Study Title: CTN-0080: Medication treatment for Opioid use disorder in expectant Mothers (MOMs): a pragmatic randomized trial comparing extended-release and daily buprenorphine formulations

NCT03918850

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UNIVERSITY OF CINCINNATI MEDICAL
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

Study Title: CTN-0080: Medication treatment for Opioid use disorder in expectant Mothers (MOMs): a pragmatic randomized trial comparing extended-release and daily buprenorphine formulations

UC IRB Study #: 2019-0429 **Sponsor Name:** NIDA
Marshall IRB Study#: 1839138

Local Site Name: Marshall Division of Addiction Sciences

Investigator Information:
Zachary Hansen, MD 304-691-6404
Principal Investigator Name Telephone Number 24 hr Emergency Contact

Subject Name: _____ Date of Birth: _____/_____/____

KEY INFORMATION

Purpose of the Study:	*The primary purpose of this study is* to compare extended-release buprenorphine (CAM2038) to buprenorphine placed under the tongue (sublingual) in pregnant women with opioid use disorder to see if CAM2038 is as effective as sublingual buprenorphine.
Length of the Study:	You and your as-yet-unborn infant would be in this study from the moment you sign this consent form through approximately 12 months postpartum; between about 13 and 21 months total with up to between about 63-102 total visits, including weekly Medication Check visits and Research visits. These visits may coincide, possibly reducing the number of total visits.
Risks:	The most common side effects of buprenorphine are headache, infection drug withdrawal syndrome, and decrease in sleep (insomnia). The most common side effect of CAM2038 is injection site pain. See section titled, “What Are the Risks and Discomforts of the Research Study?” for additional risks related to the study.
Benefits of the Study:	There may not be a direct medical benefit to you or your as-yet-unborn infant.
Alternative procedures:	Enrollment in your health care provider’s standard opioid use disorder treatment program, without needing to enroll in this study. Your participation in this research study is entirely voluntary.

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INTRODUCTION:

A biomedical or health-related research study is performed to answer specific questions about a disease.

Before you agree to participate in this research study, it is important that you be told the purpose, procedures, benefits, risks, discomforts, and precautions of the research. You should also be told what alternative procedures are available to you if you do not participate in the research study. The informed consent document is a written summary of this information. Be sure to ask questions while you read this consent document and ask questions if there is anything that you do not understand.

Your participation in this research study is entirely voluntary, as is the participation of your unborn infant. By signing this consent form, you are also consenting on behalf of your as-yet-unborn infant for this study and authorizing parties listed in "HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE AND CONFIDENTIAL?" detailed later in this consent document, to access his/her medical health records.

You may choose either to take part or not to take part in this research study. If you decide to take part, you may decide to leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to you or your as-yet-unborn infant to which you are otherwise entitled.

The researcher and sponsor of this study do not promise that you will receive any benefits from this study.

WHY IS THIS RESEARCH BEING DONE?

This research study is being done to compare the effectiveness of two treatments for pregnant women with opioid use disorder.

One of the treatments is injectable, extended-release buprenorphine (CAM2038). CAM2038 is given by a health professional with a small needle (injection under the skin). The other treatment is buprenorphine that is placed under the tongue (sublingual).

Sublingual buprenorphine is Food and Drug Administration (FDA)-approved for patients with opioid use disorder. It is often used to treat pregnant women with opioid use disorder. Patients typically take it once per day.

The FDA gave "tentative approval" of CAM2038. CAM2038 was found to be safe and effective but cannot be sold in the United States yet because a similar product is already on the market. This study cannot use the already-marketed product because it has an ingredient that is unsafe for unborn infants. CAM2038 has a weekly version that does not have this ingredient. The FDA has given us permission to conduct this study with the weekly version.

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WHY HAVE YOU BEEN ASKED TO TAKE PART IN THIS RESEARCH STUDY?

You are being asked to take part in this research study because you are: between 18-41 years old; between 6-30 weeks pregnant and not planning to terminate the pregnancy; have opioid use disorder, and are enrolled or are planning to enroll in outpatient buprenorphine treatment at Marshall Addiction Recovery Center (MARC program) part as of Marshall University's Division of Addiction Sciences. Enrollment in outpatient addiction treatment at Marshall University's Division of Addiction Sciences is required for randomization in this research study. You are also being asked to allow your as-yet-unborn infant to take part in this research study.

HOW LONG WILL YOU BE IN THE RESEARCH STUDY?

You and your as-yet-unborn infant, if enrolled into this research study, will be in the research study from when you sign the consent form through about 12 months after you give birth.

The researcher may decide to remove you from this research study at any time. Reasons for this may include:

- If it becomes no longer safe for you or your unborn infant to continue participation
- If new information is released that indicates new safety concerns for continuing the medication
- If study funding is stopped.

