KEY INFORMATION FOR

PRAGMATIC, RANDOMIZED, BLINDED TRIAL TO SHORTEN PHARMACOLOGIC TREATMENT OF NEWBORNS WITH NEONATAL OPIOID WITHDRAWAL SYNDROME (NOWS)

INFORMED CONSENT FOR CAREGIVER ONLY

NOTE: The terms "you/your baby" and "your baby," as well as "you" are used in this consent. However, this consent **only covers the caregiver** and is specifically for questionnaires that the caregiver answers about the caregiver himself/herself and/or the caregiver's family environment. "You/your" is intended to be the person currently providing care for the baby, such as a foster parent or relative. "Your baby" means the baby currently in your care. You will be asked to participate in this study as a caregiver, using this form, only if your baby's legal guardian has agreed that your baby is also joining the study. Your baby's study activities are described in the "Informed Consent for Infant Only" that your baby's legal guardian signs.

We are asking you to choose whether or not you want to participate in a clinical trial (research study) about babies who have neonatal opioid withdrawal syndrome (NOWS). Neonatal opioid withdrawal syndrome can cause a number of problems. These problems may include tremors, seizures, fussiness, vomiting, and poor feeding. Babies can develop NOWS if their mothers took drugs called opioids while the babies were still inside their mothers. There are many different names for opioids. Some brand names, generic names, and street names are listed on the last page of this form.

Your baby has NOWS and is currently being given a drug (either morphine or methadone) by his/her doctor to help him or her get over NOWS. Your baby will need to be weaned (slowly stop getting) from the drug so that your baby will get better. The question the researchers want to answer is whether or not there is a difference between a slow weaning method and a fast weaning method.

This page and the next 2 pages give you key information to help you decide whether to participate. We have included detailed information after the second page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn about the best way babies can stop getting the morphine or methadone the doctors are using to treat your baby's NOWS symptoms.

Some of this study will occur while your baby is still in the hospital. While your baby is in the hospital, your baby will be placed in one of two groups, "slow weaning" or "fast weaning." In

some hospitals, doctors use a SLOW WEANING approach, in which the baby spends more time on morphine or methadone, and in other hospitals doctors use a FAST WEANING approach, in which the baby spends less time on morphine or methadone. Nobody knows which approach is better for the baby. The question the researchers want to answer is whether one of these 2 approaches is better than the other. Details about these groups are given in the section "What will happen if I say yes, I want to be in this study?" in the main part of the consent form. During your baby's hospital stay, medical and research staff will complete the weaning process, collect information about what medicines are used and how much is given, The staff will also track your baby's health. The research team will check your baby's size and weight when your baby is ready to leave the hospital. After your baby leaves the hospital the research team will ask you to answer questionnaires that will occur via phone, electronically, or in person. These questionnaires ask about how well you are doing. The questionnaires will include things like how you feel, how you feel when you are caring for your baby.

Your participation in this research will take about 1 hour over the course of about 2 years after your baby has been discharged from the hospital. There will be a total of 6 contact times. The first (at discharge) and last (when your baby is 24-months old) could be in person. The other 4 times will be either phone calls, home visits, or be done electronically.

WHY MIGHT I CHOOSE TO VOLUNTEER FOR THIS STUDY?

You/your baby may not benefit directly from being in this study.

For a complete description of benefits, refer to the Full Consent.

WHY MIGHT I CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

The reason(s) you may not want to volunteer for this study include:

- You might be uncomfortable sharing private health information with the research team.

For a complete description of risks, refer to the Full Consent.

Your baby's participation in this study is not determined by this consent. Your baby's legal guardian will determine if your baby will be a participant in this study. If you chose not to be part of this study,it will not affect your baby's participation or his/her treatment.

For a complete description of alternate treatment/procedures, refer to the Full Consent and/or ask your doctor.

DO I HAVE TO TAKE PART IN THE STUDY?

