The Children's Hospital *of* Philadelphia®

Informed Consent Form and HIPAA Authorization

Study Title: **Utility of nasal steroids for treatment of childhood obstructive sleep apnea (SPARK)**

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You, or your child, may be eligible to take part in a research study. This form gives you important information about the study. It describes the purpose of this research 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 problems breathing during sleep (obstructive sleep apnea) or you have symptoms of obstructive sleep apnea.

What is the purpose of this research study?

The purpose of this research study is to determine if a nasal spray medicine (intranasal fluticasone) is an effective treatment for obstructive sleep apnea. Intranasal fluticasone is a medicine that is approved by the US FDA for use in children for other reasons (for example, nasal allergies) and is not an experimental medicine. It has not been well studied in children with obstructive sleep apnea. We will also determine whether a 3-month treatment with intranasal fluticasone is as effective as a 12-month treatment.

How many people will take part?

About 318 children will take part in this study, all at Children's Hospital of Philadelphia.

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 3 or 12 months and will involve 3 or 6 study visits, and monthly phone calls. Some children will be in the study for about three months, others for about 1 year.

What are the study procedures?

The study involves the following tests and procedures.

(A) Screening

First, to see if you are eligible for this study, your medical records will be reviewed to be sure that you can be in this study. Information such as medicines used, past medical problems and surgeries will be reviewed.

- If you have not had a sleep study, you will have a sleep study as part of the research.
- If you have already had a recent sleep study you will not need another at this point of the research

A sleep study is a standard clinical test that is not experimental. It will tell us if you have obstructive sleep apnea or not. The sleep study is done overnight in the sleep lab at the Children's Hospital of Philadelphia. Small patches will be placed on your skin on your head, face, chest and legs. These patches will be connected by wires to machines in a separate monitoring room to monitor your breathing, heart rate and sleep stage. You will wear stretchy belts around your chest and abdomen and a tube under your nose to measure your breathing. You will also be videotaped, so that the doctor can see your breathing pattern during sleep. Your mom or dad or other designated adult caregiver will sleep in the same room as you.

How the sleep study findings are used to determine study eligibility

You will continue in the study only if your sleep study is mild to moderately abnormal and you meet other criteria for the study.

You will not continue in the study if your sleep study is normal or if you have high levels of obstructive sleep apnea. If this is the case, your clinical doctor will be sent the results and will decide on the best treatment for you.

(B) Baseline Tests

During the first visit, you will have a number of tests done. These will take about a day all together. Some must be done in a certain order in the morning. There will be breaks and lunch, so that you don't get tired.

(i) A blood test will be taken to check your levels of hormones that may be affected by fluticasone. The test will also check for signs of inflammation. Numbing cream will be put on your arm to ease the discomfort of the blood draw. This will take about 2 teaspoons of blood

(ii) Physical exam:

(iii) Behavior tests: You will do some tests of concentration and coordination

(iv) Parent questionnaires: We will ask your parents to fill out brief questionnaires. The questions are about your behavior, quality of life, symptoms of obstructive sleep apnea, and nasal symptoms that may bother you.

(v) DXA scan: This test will be used to check how thick your bones are. Because this is an Xray, girls who are aged 10 and older or who have started their period will have a urine pregnancy test before the DXA scan. Positive pregnancy results will

be shared with you and not with your parent(s). We encourage you tell your parent(s) the results. If the test is positive, you will be taken out of the study.

(vi) Knee height measurement: You will sit in a special chair while your knee is measured.

(vii) Nasal swab: Your nose will be gently swabbed to get secretions. These secretions will be tested for genetics and to measure inflammation.

(viii) Ophthalmology (eye) evaluation: An eye specialist will check your eye pressure and look into your eyes with a special light to make sure everything is fine.

(ix) Airway size measurement: You will wear clips on your nose and breathe for a few minutes into a machine. This measures how big your throat is.

(x) Spirometry: This measures your lung function (how well your lungs work). You will breathe through a mouthpiece while wearing nose clips, take a deep breath and blow hard into a machine. It is like blowing candles on a birthday cake. You will do this a few times.

