ETHOS RESEARCH AND DEVELOPMENT

SUBJECT INFORMATION AND INFORMED CONSENT FORM

Study Title:	Pilot Study: Impact of Biomarker-Guided Dietary Supplementation on Quality-of-Life Measures in Subjects with Chronic Pain
Sponsor:	Ethos Research & Development, LLC.
Site:	Ethos Research & Development, LLC.
Protocol Number:	ERD20231
Protocol Date:	19-OCT-2023
Principal Investigator:	Joshua Gunn Ph.D. 29 E 6th St, Newport, KY 41071 513-400-3057

INTRODUCTION AND BACKGROUND

You are being invited to take part in a research study and your participation is voluntary. You were selected as a possible participant in this study because you experience chronic pain and previously submitted a urine sample for urinary biomarker testing. This urine biomarker test was ordered by your treating physician as this test has been validated to identify vitamin deficiencies and markers of inflammation and oxidative stress that might be contributing to your symptoms. The results of this test qualified you to be invited to participate in this study. This research study will investigate the impact of targeted nutritional supplement formulas specifically designed for urinary biomarker levels indicating oxidative stress, inflammation, or nutritional deficiencies. This study provides you with one of three supplement formulas based on your urinary biomarker test results and assesses changes in your urinary biomarker levels and your quality of life as it relates to your pain over a 3-month period. Ethos Research and Development is sponsoring this research study.

The researchers will explain this study to you. Research studies, including this one, are voluntary and include only people who choose to take part. Please take your time about deciding whether to participate in this study. If you have any questions, you can ask for more information or

clarification. The study staff can explain words or information that you do not understand. Reading this form and talking to your doctor or staff may help you decide whether to take part or not. If you decide to take part in this study, you must sign your name at the end of this form. If you decide to take part in this study, you may withdraw at any time, for any reason.

We will give you a signed copy of this form for your records.

KEY INFORMATION

- PURPOSE: The purpose of this study is to evaluate the impact of targeted dietary supplementation on urinary biomarker levels and your quality of life as it relates to your pain.
- EXPERIMENTAL: The nutritional supplement is experimental, which means that it is being tested and is not approved by the United States Food and Drug Administration (FDA). You may receive standard of care in addition to the experimental supplement.
- VOLUNTARY PARTICIPATION: Your decision to be in this study is voluntary.
- WITHDRAWAL: If you decide to be in this study and then change your mind, you can leave the study at any time without penalty.
- PROCEDURES: Your participation is expected to last up to 7 months. During that time, you will have 8 study visits. You will take an oral nutritional supplement daily for 3 months; answer personal questions, such as questions about your health, lifestyle, and pain virtually, over zoom, with study staff and on an electronic device; and submit urine samples for testing. 75 individuals with chronic pain will participate in this study.
- TIME INVOLVED: After screening and during the 3-month study, you will attend six virtual (zoom) 45-minute visits; one 10-minute phone call two weeks after you finish taking the supplement; and a one hour virtual zoom visit three months after you finish taking the supplement.
- COMPENSATION: If you complete all parts of the study, you will receive up to $480 in amazon or other gift cards for your time.
- RISKS: Possible risks include side effects from the nutritional supplement; loss of privacy; and discomfort answering personal questions.
- BENEFITS: There is no guarantee that you will receive direct benefit as a result of your participation; however, you will have the chance to contribute to research that may be helpful to you or others with chronic pain.
- ALTERNATIVES TO PARTICIPATION: You may refuse to sign this document and seek treatment for your condition. Consult with your doctor about alternatives.
- COSTS: The study sponsor will provide the study product and study-related procedures at no charge to you.
- CONFIDENTIALITY: There are provisions in place by the study protocol and study site to help protect the privacy and confidentiality of your personal health information and study information.

This overview does not include all of the information you need to know before deciding whether or not to take part. Much additional detail is given in the full consent document, which can be

found on the pages that follow. Be sure to review the rest of this consent form before deciding about participation.

This consent form explains the research study. Before you decide to be a part of this study, you need to know why the research is being done, what it will involve and the risks and benefits. Ask the study staff to explain anything in this form or if you want more information. Please take time to read this form carefully. Feel free to discuss it with your relatives, friends and your primary care physician. If you agree to take part in this research study, you must sign this consent form.

