Document Coversheet

Study Title: Cardiovascular, Immune and Psychosocial Benefits of Reduced Cocaine Use; Randomized Clinical Trial (04)

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	1/9/2024
NCT Number:	NCT03224546
IRB Number	42360
Coversheet created:	1/19/2024

CONSENT TO PARTICIPATE
IN A RESEARCH STUDY
University of Kentucky Medical Center

TITLE OF STUDY:
Randomized Clinical Trial (04)

INVESTIGATOR INFORMATION:

William W. Stoops, Ph.D. (859) 257-5388
Lon R. Hays, MD, MBA (859) 323-6021 x 79015
Abner O. Rayapati, MD (859) 257-9175

WHY AM I BEING INVITED TO TAKE PART IN THIS RESEARCH*?*

You are being invited to take part in a research study about your behavior that will take place over approximately 36 weeks. You are being asked to participate because you are 18 years or older with a recent history of cocaine use and a desire for treatment for your cocaine use. You are also being asked to participate because you have expressed interest in participating in this study and it is unlikely that you will react badly to the laboratory setting. You must be between the ages of 18 and 65 to participate in this research study and you will be asked to provide legal proof of age. If you volunteer to take part in this study you will be one of about 300 people to do so over the next five years at the University of Kentucky.

WHO IS DOING THE STUDY?

This study is being conducted under the scientific and administrative supervision of William W. Stoops, Ph.D., Department of Behavioral Sciences at the University of Kentucky College of Medicine and the medical supervision of Lon R. Hays, MD, M.B.A. and Abner O. Rayapati, M.D., Department of Psychiatry, at the University of Kentucky College of Medicine. There may be other people on the research team assisting at different times.

WHAT IS THE PURPOSE OF THIS STUDY?

The purpose of this experiment is to understand how changes in your cocaine use affect your physical, mental and social health. We will also inject candida yeast into your skin to test your immune response. The results of this study will be shared with the sponsor providing financial support for the study (the National Institute on Drug Abuse), the Food and Drug Administration and other federal agencies, if required. The information we get from this study may help us develop better ways to monitor and change cocaine use behaviors.

ARE THERE REASONS WHY YOU SHOULD NOT TAKE PART IN THIS STUDY?

You should not participate in the study if you are under 18 years of age or over 65 years of age. You should not participate if you have a history of serious physical disease or current physical disease (e.g., physical dependence on any drug requiring managed detoxification, unstable angina, uncontrolled abnormal heart rhythm, compromised immune function, allergy to candida yeast). You should not participate if you have a history of serious psychiatric or current psychiatric disease. You should not participate if you have a history of other significant medical problems.

WHERE IS THE STUDY GOING TO TAKE PLACE AND HOW LONG WILL IT LAST?

The research procedures will be conducted in the Laboratory of Human Behavioral Pharmacology (LHBP) and Clinical Services Core (CSC) at the University of Kentucky Medical Center. During the time

you participate, you must agree to participate as an outpatient at the LHBP and CSC. The timeline for study participation, and measures that you will be asked to complete are shown in the table below. Overall, you will be asked to attend approximately 43 appointments at the LHBP and CSC over about 36 weeks. Thirty six of these appointments will take place during the first 12 week intervention period. These visits will be scheduled every Monday, Wednesday and Friday for the 12 week period at approximately 8:00 AM. The 12 week intervention period is when you can receive payments for providing observed urine samples or samples that are negative for cocaine and its metabolites, as well as receiving supportive behavioral therapy (see below). Each appointment will last approximately between 1 and 4 hours. The remaining 7 appointments will take place during the 24 week follow up period and will be scheduled on a day that is convenient for you. These follow up visits can last up to approximately 4 hours. You will be expected to attend each appointment as scheduled and must agree to follow the general rules of the LHBP and CSC.

WHAT WILL YOU BE ASKED TO DO?

Once you finish screening and if you consent to participate, you will be randomly assigned to one of three groups for the duration of your participation (i.e., you have a 33% chance of being assigned to any one group). In one group, you will receive payment for providing observed urine samples during the first 12 weeks of the study. In the other two groups, you will receive payments for providing observed urine samples that are negative for cocaine and its metabolites during the first 12 weeks of the study. These payments will be in addition to money you earn for attending study visits and for travel, as outlined below. You will receive supportive behavioral counseling about your cocaine use throughout your participation in the first 12 weeks of the study. Throughout this time, and during a 24 week follow-up period, you will be asked to complete a number of measures that evaluate your cardiovascular, immune and general health, as well as your psychosocial function during study appointments.