No. It is okay to say no. If you decide to take part in the study, it should be because you really want to volunteer for yourself. You/your baby will not lose any services, benefits, or rights you/your baby would normally have if you choose not to volunteer.

WHAT IF I HAVE QUESTIONS, SUGGESTIONS, OR CONCERNS?

You can contact the person in charge of the study, [TO BE INSERTED *PI Name and affiliation*, with any questions, suggestions, or concerns at TO BE INSERTED *contact information*.

If you have any questions, suggestions, or concerns about your rights as a volunteer in this study, or wish to speak to someone not directly involved in the research, you can call the UAMS Institutional Review Board at 501-686-5667 during business hours. An institutional review board is a group of people who review research to protect the rights and well-being of research participants.

If you want to know more about the research, let the study team know so they can give you more information.

Also tell the study team if you have decided you don't want to be in the study. It is perfectly okay to say no.

<Insert local institution name>

Informed Consent Form

- **We are asking you to be in a clinical trial (research study). You do not have to join the study.**
- **You/your baby will still get medical care from [insert local context here] even if you/your baby are not in the study.**
- **Please take as much time as you need to read this form and decide what is right for you.**

Why am I being asked to be in this clinical trial (research study)?

- We want to learn more about how to help babies born with Neonatal Opioid Withdrawal Syndrome (NOWS). Babies who, while growing inside their mothers, have been exposed to opioids can have NOWS. There are many names for opioids. Some of the brand names, generic names, and street names are listed on the last page of this form. The signs of NOWS are different in different babies. Signs can include tremors, seizures, fussiness, vomiting, poor feeding, as well as many other symptoms.
- This study may help us learn more about which method(s) might work better than others for treating NOWS. Specifically, the research team is testing whether it may be better to wean babies fast or slow from the methadone or morphine that is being used to treat babies' NOWS symptoms.
- We are asking people like you, who have babies with NOWS, to help us.
- Approximately 502 babies who are being treated with methadone or morphine for NOWS will be in this study. The babies' parent/legal guardian (or caregivers) will also be in the study.
- This clinical trial (research study) is sponsored by the National Institutes of Health and is being conducted at about 24 hospitals across the United States.

What if I don't understand something?

- This form may have words you don't understand. If you'd like, research staff will read and explain it with you.
- You are free to ask questions at any time - before, during, or after you are in the study.
- Please ask as many questions as you like before you decide whether you want to be in this study.

What will happen if I say yes, I want to be in this study?

We first will see if your baby's legal custodian/guardian signed the baby-only informed consent for this study.

You cannot be in this study if your baby's legal guardian has not given permission for your baby to be in this study. Additionally your baby cannot be in the study if he/she has (or had) certain medical problems or does not meet the qualifications given in the baby-only consent. The person who is going over this consent with you can list these problems if you want to know what they are.

If you/your baby qualify, we will do these things:

- Ask you to sign this consent form.
- We will assess your and your family's well-being using questionnaires. Questionnaires will be done electronically, over the phone, or in person. You do not have to answer any questions you do not want to answer. The description and schedule for these questionnaires are listed in the "Contact Times" section below.

NOTE: The items listed below in this section are baby-specific and will be done under the baby-only consent, but are included here for full disclosure and to help the you (the caregiver) understand the study as a whole. The sections that are covered under the baby-only consent are *italicized*.

- *Make sure that your baby is getting morphine or methadone to treat NOWS and is stable on the amount he/she is getting.*
- *The amount (dose) of morphine or methadone your baby will receive will be lowered in steps. If your baby is showing signs that he/she is having problems with the lowered amount, the amount will be raised to help your baby.*
- *Tell you that your baby will be placed in 1 of 2 different groups. Your baby will continue to receive the medication that her or his doctor is currently prescribing (morphine or methadone). However, the step used to decrease the dose in group 1 will be different than the steps used to decrease the dose in group 2. One group will have medication decreased faster than the other group. The chances your baby will be in either group is the same as flipping a coin and getting either heads or tails. You will not know if your baby was put in the fast weaning or slow weaning group. Your doctor and nurses will not know if your baby was put in the fast weaning or slow weaning group. However, we can find out which group your baby is in if we need to in an emergency.*
    - *Babies in both groups will go through 8 steps of study drug. Babies in the slow weaning group will have the dose of the drug decreased in 8 steps. Babies in the fast weaning group will have the dose decreased in 5 steps, and then they will receive a placebo (no medicine, like salt water) for 3 steps. The steps will be*