DISCLOSURE OF FINANCIAL INTERESTS

Ethos Research and Development, the sponsor of this study, is providing funds on a per subject basis for conducting this research study.

BRANY maintains a financial interest disclosure process by which people who conduct research must disclose any financial investments (for example stock shares or patent holdings), or payments (for example, for consulting or speaking engagements) that are related to the research.

For the study you are considering joining, Joshua Gunn, the Principal Investigator, disclosed information about his role as the Chief Scientific Officer for Ethos Research and Development. Ethos Research and Development receives compensation for the urinary biomarker testing used in this protocol. If you would like more information about this matter, please ask the researchers and they will assist you.

DESCRIPTION AND PURPOSE OF STUDY

You are being asked to participate in this research study because you experience chronic pain and recently underwent a urinary biomarker test. This study will look at how your urinary biomarker levels and quality of life change with targeted nutritional supplementation. We hope that it will help improve these things, but we don't know this for sure. About 75 subjects in the United States are expected to participate in this study. Your participation in this study is expected to last up to 7 months. All visits will be held virtually over zoom video conferencing, which requires a WIFI connection. You are being asked to use your own personal phone or computer to attend visits and answer questions.

PRESCREENING

You previously submitted a urine sample for a biomarker test. This test helps to highlight some of the levels of biological processes that may be contributing to your chronic pain. You are being asked to participate because you experience chronic pain and two or more of the urinary biomarkers were abnormal.

INITIAL VISIT

Before any study-related tests and procedures are performed, you will be asked to read, sign and date this consent document. This helps you identify if this study is right for you.

If you decide to volunteer for this study this first appointment will take approximately 1 hour over two visits to complete. This visit is to find out if you qualify for the study. We will ask you questions about your health and mood. You will give a urine sample and have your medical history reviewed. The urine sample will be used for another urinary biomarker test to classify you in the proper targeted nutritional supplement group based on those results.

The following screening tests and procedures will be performed to determine if you qualify for this study:

- Provide your age, race, ethnicity and sex at birth.
- Provide a urine sample for urinary biomarker testing.
- If female, you will be asked about your birth control methods.
- Give your medical history, pain history and any medications, prescriptions, or over-the-counter supplements you are taking currently or in the past 30 days.
- Answer questions about health and mental health.

This visit is broken up into two separate days. The first day you will meet with research staff to review your medical and pain history, medication list and complete questionnaires about your health. If eligible after this first part, urinary biomarker collection supplies will be sent to your home. The second visit will include a meeting with research staff to discuss the collection process and how to send your sample back for testing. You may also be asked additional questionnaires on this visit.

Study staff will contact you regarding your eligibility and schedule your next visit. If eligible, the nutritional supplement tailored for your specific urinary biomarker results will be mailed to your home.

DURING THE STUDY

- **Baseline Visit:** If you are a good fit for this study, your study supplement will be shipped directly to your home. Once received, you will meet virtually, over zoom, with research staff to review the dosing schedule and train you on how to report taking your study supplement daily. You will also answer more questions about yourself including lifestyle habits such as alcohol, marijuana and tobacco use, sleep quality, mood etc. This visit will take about 1 hour.
- **Trial Phase:** The day you start your study supplement is known as day 1. After day 1 you will complete 5 more virtual zoom visits over the 3-month trial. These occur at week 2, week 4, week 8, week 10 and week 12. During these visits, we will ask you similar questions to the baseline visit. We will also ask how you have been feeling to document any side effects you may be experiencing. Research staff will also ask that you bring your study supplement to the visit to discuss any missed or lost doses.
- For 90 days you will use your mobile device or computer to let us know when you've taken your medication and to assess your pain. These questions take less than a minute to complete.

