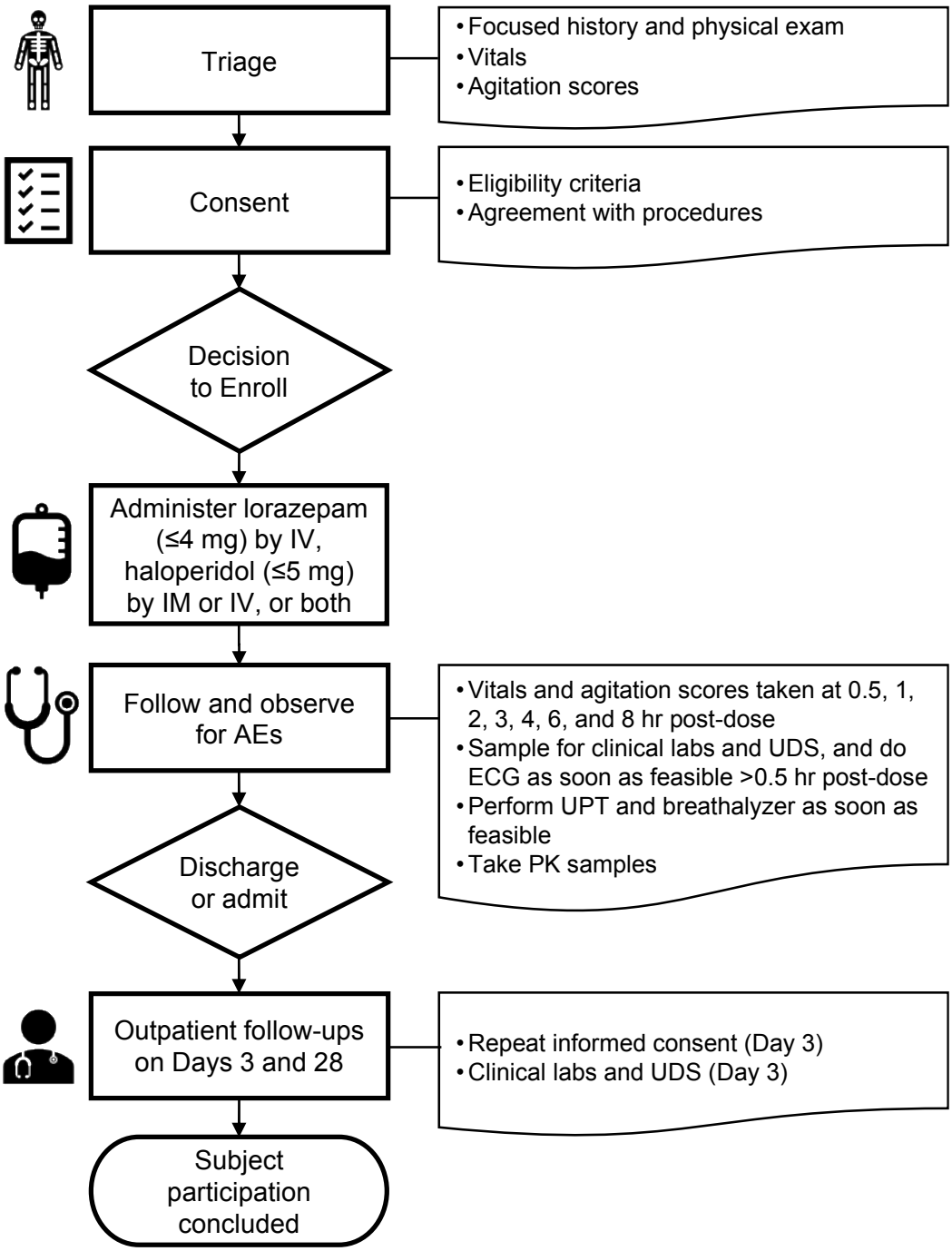
The following tests and procedures will occur as shown in the picture below.

- Physical and neurological (relating to your nervous system) examinations: A check-up of your health, which will include examining your head, ears, eyes, nose, throat, neck, heart, chest, lungs, abdomen, arms and legs, skin, and any other physical conditions of note. Your height and weight will also be measured.
- Medical, medication, and psychiatric history: You will be asked some questions about your health, including allergies or other illnesses, any medications you have taken, and if you have used methamphetamine in the past 24 hours.
- Vital signs: Your heart and breathing rate, blood pressure, body temperature, and blood oxygen levels will be measured.
- Mental health: You will be asked some questions about if you think about killing yourself or have tried to kill yourself.
- You will be asked questions about your drug use and how it felt after participating in the study.

