The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: **Dose Escalation Pharmacokinetic Study of Intranasal Atomized Dexmedetomidine in Pediatric Patients with Congenital Heart Disease**

Version Date: July 20, 2020

Principal Investigator:	**Kelly Grogan, MD**	Telephone: (410) 279-6994
Emergency Contact:	**Kelly Grogan, MD**	Telephone: (410) 279-6994

Your child may be eligible to take part in a research study. This form gives you important information about the study. It describes why we are doing the study, and the risks and possible benefits of participating.

If there is anything in this form you do not understand, please ask questions. Please take your time. You do not have to take part in this study if you do not want to. If you take part, you can leave the study at any time.

In the sections that follow, the word "we" means the study doctor and other research staff. If you are a parent or legal guardian who is giving permission for a child, please note that the word "you" refers to your child.

Why are you being asked to take part in this study?

You are being asked to take part in this research study because you have congenital heart disease and are having a heart catheterization.

What is the purpose of this research study?

The purpose of this research study is to help determine when is the best time to give Dexmedetomidine to provide sedation and how much of the drug should be given to achieve the best result in children.

When children have surgery or an invasive procedure like a cardiac catheterization, they often are given a medication by mouth or in their IV to help relieve anxiety, allow a smooth separation from their parents, and ease the beginning of anesthesia. These same medicines may also be sprayed in the nose, but this may be irritating to some patients and therefore are not often given that way.

Dexmedetomidine is approved by the US Food and Drug Administration for use in adult patients when given in an IV. It is not approved in kids. Despite this, it is used safely at CHOP in children, including children with congenital heart disease, every day. Dexmedetomidine is not approved by the US Food and Drug Administration for use in adults or children when given intranasally (sprayed in the nose). Despite this, it is safely used frequently at other hospitals in children. It is not currently routinely used at CHOP.

We would like to start using intranasal Dexmedetomidine in children with congenital heart disease who are having surgery or procedures and need sedation before the procedure. In order to do this, we want to find out when we need to give the drug and how much of the drug should be given to achieve the best result. This has not been done in children.

How many people will take part?

65 children at CHOP will take part in this study.

What is involved in the study?

How long will you be in this study?

If you agree to take part, your participation will last for up to 6 hours. Your participation will not affect the length of the catheterization you are already scheduled to have. There are no follow-up appointments.

What are the study procedures?

Some of the procedures in this study will be repeated several times. Tests that are part of your regular, routine medical care will continue to be performed. The study involves the following tests and procedures.

Medical Record Review: The subject's medical record will be reviewed as part of the study.

Physical Examination: The EKG rhythm will be assessed prior to the administration of study drug.

Blood Draw: During the study, we will collect blood samples from you. By agreeing to participate in this study, you agree to give these samples to CHOP for research purposes. Your blood will be drawn several times throughout the catheterization to measure the amount of dexmedetomidine in your system. This blood will be drawn through the IV that is placed by the cardiologist to perform your heart catheterization. No IVs will be placed that you do not normally need for your care during your procedure. At most, your blood will be drawn 12 times. The total amount of blood drawn will be less than a tablespoon.

Study Drug/Intervention: You will receive the study drug one time after you are sedated or anesthetized. Dexmedetomidine will be sprayed up your nose using a device called an atomizer (See page 7 of this consent for a picture of an atomizer).

There are two groups in the study. Each group will get a different dose of dexmedetomidine:

- The dose you receive will depend on when you take part in the study. The first subjects enrolled in the study will receive the lowest dose of the drug.
- We will look at the information from the first group before giving a higher dose of drug to the second group.

We think that the dose that will provide the best sedation is the higher dosing group. However, we want to look for side effects that may also increase with the higher drug dose before we give it.

What are the risks of this study?

Taking part in a research study involves inconveniences and risks. If you have any questions about any of the possible risks listed below, you should talk to your study doctor or your regular doctor.

While in this study, you are at risk for the following:

Breach of Privacy and Confidentiality:

As with any study involving collection of data, there is the possibility of breach of confidentiality of data. Every precaution will be taken to secure participants' personal information to ensure confidentiality.

At the time of participation, each participant will be assigned a study identification number. This number will be used on data collection forms, blood samples, and in the database instead of names and other private information. A separate list will be maintained that will links each participant's name to the study identification number for future reference and communication.

