UF | Institutional Review Board
UNIVERSITY of FLORIDA

INFORMED CONSENT FORM
to Participate in Research, and

AUTHORIZATION
to Collect, Use, and Disclose Protected Health Information (PHI)

INTRODUCTION

Name of person seeking your consent:_____

Place of employment & position: _____

GENERAL INFORMATION ABOUT THIS STUDY

1. Name of Participant ("Study Subject")

_____

2. What is the Title of this research study (this "Research Study")?

A phased clinical trial of dietary supplemental kava: kava biomarker

3. Whom do you call if you have questions about this Research Study (the "Study Team")?

Principal Investigator: Carol A Mathews MD (352) 294-4900

Other research staff: Robyn Nelson (352) 294-5563

4. Who is paying for this Research Study?

The sponsor of this study is the National Institutes of Health

5. In general, what do you need to know about this Research Study?

Agreeing to become involved in any research is always voluntary. By signing this form, you are not waiving any of your legal rights. If you decide not to participate in this research, you will not be penalized in any way and you will not lose any benefits to which you are entitled. If you have questions about your rights as a research subject, please call the University of Florida Institutional Review Board (IRB) office at (352) 273-9600.

a) In general, what is the purpose of the research, how long will you be involved?

The main purpose of this research is to better understand how your body processes the dietary supplement kava and how it may affect symptoms of anxiety. You will be in this study for a total of 13 weeks.

b) What is involved with your participation, and what are the procedures to be followed in the research?

You will complete an initial screening visit which will include a blood draw, collection of vital signs, questionnaires to assess mental health and medical history, urine drug screen, and urine pregnancy screen (for women of childbearing potential) to determine your eligibility. This visit should take approximately 2 hrs. Once you have completed the screening visit and have met the criteria for the study, you will return to the research office and the study team will provide you with study medication to take at home for 7 days. After you have completed the 7 days of study medication, you will return for 4 follow-up visits (1, 4, 8, 12 weeks) for additional testing which will include a blood draw at each visit. Less than two tablespoons of blood will be collected at each time point.

c) What are the likely risks or discomforts to you?

You may experience nausea and fatigue after taking kava. Some individuals may experience soreness and possibly dizziness during blood draws. Although in very rare cases, use of kava has been shown to cause liver problems, this study uses a form of kava that does not contain the compounds that are thought to cause liver damage.

d) What are the likely benefits to you or to others from the research?

Some participants may experience a decrease in anxiety symptoms.

e) What are the appropriate alternative procedures or courses of treatment, if any, that might be helpful to you?

This study is voluntary and you are not required to participate. If you are experiencing symptoms of anxiety or any other psychological disorder, you have the option to seek and receive treatment.

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.

Additional and more detailed information is provided within the remainder of this Informed Consent form, please read before deciding if you wish to participate in this study.

WHAT CAN YOU EXPECT IF YOU PARTICIPATE IN THIS STUDY?

6. What will be done as part of your normal clinical care (even if you did not participate in this Research Study)?

During the study, you will be asked to avoid taking any new medication until you have discussed the medication with the study team or Dr. Mathews. Starting a new medication can affect your ability to remain in the study. If you find that you are not able to avoid taking a new medication, please contact the study team as soon as possible to discuss the option of continuing in the study and the risks. While your participation in this study should not affect your normal clinical care, it is important that we know about any treatment that you are receiving as it may affect the results of the study.

7. What will be done only because you are in this Research Study?

The screening visit will include the review and signing of this informed consent document, a physical exam, a blood collection to test basic metabolic and liver function and if your genetics affect the way your body uses the study drug, a urine drug screen, a urine pregnancy screen for women of childbearing potential and screening questionnaires to assess for psychiatric disorders, your medical history, and demographic information. Genetic information will be collected from you to examine if the way your body processes the study drug affects the biomarker assays.

You must meet the following criteria to be eligible for participation in the study (a) be between the ages of 18 and 50 years, and (b) women of potential childbearing status must complete a pregnancy test to confirm you are not pregnant. You will be excluded if any of the following are true at the time of screening or baseline visit: You

a) Have not been stable on your current psychotropic medication for at least 6 weeks at the baseline visit.