- You will be asked if you agree to have an IV line inserted so that you can be given study medications and if you agree to have blood drawn several times.
- You will be assessed for agitation or sleepiness frequently.
- Electrocardiogram (ECG): A technician will place patches (sticky pads) on your chest that will be connected by wires to a machine. The machine will record the electrical activity of your heart.
- You will be given a Breathalyzer test to check for alcohol.
- Laboratory tests: Blood and urine samples will be collected.
    - A blood sample will be taken to measure the methamphetamine in your blood. About 10 mL (1-2 teaspoons) of blood will be taken.
    - A blood sample will be taken for various blood tests to evaluate your general health (the cells and chemicals in your blood, etc.). About 10 ml (1-2 teaspoons) of blood will be taken at least 30 minutes after you receive the study drug and again 2 days later.
    - A urine sample will be taken to test your health and to perform a drug test.
        - If you are a female who is able to have children, a urine sample will be collected to test whether or not you are pregnant.

The following picture shows what procedures and assessments will occur at which visit(s). In addition to the visits described below, the study doctor may do some additional tests, if necessary for your safety.

Study Outline



Abbreviations: IM, intramuscular; IV, intravenous; min, minutes.

What do I have to do?

During the study, you will have the following responsibilities:

- Follow the study instructions given by the study staff and doctor.
- Tell the study doctor of any illnesses or injuries, side effects, or other problems that occur during your participation in this study.
- Tell the study doctor or staff of any new medications (prescription or over-the-counter) that you start taking after signing this consent form.
- Return to the clinic as instructed by the study staff and doctor.
- You should continue to make regular visits to your family/personal doctor or any other special doctors you were seeing before starting the study because being in the study does not replace regular medical care.
- Contact the study doctor if you find you have any questions about the study after you sign this form.

What are the risks and possible discomforts?

Any study has risks, which may include things that could make you sick, make you feel uncomfortable, or harm you. You might experience side effects while participating in the study. All participants in the study will be watched carefully for any side effects. The study team may give you medicines to help reduce side effects. These side effects may be mild or serious. In some cases, these side effects might be long lasting or permanent and may even be life-threatening.

In this research study, you will receive lorazepam and/or haloperidol.

Possible risks/side effects associated with lorazepam include:

- Lorazepam is a benzodiazepine that is approved by the US FDA for short-term relief of anxiety symptoms. Lorazepam is often given to relieve anxiety or to cause sedation. This is a medication that is commonly used to treat non–life-threatening symptoms of a methamphetamine overdose.
- Side effects of lorazepam include drowsiness, tiredness, amnesia (memory loss), and loss of balance.
- It is possible that lorazepam may increase the risk of respiratory depression (slow ineffective breathing), especially if combined with another sedative medication.

Possible risks/side effects associated with haloperidol include:

- Haloperidol is approved to treat some mental or mood disorders. Haloperidol is often given to help you think more clearly, feel less nervous, and reduce aggression. This medication is commonly used to treat non–life-threatening symptoms of a methamphetamine overdose.
- Side effects of single doses of haloperidol given over a short period of time include dizziness, lightheadedness, drowsiness, difficulty urinating, sleep disturbances, headache, and anxiety.

Other risks include:

- Blood samples: Over the whole study, you may have approximately 30 ml (2 tablespoons) of blood taken. You might feel lightheaded, pain, or have bruising or bleeding when blood samples are taken (infection rarely happens).
- ECG: Skin irritation is rare but could occur during an ECG from the electrode patches (which are sticky) or gel that is used.
- You will have a catheter inserted (IV line) to be dosed with medications if needed. There is a small risk of infection from the IV insertion.