- During week 4, in addition to the questionnaires, you will be asked to provide another urine sample for testing. Materials will be shipped directly to your home and research staff will review the collection and shipment process with you.
- **End of Study visit:** At the end of the 12-week study, you will complete a final virtual zoom visit. This visit takes about 1 hour. This visit is similar to the baseline visit where we will ask you questions about yourself, your mental health, feedback about the study and collect another urinary biomarker sample. We will do a final review of your supplement to document any remaining capsules and discuss shipping back the remainder of the product.
- **After you finish the study medicine:** You will complete a brief follow up phone call 2 weeks after you stop the study supplement. 3 months after you finish the study supplement you will be asked to meet virtually over zoom with research staff to answer the same questions about yourself as before. This visit will take about 1 hour.

SUBJECT RESPONSIBILITIES

As a subject in this study, you will have certain responsibilities, including the following:

- Use your personal phone or computer to attend virtual visits via Zoom

  • Attend all study visits and, if needed, reschedule appointments as soon as possible

  • Follow the instructions of the study staff

  • Take the study supplement as directed

  • Tell the study staff all medications that you are taking and check with the study staff before taking any new medicines or changing medications (including prescription, over-the-counter, vitamins and herbal supplements)

  • Tell the study staff any time you do not feel well or if you have any side effects or have hospital or doctor visits

SCHEDULE OF ASSESSMENTS

Study phase	**Screening**	**Baseline**	**Study Week**				**End of study**	**3 month follow up**
Week	**-2 to -1**	**1**	**2**	**4**	**8**	**10**	**12**	**24**
Informed consent	X							
Urinary biomarker test	X			X			X	
Interviews & Questionnaires	X	X	X	X	X	X	X	X
Electronic device assessments		X	X	X	X	X	X	X

*You will also complete a brief 10-minute phone interview 2 weeks after you completely stop the study supplement.

HOW LONG WOULD YOU BE IN THIS STUDY?

Each person will participate in the study for up to 7 months, including 2 weeks of screening, 3 months during the trial phase, one end-of-study visit during the week you stop the study supplement, a telephone contact ~2 weeks after completing the trial for a safety follow-up and a 3 month follow up.

PARTICIPATION

The principal investigator, sponsor, or BRANY Institutional Review Board (IRB) may remove you from the study without your consent for any of the following reasons:

- If it appears to be medically harmful to you;
- If you fail to keep appointments or complete study procedures;
- If it is discovered that you do not meet the study requirements;
- You are in a confined or controlled environment;
- You have a psychiatric crisis;
- You have a physical illness that prevents you from taking the study drug;
- If the study is canceled.

RISKS AND DISCOMFORTS

You must tell the study staff about any health problems you have while you are taking part in this study. Giving false, misleading or incomplete information about your medical history, including past and present use of other medications could affect your well- being while taking part in this study.

- **Study medication risks:** Although nutritional supplements are relatively low risk, there may be risks that are currently not known. Some known side effects include:

Supplement Name	Side effects
Nerve Health Formula	Headache; nausea; vomiting; diarrhea; fatigue or weakness; tingling sensation in hands and feet; altered sleep patterns; heartburn; difficulty concentrating; irritability; confusion; weight loss; dermatological lesions; and photosensitivity.
Redox Support Formula	Headache; nausea; vomiting; diarrhea; loss of appetite; skin rash; flushing; stomach pain; constipation; tinnitus; chills; fever; insomnia; body odor; fatigue; itching; cough; decreased blood pressure; facial swelling; increased sweating; restlessness; brittle hair or nails; loss of hair or nails; dizziness; and trouble breathing.
Inflammation Support Formula	Headache; nausea; vomiting; coughing, dizziness, stomach pains, acid reflux; heart burn; nasal congestion; cold or flu symptoms; decreased appetite; and weight loss.

Biomarker Group	Supplement Name	Ingredients
Nerve Health	Nerve Health Formula	Vitamin B6; Vitamin B12; L-Methylfolate; Betaine
Oxidative Stress	Redox Support Formula	N-Acetylcysteine; CoenzymeQ10; Acetyl-L-Carnitine; Alpha-Lipoic Acid; Benfotiamine; Selenium; Riboflavin; Zinc; Copper
Inflammation	Inflammation Support Formula	Turmeric Extract; Olive Leaf Extract; Ashwagandha; Bioperine

You should not take these supplements if you are allergic to any of the ingredients listed above. Please notify study staff if you have any allergies to these ingredients. Please notify study staff if you have liver or kidney disease as these supplements may not be right for you.