You may withdraw from the study or stop taking the medication at any time. If you decide to stop taking the medication or to stop participating in the study in general, we encourage you to talk to the researcher and your regular doctor first. They can help you understand any safety concerns associated with stopping and what follow-up care and testing could be most helpful to you. In most cases, people who have been taking buprenorphine and wish to stop should be monitored by a doctor and they should not stop taking the medication suddenly. If you do not wish to continue taking buprenorphine, the study may provide you with enough buprenorphine for up to a two-week taper. You may continue with the research visits even if you decide to stop taking the study medication.

You may be contacted in the future by representatives of the University of Cincinnati who are interested in asking you survey questions about your participation in this research study. If you choose to participate in the survey, your responses will be used for quality assurance purposes only.

WHO IS CONDUCTING THE RESEARCH STUDY?

This research study is sponsored and directed nationally by T. Winhusen, PhD., a researcher at the University of Cincinnati, with support provided by The National Institute on Drug Abuse.

The local principal investigator for this study is Dr. Zachary Hansen, at Marshall Division of Addiction Sciences. Medical monitoring for the study is provided locally by Dr. Zachary Hansen.

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HOW MANY PEOPLE WILL TAKE PART IN THE RESEARCH STUDY?

About 25 people will take part in this study at **Marshall University's Division of Addiction Sciences**. A total of about 200 pregnant women will take part across the country.

WHAT IS INVOLVED IN THE RESEARCH STUDY?

If you choose to participate in this research study, you will need to receive outpatient buprenorphine treatment and related substance use disorder treatment services offered by **Marshall University's Division of Addiction Sciences**.

You will meet with study staff for a screening/baseline visit(s). If you qualify for the study, you will be randomly placed into a study group. One group will receive CAM2038. The other group will receive sublingual buprenorphine. Once you are placed in a study group, you will have weekly visits until 12 months post-delivery. While you are in the study, we ask that you attend regular clinic visits for opioid use disorder treatment. Study staff will try to schedule your weekly visits on the same day as your regular clinic visits. With your permission, study staff will get information about your treatment for opioid use disorder from your clinic records. We will also ask you to give us permission to get health information about you and your as-yet-unborn infant from your other healthcare providers and delivery hospital.

We may contact you by various means, such as phone calls, mail, e-mail and messaging by text or social media. We will get your permission to use these means to contact you or chosen study contacts before using any of these. These will be used for follow-up, providing more information if needed, trying to find you if you miss a visit, confirming appointments, and just checking in with you.

While ideally all main study visits will occur at [Site], alternate arrangements may be made at our study team's discretion to accommodate your needs and safety concerns. This may include your home or other appropriate locations within the community.

SCREENING/BASELINE

These screening procedures will help us to see whether this study is suitable for you and your as-yet-unborn infant. Screening will take about 3-3.5 hours to complete. The things that will happen during screening are done only for this research study and are not part of any other routine healthcare you may receive at Marshall Health or Cabell Huntington Hospital. For screening, you will be asked to:

- Sign release of information form(s) for the hospital(s) where you are likely to deliver, for your addiction treatment clinic, and for your prenatal care clinic.
- Complete a locator contact form & sign release of information forms for your locator contacts.
- Provide a urine sample for drug screening and pregnancy testing.
- Provide a blood sample unless your medical records include up-to-date clinical lab results.
- Provide an estimated gestational age, either by ultrasound or by providing date of last menstruation.

- Answer questions about your demographics; any other research studies you may be a part of; your drug, tobacco, and alcohol use history; your physical and mental health; previous testing for HIV and Hepatitis C; any trauma you may have suffered in your past; your health-related quality of life; your use of non-study healthcare services; information about conditions at home or in your personal life; other medications you are taking; addiction treatment services you receive; your attitude towards abstinence; self-report of opioid craving and withdrawal, and any opioid overdose events you may have had.

RANDOMIZATION

If you are eligible based on screening, you will be randomized. Randomization means that you are put into a group completely by chance. You have a 50-50 chance of being randomized to either group, like the flip of a coin. Study staff have no control over which group you are randomized to. You will be randomized to receive either:

1) a weekly administration of CAM2038 during pregnancy or while breastfeeding after delivery followed by a monthly administration of CAM2038 through 12 months post-delivery if you are not breastfeeding; or

2) daily sublingual study medication, which will be sublingual buprenorphine or the sublingual buprenorphine/naloxone combination (whichever is typically prescribed by your provider) from randomization through the 12-month post-delivery phase.

If you are randomized into the study, you will complete two types of study visits. Medication Check visits occur about once a week. Research visits occur less frequently. Ideally, the research visits will be combined with the medication check visit for that week.