Confidentiality risks include:

- To enroll in this study, you must admit to using methamphetamine. We will protect the information about you and your taking part in this research study to the best of our ability, but there is a risk of loss of confidentiality.
- This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use information, documents, or samples that may identify you in any action or suit unless you say it is okay. They also cannot provide them as evidence unless you have agreed. This protection includes federal, state, or local civil, criminal, administrative, legislative, or other proceedings. An example would be a court subpoena.
- There are some important things that you need to know. The Certificate DOES NOT stop reporting that federal, state, or local laws require. Some examples are laws that require reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate CANNOT BE USED to stop a sponsoring US federal or state government agency from checking records or evaluating programs. The Certificate DOES NOT stop disclosures required by the US FDA. The Certificate also DOES NOT prevent your information from being used for other research if allowed by federal regulations.
- Researchers may release information about you when you say it is okay. For example, you may give them permission to release information to insurers, medical providers, or any other persons not connected with the research. The Certificate of Confidentiality does not stop you from willingly releasing information about your involvement in this research. It also does not prevent you from having access to your own information.

In addition to these risks, taking part in this research may harm you in unknown ways.

What are the benefits of being in this study?

There is no guarantee that you will receive any benefits. However, you will be helping others by contributing to medical research. Possible benefits to others include the continued development of a medication to treat a methamphetamine overdose. Your condition will be checked as long as your participation in the study lasts. However, services provided and evaluations carried out as part of the study should not be seen as

a substitute for a careful evaluation, ongoing medical care, or follow-up by your family/personal doctor.

You have the right to be informed of the overall results of the study.

What other options are available if I do not take part in this study?
You do not have to take part in the study to treat your mild to moderate methamphetamine toxicity. Instead of being in this research study, your choices may include the following:

- You may choose to be treated by the emergency department doctor as he or she would normally do if you were not in the study. This may include treatment with lorazepam, haloperidol, or other similar drugs to calm or sedate you. Other drugs to reduce blood pressure may be added as needed.
- You may also choose to not have further treatment for your symptoms.

Your study doctor will discuss these options, and their risks and benefits, with you.

What if I get harmed or injured during the study?
If you require medical treatment for an illness or injury that is a direct result of participating in the study, call the study doctor immediately. The study doctor will provide emergency medical treatment or refer you for treatment. Your insurance may be billed for this treatment. The Sponsor will pay any charges that are not covered by your insurance policy or the government, provided the injury was not due to your underlying illness or condition and was not caused by you or some other third party. No other payment is routinely available from the study doctor or Sponsor.

What are the costs for participation?
You will not be charged for any study doctor visits, laboratory work, tests, or procedures that are needed for the study. You or your insurance company will have to pay for routine care you would receive whether or not you are in the study. You may talk to the study staff and your insurance company about what is covered.

Will I be paid?
[You will receive no direct payment for taking part. However, you will be compensated for your time and reimbursed for transportation or parking payments related to visiting the study center.

OR You will receive $XX for each completed study visit.

OR You will not receive any payment for taking part in this research study.]

Do I have to take part in the study?
Taking part in this study is voluntary. You can choose not to participate or you can withdraw later at any time for any reason. Your decision not to participate or to stop study participation will not result in any penalty or loss of benefits to which you are otherwise entitled. Your regular medical care will not be affected.

If you are considering or have already decided to leave the study, you should contact the study doctor to discuss the safest way to leave the study. This may involve completing some final tests and examinations. You should also contact your primary/family doctor so he or she can provide you with the best course of continuing care.

New information
If new findings that would affect your safety and willingness to participate in the study are identified while you are in the study, you will be told as soon as possible so you can decide whether to leave the study or continue. If you decide to continue, you will be required to sign a new informed consent form.

Could I be withdrawn from the study?
Sometimes the study doctor or InterveXion Therapeutics, LLC may decide it best for you to stop your participation and remove you from the study (even if you do not agree). The study doctor will discuss this with you. Possible reasons for doing so include the following:

- It is in your best interest.
- You have a side effect that requires stopping the research.
- You do not follow the instructions given by the study staff or doctors.
- You no longer qualify after further questioning or testing.
- Your blood samples do not contain any methamphetamine.
- The research is canceled by the US FDA or the Sponsor.
- You are unable to keep your scheduled appointments.

What medical care will I receive when my participation in this study stops?
After your participation in this research study, you will no longer have access to the study. If you return to the emergency department with a methamphetamine overdose, you will be treated as usual. You cannot enroll in the study more than once.

What will happen to the samples that I provide?
Data or specimens collected in this research might be deidentified (your personal information is removed) and used for future research or distributed to another investigator for future research without your consent. The blood and urine samples that you provide may be transferred to a commercial organization for testing and storage; however, the samples will be deidentified first. This commercial organization will have ownership of the research results and may file patents or otherwise protect and

commercialize any research results; you will not benefit from any future commercialization.