You should also notify staff if you have recently had a bacterial or viral infection during the past 3 months, if you have any psychiatric disorders, a history of cancer, an immune disorder, taking corticosteroids or other immunosuppressive drugs, or are pregnant, breastfeeding or planning to become pregnant in the next 4 months.

- **Questionnaires:** Some of the questions about your life and health may cause you to feel uncomfortable answering them. If a question makes you feel comfortable you may discuss the importance and need to answer it with your study staff. You may refuse to answer any question if this occurs.
- **Loss of confidentiality:** As this study involves the use of your identifiable, personal information there is a chance that a loss of confidentiality of privacy will occur. We have procedures in place to reduce the chance of this happening (See "confidentiality" section below)

You will be notified in a timely way if important new findings become known that may affect your willingness to continue in the study.

As the results obtained during the research study are for research purposes only and are not for medical diagnosis, you will not receive individual results. In some circumstances, if the study doctor learns information related to your health from the study procedures, the study doctor will discuss this information and your options with you.

NEW INFORMATION
You will be notified in a timely way if important new findings become known that may affect your willingness to continue in the study.

<u>Clinically Relevant Research Results</u>
As the results obtained during the research study are for research purposes only and are not for medical diagnosis, you will not receive individual results. In some circumstances, if the study doctor learns information related to your health from the study procedures, the study doctor will discuss this information and your options with you.

BENEFITS

The benefits of these nutritional supplements as it pertains to chronic pain are unknown. We cannot promise any benefit to you or others from your participation in this research. You will have the chance to contribute to research that may be helpful to you or others in the future. Information found by this study may be used to help physicians better understand chronic pain and new treatment options. Even if the study supplement helps you, it may not be available to you after the study is over.

There is no expectation that you will benefit from your participation in this study. However, the information learned from this study may help other people in the future by improving treatment for chronic pain.

PAYMENT

You will be paid in Amazon gift cards or other gift cards available on Amazon. This is based on your choice. You will be paid for the visits you complete, even if you decide to stop the study early for any reason. Payments for each visit are documented in the following schedule:

Screening	$20
Biomarker sample at screening	$20
Baseline	$40
Week 2	$40
Week 4	$50
Biomarker sample at week 4	$20
Week 8	$40
Week 10	$40
Week 12	$50
Biomarker sample at week 12	$20
Daily medication	$1 a day for reporting (up to $90)
Phone call	$10
3 month follow up	$40
Total:	$480

Tax law may require the payer (e.g. research institution or third party) to report the amount of payment you receive from that payer to the Internal Revenue Service (IRS) or other agencies, as applicable. Generally this reporting would take place if you received $600 or more from the payer in a calendar year. You would be responsible for paying the taxes on the payment you received from the study.

You will not receive payment of any kind for your information or specimens (even if identifiers are removed) or for any tests, treatments, products or other things of value that may result from this research study.

ALTERNATIVES

You may choose not to participate in this study.

You do not have to participate in this study to receive treatment for your condition. There are alternative treatment options for chronic pain. If necessary, talk to your doctor about your options before you decide whether or not you will take part in this study.

COSTS OF PARTICIPATION

There will be no charge to you for your participation in this study. Your insurance will not be involved or notified of your involvement in this study. You will receive the study supplement, urinary biomarker test and procedures at no cost.

WHO TO CONTACT IF YOU HAVE A STUDY-RELATED INJURY, ILLNESS OR DISTRESS

For medical emergencies, call 911 immediately. If you become ill or are hurt while you are in this study, contact your study staff immediately. The study doctor will assist you in obtaining appropriate medical treatment. The sponsor will not be responsible for the costs of treatment caused by the properly performed study procedures and/ or study drug.

The sponsor will pay for reasonable and necessary medical treatment of injuries and illness that are a direct result of study procedures and/or study drug/device that are required by the study protocol and that were done correctly and only because you were in this study.