(xi) Allergy skin prick test: This test involves pricking your arm about 10 times with a very small needle. This introduces allergy extracts under the skin, to see if you have any allergies.

(C) Randomization

At the end of these tests, if you DO have problems with your hormones, bone density or eyes, you will not be able to continue in the study. Tests results will be forwarded to your doctor and you will be referred to specialist(s) for clinical care.

If you DO NOT have problems with your hormones, bone density or eyes, you will be randomly assigned to one of the study groups. Randomly assigned means you are put into a group by chance. It is like flipping a coin. Since the group assigned to the study drug will be larger than that assigned to placebo, you will have more chances to be in the study group. Your study doctor will not know which group you are in until after the study is finished.

One group will receive intranasal fluticasone and the other will receive placebo. A placebo is a nasal spray that does not contain active medication. Both groups will receive the nasal spray for 3 months.

The bone density results may not be immediately available at the time of randomization, and may take up to a couple of weeks. If the bone density results come back abnormal, then you will be taken off the study and referred for clinical treatment. There is no harm to the bones from being on the study medication for a couple of weeks.

(D) Treatment

You will use the nasal spray every night (one spray into each nostril) until the study is over. You will keep a diary of any illnesses or medical problems. You will receive a phone call by the study research coordinator after the treatment initiation to check how everything is going. You will be asked if you have been to a doctor, emergency room, or if you have taken any medication for any reason.

You will come back to CHOP for a visit 3 months after the treatment started. You will have all the tests that were done at the baseline visit except for the spirometry and skin allergy testing. We will collect all of the study spray bottles that you used. You will also have another sleep study overnight.

If problems with your hormones, bone density or eyes are seen at this visit, or if your sleep apnea on the sleep study is much worse, you will be referred to specialist(s) and you will no longer stay in the study.

Importantly, your participation in the study may end even if you do not have any of the problems during testing. Your participation may end after three months in the Treatment phase. You will be told if your participation in the study has ended at the end of the visit, and refer you to your doctor for clinical care if you still have obstructive sleep apnea. The investigators will not know whether you received the study drug or placebo until the study is completed.

Second Randomization**:** You will be told if you can continue in the study. If you continue in the study, you will be randomized again to treatment with intranasal fluticasone or placebo. Both groups will be treated for 9 months.

(E) Follow-up

This phase of the study will last 9 months.

You will take the nasal spray every day and keep a diary of any medical problems or illnesses. You will receive a phone call by the study research coordinator every month, unless you have to come for a visit. These calls are to check how everything is going.

3 and 6 months after the second randomization, you will come to CHOP for a short visit that will include a medical history, blood pressure, heart rate, height, weight, medications you have taken, and two brief symptoms questionnaires. You have to bring the study nasal sprays as well.

9 months after the second randomization, you will come to CHOP for a long visit. All the baseline tests will be repeated except for the spirometry and skin allergy test. You will have a final sleep study. You may be referred to your doctor for clinical care if needed.

This will end your study participation.

Visit Schedule

The table below provides a brief description of the purpose and duration of each study visit.

Visit	Purpose	Main Procedures	Duration
Screening	Screening visit	History, height, weight, sleep study	overnight
Visit 1, Day 0	Baseline Tests and first randomization	Routine procedures, physical, questionnaires, behavioral testing, blood tests, urine pregnancy test (if appropriate), DXA scan and knee measurement, airway measurement, nasal swab, allergy skin test, ophthalmology exam, spirometry, randomization	One day