MEDICATION CHECK VISITS

About once every week from randomization through the 12-month follow up visit, we will ask you to:

- Report any new or changed medical or psychological problems since your last study visit.
- Provide a urine sample for drug screening purposes. The sample will also be used to check for a new pregnancy for women receiving the monthly CAM2038 injection after delivery.
- For those in the sublingual medication group, you will answer questions about how you are taking your sublingual study medication. For those in the CAM2038 group, you will get your CAM2038 injection and let medical clinicians examine the site of the CAM2038 injection.
- Post-delivery, while you are feeding your infant breastmilk or formula, answer questions about signs of sedation in your infant.

If you are not currently receiving buprenorphine treatment, you may receive two initial injections. These two injections would be at a smaller dose, rather than one full dose. We may ask you to attend one extra medication visit for this purpose.

RESEARCH VISITS

During these visits, we will ask you questions about: your mental health; other medications you are currently taking; symptoms of opioid withdrawal; severity of cravings for opioids; any opioid overdose events you may have experienced since the last study visit; your health-related quality of life; and your use of addiction treatment and non-study healthcare services.

WEEK 3 RESEARCH VISIT
This visit will take about 30 minutes to complete.

MONTHLY RESEARCH VISITS DURING PREGNANCY
You will have study visits once a month between randomization and delivery (first monthly visit is at study week 5); these visits will last about 1 hour each. The number of these visits will depend on the amount of time between randomization and delivery.

1-, 3-, and 9-MONTH POST-DELIVERY RESEARCH VISIT
You will have visits at about 1, 3, and 9 months post-delivery. These visits will last for about 1 hour. At the 1-month post-delivery visit you will be asked to report any new or changed medical problems for your infant since delivery. *

*If you are not the infant's caregiver, the caregiver will be asked to complete some or all of the questions in these assessments.

6-MONTHS POST-DELIVERY RESEARCH VISIT
About 6 months post-delivery, you will be asked to attend a follow-up study visit; this visit will last for about 1 hour. During this visit, we will ask you questions about your infant's development and conditions at home if you are the infant's caregiver. If you are not the infant's caregiver, the caregiver will be asked to complete some or all of the questions in these assessments.

12-MONTHS POST-DELIVERY RESEARCH VISIT
About 12 months post-delivery, you will be asked to attend your final study visit; this visit will last about 80 minutes. During this visit, we will ask you to:

- For those in the sublingual medication group, answer questions about how you are taking your sublingual study medication. For those in the CAM2038 group, let medical clinicians examine the site of the CAM2038 injection
- Answer questions about your infant's development and conditions at home if you are the infant's caregiver. If you are not the infant's caregiver, the caregiver will be asked to complete some or all of the questions in these assessments.

COLLECTING THE HEALTH RECORDS OF YOUR INFANT After delivery, we would like to follow-up on the health of your newborn infant. As part of the research study, we will be collecting the health records of your infant post-birth until s/he is discharged from the hospital to record data about your infant's health and development.

ADDITIONAL INFORMATION
We may ask you to fill out a medical release of information form, to get medical/pharmacy records for you and/or your infant. This may happen if you have any new or changed medical or psychological problems or a change in your treatment provider. We may also ask you to sign releases of information for other potential caregivers as needed.

If you become a prisoner, we would still like to find out how you are doing. Being a prisoner includes: being in jail or prison, being on probation or parole, or being under house arrest or electronic monitoring. If needed, we will try to collect follow-up data from you over the phone or in person. Please note that your continued participation would have no effect on your criminal case, or release or parole from jail or prison, or probation case.

WHAT ARE THE RISKS AND DISCOMFORTS OF THE RESEARCH STUDY?

Buprenorphine

Both the sublingual study medicine and CAM2038 contain buprenorphine, which is an opioid medication.

Side effects that occurred in people in a 16-week study of sublingual buprenorphine include:

The most common side effects that occurred in about 20 to 34 out of 100 people were

- Headache
- Decrease in sleep (insomnia)
- Pain
- Drug withdrawal syndrome
- Infection

The following side effects occurred in less than 15 out of 100 people

- Weakness or lack of energy
- Back pain
- Constipation
- Nausea
- Anxiety
- Depression
- Nasal Inflammation (Rhinitis)
- Sweating

The following side effects occurred in less than 10 out of 100 people in the study.

- Abscess
- Fever
- Chills
- Diarrhea
- Indigestion
- Vomiting
- Flu-like symptoms
- Dizziness
- Feeling nervous
- Sleepiness
- Increased Coughing
- Sore Throat
- Runny Eyes

On January 12, 2022, the FDA posted a Drug Safety Communication for buprenorphine medicines dissolved in the mouth (BUP-SL formulations) warning of dental problems being reported in patients, even those with no history of dental issues. These dental problems can be serious, and include:

- Tooth decay
- Cavities
- Oral Infections
- Loss of teeth

In this report, the FDA indicates that despite these additional risks, buprenorphine is an important treatment option for opioid use disorder and pain, and the benefits of these medicines clearly outweigh the risks. Inform your healthcare professional if you have a history of tooth problems, including cavities.