During your participation, you must agree to come to the laboratory on scheduled days (e.g., Monday, Wednesday and Friday) at the specified times (i.e., approximately 8:00 AM) for scheduled appointments. Each appointment will require you to remain at the laboratory for approximately 1-4 hours. During each appointment, you will be asked to provide an observed urine sample and complete several questionnaires. You will be allowed to take breaks between questionnaires. If you are a woman, you will receive a urine pregnancy test monthly. You may also be asked to go to the CSC for blood draws, as well as cardiovascular and immune measurements. On days when we ask you to do these measurements, you will also need to be fasting prior to your appointment. These measurements include administration of candida yeast injected into your skin to assess immune function.

It is important that you attend all of your scheduled appointments. You will be provided with a calendar showing all of your scheduled appointments at the beginning of your participation. If you attend the clinic as scheduled, you will receive bonus payments, which are described in more detail below.

If you are unable to attend any of your scheduled appointments, you are asked to contact us to reschedule. You are asked to complete the tasks during the sessions to the best of your ability.

If you must take a non-prescription medication, you should refrain from using it for 12 hours before a research session. Pain relievers containing only aspirin, ibuprofen, or acetaminophen, are acceptable for normal use without special permission. You must agree to be sober when you arrive for each session. You must agree to abstain from caffeine or any stimulants (not including smoking cigarettes) for 4 hours prior to each scheduled appointment. You must agree to abstain from smoking during session participation. You must also agree to give observed urine samples upon request and to take a breathalyzer test to allow the investigators to monitor your compliance with these restrictions.

Below is a table outlining what measurements you will complete throughout your participation and when you will complete them as marked by an X (for baseline and follow up appointments) or described as a frequency for the 12 week intervention. For example, if the table states that a measure will be collected 3 days/week during the 12 week intervention, it will be completed every Monday, Wednesday

and Friday at your scheduled visit. If it is once weekly, it will only occur at either the Monday, Wednesday or Friday visit.

Measurement	**Activity at Baseline Appointment (Approximately 4 hours)**	**Frequency of Measure Collection during 12 Week Intervention**	**Activity at 4 Week Follow up***	**Activity at 8 Week Follow up**	**Activity at 12 Week Follow up***	**Activity at 24 Week Follow up***
Height	X					
Drug Urine Screens	X	3 Days/Week	X	X	X	X
Weight	X	3 Days/Week	X	X	X	X
Breath Carbon Monoxide	X	3 Days/Week	X	X	X	X
Vital Signs	X	3 Days/Week	X	X	X	X
Sleep Questionnaire	X	3 Days/Week	X	X	X	X
Depression Questionnaire	X	Once Weekly	X	X	X	X
Cognitive Tasks	X	Once Weekly	X	X	X	X
Risk Behavior Questionnaire	X	Once Weekly	X	X	X	X
Adverse Events Questionnaire	X	Once Weekly	X	X	X	X
Supportive Behavioral Counseling		Once Weekly				
Blood Draw to assess cardiovascular, immune and general health	X	One time during both Weeks 6, 12	X		X	X
Candida Yeast Administration	X	One time during both Weeks 6, 12	X		X	X
Addiction Severity Index Questionnaire	X	One time during both Weeks 4, 8, 12	X	X	X	X
Timeline Follow Back Drug Use Questionnaire	X	One time during both Weeks 4, 8, 12	X	X	X	X
Peripheral Arterial Tonometry Test (This is a non-invasive test of your cardiovascular function).	X	One time during Week 12	X		X	X
Short Inventory of Problems - Cocaine	X	One time during Week 12	X		X	X
Structured Clinical Interview	X	One time during Week 12	X		X	X
Microbiome (IM)	X	Week 12				

Electrocardiogram	X	One time during Week 12	X		X	X

We will schedule you to return to the LHBP 48 hours after your 4, 12 and 24 Week Follow Up visits in order to evaluate your response to Candida Yeast Administration. You will earn $15 for these visits and $10 for travel to the clinic visit, which are expected to last 30-60 minutes.

WHAT ARE THE POSSIBLE RISKS OR DISCOMFORTS?