What happens with my data and other personal information?
All data collected on Day 1 will be used in the study analyses. However, no data will be collected on Day 3 or Day 28 if consent is not obtained from the participant on Day 3.

All information that you give will be kept strictly confidential. The information collected about you usually will not directly identify you (for example, by name, address, or social security number). Instead, a coded identification number will be used for your information.

Your records may be reviewed by:

- Study Sponsor (the sponsor) and its affiliates
- Individuals and/or companies that act on the Sponsor's behalf, including Syneos Health.
- The Institutional Review Board (IRB).
- Data safety monitoring committees
- Accrediting agencies that monitoring the accuracy and completeness of the research data
- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- NIDA
- Other regulatory agencies

These people may look at your records to make sure the study has been done the right way. They also want to make sure that your health information has been collected the right way, or for other reasons that are allowed under the law.

If information about this study is published, you will not be identified.

A detailed description of what will happen to your data and other personal information is included in the HIPAA Authorization that you should read and sign to be able to participate in this study.

Whom should I reach if I have a question?
If you have questions, concerns, or complaints, or think this research has hurt you or made you sick, talk to the research team at the phone number(s) listed above on the first page.

This research is being overseen by an Institutional Review Board ("IRB"). An IRB is a group of people who perform independent review of research studies. You may talk to them at 1-855-818-2289 or Researchquestions@wcgirb.com if:

- You have questions, concerns, or complaints that are not being answered by the research team.
- You are not getting answers from the research team.
- You cannot reach the research team.
- You want to talk to someone else about the research.
- You have questions about your rights as a research subject.

Participant Consent to Participate

By signing this informed consent form, I agree to the following:

- I have read and I understand this informed consent form.
- I have been given the chance to ask any questions that I had about the study, and all questions that I asked were answered to my satisfaction.
- I understand the risks of taking part in this study as described in this informed consent form.
- I freely consent to be treated under the study doctor's care. I understand that there is no guarantee that I will receive any benefits from taking part in this study.
- I understand that I am free to withdraw from the study at any time for any reason. I will tell the study doctor if I decide to withdraw so that participation may end in an orderly manner and my future care can be discussed. I understand that the study doctor can stop my participation in the study at any time.
- I understand that I will be told of any new information that might relate to my willingness to continue in the study.
- I understand that I cannot participate in another research study while taking part in this one.
- I understand that I will receive a signed and dated copy of this informed consent form for my records.

My consent to participate in this study does not take away any legal rights in the case of negligence (carelessness) or other legal fault of anyone who is involved with this study.

_____
Name of participant (print)

_____ _____
Signature of participant Date (dd/Mmm/yyyy)

I confirm that all the contents of this informed consent form were discussed and that any questions have been answered. I confirm that this participant was found capable of consent by administration of the UCSD Brief Assessment of Capability to Consent.

_____
Name of study doctor or person administering consent (print)

_____ _____
Signature of study doctor or person administering consent Date (dd/Mmm/yyyy)

Impartial Witness
I am an impartial witness, and I confirm I was present during the entire informed consent discussion. I attest that the information in this informed consent form was accurately explained, apparently understood, that the consent to participate was given freely by the participant.

_____
Name of impartial witness (print)

_____ _____
Signature of impartial witness Date (dd/Mmm/yyyy)

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the informed consent process, and
- who reads the informed consent form and any other written information supplied to the participant if necessary.

HIPAA AUTHORIZATION TO USE AND/OR DISCLOSE PERSONAL HEALTH INFORMATION

In this form, the terms “you” and “your” refers to the research subject.

Federal laws and regulations give you certain rights related to “protected health information” or which might identify you. These include the right to know who will receive your protected health information and how it will be used. The study doctor must obtain your authorization (permission) to use or share any of your protected health information. This authorization form, which is attached to your consent for participation in the research study, helps explain to you how your protected health information collected in the Study will be used and shared with others.

Data to Be Collected and Processed: The study staff will collect, use and share protected health data about you for the study. This data may include your name or initials, date of birth, gender, contact details, and information needed for payment processing. In addition, the following sensitive personal data about you may be collected: health, ethnicity, and race.

Except when required by law, you will not be identified by name, address, telephone number or other facts that could identify the health information as yours.