The long-term side effects of buprenorphine are unknown at the present time. Buprenorphine itself causes physical dependence and can result in withdrawal symptoms when buprenorphine is stopped. Buprenorphine can also cause drowsiness and breathing that is slow and shallow.

A number of deaths have been reported in people who abuse buprenorphine in combination with benzodiazepines, such as Valium or sleeping pills. Combining buprenorphine with alcohol or other drugs is dangerous. You must not drink alcohol-containing beverages or take other drugs including benzodiazepines, like Valium or sleeping pills, or narcotic pain relievers, while using buprenorphine.

Buprenorphine may also impair mental or physical abilities involved in such activities as driving or operating machinery. You are advised not to engage in such activities for at least 6 hours after taking the first dose of sublingual study medicine or after the first injection of CAM2038.

Sublingual buprenorphine formulations
There are two sublingual buprenorphine (BUP-SL) formulations; one formulation contains only buprenorphine while the other contains both buprenorphine and naloxone. The formulation with naloxone has no additional risks over those for buprenorphine alone when taken as prescribed.

Naloxone is added to buprenorphine to decrease the likelihood of misuse of the combination drug product. When these combination products are taken as sublingual or films, buprenorphine's opioid effects dominate, and naloxone does not bring on opioid withdrawals. If the sublingual films are made into a solution and injected, however, the naloxone effect dominates and can bring on opioid withdrawal symptoms such as pain, cramps, vomiting, diarrhea, anxiety, sleep problems, and cravings.

CAM2038
In addition to the side effects associated with buprenorphine, common (incidence of equal to or greater than 5 out of 100 people) side effects for CAM2038 include:

- Injection site pain (occurred in about 12 out of 100 people)
- Injection site swelling (occurred in about 8 out of 100 people)

- Reddening of the skin around the injection site (occurred in about 7 out of 100 people)
- Urinary tract infection (occurred in about 5 out of 100 people)
- Nasopharyngitis (Common cold) (occurred in about 5 out of 100 people)

There are two formulations of CAM2038; one formulation is for weekly administration and one formulation is for monthly administration. While you are pregnant or breastfeeding, you will receive the weekly formulation. The weekly CAM2038 contains additional ingredients not contained in sublingual buprenorphine. These ingredients are described below in "What are the Reproduction Risks?" Potential side effects from the extra ingredients in the monthly formulation are reflected in the side effects described above.

Other Prescription Drugs
There are several prescription drugs that may cause problems when taken with the study drugs. The doctor will carefully review all the drugs you are taking before giving you the study drugs. If any other health care provider prescribes any new drug(s) for you while you are in this study, please tell the study doctor before you take the new drug. You could also have that provider talk to the doctor before prescribing the new drug.

Risks of a blood draw may include:
- momentary discomfort at the draw site
- bruising
- redness and/or swelling around the site
- bleeding at the site
- feeling of lightheadedness when the blood is drawn

Rarely:
- infection at the site of the blood draw

WHAT ARE THE RISKS OF STOPPING YOUR CURRENT TREATMENT?

If you are currently prescribed and taking buprenorphine for the treatment of opioid use disorder, you will continue taking buprenorphine for opioid maintenance therapy as provided by this study. However, you may be switched to the injectable CAM2038 form of buprenorphine for this study. Studies showed there is no known risk related to switching from sublingual buprenorphine to the corresponding dose of CAM2038.

If you are currently taking methadone, you should continue your treatment and should not participate in this study. If you are taking Vivitrol, you should continue your treatment and should not participate in this study.

WHAT ARE THE REPRODUCTION RISKS?

Limited data in women taking buprenorphine for opioid use disorder during pregnancy have not shown an increased risk of major birth defects. However, these studies were not designed to assess risk of long-term buprenorphine maintenance. Recent data in women prescribed opioids in early pregnancy suggest a small increase in birth defects. However, buprenorphine was not

studied in the analysis, and the American College of Obstetrics and Gynecology recommends buprenorphine for use during pregnancy.

Use of opioids during pregnancy can cause neonatal opioid withdrawal syndrome (NOWS). NOWS may be life-threatening if not recognized and treated.

Neonatal opioid withdrawal syndrome (NOWS) has been reported in the infants of women treated with buprenorphine during pregnancy. NOWS occurs 1 to 8 days after birth with most cases occurring on Day 1. About half of infants born to women on opioid maintenance treatment (e.g., buprenorphine or methadone) will experience NOWS. Medicines to treat or manage severe withdrawal symptoms may be needed.