Risks associated with Dexmedetomidine:

The main risks of Dexmedetomidine are:

- Bradycardia, which is when your heart rate is lower than normal. This has been seen in up to 10% of children and adults who receive dexmedetomidine when given in the IV. It has been seen in up to 10% of children who receive dexmedetomidine when given intranasally. The bradycardia is generally mild and usually does not need any treatment.
- Hypotension, which is when your blood pressure is lower than normal. This has also been seen in up to 25% of children and adults who receive dexmedetomidine when given in the IV. It has been seen in up to 10% of children who receive dexmedetomidine when given intranasally. The hypotension is generally mild and usually does not need any treatment.
- Transient hypertension, which is when your blood pressure is higher than normal. This can be seen briefly when dexmedetomidine is given in the IV in up to 12% of adults. It has not been reported when given intranasally, but it may occur.
- Sedation. This is actually the desired effect of Dexmedetomidine. However, in this study we are not evaluating the degree of sedation since you will already be under sedation or anesthesia when the drug is given. Most of the drug should be cleared from your system by the end of the catheterization. Since it is being added to the other medications you will be receiving for your sedation and anesthesia, there may be an additional sedation effect. The nurses or anesthesiologist giving the other drugs will alter those doses, if needed.

Other Risks:

In neonatal and infant animals, sedative and anesthetic agents adversely affect brain development. This includes loss of brain cells. This may result in long-term changes that may be permanent in learning and behavior. For the most

part, these effects happen after prolonged periods of sedation or anesthesia (greater than 3 hours). These effects also appear when rapid brain development is taking place. In children, this is when they are less than 3 years of age. It is not known if similar adverse effects occur in humans.

You should know that anesthetic drugs are needed to perform your child's procedure. They may have the potential to increase the loss of nerve cells in their developing brain. The clinical significance of any such changes is not yet known. Some animal studies suggest that dexmedetomidine may be better for a growing infant's brain than other drugs. However, the effects of dexmedetomidine on the developing brain have not been completely tested.

Are there any benefits to taking part in this study?

There will be no direct benefit to you from taking part in this study. The knowledge gained from this study will help doctors determine at what dose and at what time Dexmedetomidine should be given to children with congenital heart disease who would benefit from having sedation before procedures or surgery.

Do you need to give your consent in order to participate?

If you decide to participate in this study, you must sign this form. A copy will be given to you to keep as a record.

What happens if you decide not to take part in this study?

Participation in this study is voluntary. You do not have to take part in order to receive care at CHOP.

If you decide not to take part or if you change your mind later there will be no penalties or loss of any benefits to which you are otherwise entitled.

Can you stop your participation in the study early?

You can stop being in the study at any time. You do not have to give a reason.

Can the study doctor take you out of the study early?

The study doctor may take you off of the study if:

- The study is stopped.
- The study drug is no longer available.
- New information suggests taking part in the study may not be in your best interests.

What about privacy, authorization for use of Personal Health Information (PHI) and confidentiality?

As part of this research, health information about you will be collected. This will include information from medical records, procedures, interviews, exams, and blood tests. Information related to your medical care at CHOP will go in your medical record. Medical records are available to CHOP staff. Staff will view your records only when required as part of their job. Staff are required to keep your information private.

Information that could identify you will not be shared with anyone - unless you provide your written consent, or it is required or allowed by law. The laboratory results obtained in this study will not be part of your medical record. We will do our best to keep your personal information private and confidential. However, we cannot guarantee absolute confidentiality. Your personal information may be disclosed if required by law.

The results of this study may be shown at meetings and published in journals to inform other doctors and health professionals. We will keep your identity private in any publication or presentation.

Several people and organizations may review or receive your identifiable information. They will need this information to conduct the research, to assure the quality of the data, or to analyze the data or samples. These groups include:

- Members of the research team and other authorized staff at CHOP
- People from agencies and organizations that perform independent accreditation and/or oversight of research; such as the Department of Health and Human Services, Office for Human Research Protections.
- The Bio Analytical Core of the Center for Clinical Pharmacology Laboratory, who is testing your blood sample(s)
- The Food and Drug Administration.

By law, CHOP is required to protect your health information. The research staff will only allow access to your health information to the groups listed above. By signing this document, you are authorizing CHOP to use and/or release your health information for this research. Some of the organizations listed above may not be required to protect your information under Federal privacy laws. If permitted by law, they may be allowed to share it with others without your permission.