The behavioral and physiological assessment procedures employed in this study are benign. The primary risks those related to the blood draws, which can lead to pain, soreness, bleeding, fainting, bruising, discomfort or infection, and administration of the candida yeast into your skin, which can lead to inflammation and discomfort.

There is also the risk that others may see your Protected Health Information (PHI). PHI is considered individually identifiable health information transmitted or maintained in any form (electronic means, on paper, or through oral communication) that relates to the past, present or future physical or mental health conditions of an individual that may be used or disclosed. The following PHI will be collected as part of this project: names (individual, employer, relatives, etc.), addresses (individual, employer, relatives, etc.), telephone number, Social Security number (necessary for payment), dates (birth, admission, discharge), medical record numbers, driver's license numbers, mental and physical health history, drug use history, results from mental and physical health screening, results from questionnaires and other experimental measures.

There may be other risks of being in this research study, which are not known at this time.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

There may be no benefit from being in this study, but we might learn something that could help researchers better understand how drug use relates to cardiovascular, immune and psychosocial function. You may benefit from the monitoring of your physical and mental health, as well as from the supportive behavioral counseling provided during the 12 week intervention.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any benefits or rights you would normally have if you choose not to volunteer. You can stop at any time during the study and still keep the benefits and rights you had before volunteering.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?

If you do not want to be in the study, there are no other choices except not to take part in the study.

WHAT WILL IT COST YOU TO PARTICIPATE?

Participating in this research study will include $10 for the expense of travel to and from the laboratory. All costs for screening and follow up appointments will be paid by a grant from the sponsor (National Institute on Drug Abuse).

The University of Kentucky may not be allowed to bill your insurance company, Medicare or Medicaid for the medical procedures done strictly for research. Therefore, these costs will be paid by the sponsor (National Institute on Drug Abuse).

You and/or your insurance company, Medicare or Medicaid will be responsible for the costs of all care and treatment you receive during this study that you would normally receive. These are costs that are considered medically reasonable and necessary and will be part of the care you receive if you do not take part in this study.

WHO WILL SEE THE INFORMATION THAT YOU GIVE?

Every effort will be made to maintain the confidentiality of your study records. The data from the study may be published; however, you will not be identified by name. Your identity will remain confidential, unless you give prior written approval or unless disclosure is required by law. Your name, address and social security number will be listed on the receipt for payment that you receive, as required by the Internal Revenue Service; but no information about your participation in this research project will be released. We will be collecting your social security number for payment purposes. You cannot participate in this research if you withhold your social security number. To help us protect your privacy, we have obtained a Certificate of Confidentiality from the National Institutes of Health. The researchers can use this Certificate to legally refuse to disclose information that may identify you in any federal, state, or local civil, criminal, administrative, legislative, or other proceedings, for example, if there is a court subpoena. 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, employer, or other person obtains your written consent to receive research information, then the researchers may not use the Certificate to withhold that information. The Certificate of Confidentiality will not be used to prevent disclosure to state or local authorities of abuse of a child or elderly person or that you intend to harm yourself. Also, because this research is regulated by the National Institute of Health (NIH) and The University of Kentucky, staff from these and other DHHS agencies may review records that identify you. However, it is the policy of these agencies and of these investigators that every attempt will be made to resist demands to release information that identifies you. When results of this study are published, your name will not be used.

CAN YOUR TAKING PART IN THE STUDY END EARLY?

If you decide to take part in the study you still have the right to decide at any time that you no longer want to continue. You will not be treated differently if you decide to stop taking part in the study. You should understand, however, that if you decide to withdraw from the study early you will not receive any of the completion bonus described below. You will only receive the payment you were paid for the sessions you completed.

You should understand the principal investigator on this project, William W. Stoops, Ph.D., can terminate your participation for the following reasons: 1) failure to adhere to patient rules for the LHBP or CSC, 2) if you verbally or physically assault another volunteer, patient or staff member on the LHBP or CSC, 3) if your behavior is disruptive to other ongoing studies that are conducted on the LHBP or CSC, 4) if your behavior is disruptive to the other volunteers, patients, research staff or medical staff on the LHBP or CSC, 5) failure to comply with the drug use restrictions, 6) failure to complete a scheduled appointment, and/or 7) failure to perform the behavioral tasks to the best of your ability. If you are terminated for any of these reasons, it will be deemed that you did not complete all of your scheduled experimental sessions and follow-ups and you will not receive the completion bonus described below.