(b) Have current liver disease or a history of liver disease, as indicated by self-report or via blood tests. All abnormal test results will be reviewed by the study's medical monitor. Individuals will be referred to their primary care provider for follow up examination and care advice if appropriate. No treatment will be offered by the study team as a result of the testing performed as part of the screening procedures.

c) Have a current active medical, psychiatric, or neurological condition besides Generalized Anxiety Disorder that is not currently controlled.

d) are a current smoker,

e) Are unable to abstain from drinking alcohol during the 1 week of active medication administration and for 72 hours before your baseline visit.

For the baseline visit, the study team will ensure that you continue to meet all of the inclusion and none of the exclusion criteria. Once all of these items have been determined, using a method much like flipping a coin, you will be assigned to receive either the study drug or a placebo. A placebo is a substance that looks like and is

given in the same way as an experimental treatment but contains no medicine, for example, a sugar pill. This study is a double-blinded study meaning that neither you nor the study team will know which category you are in. In the case of a medical emergency, the PI of the study will be able to learn if you are taking the study drug or placebo. It will be important for you to keep a diary of the dates and times you take the study medication and that you avoid missing any doses. If you experience any type of side effect or miss a dose, please contact the study team to discuss how to proceed. This study medication will be taken as directed on the label for 7 days. You will be scheduled to return to the research office on the 7th day for a 1 week follow up. You will have follow up visits which will include a blood draw at week 1, 4, 8, and 12 after taking the study drug.

Biological samples that are collected as part of this study will be submitted to SomaLogic, a laboratory which performs the biomarker assay needed for sample analysis. SomaLogic may use the results of the lab work and/or also some of the clinical information we have collected from you for commercial purposes. All of this information will be provided to them in an anonymous manner. No identifying information will be shared with them.

Once this research study is completed, any information that could identify you **might** be removed from any identifiable private information or identifiable biospecimens collected and that, after such removal, the information or biospecimens could be used for future research studies or distributed to another investigator for future research studies without additional informed consent from you or your legally authorized representative.

If you have any questions now or at any time during this Research Study, please contact one of the Research Team members listed in question 3 of this form.

8. What identifiable health information will be collected about you and how will it be used?

The Research Team will collect your name, address, date of birth, phone number, complete medical and psychiatric history, social security numbers, and medication and substance use.

The Research Team may collect this information from other healthcare providers, such as laboratories, which are a part of this research, as well as healthcare providers that are not part of this research (other doctors, hospitals or clinics). Other professionals at the University of Florida or Shands Hospital who provide study-related care, and the University of Florida Institutional Review Board (IRB), may also collect your health information.

The Research Team listed in question 3 above will use or share your health information as described below to carry out this research study.

9. With whom will this health information be shared?

This health information may be shared with:

- the study sponsor (National Institutes of Health);
- United States governmental agencies which are responsible for overseeing research, such as the Food and Drug Administration, the Department of Health and Human Services, and the Office of Human Research Protections;
- The IRB that reviewed this Research Study and ensures your rights as a Study Subject are protected

Otherwise, your identifiable health information will not be shared without your permission unless required by law or a court order. Once your health information is shared with those listed above, it is possible that they could share it without your permission because it would no longer be protected by the federal privacy law.

10. How long will you be in this Research Study?

Your participation in this research study will last 13 weeks.

This Authorization to use and share your health information expires at the end of the study, unless you revoke it (take it back) sooner.

11. How many people are expected to take part in this Research Study?

In total, 26 people will complete this research study.

WHAT ARE THE RISKS AND BENEFITS OF THIS STUDY AND WHAT ARE YOUR OPTIONS?

12. What are the possible discomforts and risks from taking part in this Research Study?

In the past, kava use has very rarely been associated with liver toxicity, including liver failure. The reported risk of liver toxicity occurring with a single dose is less than 1 per million. This study has minimized this already very low risk by using a form of kava that does not include the chemicals that are thought to have caused liver problems in the past. Nevertheless, we will carefully monitor you for any signs or symptoms of liver problems. We will closely monitor your liver after you take kava. We will test your liver at weeks 1, 4, 8, and 12. Although the timing of any potential liver toxicity with kava is not known, symptoms related to liver toxicity include nausea and fatigue. It is likely that if you experience these symptoms, it will be between 2 weeks and 12 weeks after taking the 1st dose of the study medication. You are encouraged to contact the study team for any concerning symptoms that you may have for up to 6 months after taking kava to ensure that no delayed reactions, no matter how unlikely, are missed. We will carefully educate you about symptoms to watch for throughout the study and following treatment. You will be free to discontinue your participation at any time if you feel that it is causing unacceptable distress or discomfort.