Phone Contact 1, Day 30	Checking in	Routine procedures	20 minutes
Phone Contact 2, day 60	Checking in	Routine procedures	20 minutes
Visit 2, day 90	Tests and second randomization	History, physical, questionnaires, behavioral testing, blood tests, urine pregnancy test (if appropriate), DXA scan and knee measurement, airway measurement, ophthalmology exam, nasal swab, sleep study, and randomization	One day and overnight
Your participation may end after visit 2			
Phone Contact 3, Day 120	Checking in	Routine procedures	20 minutes
Phone Contact 4, Day 150	Checking in	Routine procedures	20 minutes
Visit 3, Day 180	Symptoms evaluation	Routine procedures, physical, height, weight, , symptoms questionnaires	60 minutes
Phone Contact 5, Day 210	Checking in	Routine procedures	20 minutes
Phone Contact 6, Day 240	Checking in	Routine procedures	20 minutes
Visit 4, Day 270	Symptoms evaluation	Routine procedures, physical, height, weight, , symptoms questionnaires	60 minutes
Phone Contact 7, Day 300	Checking in	Routine procedures	20 minutes
Phone Contact 8, Day 330	Checking in	Routine procedures	20 minutes
Visit 5, Day 365	Final visit	Routine procedures, physical, questionnaires, behavioral testing, blood tests, urine pregnancy test (if appropriate), DXA scan and knee measurement, airway measurement, ophthalmology exam, nasal swab and sleep study	One day and overnight

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 side effects:

Risks associated with treatment delay:

The possible side effects of untreated obstructive sleep apnea may include snoring and behavioral problems. However, considering that most children with obstructive sleep

apnea have been snoring for a lot longer than 12 months, we believe that a 3 and a 12 month wait is within a safe range. We will talk to you or see you every month to see if you are developing any new or worsening problems. If you develop significant problems related to obstructive sleep apnea, we will refer you for clinical care (which may include surgery to take out your tonsils and adenoid).

- Children with higher levels of obstructive sleep apnea will be excluded from this study
- A Medical Safety Officer, who is an outside pediatrician who is not part of the study, and a safety board will review the study for safety. If you develop problems during the study, the Medical Officer, the safety board, and the principal investigator will decide whether it is safe for you to continue in this study.

Risks associated with study intranasal fluticasone:

- Most severe risks: hormonal dysfunction that is extremely rare at low doses such as the used in this study, eye cataracts, and decrease in growth velocity.
- Less severe risks: nasal dryness or irritation, nose bleeds

Risks associated with placebo:

- Minimal risks: You may experience transient discomfort.

Risks associated with sleep studies:

- There are no risks related to the sleep study itself except for possible minor skin irritation from the patches put on the skin.
- Sleeping away from home may make your child uncomfortable. However, another family member will sleep in the same room.

Risks associated with physical exam/vital signs:

- There are no more than minimal risk associated with these exams.

Risks associated with blood tests:

- Taking blood may cause some pain, bleeding or bruising at the spot where the needle enters your body.
- Rarely, taking blood may cause fainting or infection.
- Very rarely, the numbing cream can cause an allergic reaction.

Risks associated with urine pregnancy tests:

You may feel embarrassed by providing a urine sample. However, the sample will be collected in a private location. If you are pregnant, you will not continue in this research study as there is a risk that the DXA scan radiation can hurt an unborn baby.

Risks associated with behavioral tests:

Some people find taking the behavior tests mildly stressful. To help with this, testing will be conducted in a quiet, private area and you will be offered breaks as needed. The examiners are well-trained in testing children.

Risks associated with DXA scan:

This research study involves exposure to a small dose of radiation from a DXA scan. This radiation dose is not necessary for your medical care and will occur only as a result of your participation in the study. At doses much higher than you will receive, radiation is known to increase the risk of developing cancer after many years. At the doses you will receive, it is unlikely that you will see any effects at all.

Risks associated with ophthalmological exam:

The risks associated with eye exams are no more than minimal.

Risks associated with allergy skin test:

You may experience pain, discomfort, itching, redness or swelling at the site of the skin test. This usually goes away within 30–60 minutes after the skin test, although it can last for up to 24–48 hours. Very rarely, skin tests can cause anaphylaxis (a severe allergic reaction). Skin tests may also bring on an asthma attack, especially if you have active asthma symptoms on the day of testing. However, this is also very rare. A doctor will be there in case there are any problems.

