INDIANA UNIVERSITY INFORMED CONSENT STATEMENT

AND AUTHORIZATION FOR RESEARCH

Phase IIa Clinical Trial to Evaluate Pharmacokinetics and Safety of Slow Release DHEA

Sponsor: National Institutes of Health

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ABOUT THIS RESEARCH

You are being asked to participate in a research study. Scientists do research to answer important questions which might help change or improve the way we do things in the future.

This consent and Authorization form will give you information about this study to help you decide whether you want to participate. It is your choice whether you want to be in this research study. Please read this form, and ask any questions you have, before agreeing to be in this study.

STUDY SUMMARY

This information gives you an overview of the research. More information about these topics may be found in the pages that follow.

TAKING PART IN THIS STUDY IS VOLUNTARY

You may choose not to take part in the study or may choose to leave the study at any time. Deciding not to participate, or deciding to leave the study later, will not result in any penalty or loss of benefits to which you are entitled, and will not affect your relationship with Indiana University or IU Health.

WHY IS THIS STUDY BEING DONE?

We would like to explore if taking dehydroepiandrosterone (DHEA), a supplement for a hormone that your body naturally produces, would be a safe treatment for asthma.

WHAT WILL HAPPEN TO ME DURING THE STUDY?

If you agree to participate, then you will be asked to attend 11 study visits at Indiana University School of Medicine/Riley Hospital for Children. During study visits we will perform a physical exam, collect blood, and ask you to complete breathing tests to measure your lung function. You will take DHEA to see if additional amounts affect your asthma. DHEA is available as an over-the-counter supplement that can be purchased without a prescription; however, its use in this study, as a potential treatment for asthma, is considered *investigational*, which means the FDA has not approved using DHEA in this way. Additionally, for this study, you will take DHEA that is made to release in your body slower than the currently available over-the-counter form. We will ask you to complete questionnaires about how you have been feeling and ask you about your medical history.

HOW LONG WILL I PARTICIPATE?

Approximately 8 weeks (about 2 months).

WILL I BENEFIT FROM THE STUDY?

It is possible that you may benefit from taking part in this study, however, there is no guarantee that it will help you.

WILL TAKING PART IN THIS STUDY EXPOSE ME TO RISKS?

Taking part in this research may expose you to significant risks. It is important that you understand the risks before you decide whether to participate. Some of the most common risks include: loss of confidentiality, risks associated with DHEA, bruising or slight pain associated with the blood draw. There are other possible risks not listed here but described later in this consent.

WILL I BE PAID TO PARTICIPATE?

Payment for your time and travel is available if you decide to take part in this study.

WILL IT COST ME ANYTHING TO PARTICIPATE?

You will not be responsible for any costs related to the research, however, you or your insurance company will still be responsible for the cost of your normal medical care.

Please review the rest of this document for more details about this study and the things you should know before deciding whether to participate in this study.

WHY IS THIS STUDY BEING DONE?

The purpose of this study is to determine the pharmacokinetic (PK) effects of supplemental dehydroepiandrosterone (DHEA) on your body. PK is the study of what a specific drug does to your body: how it is absorbed, how it moves through the body, how it is broken down and how it is eliminated. Understanding these processes with regards to a specific drug allows doctors to prescribe medications that will provide the greatest benefit with the lowest risk, and to make adjustments as necessary.

There is evidence to suggest that DHEA-based treatment could be beneficial to patients with asthma, yet one of the main treatments for asthma (taking glucocorticoids, a hormone that is effective in reducing inflammation), suppresses the production of DHEA. In this study, we want to test and evaluate the safety of DHEA-based treatment.

We are asking you if you want to be in this study because you have asthma.

The study is being conducted by Drs. Kirsten Kloepfer, Jim Chmiel, and Ben Gaston at Indiana University School of Medicine. It is funded by the National Institutes of Health.

HOW MANY PEOPLE WILL TAKE PART?