The sponsor will not cover the costs of your study-related injury or illness if:

- The sponsor and/or the study doctor do not think the condition or injury is a direct result of your being in the study;
- The injury is attributable to the underlying disease or a pre-existing medical condition or the natural progression of an underlying disease;
- The injury was the result of a failure to follow the study protocol or instructions or misconduct by the study staff.

No other compensation will be offered by the sponsor or Biomedical Research Alliance of New York, including for things such as lost wages or discomfort. You are not waiving any legal right to seek additional compensation through the courts by signing this form.

You should inform all healthcare professionals treating you that you are participating in this study.

CONFIDENTIALITY

To the extent allowed by law, every effort will be made to keep your personal information confidential. However, information from this study will be submitted to the study sponsor and to the U.S. Food and Drug Administration. It may be submitted to governmental agencies in other countries where the study product may be considered for approval. Medical records, which

identify you and the consent form signed by you, will be looked at by the sponsor or the sponsor's representatives and may be looked at by the FDA and other regulatory agencies, the Institutional Review Board, and the Biomedical Research Alliance of New York. While these parties are aware of the need to keep your information confidential, total confidentiality cannot be guaranteed. The results of this research project may be presented at meetings or in publications; however, you will not be identified in these presentations and/ or publications.

If you take part in this study, you will be assigned a unique subject code to help protect your privacy. Your study records and study samples will be labeled with this code that does not directly identify you. The study site staff securely stores the linking code between your name and study information.

AUTHORIZATION TO USE AND DISCLOSE PERSONAL HEALTH INFORMATION

Federal regulations give you certain rights related to your health information. These include the right to know who will be able to get the information and why they may be able to get it. The study staff must get your authorization (permission) to use or give out any health information that might identify you. If you choose to be in this study, the study staff will get personal information about you. This may include information that might identify you. The study staff may also get information about your health, including:

- Your name
- Address
- Phone number
- Age
- Medical history
- Information from your study visits, including all laboratory test results
- Records about phone calls made as a part of this research
- Records about your study visits

Information about you and your health that might identify you may be given to others to carry out the research study. The sponsor will analyze and evaluate the results of the study. Health data may come from your study records or from existing records kept by your doctor or other health care workers. For this study, the study staff may share health data about you with authorized users. Authorized users may include:

- Ethos Laboratories
- Ethos Research and Development
- Biomedical Research Alliance of New York (BRANY)
- Medical Monitor appointed by Ethos Research and Development

Your personal health information may be further shared by the groups above. If shared by them, the information will no longer be covered by the U.S. federal privacy laws. However, these groups are committed to keeping your personal health information confidential. If you give permission to give your identifiable health information to a person or business, the information may no longer be protected. There is a risk that your information will be released to others

without your permission.

Your health data will be used to conduct and oversee the research, including for instance:

- To see if the study supplement is safe
- For other research activities related to the study

Ethos Research and Development is required by law to protect your health information. By signing this document, you authorize Ethos Research and Development to use and/or disclose (release) your health information for this research. Once your health data has been shared with authorized users, it may no longer be protected by federal privacy law and could possibly be used or disclosed in ways other than those listed here.

Your permission to use and share health data about you does not have an expiration date. If you do not withdraw this authorization in writing, it will remain in effect indefinitely.

By signing this consent form, you are giving permission to use and give out the health information listed above for the purposes described above. You do not have to sign this consent form. If you choose not to sign this consent form, you will not be able to be in this research study. Your decision not to sign this consent form will not have any effect on your medical care and you will not lose any benefits or legal rights to which you are entitled. You have the right to review, correct and copy your health information. However, if you decide to be in this study and sign this permission form, you may not be allowed to look at or copy your information until after the research is completed.

You may withdraw or take away your permission to use and disclose your health information at any time. You do this by sending written notice to the study doctor at the address on the front of this informed consent form. If you withdraw your permission, you will not be able to continue being in this study, but you will not have any penalty or loss of access to treatment or other benefits to which you are entitled. When you withdraw your permission, no new health information which might identify you will be gathered after that date. Information that has already been gathered may still be used and given to others. This would be done if it were necessary for the research to be reliable.

Your right to access your health data in the study records will be suspended during the study to keep from changing the study results. When the study is over, you can access your study health data.