Symptoms associated with the neonatal withdrawal syndrome include:
- Stiffness in the muscles
- Neonatal tremor
- Neonatal agitation
- Muscle twitches and/or spasms

With neonatal withdrawal syndrome, there have also been reports of:
- Convulsions
- Temporary cessation of breathing
- Respiratory depression
- Slower-than-normal heart rate

Low amounts of buprenorphine and its metabolite (norbuprenorphine) have been found in the breast milk of women taking buprenorphine or CAM2038. If you are breast feeding, this could cause your baby to be drowsy. We will be checking to see if there is sedation effect of buprenorphine on infants being fed with breast milk compared with infants fed with formula only.

No information is available on the presence of naloxone in breast milk. Because naloxone has essentially no effect when taken orally, it is unlikely to affect an infant fed with breast milk.

Weekly CAM2038 has small amounts of phosphatidylcholine; glycerol dioleate (GDO); and alcohol in the form of ethanol. You will be exposed to small amounts of these substances while on the study. The risks of being exposed to low levels of these substances is unknown.

1) phosphatidylcholine

- Choline is a nutrient found in meats, dairy products, eggs, peanuts, and vegetables. Choline supplements of 450 milligrams per day during pregnancy have been recommended.
- The total amount of choline you could receive on this study during your pregnancy is about 9 grams. If you took a choline supplement for the same amount of time you would receive about 100 grams of choline.

- The total amount of choline you would receive post-delivery would be about 13 grams. If you took a choline supplement for the same amount of time you would receive about 160 grams of choline.

2) glycerol dioleate (GDO)

- GDO is naturally found in human blood. It is also found in foods like mayonnaise, salad dressings, margarine, and icing.
- The total amount of GDO you could receive during pregnancy is about 9 grams. That is less than one tablespoon.
- The total you could receive post-delivery is about 13 grams. That is about one tablespoon.

3) Alcohol in the form of ethanol.

Drinking alcohol during pregnancy can lead to birth defects. There is no known safe amount of alcohol use during pregnancy. A standard alcoholic drink has 14 grams of ethanol. The total amount of ethanol you could receive during pregnancy is about 2 grams.

Alcohol use is not encouraged in breastfeeding women. However, the CDC notes that up to 1 standard drink per day is not known to be harmful to the infant. The total amount of ethanol you could receive while breast feeding is about 2 grams.

If you become pregnant again during the 12-month post-delivery period, tell study staff or your study-related provider immediately. The medical clinician will work with you and the principal investigator to decide the best course of study-related treatment for you and your newly as-yet-unborn infant. We would also like to collect follow-up data regarding this infant's health and development. We may ask you to sign additional medical releases of information.

ARE THERE BENEFITS TO TAKING PART IN THE RESEARCH STUDY?

If you agree to take part in this research study, there may not be a direct medical benefit to you or your as-yet-unborn infant. We hope the information learned from this research study will benefit other pregnant women with opioid use disorder, and their unborn infants, in the future. Potential benefits to you and your as-yet-unborn infant may include more frequent than usual medical visits. You will also be receiving, as part of this study, a medication for opioid use disorder free of charge. You may be informed of any clinically significant findings as a result of study procedures and may be offered referrals for further evaluation or care.

WHAT OTHER CHOICES FOR CARE ARE THERE?

Enrollment in your health care provider's standard opioid use disorder treatment program, without needing to enroll in this study, is an option. There may be other treatment options, including but not limited to methadone treatment. Ask your physician if you would prefer to seek out one of these other choices.

WHAT IS THE CLINICAL TRIALS REGISTRY?

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 results. You can search this Web site at any time.

DATA-SHARE WEB SITE

Data from this study will be available to researchers on another website, https://datashare.nida.nih.gov/ after the study is complete and the data has been analyzed. This website will NOT include information that can identify you. You can view this website at any time.

WHAT IS A CERTIFICATE OF CONFIDENTIALITY?

To further protect your privacy and the privacy of your as-yet-unborn infant, this study is covered by a Certificate of Confidentiality from the Department of Health and Human Services (HHS). With this certificate, the researchers may not disclose information (for example by court order or subpoena) that may identify you or your as-yet-unborn infant in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. Disclosure will be necessary, however, upon request of HHS for audit or program evaluation purposes.

A Certificate of Confidentiality does not prevent you from voluntarily releasing information about yourself, your infant or your or your infant's involvement in this research.

Even with the Certificate of Confidentiality, if the investigator learns about abuse of an infant or elderly person or that you intend to harm yourself or someone else, about certain communicable diseases, or about any other information that requires reporting according to state and local laws, they will report that to the proper authorities. If keeping information private would immediately put you or someone else in danger, the researchers would release information to protect you or another person.

AVAILABILITY OF INFORMATION

You will receive a copy of this signed and dated consent form.

You will be told about any new information from this or other studies that may affect your health, welfare, willingness to keep your infant in this study, or your own willingness to stay in this study.

WHAT ARE YOUR COSTS TO BE IN THIS STUDY?