A needle will be used to perform blood collection at screening, baseline, week 1, 4, 8, and 12. The risks associated with a needle stick include pain at the puncture site,

swelling, clotting, bruising, and rarely infection. An aseptic technique will be used to collect the blood and all precautions will be taken to prevent clotting, infection, and discomfort.

It is possible that answering questions about your state of mind may increase feelings of sadness you might already have. If this should occur, you may stop the testing at any time. You may also refuse to answer questions or to complete a questionnaire if you find them too upsetting. Should you confirm questions about depression or suicidality in any of the questionnaires you may be asked follow-up questions to assess your risk of self-harm. If you show a significant risk of harming yourself research staff will escort you to emergency services to receive care.

All research material will be treated in a confidential manner and only research staff will have access to the data. Confidentiality will be maintained by assigning a unique ID number to your sample and data; all data entered into computer databases will use only this identifier. This consent form and the key for identification of your name corresponding to your ID number will be stored in a separate file cabinet. Your name and files are kept confidential and your name will not be used in the data files, only identifying codes. Once the study is complete, the code will be destroyed and all of your data will be de-identified.

A Federal law, called the Genetic Information Nondiscrimination Act (GINA), makes it illegal for health insurance companies, group health plans, and most employers to discriminate against you based on your genetic information. Additional information can be obtained at: http://irb.ufl.edu/gina.html or call 1-800-669-3362. If you think this law has been violated, it will be up to you to pursue any compensation from the offending insurance company and/or employer. This Research Study may also include risks that are unknown at this time.

Please note, participating in more than one research study or project may further increase the risks to you. If you are already enrolled in a research study, please inform one of the Research Team members listed in question 3 of this form or the person reviewing this consent with you before enrolling in this or any other research study or project.

During the study, the Research Team will notify you of new information that may become available and might affect your decision to remain in the study.

The University of Florida is required by law to protect your health information. Your health information will be stored in locked filing cabinets or on computer servers with secure passwords, or encrypted electronic storage devices, as required by University policy. However, there is a slight risk that information about you could be released inappropriately or accidentally. Depending on the type of information, a release could upset or embarrass you, or possibly affect your ability to get insurance or a job.

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 have been informed that a Certificate of Confidentiality does not prevent you 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. That is, if you give written consent for the release of information, we cannot withhold that information and we cannot hold responsibility for how that person may use your information.

The Certificate of Confidentiality does not prevent the researchers from disclosing voluntarily, without your consent, information that would identify you as a participant in the research project under the following circumstances. If we learn about child abuse, elder abuse, or intent to harm yourself or others, we will report that information to appropriate authorities.

If you wish to discuss the information above or any discomforts you may experience, please ask questions now or call one of the Research Team members listed in question 3 in this form.

13a. What are the potential benefits to you for taking part in this Research Study?

Some participants may experience and decrease in anxiety symptoms.

13b. How could others possibly benefit from this Research Study?

Participation in this study could advance our understanding of how the body processes kava and eventually lead to new insights into more innovative approaches to the treatment of pathologic anxiety.

13c. How could the Research Team members benefit from this Research Study?

In general, presenting research results helps the career of a researcher. Therefore, the Research Team listed in question 3 of this form may benefit if the results of this Research Study are presented at scientific meetings or in scientific journals.

14. What other choices do you have if you do not want to be in this study?

Taking part in this research study is voluntary. Your alternative is to not take part in the study. If you choose to not take part, your Healthcare at the University of Florida will not be affected. If you are experiencing symptoms of anxiety or any other psychological disorder you have the right to seek and receive treatment with a healthcare provider of your choice.

You may also refuse to authorize the use of your health information, but if you refuse, you may not be allowed to be in this research study or receive any research-related treatment that is only available in this research study. However, your decision not to sign this Authorization will not affect any other treatment you may be eligible to receive.

15a. Can you withdraw from this study?

You may withdraw your consent and stop participating in this Research Study at any time. If you do withdraw your consent, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. If you decide to withdraw your consent to participate in this Research Study for any reason, please contact the Research Team listed in question 3 of this form. They will tell you how to safely stop your participation.