You should also understand that the medical doctors on this project, Lon R. Hays, MD, M.B.A. and Abner O. Rayapati, M.D., can terminate your participation if they do not feel that it is medically safe for you to continue. If your participation is terminated for medical reasons, you will receive the completion allowance for each of the appointments you completed.

If you choose to withdraw from the study early, the data collected until that point will remain in the study database and may not be removed. The individuals conducting the study may need to withdraw you from the study and the study intervention and/or medication will no longer be provided by the investigator and may not be accessible commercially. This may occur if you are not able to follow the directions they give you, if they find that your being in the study is more risk than benefit to you, or if the agency funding the study decides to stop the study early for a variety of scientific reasons. It is not

anticipated that withdrawing you from the study would lead to any risks in your health and welfare, but the investigators may request to schedule follow up appointments if you are withdrawn from the study.

ARE YOU PARTICIPATING OR CAN YOU PARTICIPATE IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?

You may not take part in this study if you are currently involved in another research study. It is important to let the investigator/your doctor know if you are in another research study. You should also discuss with the investigator before you agree to participate in another research study while you are enrolled in this study.

WHAT HAPPENS IF YOU GET SICK OR HURT DURING THE STUDY?

If you believe you are hurt or if you get sick because of something that is due to the study, you should call Lon R. Hays, M.D., M.B.A. at (859) 323-6021 x 79015 or Abner O. Rayapati, M.D. at (859) 257-9175 immediately. You can also call 911 in the case of an emergency. Dr. Hays or Dr. Rayapati will determine what type of treatment, if any, is best for you at that time. The medical costs related to your care and treatment because of research related harm will be your responsibility.

The University of Kentucky Medical Center has no mechanism to provide compensation for research subjects who may incur injuries as a result of participating in biomedical and behavioral research. This means that while all investigators will do everything possible in providing careful medical care and safeguards in conducting this research, there is no way in which the institution can pay for the unlikely occurrence of injury resulting solely from the research itself. You may contact the principal investigator for this study, William W. Stoops, Ph.D., if you have questions about this policy. You do not give up your legal rights by signing this form.

It is important for you to understand that the University of Kentucky does not have funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, the University of Kentucky will not pay for any wages you may lose if you are harmed by this study. The medical costs related to your care and treatment because of research related harm will be your responsibility.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?

You will be paid for attendance during the 12 week intervention period. For the short appointments (i.e., approximately 1 hour) that occur about two times per week (e.g., Monday and Wednesday), you will earn $15. For medium appointments (i.e., approximately 2 hours), that occur about one time per week (e.g., Friday), you will earn $30. For long appointments (i.e., approximately 3 hours) that occur about one time per month, you will earn $45. For the longest appointments (i.e., approximately 4 hours) that occur about one time every six weeks, you will earn $60. You will earn $60 for the 4, 8, 12 and 24 week follow up appointments and can expect those to last approximately 4 hours. You will also earn $15 for visits scheduled 48 hours after the 4, 12 and 24 week follow up appointments when we will assess your response to candida yeast. You can expect those visits to last 30-60 minutes. You will receive half of the visit payment (e.g., $7.50 for short visits) at the end of each study visit. The remaining half will be paid to you if you complete the study. If you complete all study appointments as scheduled, you can earn a total of approximately $1,230 in study payments.

You can also earn money based on providing observed urine samples. Depending on the group you are assigned to, you will earn money for providing an observed urine sample or for providing a urine sample that is negative for cocaine and its metabolites. These payments will be added to the amount of money you will be paid at the end of each study visit.

If you are assigned to the group that will receive money for providing observed urine samples, the amount you will receive is $13 per sample.

If you are assigned to one of the groups that will receive money for providing observed urine samples that are negative for cocaine and its metabolites, you will receive $55 for a negative sample.

If you are assigned to the other group that will receive money for providing observed urine samples that are negative for cocaine and its metabolites, you will receive $13 for a negative sample.

If you are in either of the two groups that are paid for negative samples, and provide a cocaine/cocaine metabolite positive sample during an appointment, you will not earn any money for that sample. The maximum amount you can earn for providing urine samples or cocaine/cocaine metabolite negative samples is approximately $500-$2000. Thus, the maximum you can earn in this study is approximately $3,250. Participating in this research study will include $10 for the expense of travel to and from the laboratory, which will be paid at the end of each scheduled appointment along with the other money you receive based on your group assignment and attending study visits.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS, CONCERNS OR COMPLAINTS?