changed based on how your baby is doing and his or her needs. The amount of time your baby is in the hospital will be the same no matter which group the baby is assigned to.

- *Your baby will continue to get morphine or methadone until he or she is stable without either morphine or methadone.*
- *The length of time your baby is in this study will depend on how he/she responds to the lowering of the amount of morphine or methadone.*
- *We will assess your child's behavior and development. This will be done on your baby 24 to 48 hours after your baby has stopped getting methadone or morphine. This will help the medical team evaluate your baby's behavior. The assessment includes determining how calm or excitable the baby is, how well she or he takes to being handled, and how easily he or she can be made more comfortable. This is a physical exam. It involves moving your baby's arms and legs and watching the baby closely.*
- *Your baby will be watched in the hospital for 48 to 72 hours after he/she stops getting study drug. The medical team will watch closely for any signs of NOWS.*
- *During your baby's hospital stay, you/your baby will receive your hospital's usual care except for the following:*
  - ✓ *Your baby's medical team will not decide how fast or slow your baby is weaned from methadone or morphine. Instead, your baby will be randomly put into either the "fast weaning group" or the "slow weaning group." The chance of your baby being in either group is like the chance of getting heads or tails when you flip a coin. The chance your baby will be into the fast weaning group is exactly the same as the chance your baby will be put into the slow weaning group.*
  - ✓ *Your baby will be assessed for nervous system, behavioral, and motor development.*
  - ✓ *Collection of information about your baby when your baby is discharged from the hospital. This information will be from the hospital records of you and your baby and will include things like your baby's size and weight and medication(s) used.*

Description of Post-Discharge Assessments

- You will be asked questions about how you are doing. The questions will be about things like feeling anxious, depressed, distressed or upset. This series of questions will take about 10 minutes to answer.
- You will be asked questions about how you and your baby are doing. This series of questions will take about 5 minutes.

Contact Times (Discharge and Post-discharge)

- Contact 1 – at hospital discharge (of your baby)
  - ✓ Ask you to provide/verify your contact information
- Contact 2 – by phone, home visit, or electronically at 1 month after your baby is discharged from the hospital
  - ✓ Ask you questions about how you are doing. The questions will be about things like feeling anxious, depressed, distressed or upset. This series of questions will take about 10 minutes to answer.
  - ✓ Ask you questions about how you and your baby are doing together. This series of questions will take about 5 minutes.
  - ✓ Ask you to provide or verify contact information
- Contact 3 – by phone, home visit, or electronically when your baby is 6 months old
  - ✓ Ask you to provide or verify contact information
- Contact 4 – by phone, home visit, or electronically when your baby is 12 months old
  - ✓ Ask you to provide or verify contact information
- Contact 5 – by phone, home visit, or electronically when your baby is 18 months old
  - ✓ Ask you to provide or verify contact information
- Contact 6 - when your baby is 24 months old
  - ✓ Ask you questions about how you are doing. The questions will be about things like feeling anxious, depressed, distressed or upset. This series of questions will take about 10 minutes to answer.

How long will this clinical trial (study) take?

Your participation in this research will take about 1 hour over the course of 2 years. There will be a total of 6 contact times (either by phone, home visits, or electronically). The first contact is at discharge and last contact is when your baby is 24-months old. The last contact time could be in person. The time needed to complete these calls or electronic sessions will range from about 10 minutes to about 35 minutes.