If you have any questions about the study or your rights as a research participant, the procedures, risks or benefits you may call us at 513-400-3057 or email us at info@ethosrd.com.

If you have any questions about your rights as a research participant, you may contact the Institutional Review Board overseeing this study at 1981 Marcus Avenue, Suite 210 Lake Success, NY 11042 or by phone at 516-470-6979.

Notice Concerning HIV-Related Information: HIV-related information that either is collected as part of the research or that may already exist in your medical record might be accessed for the research by the research staff and the study sponsor, but will not be shared with others without

your authorization, unless federal or state law requires the disclosure. You have a right to request a list of people who may receive or use your HIV-related information without authorization. If you experience discrimination because of the release or disclosure of HIV-related information, you may contact the agencies that are responsible for protecting your rights.

Your information and biospecimens collected as part of this research study, even if identifiers are removed, will not be used or distributed for future research studies.

VOLUNTARY PARTICIPATION AND WITHDRAWAL

This study is completely voluntary, you do not have to be in this study if you do not want to be. Even if you decide to be in this study, you can change your mind and stop at any time. If you choose not to be a part of this study or decide to stop participating, there is no penalty. Refusing to participate in or stopping the study will not affect your current or future relationship with your primary care physician, Ethos Laboratories, Ethos Research and Development or the research team.

You may be withdrawn from the study for any reason at any time without your consent by your study doctor, the study sponsor, the FDA or other regulatory authorities. Reasons this may happen include: it is believed to be in your best interest, you do not follow the study instructions; regulatory authorities end your participation in the study or for other administrative reasons.

If you choose to stop participating in this study or the research team stops your participation for any reason, you will be asked to undergo a final virtual zoom visit to get your feedback on the study and complete end of study procedures such as a final urinary biomarker sample. If you want to stop, it is important to tell us.

WHO CAN YOU CONTACT IF YOU HAVE QUESTIONS ABOUT THIS STUDY?

The Research Team: You may contact Dr. Joshua Gunn by email at DrGunn@ethosrd.com with any questions or concerns about the research or your participation in this study. Additionally, you may contact research staff Brianna Krause by email at Brianna.Krause@ethosrd.com or info@ethosrd.com.

BRANY Institutional Review Board:
If you have any questions about your rights as a research subject or complaints regarding this research study, or you are unable to reach the research staff, you may contact a person independent of the research team at the Biomedical Research Alliance of New York Institutional Review Board at 516-318-6877. Questions, concerns or complaints about research can also be registered with the Biomedical Research Alliance of New York Institutional Review Board at www.branyirb.com/concerns-about-research. The IRB is a committee that reviews research studies to help protect the rights and welfare of study subjects.

CLINICAL TRIALS REGISTRATION

A description of this clinical trial will be available for you to access at https://www.clinicaltrials.gov, as required by US Law. This website will not include information

that can identify you. At most, the website will include a summary of results. You can view this website at any time.

STATEMENT OF CONSENT

STATEMENT OF CONSENT - SIGNATURES

By signing this form, I confirm the following:

- I have read all of this consent form.
- All of my questions have been answered to my satisfaction.
- I can leave the study at any time without giving a reason and without penalty.
- I agree to the collection, use, sharing and analysis of my personal health information and study information and samples collected as part of this study by the sponsor and other authorized persons and regulatory agencies as described in this form.
- I agree that the study staff may contact my other doctor(s) about my participation in this study and to collect relevant medical information as needed for my care.
- I will be given a copy of this signed and dated consent form to keep.
- I do not give up any legal rights that I would otherwise have if I were not in this study.

I voluntarily agree to participate in this study.

_____

Subject: Name (Print) Signature Date

I have explained this research study to the study subject named above, answered all their questions to the best of my ability, believe they understand what has been explained and have consented voluntarily.

_____

Person Obtaining Consent: Name (Print) Signature Date

Please choose if you agree or disagree to be re-contacted for future studies. This does not hinder your participation in the study being discussed. Your first name and contact number will be securely stored for future contact. If you choose to agree, you may opt out at any time.

___ Yes, I agree to be recontacted for future studies.

___ No, I do not agree to be recontacted for future studies.