Risks associated with spirometry:

The risks associated with spirometry are no more than minimal.

Risks associated with airway measurement:

The nose clips may be uncomfortable during the procedure that is very short (5 minutes).

Risks associated with nasal swab:

This may cause some pain, bleeding or bruising at the spot where the swab enters the nostril. However, these risks are very low as this is a fast procedure.

Are there any benefits to taking part in this study?

You might benefit if we identify any disease that needs attention, for instance high blood pressure. However, we cannot guarantee or promise that you will receive any direct benefit by participating in this study. The knowledge gained from this research may help doctors determine whether intranasal fluticasone is an effective treatment for children with obstructive sleep apnea. If intranasal fluticasone is proven effective for the treatment of OSAS, the participants who receive this medication will benefit from it. However, you will not know whether you were on fluticasone or placebo.

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. Please consider the study time commitments and responsibilities as a research subject when making your decision about participating in this study

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:

- Your condition worsens.
- The study is stopped.
- The study drug is no longer available.
- You cannot meet all the requirements of the study.
- New information suggests taking part in the study may not be in your best interests.

What choices do you have other than this study?

There are options for you other than this study including:

- Not participating in this study. If you do not participate, you will have usual clinical care which is often surgery to take out your tonsils and adenoid.

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 and tests that are part of this research. In addition, we will access you medical record to see how many times you go to the doctor or emergency room. Laboratory test results will appear in your medical record with the exception of psychological tests and parent questionnaires, which are performed only for this research study. 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
- Groups monitoring the safety of this study
- The National Institutes of Health who is sponsoring this research;
- Public health authorities that are required by law to receive information for the prevention or control of disease, injury or disability

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.

To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. With this Certificate, the researchers cannot be forced to disclose information that may identify you, even by a court subpoena, in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings. The researchers will use the Certificate to resist any demands for information that would identify you, except as explained below.

The Certificate cannot be used to resist a demand for information from personnel of the United States Government that is used for auditing or evaluation of Federally funded projects or for information that must be disclosed in order to meet the requirements of the federal Food and Drug Administration (FDA).

You should understand that a Certificate of Confidentiality does not prevent you or a member of your family from voluntarily releasing information about yourself or your involvement in this research. If an insurer, medical care provider, or other person obtains your written consent to receive research information, then the researchers will not use the Certificate to withhold that information.

The Certificate of Confidentiality does not prevent the researchers from disclosing, without your consent, information that they are required by law to disclose to government authorities. For example, researchers must comply with laws requiring the reporting of suspected child abuse and neglect and communicable diseases.

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, you must tell the investigator in writing.

Dr. Ignacio E. Tapia
The Children's Hospital of Philadelphia
34th Street and Civic Center Blvd.
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

A Data Safety and Monitoring Board, an independent group of experts, will be reviewing the data from this research throughout the study.

You will be informed if changes to the study are needed to protect your health. You will be told about any new information that could affect your willingness to stay in the study, such as new risks, benefits or alternative treatments.

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?

The National Institutes of Health is providing financial support and material for this study and research procedures, medications and study visits:

Will you be paid for taking part in this study?

Yes. The compensation details are below.

If you are 8 years or younger, your compensation for participation will be given in trust to your parents as follows:

- The parent/caregiver accompanying the child to the sleep study will receive $100 cash for each sleep study (screening visit if you have not had a recent one, and visits 2 and 5) performed as a reimbursement for transportation, parking, meals, and baby-sitting costs for siblings.
- The parent/caregiver accompanying the child to daytime visits (1, 2, and 5) will receive $100 cash as a reimbursement for transportation, parking, meals, and loss wages.
- The parent/caregiver accompanying the child to daytime visits (3 and 4) will receive $50 cash as compensation for time and effort.

If you are 9 years or older:

- The parent/caregiver accompanying the child to the sleep study will receive $50 cash for each sleep study (screening visit if you have not had a recent one, and visits 2 and 5) performed as a reimbursement for transportation, parking, meals, and baby-sitting costs for siblings.