NOTE: To help you understand the timing of the entire study, the following information from the baby-only consent is being provided:

> The in-hospital portion of the study will take about 1 month. The length of the hospital stay will depend on your baby's responses to treatment

What if I say no, I do not want to be in this study?

- Nothing bad will happen.
- You/your baby can still get treatment with either morphine or methadone.

What happens if I say yes, but change my mind later?

- You can stop being in the study at any time.
- Nothing bad will happen.
- You/your baby can still get medical care at [insert local context here].
- If you decide to stop being in the study, call (*insert head researcher name*) at (*insert phone #*).

Will it cost me anything to be in the study?

The study will not cost you anything. You or your insurance company will be responsible for your regular medical care, as usual.

Will I be paid for being in the study?

Yes. We will give you the following:

- 1 month post-discharge - $25.00
- 24 months post-discharge, when baby is 24 months old - $20.00

If you participate in the 1 month post-discharge "questionnaire-only" contact time - plus the contact time when the baby is 24 months old –you will be paid a total of $45.00. This is to thank the you for your time.

We will *(LOCAL CONTEXT - insert time and method of payment)*. If you change your mind and decide not to to be in the study, you will only be paid for the contact times for which you answered questionnaires or came for an in-person visit. You will receive payment at – or near – the participation contact time.

If more than $600 in one year (January-December) from *(insert local context/institution)* we may send that person a tax form, if required by law.

Will being in this study help me or my baby in any way?

Being in the study may or may not help you/your baby.

To help you understand the entire study, the following is being provided from the companion baby-only consent. Note that your baby's legal guardian is the person authorizing your baby's participation in this study.

- *If faster weaning is successful, infants in the faster wean group will receive less morphine or methadone.*
- *The information gathered may help babies with NOWS in the future in the following ways:*
  - *Shorten treatment time with methadone or morphine.*
  - *Shorten hospital stays for babies.*
  - *Decrease symptoms.*
  - *Lower chance of return of NOWS symptoms.*

What are the risks of being in this study?

The risks are:

- Someone could find out that you were in the study and learn something about you/your baby that you did not want others to know. We will do our best to protect you/your baby's privacy.
- The questions we ask may make you sad or upset.
- The *italicized* risks are risk to the baby <u>if the baby's legal guardian has given his/her persmission</u> for your baby to be in this study. The risks are being included in your (caregiver) consent so that you can more fully understand the study.
  - *Your baby's NOWS symptoms may return in both groups, but possibly more frequently in the fast weaning group.*
  - *Your baby may have a harder time getting used to being home. This may be more likely if your baby is part of the fast weaning group.*
  - *Problems among babies being treated for NOWS are not common. These problems include:*
    - *seizures*
    - *diarrhea*
    - *breathing problems*
    - *feeding problems*
- Your doctor or study team member [insert local context as appropriate – 'may' vs 'are required to'] report suspected child abuse or neglect to appropriate authorities.

- Participation in this study does not change any need to report a newborn baby was exposed to opioid(s). Local reporting requirements for neonatal opioid exposure will be followed. These requirements are <insert local reporting requirements here>.
- There may also be risks that are not known at this time. You will be given more information if other risks are found.

What if I gets sick or hurt while in this study*?*

If you get hurt when you/your baby are in the hospital for the study, we will help you get the care you need. This may include first aid, emergency care, and/or follow-up care.

- If you are home and get hurt or sick, and think it is because of the study, do these things:
  - ✓ call your doctor or if an emergency, call 911
  - ✓ give your doctor or ER staff
    - the name of this study. *Pragmatic, Randomized, Placebo-Controlled Trial to Shorten Pharmacologic Treatement of Newborns with Neonatal Opioid Withdrawal Syndrome (NOWS) – short title "Weaning"*
    - the name of the head researcher for this study, *(insert researcher name)*
    - a copy of this form if you have it
  - ✓ call the head of the study, *(insert researcher name and 24 hour phone #)*
- This treatment may be billed to you or your insurance company in the normal manner. No other form of payment is available.
- INSERT ADDITIONAL LOCAL CONTEXT AS NEEDED WITH REGARD TO BILLING

What are the alternatives to being in this study?