Examples of the information that may be used are:

- Medical records (from any doctor, hospital or other healthcare provider)
- Information created or collected during the research. This could include your medical history, and dates or results from any physical exams, laboratory tests or other tests.

Who May Receive Your Personal Health Information: The study doctor and study staff will receive your protected health information. Additionally, individuals from the following organizations may also receive your protected health information:

- Study Sponsor (the sponsor) and its affiliates
- Individuals and/or companies that act on the Sponsor's behalf, including Syneos Health.
- Institutional Review Board (IRB)
- Data safety monitoring committees
- Accrediting agencies that monitoring the accuracy and completeness of the research data
- The U.S. Food and Drug Administration (FDA)
- Department of Health and Human Services (DHHS) agencies
- NIDA
- Other regulatory agencies

The sponsor and the groups above will use your health information:

- to complete this research
- to evaluate the results of the study
- to check that the study is being done properly
- to obtain marketing approval for new products resulting from this research

The information that is shared with those listed above may no longer be protected by federal privacy rules or this authorization form and may be released without your permission.

With your permission, the study doctor will tell your primary doctor about your role in this study. In unusual cases, the study doctor may be required to release your protected health information in response to an order from a court of law.

How Your Personal Data Will Be Used: The protected health information collected about you will be recorded in your study file by the study staff to run the study and to monitor your safety as a participant. Your protected health information may be processed on a computer, on paper, or both. The collection of this data is necessary to conduct the study and comply

with applicable laws. You will not be able to participate in the study if you fail or refuse to provide your information.

If you do not consent to the collection and use of your personal information, you will not be able to be in the study.

Results of this study may be presented at meetings or in publications; however, your identity will never be shared. Your personal data will not be used for any direct marketing purposes.

Storage of Your Personal Data: Your personal health information will be stored in the study databases and/or paper files for whichever time period is longer, as required by applicable laws:

- at least 30 years after the study ends, OR
- at least 2 years after the drug being studied has received its last approval for sale, OR
- at least 2 years after the drug's development has stopped.

Confidentiality: To keep your identity private, all data that is sent or provided outside of the study center will show only a coded identification number instead of your name. Only the study doctor and authorized personnel will be able to connect this code to your name. They will use a list that will be kept in a secure place to link this code to your name in case of an emergency.

You may not be able to review some of your records related to the study until after the study is over. When the study is over, you may contact the study doctor to see your health data from the study and to correct any errors.

Right to Refuse Use of Protected Health Information: Your authorization to disclose your protected health information for this research study is voluntary. However, if you do not authorize the use of such protected health information, you will not be allowed to participate in this study. If you withdraw your authorization during the study, you will be removed from the study.

Right to Revoke or Withdraw Use of Your Protected Health Information: You may withdraw the authorization for use of your protected health information at any time or choose not to participate. Neither decision will result in any penalty or loss of benefits to which you are otherwise entitled. If you wish to withdraw your authorization for use of your protected health information, you must inform the study doctor in writing.

If you stop participating in or are removed from the study, no new information about you will be collected for the study unless you have a side effect related to the study. Any protected health information already recorded as a result of your participation in the study may continue to be used and disclosed by the study doctor for the purposes outlined above.

If you withdraw from the study but do not withdraw your Authorization, new health information may be collected until this study ends.

If you do not withdraw this Authorization, it will remain in effect.

If the research site is located in California, Delaware, Indiana, Washington, or Wisconsin this authorization will expire on 31Dec2070.

There is no expiration of this authorization except for research conducted in the states listed above.

AUTHORIZATION

By signing this form, I allow the use or disclosure of my health information. I will receive a signed and dated copy of this Authorization.

_____

Name of participant (print)

_____ _____

Signature of participant **Date (dd/Mmm/yyyy)**

Impartial Witness (when applicable*)

I am an impartial witness, and I confirm I was present during the entire Authorization discussion. I attest that the information in this form was accurately explained, apparently understood, that Authorization was given freely by the participant.

_____

Name of impartial witness (print)

_____ _____

Signature of impartial witness **Date (dd/Mmm/yyyy)**

An impartial witness is:

- a person who is independent of the trial,
- who cannot be unfairly influenced by people involved with the trial,
- who attends the Authorization process, and
- who reads the Authorization and any other written information supplied to the participant if necessary.