- The parent/caregiver accompanying the child to daytime visits (1, 2, and 5) will receive $50 cash as a reimbursement for transportation, parking, meals, and loss wages.
- The parent/caregiver accompanying the child to daytime visits (3 and 4) will receive $25 cash as compensation for time and effort.
- Participants will receive $50 cash for each sleep study performed (screening visit if you have not had a recent one, and visits 2 and 5) as compensation for time and effort.
- Participants will receive $50 cash for daytime visits (1, 2, 3and 5) as compensation for time and effort.
- Participants will receive $25 cash for daytime visits (3 and 4) as compensation for time and effort.
- Please remember that it is possible that your participation in the study may end at the end of visit 2.

Who is funding this research study?

The National Institutes of Health is providing funding for this study.

What if you have questions about the study?

If you have questions about the study, call the study doctor, Dr. Tapia at 267-426-5842. 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. Tapia at (267)426-5842. 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 sleep studies, tests on behavior, blood tests, nasal secretions tests, questionnaires, spirometry, skin allergy tests, DXA scans, and airway measurement. We may wish to use this information or samples in a future study about sleep in children. Information that can identify you or your sleep studies, questionnaires, and blood or nasal swab samples may be kept permanently in a password protected electronic file 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 your 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 data or samples to be used for future research by putting your initials next to one of the following choices:

_____ (initials) My _____data or specimens may be used for this study only.

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

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 take part in this research study and you are legally authorized to consent to your child's participation. You are also agreeing to let CHOP use and share your child's health information as explained above. If you don't agree to the collection, use and sharing of your child's health information, your child cannot participate in this study. **NOTE:** *A foster parent is not legally authorized to consent for a foster child's participation.*

Name of Subject	
Name of Authorized Representative (if different than subject)	Relation to subject: ☐ Parent ☐ Legal Guardian
Signature of Authorized Representative	Date

Child Assent to Take Part in this Research Study

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent Date

This study has been explained to me and I agree to take part.

_____ _____
Signature of Subject (optional) Date

For children unable to assent:

I certify that _____ was not capable of understanding the procedures involved in the study sufficiently to assent to study participation.

_____
Person Responsible for Obtaining Assent

_____ _____
Signature of Person Responsible Date

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

Name of Subject

Name of Authorized Representative (if different than subject)

Relation to subject:
☐ Parent ☐ Legal Guardian

The research study and consent form have been explained to the subject or parent/legal guardian.

By signing this form, you are indicating that you have answered the subject's or parent's/legal guardian's questions, they have agreed to take part in this research study and they are legally authorized to consent to their or their child's participation. They have also agreed to let CHOP use and share their or their child's health information as explained above. If they don't agree to the collection, use and sharing of their or their child's health information, they cannot participate in this study.

Person Obtaining Consent

Signature of Person Obtaining Consent

Date:

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining consent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining consent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining consent (including responses to the subject's questions) and responded affirmatively.

Name of Witness/Interpreter

Signature of Witness/Interpreter

Date: _____

Child Assent to Take Part in this Research Study

For children capable of providing assent:

I have explained this study and the procedures involved to _____ in terms he/she could understand and that he/she freely assented to take part in this study.

_____
Person Obtaining Assent

_____ _____
Signature of Person Obtaining Assent | Date

Witness/Interpreter

By signing this form, you are indicating that

- The information in the Summary Document as well as any additional information conveyed by the person obtaining assent was presented to the subject in a language preferred by and understandable to the subject; and
- The subject's questions were interpreted and the responses of the person obtaining assent were presented in a language preferred by and understandable to the subject.
- At the conclusion of the consent conference, the subject was asked in a language preferred by and understandable to the subject if s/he understood the information in the Summary Document as well as any additional information conveyed by the person obtaining assent (including responses to the subject's questions) and responded affirmatively.

_____ _____
Name of Witness/Interpreter | Signature of Witness/Interpreter

Date: _____