You do not have to be in this study.

If you do not want to be in this study, you can choose to receive the hospital's usual care for youself.

Can I be taken out of the study even if I want to continue?

Yes, the study doctor (or head researcher) can take you out of the study if:

- It is not in you/your baby's best interest to continue.
- Your baby has an side effect or complication related to NOWS which is considered serious and may prolong the stay in the hospital (seizure, unable to take medication by mouth either due to increased stools, breathing or feeding difficulties).
- The study is stopped for any reason.

What information will be collected about me in the study?

During the study, we will need to learn private things about you/your medical condition, including information about:

- Your background and how to contact you. Information to be collected includes your name, address, telephone number, and other similar types of information. You may be contacted by text, phone call, mail, home visit, or email.
  - ✓ If we cannot contact you from the information that you provide, we may access your/your baby's medical record to obtain contact information from your/your baby's medical record. Use of information available in the public domain may also be used to make contact.
- We may also collect the name of the baby so that we can match information if another person or government agency signs the baby-only consent.
- If you are the biological mother, information about your pregnancy, including physical and mental health conditions, smoking, and whether you took medications or other substances during pregnancy.
- Your drug-test results, if applicable .
- Your responses to questionnaires, including responses to questions about your emotional well-being and your relationship with your baby.
- The person who is going over this consent with you can tell you exactly what information will be collected if you want to know.

Who will see this information? How will you keep it private?

- The local study team will know your name and have access to your information.
- We will do our best to make sure no one outside the study knows you are part of the study.

  To help us stay in contact with you during the study, we may ask you if you are willing to provide name(s) and contact information of back-up contact(s). It is completely up to you to decide if you want to give us additional contact information.
  - ✓ If you decide to give us information for back-up contacts, you are giving us permission to contact those person(s). If we contact one of your back-ups, that person will likely find out that you are part of this study. You may also choose to provide or share other ways for us to stay in contact with you. If you agree to do provide this information, you are giving us permission to use these ways to contact you. Someone outside of the study team may then find out that you are part of this study.
- We will take your name off of information that we collect from you during the study.
  - ✓ We may share your information – with your name removed - with colleagues at the IDeA States Pediatric Clinical Trial Network Coordinating and Operations Center

at University of Arkansas for Medical Sciences, the Duke Clinical Research Institute Coordinating Center, and RTI International in North Carolina.

- When we share the results of the study in meetings or medical journals, we will not include your name or anything else that identifies you or your baby.
- There are people who make sure the study is run the right way. These people may see information, including information that identifies you, from the study about you. They are:
  - ✓ NIH (National Institutes of Health), the study sponsor
  - ✓ OHRP (Office for Human Research Protections), a federal agency
  - ✓ University of Arkansas for Medical Sciences (UAMS) Institutional Review Board
  - ✓ Other institutional oversight offices
  - ✓ Investigators from other sites in the study
  - ✓ RTI International
  - ✓ FDA (Food and Drug Administration)
  - ✓ IDeA States Pediatric Clinical Trial Network Data Coordinating and Operations Center at the University of Arkansas for Medical Sciences
  - ✓ Duke Clinical Research Institute Coordinating Center
- Insert local state law requirements.

  For example, state law requires that we report to the Arkansas Department of Health cases of certain diseases that a sick person could give to someone else. If we learn you have such a disease, we will share your name and contact information with the health department.

  State law requires we tell the authorities if we learn about possible child or adult abuse or that you might hurt yourself or someone else

Where and how long will my information be kept?