There is no set time for destroying the information that will be collected for this study.

Your permission to use and share the information and data from this study will continue until the research study ends and will not expire. Researchers continue to analyze data for many years and it is not possible to know when they will be completely done.

Can you change your mind about the use of personal information?

You may change your mind and withdraw your permission to use and disclose your health information at any time. To take back your permission, it is preferred that you inform the investigator in writing.

Dr. Kelly Grogan, MD
The Children's Hospital of Philadelphia
Department of Anesthesiology and Critical Care Medicine
3401 Civic Center Blvd, Suite 12NW40
Philadelphia, PA, 19104

In the letter, state that you changed your mind and do not want any more of your health information collected. The personal information that has been collected already will be used if necessary for the research. No new information will be collected. If you withdraw

your permission to use your personal health information, you will be withdrawn from the study.

Additional Information

An Independent Medical Monitor will be reviewing the data from this research throughout the study.

Financial Information

While you are in this study, the cost of your usual medical care – procedures, medications and doctor visits – will continue to be billed to you or your insurance.

Will there be any additional costs?

There will be no additional costs to you by taking part in this study.

CHOP is providing financial support and material for this study. The following research materials will be paid for by CHOP:

- Cost of Dexmedetomidine
- Cost of atomizers to administer the Dexmedetomidine
- Blood tests for determining Dexmedetomidine blood levels

Will you be paid for taking part in this study?

You will not receive any payments for taking part in this study.

Who is funding this research study?

The Division of Cardiothoracic Anesthesia at the Children's Hospital of Philadelphia is funding this research study.

One of the investigators on this study, Dr. Athena Zuppa, has served as a consultant to Pfizer. Her participation in this study has been reviewed and approved by CHOP's Conflict of Interest (COI) Office.

If you have any questions or concerns about how this study is funded, you may contact Dr. Grogan or the COI Office at COI@email.chop.edu/267-426-6044.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Grogan at 410-279-6994. You may also talk to your own doctor if you have questions or concerns.

The Institutional Review Board (IRB) at The Children's Hospital of Philadelphia has reviewed and approved this study. The IRB looks at research studies like these and makes sure research subjects' rights and welfare are protected. If you have questions about your rights or if you have a complaint, you can call the IRB Office at 215-590-2830.

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.

What happens if you are injured during the study?

If you are hurt or get sick from something that was done as part of this study, doctors at the clinic or hospital can arrange for emergency medical care. The Hospital does not offer financial compensation or payment for injuries due to participation in this research.

You and your insurance company will be billed for the costs of any care or injuries.

If you think you have been injured from taking part in this study, call Dr. Kelly Grogan at (410)-279-6994. She can go over things with you, let you know of resources that may be available and give you information on what you need to do.

In case of injury resulting from this study, you will not lose any legal rights by signing this form.