You will be required to be enrolled in treatment at Marshall University's Division of Addiction Sciences in order to qualify for this study. You will be responsible for payment for your treatment visits, procedures, and medical tests associated with that treatment.

In addition, you will be responsible for all costs associated with prenatal care, delivery, neonatal care, and hospital stay. Insurance may cover some of these costs.

The study will provide all study medication in this research study at no cost to you. Any procedures, visits, or tests performed for this research, including the weekly urine drug screens, will be provided at no cost to you.

WILL YOU BE PAID TO PARTICIPATE IN THIS RESEARCH STUDY?

You will be paid for your time and travel costs related to taking part in this study. Payments will be made in the form of a ClinCard that will be given to each participant and will be loaded with the amount allotted for each visit once the visit is completed. The $120 Screening/baseline payment will be separated into four individual payments to allow for visit activities to be completed more in line with your schedule. If you are determined to be ineligible for the study based on screening criteria, you will receive the whole payment.

Compensation for visits during pregnancy:
The number of visits that you can participate in during pregnancy depends on the number of weeks you are pregnant when you are randomized into the study and at the time you deliver. If you attend all scheduled visits while you are pregnant, you will be compensated between $420 and $1360.

Table A

Visit	Total per Visit ($)	Total # of Visits	Grand Totals ($)
Screening/baseline			$120
Week 2 visit	$40	1	$40
Weekly Medication Check visits during pregnancy (if not corresponding to a research visit)	$20	7-36	$140-$720
Monthly Research visits during pregnancy	$60	2-8	$120 - $480
Total			$420 - $1,360

Compensation for visits post-delivery:
If you attend all scheduled visits post-delivery, you will be compensated up to $1,350.

Table B

Visit	Total per Visit ($)	Total # of Visits	Grand Totals ($)
Weekly Medication Check visits post-delivery (if not corresponding to a research visit)	$20	48-52	$960-$1,040
Post-delivery Research visits (1, 3, 6, 9 months)	$60	4	$240
Post-delivery visit month 12	$70	1	$70
Total			$1,270-$1,350

Compensation for infant-related assessments:
If you are the caregiver for the infant, you will be compensated $60 for completing the infant-related assessments at 6 and 12 months post-delivery.

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Table C

Visit	Total per Visit ($)	Total # of Assessment Points	Grand Totals ($)
6-month post-delivery assessments	$30	1	$30
12-month post-delivery assessments	$30	1	$30
Total			$60

The reimbursement amounts listed in Tables A and B will be reduced by $10 if you do not travel to attend the visit

If you receive payments for being a part of this research study, you may be asked to complete an Internal Revenue Service (IRS) form. The amount you receive may count as income and may affect your income taxes. Your social security number will be required to complete the IRS form.

WHAT COMPENSATION IS AVAILABLE IN CASE OF INJURY?

If you or your as-yet-unborn infant become ill or injured from participating in this research study, emergency medical care will be provided to you. The **Marshall University's Division of Addiction Sciences** will decide on a case-by-case basis whether to reimburse you for your out-of-pocket health care expenses.

If you think that you or your as-yet-unborn infant have been hurt by taking part in this research, call Dr. Zachary Hansen at 304-691-6404, as soon as possible. If needed, emergency medical care will be provided. If the injury is a direct result of a study-related procedure or because you are taking either sublingual buprenorphine or CAM2038, the cost of the emergency medical care will be paid by **Marshall University's Division of Addiction Sciences** only if it is not paid by your health insurance, a government program, or other third party. The Sponsor has no plans to pay for medical care for any other injury whether or not it might be related to taking part in this research.

WHAT ARE YOUR RIGHTS AS A PARTICIPANT?

You may choose either to take part or not to take part in this research study. If you decide to take part, you may decide to leave the study at any time. Leaving the study will not result in any penalty or loss of benefits to you or your as-yet-unborn infant.

The investigators will tell you about new information that may affect your health, welfare, the health and welfare of your infant, your willingness to keep your infant in this study, or your own willingness to stay in this study.

If you have questions about the study, you will have a chance to talk to one of the study staff or your regular doctor. Do not sign this form unless you have had the chance to ask questions and have received satisfactory answers.

Nothing in this consent form waives any legal rights you or your infant may have nor does it release the investigator, the sponsor, the institution, or its agents from liability for negligence. If you choose to withdraw from the study, we may still ask you to return to assess your safety and the safety of your unborn infant.

HOW WILL INFORMATION ABOUT YOU BE KEPT PRIVATE AND CONFIDENTIAL?