Before you decide whether to accept this invitation to take part in the study, please ask any questions that might come to mind now. Later, if you have questions, suggestions, concerns, or complaints about the study, you can contact the principal investigators, Dr. Stoops at (859) 257-5388. If you have any questions about your rights as a volunteer in this research, contact the staff in the Office of Research Integrity at the University of Kentucky at (859) 257-9428 or toll free at 1-866-400-9428. We will give you a signed copy of this consent form to take with you.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?

If the investigator on this project, Dr. William W. Stoops, Ph.D., learns of new information regarding this study, and it might change your willingness to stay in this study, the information will be provided to you. You may be asked to sign a new informed consent form if the information is provided to you after you have joined the study. If you choose not to continue, you will not lose any of your earnings.

CONTACTING RESEARCH SUBJECTS FOR FUTURE STUDIES

Do you give your permission to be contacted in the future by Dr. Stoops or his staff regarding your willingness to participate in future research studies about how to prevent, detect, or treat substance use disorders?

☐ *Yes* ☐ *No* _____*Initials*

WHAT ELSE DO YOU NEED TO KNOW?

This project will be funded by a grant from the National Institute on Drug Abuse (R01DA043938). 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.

There is a possibility that the data/specimens/blood collected from you may be shared with other investigators in the future. If that is the case the data/specimen/blood will not contain information that can identify you unless you give your consent/authorization or the UK Institutional Review Board (IRB) approves the research. The IRB is a committee that reviews ethical issues, according to federal, state and local regulations on research with human subjects, to make sure the study complies with these before approval of a research study is issued.

AUTHORIZATION TO USE OR DISCLOSE YOUR IDENTIFIABLE HEALTH INFORMATION

The privacy law, HIPAA (Health Insurance Portability and Accountability Act), requires researchers to protect your health information. This form describes how researchers may use your information. Please read it carefully.

Your health information will be used and/or released (disclosed) for the following research study: Randomized Clinical Trial (04)

You allow William W. Stoops, Ph.D. and his research staff at the University of Kentucky to create, access, use and release your health information for the purposes listed below.

Your health information that may be used and released includes:

- Demographic information (for example, information about your race, gender, socioeconomic status, and age)
- Results of psychiatric screening tests
- Results of questionnaires and study procedures
- Results of urine screens
- Medical history

Your health information will be used for:

- A study coordinated by William W. Stoops, Ph.D. examining how your drug use impacts cardiovascular, immune and psychosocial function. Your protected health information is necessary to conduct this line of research, as well as to meet legal, institutional, and accreditation requirements.

The Researchers may use and share your health information with:

- The University of Kentucky's Institutional Review Board/Office of Research Integrity,
- University of Kentucky Medical Center, Investigational Drug Service, Center for Clinical and Translational Sciences, Clinical Services Core, and Clinical Research Organization,
- The Medical University of South Carolina
- Temple University
- Law enforcement agencies when required by law
- The National Institute on Drug Abuse
- The Food and Drug Administration

The researchers agree to only share your health information with the people listed in this document.

Should your health information be released to anyone that is not regulated by the privacy law, your health information may be shared with others without your permission; however, the use of your health information would still be regulated by applicable federal and state laws.

You will not be allowed to participate in the research study if you do not sign this form. If you decide not to sign the form, it will not affect your:

- Current or future healthcare at the University of Kentucky
- Current or future payments to the University of Kentucky
- Ability to enroll in any health plans (if applicable)
- Eligibility for benefits (if applicable)

After signing the form, you can change your mind and NOT let the researcher(s) release or use your health information (revoke the Authorization). If your revoke the authorization:

- You will send a written letter to: William W. Stoops., Ph.D. 465 E. High Street, Suite 204B, Lexington, KY 40507 to inform him of your decision.
- Researchers may use and release your health information already collected for this research study.
- Your protected health information may still be used and released should you have a bad reaction (adverse event).
- You will not be allowed to participate in the study.

If you have not already received a copy of the Privacy Notice, you may request one. If you have any questions or concerns about your privacy rights, you should contact the University of Kentucky's Privacy Officer at: (859) 323-9817.

You are the subject. You have read this information, and you will receive a copy of this form after it is signed.

_____ _____

Signature of research subject Date

_____

Printed name of research subject

_____ _____

Name of person obtaining informed consent/ HIPAA authorization Date

_____

Signature of Investigator