Consent for Use of Data or Specimens for Future Research

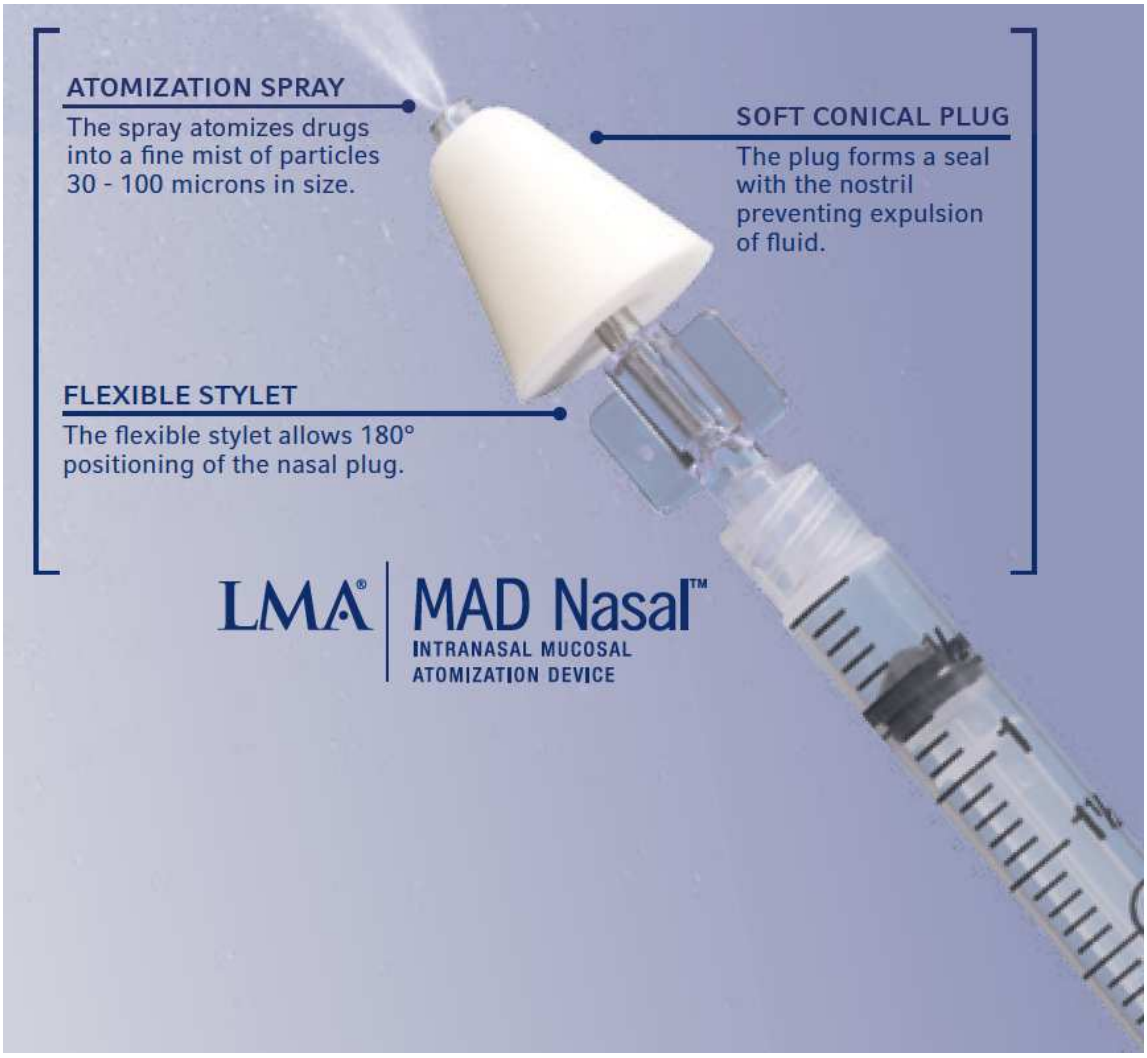
As part of the study, we will collect data (information) about you and blood samples. We may wish to use this information or blood samples in a future study about the sedative effects of intranasal dexmedetomidine in pediatric patients with cardiac disease. The information and samples will be given a unique code and will not include information that can identify you. Information that can identify you or the blood samples may be kept permanently in a computer database at CHOP. Only the study doctors and those working with them on this study will be able to see information that can identify you.

If you leave the study, you can ask to have the data collected about you removed or the samples destroyed. You can also ask us to remove information that identifies you from the data or samples.

Please indicate whether you will allow your stored information or blood samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) The data and blood specimens may be used for this study only.

_____ (initials) The data and blood specimens may be used for other future research studies. If the data or blood specimens are shared outside of CHOP, no identifiable information will be included.


ATOMIZATION SPRAY
The spray atomizes drugs into a fine mist of particles 30 - 100 microns in size.
SOFT CONICAL PLUG
The plug forms a seal with the nostril preventing expulsion of fluid.
FLEXIBLE STYLET
The flexible stylet allows 180° positioning of the nasal plug.
LMA® MAD Nasal™
INTRANASAL MUCOSAL ATOMIZATION DEVICE

Consent to Take Part in this Research Study and Authorization to Use and Disclose Health Information for the Research

The research study and consent form have been explained to you by:

Person Obtaining Consent	Signature of Person Obtaining Consent
	Date

By signing this form, you are indicating that you have had your questions answered, you agree to allow your child to take part and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share the health information that will be collected for this study, as explained above. If you don't agree to the collection, use and sharing of health information, you cannot participate in this study.
NOTE: *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Child Subject

Both Parents Must Sign this Consent Form

Name of Authorized Representative #1	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #1	Date
Name of Authorized Representative #2	Relationship to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative #2	Date

If the second representative is unavailable, per §46.408(b) / §50.55(e)(2), explain the reason.