You will be one of 9 participants taking part in this study.

WHAT WILL HAPPEN DURING THE STUDY?

During this study, you will come to the study site 11 times over a period of 8 weeks and complete the following:

Informed Consent: We will explain the study to you. If you decide to participate you will be asked to review, sign, and date the consent form.

Medical History: We will review your medical chart and record relevant medical history, including the history of your asthma, other pertinent respiratory details, and any information regarding underlying diseases such as cystic fibrosis or chronic lung disease. We will also ask you about any medications you are currently taking.

Demographic Information: We will collect information about you such as age, gender, and race.

Physical Exam & Vital Signs: The study doctor will examine your head, eyes, ears, nose, throat; heart, chest, lungs, and abdomen; extremities and skin; and any other areas as appropriate for any abnormal signs and symptoms. In addition, we will also check your vital signs which includes measuring your blood pressure, temperature, heart rate, breathing rate, pulse oximetry (the amount of oxygen in your blood), and your height and weight.

Urine Samples: All participants will be asked to provide a urine sample that will be tested for cotinine levels (to indicate whether you have been exposed to nicotine recently).

Pregnancy Testing & Contraception

Females who can get pregnant will also have a pregnancy test. Because DHEA is a hormone and we do not know how it will affect a developing baby, if you are pregnant, you cannot be in this study. Additionally, you must practice a medically acceptable form of contraception during study participation. Medically acceptable contraceptives include: (1) surgical sterilization, (2) approved hormonal contraceptives such as birth control pills, (3) barrier methods (such as a condom or diaphragm) used with a spermicide, (4) abstinence, or (5) an intrauterine device (IUD).

Blood Samples: At the screening visit, we will draw 20 ml of blood (about 4 teaspoons) for a CBC, or complete blood count, and metabolic panel. We will also use your blood sample for genotyping your ability to process DHEA (studying your genetic makeup); and measuring the level of DHEA-S. For male subjects, a portion of the 20 ml will be taken for Prostate Specific Antigen Test which checks for prostate cancer.

- At visit 1, 29 ml of blood (about 6 teaspoons) will be drawn to measure your DHEA-S levels and for cytokine studies, peripheral blood mononuclear cells (PBMC, to test protein responses to DHEA in your blood), endocrine analysis (to detect hormone levels in your blood) and genomics (to determine if certain genes are linked with better responses to DHEA) before you take DHEA. After taking DHEA, 8 ml of blood (about 2 teaspoons) will be drawn to measure DHEA-S levels at multiple time points. A total of 101 ml of blood (about 21 teaspoons) will be drawn during visit 1.
- At visit 2, 8 ml of blood (about 2 teaspoons) will be drawn to measure your DHEA-S levels before and after taking DHEA at multiple time points. A total of 80 ml of blood (about 16 teaspoons) will be drawn during visit 2.
- At visits 3A-3B and 4A-4B, 14ml of blood (about 3 teaspoons) will be drawn at each visit to measure your DHEA-S levels before and after taking DHEA at multiple time points. A total of 70 ml of blood (about 14 teaspoons) will be drawn during visits 3A-3B and 4A-4B.
- At visits 3C and 4C, 14ml of blood (about 3 teaspoons) will be drawn at each visit to measure your DHEA-S levels, for cytokine studies, and genomics before and after taking DHEA at multiple time points. A total of 28 ml (about 6 teaspoons) will be drawn during visits 3C and 4C.
- At visit 3D, 35 ml of blood (about 7 teaspoons) will be taken to measure your DHEA-S levels and for cytokine studies, PBMCs, endocrine analysis and genomics.

- At visit 4D, 45 ml of blood (about 9 teaspoons) will be taken to measure your DHEA-S levels and for cytokine studies, PBMCs, endocrine analysis, genomics and to obtain a complete blood count and metabolic panel.