Every effort will be made to maintain the confidentiality of your and your infant's medical and research records related to this study. Agents of the United States Food and Drug Administration (FDA), the University of Cincinnati, **Marshall Division of Addiction Sciences**, and the sponsor, NIDA or its designees, study monitors, auditors, Braeburn Pharmaceuticals, Inc., the Institutional Review Board (IRB), and other regulatory authorities will be granted direct access to your original medical and research records for verification of clinical trial (research study) procedures or study data without violating your confidentiality or that of your as-yet-unborn infant, to the extent permitted by the applicable laws and regulations. By signing this consent form, you or your legally authorized representative are authorizing such access. The data from the study may be published; however, you and your as-yet-unborn infant will not be identified by name. Your identity and that of your as-yet-unborn infant will remain confidential unless disclosure is required by law.

After identifiers are removed from your and your infant's identifiable private information, the information may be used for future research studies or distributed to another investigator for future research studies without additional informed consent.

WHAT WILL HAPPEN TO BIOLOGICAL SAMPLES OBTAINED DURING THE STUDY?

Biological samples (e.g., blood and urine samples) obtained as part of study procedures will be destroyed once the study has completed; samples will not be stored or distributed to be used for future research studies. No genetic information will be extracted, stored, or sequenced from these samples.

Authorization to Use and Disclose Health Information

A federal regulation known as the Privacy Rule gives you certain rights concerning the privacy of your and your infant's health information. Researchers covered by this regulation are required to get your authorization (permission) to use and disclose (share with others) any health information that could identify you or your infant. You should have received a Notice of Privacy Practices when you received health care services here. If not, let us know and a copy will be given to you.

If you sign this informed consent form, you are giving permission for the use and disclosure of your and your infant's health information for purposes of this research study to the parties listed in this document. You do not have to give this permission. Your health care and the health care of your infant outside of the study, payment for your health care and health care of your

infant, your health care benefits, and the health care benefits of your infant will not be affected if you choose not to sign this form. However, if you do not sign this form, you will not be able to participate in the study.

Who Will Use and Disclose My Health Information? The study doctor and study staff may use your health information and the health information about your infant to conduct, review, and determine the results of the study. The study team may also use your information and the information of your infant to prepare reports or publications about the study. However, neither your name nor the name of your infant will appear in any report or publication without your permission.

What Health Information will be Used and Disclosed? The study team will record your medical history, the treatment you receive, pharmacy records, and the results of examinations and tests done during the study on study forms and record the same for your infant. Additionally, the outcome of this pregnancy will be recorded. The study team will send the completed study forms to the study sponsor. Representatives from the groups identified below may need to look at your medical records and your infant's medical records to make sure that the information on the study forms is correct or that the study was conducted properly. Your medical and/or pharmacy records and your infant's medical and/or pharmacy records may include other health information about you and your infant and may include documents that directly identify you and your infant. Your study team may access the Prescription Drug Monitoring Program, if available in your state, to monitor your prescription use. Reviews like that will take place at the study center or where the medical records are stored and can take place after the study is over.

The State of West Virginia requires direct consent for use of information from patients with behavioral health disorders, including substance use disorder unless waived by an IRB under 45 CFR part 46. By signing this consent document, you are consenting to allow research staff to review your private health information only for use in the study as described.

Who Will Receive My Health Information? Your and your infant's study information or medical records (as described above) or both may be shared with the following people or groups:

- The study sponsor or its representatives, including companies it hires to provide study-related services
- Dr. T. Winhusen, the study Sponsor and Lead Investigator, and his research team at the University of Cincinnati
- Researchers who are conducting this study at other study centers, including monitors and project management personnel from the University of Cincinnati.
- UC Institutional Review Board and any other committees responsible for overseeing the research
- Staff of the UC Human Research Protection Program
- Staff of the Marshall University Institutional Review Board
- **Marshall University's Division of Addiction Sciences** employees providing service or

care to you
- Braeburn Pharmaceuticals, Inc. (the manufacturer of CAM2038)
- Federal and State agencies, such as the U.S. Food and Drug Administration (FDA), Department of Health and Human Services (HHS), the National Institutes of Health (NIH), and other US and non-US government bodies that oversee or review research

Will My Information be Protected by the Privacy Rule After it is Disclosed to Others? **Marshall Division of Addiction Sciences**, Marshall Health, and the Mountain Health Network are required by the Privacy Rule to protect your health information and the health information of your infant. After your information and your infant's information is shared with others, such as the study sponsor, it may no longer be protected by the Privacy Rule. The people who receive this information could use it in ways not discussed in this form and could disclose it to others. The sponsor will use and disclose your information and/or your infant's information only for research or regulatory purposes or to prepare research publications. In addition to using it for this study, the sponsor may reanalyze the study data at a later date or combine your information and/or your infant's information with information from other studies for research purposes not directly related to this study. The goal of any such research would be to learn more about drugs, devices, or diseases or to help design better studies in the future. When using your or your infant's information in these ways, the sponsor may share it with regulatory authorities, other researchers, its business partners, or companies it hires to provide research-related services.