- We will code your information and keep the key to the code in a locked file or other secure location at <insert local institution>.
- Your study information will also be stored, without your name, at the IDeA States Pediatric Clinical Trial Network at University of Arkansas for Medical Sciences in Arkansas and at RTI International in North Carolina.
- Your information will be stored indefinitely.
- Only *(insert local context, name/roles of persons)* will be able to link your information to you.
- We LOCAL CONTEXT: *will/will not* put study information about you in your medical record(s). *(IF yes, include state what information will be put in the participant's medical record.)*

If I stop being in the study, what will happen to any information collected from me in the study?

- We will not be able to take your information out of the study after it has started.

Will my information from the study be used for anything else, including future research?

- Yes. If you participate in this study, we will keep information from this research study. The information will be de-identified (for example, a code number will be used instead of your/your child's names) so that it cannot be linked to you or your baby. The information will be placed into an appropriate NIH-approved information repository. In the future other researchers who were not part of this study may ask to use this information. Any information released to other researchers will not identify you or your baby or your participation in this research study.

Will you tell me the results of the study?

- We will not notify you directly, but the results of the study will be available on a website (http://www.ClinicalTrials.gov, see below) and in medical journals. You may contact us at any time during or after the study if you have questions about the results.

Will you tell me anything you learn that may impact my health?

- Yes. If we learn something about you or your baby that might be important for your or your baby's health, we will tell you.

What if new information comes up about the study?

- We want you to know about anything that may change your mind about being in the study.
- The study team will let you know either by calling you or sending you a letter.

Where can I find more information about this study?

A description of this study 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 any time. The NCT number is NCT04214834.

What if I have questions?

- Please call the head researcher of the study *(insert researcher name and phone #),* if you
  - ✓ have any questions about this study
  - ✓ feel you have been injured in any way by being in this study

- You can also call the office at UAMS that supervises research if you can't reach the study team or want to speak to someone not directly involved with this study. To do so call the UAMS Institutional Review Board (IRB) at 501-686-5667.
  - ✓ You may call the UAMS IRB if you have questions about your rights as a research participant
- *[insert local context if other than researcher named above]*

By signing the document, I am saying:

- ✓ I understand that joining this study is voluntary.
- ✓ I agree to be in the study.
- ✓ Someone talked with me about the information in this document and answered all my questions.
- ✓ I have been asked if I wish to talk directly to the study doctor.

I know that:

- ✓ I can stop any and all parts of the study at any time and nothing bad will happen to me or my baby.
- ✓ I can call the office that supervises research (UAMS Institutional Review Board) at 501-686-5667 if I have any questions about the study or about my rights.
- ✓ I do not give up any of my rights by signing this form.

I agree to be part of this study:

Printed Name of Participant

Signature of Participant | Date (mm/dd/yyyy)

Name of baby: _____

I agree to being contacted for future research related to this study.

___ YES ___ NO

Printed Name of Participant

Signature of Participant | Date (mm/dd/yyyy)

Name/Signature of person obtaining consent:

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent | Date (mm/dd/yyyy)

List of Common Opioids

- **Brand Names (generic names):**
  - Demerol (meperidine)
  - Dilaudid (hydromorphone)
  - Lortab (hydrocodone)
  - MS Contin (morphine)
  - Norco (hydrocodone)
  - Opana (oxymorphone)
  - Oxycet (oxycodone)
  - Percocet (oxycodone)
  - Zohodro ER (hydrocodone)
- **Generic Names:**
  - Buprenorphine
  - Fentanyl
  - Heroin
  - Hydrocodone
  - Methadone
- **Street Names (generic names):**
  - Buse, Oranges, Subs (buprenorphine)
  - Apache, China Girl, Dance Fever, Friend (fentanyl)
  - China White, Dope, H. Horse, Junk, Smack (heroin)
  - Watson 387 (hydrocodone)
  - Amidone, Fizzies, Chocolate Chip Cookies (methadone)
  - M. Miss Emma, Monkey, White Stuff (morphine)
  - Hillbilly Heroin, O.C. Oxycet, Oxy (oxycodone)