Spirometry: This test measures how much air your lungs can hold and how fast you can breathe out. You will take a deep breath and then blow into a mouthpiece as hard as you can and for as long as you can. You might have to wear soft nose clips during the test to stop air from escaping through your nose. You will be asked to repeat this test at least 3 times. You will be asked to take a bronchodilator (a medication that relaxes and opens the airways in the lungs) such as albuterol while completing spirometry during some study visits. The study team will provide the bronchodilator used for the test.

Completion of Questionnaire & Symptom Diary: You will be asked to complete the Asthma Control Test (ACT) and the Asthma Control Questionnaire (ACQ) at several study visits. You will also be asked to complete a medication dosing and symptom diary at home between visits 3A and 3D and visits 4A and 4D.

Study Drug: DHEA is an over-the-counter supplement that is available on the market without prescription. In this study, you will be taking DHEA as a capsule that has been formulated in a specific way that the investigators expect will make it as effective as possible. You will be provided DHEA capsules as outlined below:

1. Zero capsules at the screening visit.
2. One capsule (50mg) at Visit 1 to take at the start of the 12-hour PK study.
3. One capsule (100mg) at Visit 2 to take at the start of the 12-hour PK study.
4. Six capsules (50mg each) at Visit 3A. You will take your first capsule at the start of the 72-hour PK study and continue to self-administer one capsule every 12 hours (± 1 hr) until all 6 capsules have been consumed. You will record the times you take each dose into your medication and symptom diary.
5. Six capsules (100mg) at Visit 4A. You will take your first capsule at the start of the 72-hour PK study and continue to self-administer one capsule every 12 hours (± 1 hr) until all 6 capsules have been consumed. You will record the times you take each dose into your medication and symptom diary.

At Visits 3D and 4D, please return all unused DHEA capsules and packaging to the study team.

There is also one unscheduled visit that will be used in case you need to return to the study site for any reason to finish study activities.

SCHEDULED EVENTS

Assessments and Procedures	Visit 0	Visit 1	Visit 2	Visit 3A	Visit 3B	Visit 3C	Visit 3D	Visit 4A	Visit 4B	Visit 4C	Visit 4D
	Screening Day 0	Day 14 ± 7 days	Day 28 ± 7 days	Day 42 ± 7 days	1 day (24 hours ±1 hr) after Visit 3A	2 days (48 hours ±1 hr) after Visit 3A	3 days (72 hours ±1 hr) after Visit 3A	Day 56 ± 7 days	1 day (24 hours ±1 hr) after Visit 4A	2 days (48 hours ±1 hr) after Visit 4A	3 days (72 hours ±1 hr) after Visit 4A
Informed consent	X										
Medical history and demographics	X										
Concomitant medications	X	X	X	X				X			
Asthma Control Test (ACT) & Asthma Control Questionnaire (ACQ)	X	X	X	X				X			X
Height	X										
Weight, pulse oximetry, vital signs	X	X	X	X				X			
Urine pregnancy test (when applicable)	X	X	X	X				X			
Urine cotinine test	X										
Prostate specific antigen test (when applicable)[1]	X										
Spirometry	X	X	X	X			X	X			X
Abbreviated physical exam	X	X	X	X				X			
Blood draw	X	X	X	X	X	X	X	X	X	X	X
DHEA administration		X	X	X				X			
Collect any unused DHEA capsules from subject							X				X
Adverse events	X	X	X	X	X	X	X	X	X	X	X
Give subject Dosing & Symptom Diary				X				X			
Collect Dosing & Symptom Diary							X				X

[1] This test is for male subjects only. The prostate specific antigen is a protein made by the prostate and found in blood. If the result of this test is >4 nanograms per milliliter, you will be unable to participate in the study. We will call you prior to your next visit to let you know; we will also recommend that you follow-up with your regular primary care physician.

The study team will inform you of your relevant genotyping result and if elevated, the result of the prostate specific antigen test for male subjects, but you will not receive the results of any of the other tests or procedures because they are being done for research purposes only.