What Happens if I Leave the Study Early? If you stop participating in the study early for any reason, the study team will tell the sponsor why. If the study team asks you to come to any more study visits and you agree, the study team will send the sponsor information from those visits as well. All information collected about you may continue to be used and disclosed.

Will My Authorization Ever Expire? This Authorization does not have an expiration date. The study team may need to correct or provide missing information about you even after your study participation is over and a review of your medical records may also take place after the study is over.

May I Take Back My Authorization? You have the right to take back (revoke) your Authorization at any time by writing to the person in charge of this research study whose information is listed on the front of this form. If you revoke your Authorization, the study team will not collect any new health information about you. However, they can continue to use and disclose any already-collected information if that is necessary for the reliability of the study. The sponsor can also still keep and use any information that it has already received. If you revoke your Authorization, you can no longer continue to participate in the study.

May I Look At My Study Information? You have a right to see and make copies of your medical records. However, to ensure the reliability of the study, you will need to wait to see your study records until the study is completed.

WHO DO YOU CALL IF YOU HAVE QUESTIONS OR PROBLEMS?

If you have questions, concerns, complaints and/or suggestions about this research study or to report a research-related injury, please contact the research team or Dr. Hansen by calling 304-691-6404.

Please call the University of Cincinnati Institutional Review Board at 513-558-5259 (Monday – Friday 8 am to 5 pm eastern time zone) if you:

- Think the research has hurt you.
- Have general questions about giving consent or your rights as a research participant in this research study.
- Have questions, concerns, complaints, and/or suggestions about the research.
- Cannot reach the research team or you want to talk to someone else.

You may also contact the Marshall University Office of Research Integrity or the Institutional Review Board at Marshall University at 304-696-4303.

To report complaints or concerns to an independent agency in an anonymous and confidential manner, please call the Research Compliance Hotline at 1-800-889-1547.

University of CINCINNATI

Comprehension Tool

1. My participation in this research study is entirely voluntary. T F

2. If I am eligible after screening, I will be randomized to receive buprenorphine medication either by mouth or under the skin by an injection. T F

3. Buprenorphine is an opioid and, thus, my newborn infant will still be at risk for neonatal opioid withdrawal syndrome (NOWS). T F

4. As part of my participation in this research study, I will be required to be enrolled in the opioid use disorder treatment program at Marshall University's Division of Addiction Sciences. T F

5. This study is guaranteed to end my addiction to opioids. T F

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UNIVERSITY OF CINCINNATI - Medical
CONSENT TO PARTICIPATE IN A RESEARCH STUDY

CTN-0080: Medication treatment for Opioid use disorder in expectant Mothers (MOMs): a pragmatic randomized trial comparing extended-release and daily buprenorphine formulations

UC IRB Study #: 2019-0429 **Sponsor Name:** NIDA
Local Site Name:
Investigator Information:
Zachary Hansen, MD 304-691-6404
Principal Investigator Name Telephone Number 24 hr Emergency Contact

I have read or someone has read to me, this Informed Consent Document which describes the purpose and nature of this research. I have had time to review this information and have been encouraged to ask questions. If I do not participate or if I discontinue my participation, I will not lose any benefits or any legal rights. My participation in this research is completely voluntary. I have received (or will receive) a copy of this signed and dated form for my records and future reference. I have been given the information about the use and disclosure of my health information for this research study.
I give my consent to participate, and give my consent for my as-yet-unborn infant to participate.

I authorize the release of information concerning treatment relating to…

- psychiatric condition(s)
- alcohol use
- drug abuse
- my infant

…to the parties listed in the authorization section of this consent for the purposes described above.

Participant Date Time

PERSON OBTAINING CONSENT
I have read this form to the participant and/or the participant has read this form. An explanation of the research was given and questions from the participant were solicited and answered to the participant's satisfaction. In my judgment, the participant has demonstrated comprehension of the information.

Printed Name of Person Obtaining Consent

Signature and Title of Person Obtaining Consent and Identification of Role in the Study Date

University of CINCINNATI

PERMISSION TO CONTACT YOU ABOUT FUTURE RESEARCH

We are asking your permission to contact you about future research studies conducted by the CTN-0080 MOMs investigators.

If you agree, you might be contacted about other research studies in the future. At that time, you can decide whether or not you are interested in hearing more about the study.

Your permission to allow us to contact you about future research studies would be greatly appreciated, but it is completely voluntary. If you choose not to allow us to contact you, it will not affect your care or participation in the CTN-0080 MOMs study. Please understand that giving your permission to do this is only to help us identify individuals who may qualify for one of our future research studies. It does not mean that you must join in any study.

Please initial your choice below.

_____ I agree to be contacted by the CTN-0080 MOMs investigators about future research studies

_____ I do not agree to be contacted by the CTN-0080 MOMs investigators about future research studies