You can also change your mind and take back this Authorization at any time by sending a written notice to the Research Team listed in question 3 of this form to let them know your decision. If you take back this Authorization, the Research Team may only use and disclose your health information already collected for this research study. No additional health information about you will be collected or disclosed to the Research Team. However, if you take back this Authorization, you may not be able to continue in this study. Please discuss this with a member of the Research Team listed in question #3.

15b. Can the Principal Investigator withdraw you from this Research Study?

You may be withdrawn from this Research Study without your consent for the following reasons:

1. You have a serious or unexpected adverse event.
2. You become pregnant.
3. Study doctors decide it is not in your best interest to continue the study.
4. You do not or cannot adhere to the instructions provided to you.
5. The IRB decides to stop the study early.

WHAT ARE THE FINANCIAL ISSUES IF YOU PARTICIPATE?

16. If you choose to take part in this Research Study, will it cost you anything?

No, there will be no additional costs to you or your health plan as a result of your participation in this study. There are no expected protocol-required items, services or procedures that will generate any charges at UF Health. However, if you feel you have received a bill related to this study, please contact the Principal Investigator.

If you receive any healthcare at UF Health that is not related to this study, this care will be billed as usual.

17. Will you be paid for taking part in this Research Study?

By the completion of all study visits you will have had the ability to earn up to $150 via a Visa gift card. You will not be compensated for any study visit that is not completed.

Your payment for participation in this research study is handled through the University of Florida's Human Subject Payment (HSP) Program. Your information, which will include your name, address, date of birth, and SSN, is protected. Access to the (HSP) Program site is limited to certain staff with the assigned security role. You will be randomly assigned a specific identification (ID) number and your information will be coded with that number to protect your identity.

If you have any problems regarding your payment contact the study coordinator.

If you are paid more than $75 for taking part in this study, your name and social security number will be reported to the appropriate University employees for purposes of making and recording the payment as required by law. You are responsible for paying income taxes on any payments provided by the study. Payments to ***nonresident aliens*** must be processed through the University of Florida Payroll and Tax Services department. If the payments total $600 or more in a calendar year, the University must report the amount you received to the Internal Revenue Service (IRS). The IRS is not provided with the study name or its purpose. If you have questions about the collection and use of your Social Security Number, please visit: http://privacy.ufl.edu/SSNPrivacy.html.

18. What if you are injured while in this Research Study?

If you are injured as a direct result of your participation in this study, only the professional services that you receive from any University of Florida Health Science Center will be provided without charge. These healthcare providers include physicians, physician assistants, nurse practitioners, dentists or psychologists. Any other expenses, including Shands hospital expenses, will be billed to you or your insurance provider.

You will be responsible for any deductible, co-insurance, or co-payments. Some insurance companies may not cover costs associated with research studies or research-related injuries. Please contact your insurance company for additional information.

The Principal Investigator and study physician will review your situation together and consult the IRB to determine whether your injury is related to your participation in this study.

No additional compensation is offered. The Principal Investigator and others involved in this study may be University of Florida employees. As employees of the University, they are protected under state law, which limits financial recovery for negligence.

Please contact one of the Research Team members listed in question 3 of this form if you experience an injury or have questions about any discomforts that you experience while participating in this Research Study.

SIGNATURES

As an investigator or the investigator's representative, I have explained to the participant the purpose, the procedures, the possible benefits, and the risks of this Research Study; the alternative to being in the study; and how the participant's protected health information will be collected, used, and shared with others:

_____ _____

Signature of Person Obtaining Consent and Authorization Date

You have been informed about this study's purpose, procedures, possible benefits, and risks; the alternatives to being in the study; and how your protected health information will be collected, used and shared with others. You have received a copy of this Form. You have been given the opportunity to ask questions before you sign, and you have been told that you can ask questions at any time.

You voluntarily agree to participate in this study. You hereby authorize the collection, use and sharing of your protected health information as described above. By signing this form, you are not waiving any of your legal rights.

_____ _____

Signature of Person Consenting and Authorizing Date

SomaLogic Clinical Information Sharing Consent:

Do you agree to allow your **non-identifiable** clinical information to be shared with SomaLogic for commercial purposes? Please initial below to indicate your response.

_____ Yes

_____ No