WHAT ARE THE RISKS OF TAKING PART IN THE STUDY?

The possible risks and discomforts you may experience as a result of taking part in this study are detailed below; however, there may be other risks and side effects that are not yet known.

DHEA: DHEA is commercially available without a prescription. The DHEA capsules used in this study are formulated for slow release (designed to release a drug in the body slowly over an extended period of time). Most of the known data pertaining to risks comes from studies in adults with adrenal insufficiency (a condition where your body does not produce enough hormones to control your blood pressure) who were treated with long courses of DHEA (e.g. 3-12 months). Minor side effects associated with taking the study drug from these studies include greasy skin, male-pattern hair growth in women, acne, scalp itching and increased sweating. We will ask you about any side effects at each study visit.

Blood collection: When blood samples are taken from a vein, subjects may have discomfort or pain where the blood was taken. Sometimes a person may become dizzy or faint when blood is taken. There is also a risk of infection (rare), bleeding, redness or bruising at the skin puncture. Bleeding and bruising can usually be reduced by putting pressure on the place where the blood was taken. The chance of infection is lowered by using standard skin cleaning and sterile needles. Blood will be drawn by experienced staff members.

Spirometry: There is a small risk of lightheadedness, wheezing, shortness of breath or increased cough when performing spirometry. These symptoms usually resolve quickly without the need for treatment. Withholding short-acting/long-acting bronchodilator medication prior to study visits: There is a risk of shortness of breath or breathing difficulty. Subjects will be advised that if they experience any worsening symptoms during the pre-visit withholding period, they should use their usual medication as needed and call the study team to cancel or reschedule the study visit.

Urine Collection: There are no foreseeable risks to its collection. However, there is the risk of emotional distress if a subject discovers that they are pregnant. Our research coordinators are highly trained and experienced regarding advising people who discover that they are pregnant as part of a research protocol.

Questionnaires: You may be uncomfortable while answering the survey questions. While completing the surveys, you can skip any questions that make you uncomfortable or that you do not want to answer.

Other: There is a possible loss of confidentiality. The greatest risk is the release of information from your health records. The chance that this information would be given to someone else is small. All team members listed in our study have completed education on protection of research information, which will help us protect your privacy. Some risks may not be known. We will make every effort to keep these to a minimum.

WHO WILL PAY FOR MY TREATMENT IF I AM INJURED?

If you are injured as a result of participating in this study, necessary medical treatment will be provided to you and billed as part of your medical expenses. Costs not covered by your health care insurer will be your responsibility. Also, it is your responsibility to determine the extent of your health care coverage. No money or funds are set aside to pay for these types of injuries. However, you are not giving up any legal rights or benefits to which you are otherwise entitled by signing this Informed Consent form.

WHAT ARE THE BENEFITS OF TAKING PART IN THE STUDY?

We do not think you will have any personal benefits from taking part in this study, but we hope to learn things that will help other people in the future. Participating in this study may temporarily lessen your asthma symptoms but we do not know for sure. We are doing this research study to find out the best dose of DHEA to use in future treatment studies.

WILL I BE PAID FOR PARTICIPATION?

You be paid for participating in this study according to the table below. You will receive a payment card at the first visit and compensation for subsequent visits will be loaded onto the same card after each visit.

Visit	**Estimated Length of Visit**	**Compensation Amount**
Visit 0: Screening	3 hours	$70
Visit 1: Single 50mg administration	13 hours	$300
Visit 2: Single 100mg administration	13 hours	$300
Visit 3A: Beginning of multiple 50mg administration	13 hours	$300
Visits 3B, 3C	1 hour each	$50 each for blood draws at 24 and 48 hours
Visit 3D	2 hours	$95
Visit 4A: Beginning of multiple 50mg administration	13 hours	$300

Visit	**Estimated Length of Visit**	**Compensation Amount**
Visits 4B, 4C	1 hour each	$50 each for blood draws at 24 and 48 hours
Visit 4D	4 hours	$115
Total	**65 hours**	**$1,680**

If you have to utilize the unscheduled visit option, you will receive an additional $25 for that visit. For visits longer than 6 hours, the study coordinator will provide you with a meal option. The study coordinator can also offer mileage reimbursement for your travel to and from the hospital.

If you receive $600 or more in one calendar year from Indiana University, you will need to complete a form giving us your Social Security number (SSN) or tax identification number (TIN). You will receive a 1099 tax form the following January from Indiana University and will need to report this payment as income on your federal and state tax returns. You are responsible for paying any local, state, or federal taxes. If you have questions about how this impacts your tax return, please contact a tax professional. If you do not have an SSN or TIN, the Internal Revenue Service (IRS) requires Indiana University to deduct 30% from your research payment to pay required taxes on your behalf.

WILL IT COST ME ANYTHING TO PARTICIPATE?
There is no cost to you for taking part in this study.

HOW WILL MY INFORMATION AND SPECIMENS BE USED?
The study team will collect information about you from your medical records. This information, some of which may identify you, may be used for research-related purposes. This may include making sure you meet the criteria to be in this study, gathering information about your medical history to include in the research data, reviewing results of your medical tests for safety purposes, checking on your health in the future to help answer our research question, and/or to inspect your research records for quality assurance and data analysis.

The information released and used for this research will include:

- All records related to Asthma and Respiratory Illness
- Information provided by you
- Hospital discharge summary
- Radiology films (such as X-rays or CT scans)
- Medical history / treatment
- Medications
- Consultations
- Laboratory / diagnostic tests

- EKG reports
- Pathology reports, specimen(s) and/or slide(s)
- Operative reports (about an operation)
- Pulmonary Function Test Reports
- Other: Research records, including records about your study visits and records about phone calls made as part of this research

If you agree to participate, you authorize the following to disclose your medical record information:

- Indiana University Health Hospitals
- Indiana University Health Physicians (Allergy)
- IUMG – Primary Care Physicians
- Indiana Network for Patient Care (INPC)

The following individuals and organizations may receive or use your identifiable health information:

- The researchers and research staff conducting the study
- The Institutional Review Boards (IRB) or its designees that review this study
- Indiana University
- US governments or agencies as required by law
- Data safety monitoring boards and others authorized to monitor the conduct of the study
- State or Federal agencies with research oversight responsibilities, including but not limited to:
    - Office for Human Research Protections (OHRP)
    - National Institutes of Health (NIH)
    - The United States Food and Drug Administration (FDA)

Information and specimens collected for this study may be used for other research studies or shared with other researchers for future research. If this happens, information that could identify you, such as your name and other identifiers, will be removed before any information or specimens are shared. Since identifying information will be removed, we will not ask for your additional consent.

A description of this clinical trial will be available on 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 at any time.

HOW WILL MY INFORMATION BE PROTECTED?

Every effort will be made to keep your personal information confidential, but we cannot guarantee absolute confidentiality. No information which could identify you will be shared in publications about this study. Your personal information may be shared outside the research study if required by law and/or to individuals or organizations that oversee the conduct of research studies, and these

individuals or organizations may not be held to the same legal privacy standards as are doctors and hospitals.

This research is covered by a Certificate of Confidentiality from the National Institutes of Health. This means that the researchers cannot release or use any information, documents, or specimens that could identify you in any legal action or lawsuit unless you say it is okay.

However, there are some types of sharing the Certificate does not apply to. The Certificate does not stop reporting required by federal, state, or local laws, such as reporting of child or elder abuse, some communicable diseases, and threats to harm yourself or others. The Certificate does not stop a government agency who is funding research from checking records or evaluating programs. The Certificate also does not prevent your information from being used for other research when allowed by federal regulations. The Certificate also does not stop sharing of information required by the Food and Drug Administration (FDA).

Researchers may release information about you when you say it is okay. For example, you may still give them permission to release information to insurers, medical providers, or others not connected with the research.

WHAT WILL YOU DO WITH MY GENETIC INFORMATION?

We will not use the specimens collected as a part of this study for whole genome sequencing, which involves mapping all of your DNA.

The specimens collected in this study will be used to determine the presence of the HSD3B1 gene. No further genetic studies will be performed on your DNA. You will be fully informed of the genotype results relevant to this study since you cannot be enrolled if you do not have this gene.

The genetic information in this research study is protected by the Genetic Information Nondiscrimination Act (GINA), a federal law that makes it illegal for health insurance companies, group health plans, and employers with 15 or more employees to request the genetic information we get from this research and to discriminate against you based on your genetic information. This law does not protect you against genetic discrimination by companies that sell life insurance, disability insurance, or long-term care insurance.

WHO SHOULD I CALL WITH QUESTIONS OR PROBLEMS?

For questions about the study, contact the researcher, Dr. Kirsten Kloepfer, at (317) 948-7208. After business hours, or in the event of an emergency, please call (317) 944-5000 and ask for the pediatric pulmonologist on call.

For questions about your rights as a research participant, to discuss problems, complaints, or concerns about a research study, or to obtain information or to offer input, please contact the IU Human Research Protection Program office at 800-696-2949 or at irb@iu.edu.

WHAT IF I DO NOT PARTICIPATE OR CHANGE MY MIND?

After reviewing this form and having your questions answered, you may decide to sign this form and participate in the study. Or you may choose not to participate in the study. This decision is up to you. If you choose not to participate in this study or change your mind after signing this document, it will not affect your usual medical care or treatment or relationship with Indiana University Health.

If you change your mind and decide to leave the study in the future, the study team will help you withdraw from the study safely. If you decide to withdraw, please contact the study team at (317) 948-7208.

If you choose to withdraw your authorization for use and disclosure of your protected health information, you must do so in writing by notifying **Kirsten Kloepfer, MD, Riley Hospital for Children at Indiana University Health, 705 Riley Hospital Drive, ROC 4270, Indianapolis, IN 46202**. If you withdraw your authorization, you will not be able to continue in this study. However, even if you cancel this authorization, the research team, research sponsor(s), and/or the research organizations may still use information about you that was collected as part of the research project between the date you signed this document and the date you cancelled this authorization. This is to protect the quality of the research results. Otherwise, this authorization remains valid until the research ends and required monitoring of the study has been completed.

The study doctor or sponsor can remove you from the study at any time without your consent for the following reasons:

- If it is medically harmful to you
- If you fail to follow directions for participating in the study
- If it is discovered that you do not meet the study requirements
- If the study is canceled
- For administrative reasons

AGREEMENT TO BE CONTACTED BY TEXT AND/OR EMAIL

We would like to communicate with you about this study by text message and/or email. We might use text or email to send you reminders about upcoming visits or appointments.

Text messaging and email are not secure methods of communication. The information sent over text or email, which may include sensitive or personal information, such as protected health information, could be accessed or read by someone other than you. If you would like us to communicate with you

via text or email, please initial the lines below and provide the phone number(s) and/or email address(es) you would like us to use.

_____ I authorize the researchers to send me emails related to this research study

Email address for this communication: _____

_____ I authorize the researchers to send me text messages related to this research study

Phone number for this communication: _____

You can still participate in this study even if you do not want us to contact you by text or email.

PARTICIPANT'S CONSENT AND AUTHORIZATION

In consideration of all the above, I agree to participate in this research study. I will be given a copy of this document to keep for my records.

Participants:

X	
Participant's Printed Name	**Date**
X	
Participant's Signature	
X	
Participant's Address (street, city, state, zip)	

Study personnel:

X	
Person obtaining informed consent's Printed Name	**Date**
X	
Person obtaining informed consent's Signature	