

The Ohio State University Combined Consent to Participate In Research and HIPAA Research Authorization

Study Title: The BE WELL study: Black Raspberry Beverage Working to Prevent Lung Cancer

Principal Investigator: Daniel Spakowicz

Sponsor: Intramural Research Program, The Ohio State University and National Institutes of Health (NIH)

- **This is a consent form for research participation.** It contains important information about this study and what to expect if you decide to participate. Please consider the information carefully. Feel free to discuss the study with your friends and family and to ask questions before making your decision whether or not to participate.
- **Your participation is voluntary.** You may refuse to participate in this study. If you decide to take part in the study, you may leave the study at any time. No matter what decision you make, there will be no penalty to you and you will not lose any of your usual benefits. Your decision will not affect your future relationship with The Ohio State University. If you are a student or employee at Ohio State, your decision will not affect your grades or employment status.
- **You may or may not benefit as a result of participating in this study.** Also, as explained below, your participation may result in unintended or harmful effects for you that may be minor or may be serious depending on the nature of the research.
- **You will be provided with any new information that develops during the study that may affect your decision whether or not to continue to participate.** If you decide to participate, you will be asked to sign this form and will receive a copy of the form. You are being asked to consider participating in this study for the reasons explained below.

Key Information About This Study

The following is a short summary to help you decide whether or not to be a part of this study. More detailed information is listed later in this form.

The purpose of this research:

To test whether black raspberry nectar can have positive effects on your health. In particular, whether they will change the bacteria in your gut in a way that reduces inflammation.

The study duration:

10 weeks total. For four weeks you'll drink two juice boxes per day, then take two weeks off, then another four weeks of 2 juice boxes per day.

The research procedures to be followed:

You'll be asked to avoid berries and a few other foods in your diet for the duration of the study. There are four study visits, where we'll collect (1) stool, (2) urine, (3) blood, weight, heart rate and blood pressure. Stool will be collected at home and brought into clinic. Urine will be collected for 24 hours prior to the study visit. We ask that you do not quit or start smoking during this period.

The most important risks or discomforts:

This is a food product with low risks. You may experience some upset stomach or diarrhea, and there is a low risk of an allergic reaction.

The reasonably expected benefits:

The anticipated benefits of this study are to provide scientific information regarding the effects of a black raspberry beverage on reducing inflammation, which may one day be part of a strategy to reduce the risk of developing lung cancer.

1. Why is this study being done?

The study is being conducted to examine whether a black raspberry beverage can affect the bacteria in your gut (your microbiome) and reduce inflammatory processes that may lead to lung cancer. We will examine the impact of diet and smoking on gut bacteria and inflammation in order to gain insight into the early steps in cancer development.

2. How many people will take part in this study?

Up to 96 participants will be recruited to take part in this study. 42 individuals will be randomized by gender and current smoking status (does not include vaping) so that 21 individuals are in the Berry Intervention group and 21 in the Placebo group for the first 4 weeks, followed by a 2-week washout period, and then everyone will cross over to the opposite group (Berry or Placebo) for the next 4 weeks.

3. What will happen if I take part in this study?

At the lung cancer screening visit, study staff will explain the study and will inform you if you qualify for this study. If you decide to participate in this study, the researcher will explain all details of the study and answer any questions you might have. Once you have provided consent, we will set up several follow-up appointments. You will then be scheduled for a randomization visit where you will be randomly assigned (like the "flip of a coin") to either a control beverage (containing berry flavor) or a test beverage (containing black raspberry components); however, you will not be told which beverage you have received, but the study staff will know the results of randomization. The study will require that you drink $\frac{3}{4}$ cup of the beverage twice each day and follow a special diet that excludes all types of berries and berry products (like strawberry jam) and limits the amount of a few other foods (you will keep track of this using a checklist form).

An additional 4 visits to The Ohio State University, will include measuring your weight and blood pressure, drawing blood and swabbing your nasal cavity, as well as dropping off the stool and urine samples that you will bring with you. You will receive reminders and detailed instructions prior to each visit.

A detailed breakdown of study activities for each study visit can be found below:

Visit 0: Screening and Consent, Week -4-0 (30 minutes)

- Sign informed consent, complete questionnaires
- Receive a urine collection container, stool collection materials and paperwork which will need to be completed by next visit

3 Days prior to Visit 1:

- Begin dietary compliance form

1 Day prior to Visit 1:

- Begin urine collection: collect for 24 hours
- Collect stool

Visit 1: Start of Trial, Phase I, Week 0 (30 minutes)

- Submit a completed 24-hour urine collection
- Submit stool collection tube
- Blood collection (3 tubes, ~4.5 teaspoons)
- Nasal swab
- Vital Signs (blood pressure, heart rate, and respiratory rate)
- Body measurements (weight, height)
- Receive a urine collection container, stool collection materials and paperwork which will need to be completed by next visit
- Receive nectar or placebo drink
- Receive \$50 compensation

Begin Daily Beverage Compliance Form (to be completed each day of the study while drinking beverage)

3 Days prior to Visit 2:

- Begin dietary compliance form

1 Day prior to Visit 2:

- Begin urine collection: collect for 24 hours
- Collect stool

Visit 2 End of Phase I, Begin Washout Period:

- Submit a completed 24-hour urine collection
- Submit stool collection tub and tube
- Blood collection (3 tubes, ~4.5 teaspoons)
- Nasal swab
- Vital Signs (blood pressure, heart rate, and respiratory rate)
- Body measurements (weight, height)
- Receive a urine collection container, stool collection materials and paperwork which will need to be completed by next visit
- Receive \$50 compensation

3 Days prior to Visit 3:

- Begin dietary compliance form

1 Day prior to Visit 3:

- Begin urine collection: collect for 24 hours
- Collect stool

Visit 3: Phase II, Week 6 (30 minutes)

- Submit a completed 24-hour urine collection
- Submit stool collection tube
- Blood collection (3 tubes, ~4.5 teaspoons)
- Nasal swab
- Vital Signs (blood pressure, heart rate, and respiratory rate)
- Body measurements (weight, height)
- Receive a urine collection container, stool collection materials and paperwork which will need to be completed by next visit
- Receive nectar or placebo drink
- Receive \$50 compensation

3 Days prior to Visit 4:

- Begin dietary compliance form

1 Day prior to Visit 4:

- Begin urine collection: collect for 24 hours
- Collect stool

Visit 4: End of trial, Week 10 (30 minutes)

- Submit a completed 24-hour urine collection
- Submit stool collection tub and tube
- Blood collection (3 tubes, ~4.5 teaspoons)
- Nasal swab
- Vital Signs (blood pressure, heart rate, and respiratory rate)
- Body measurements (weight, height)
- Receive \$50 compensation

4. How long will I be in the study?

The study will require 4 visits over 10-week period. At your lung screening the study coordinator will determine if you qualify for the study. If you qualify, you will be enrolled for the full 4-visit study. Each visit will last about 30 minutes and will include collection of study materials, drawing blood, a nasal swab, body measurements and giving out new materials. Home preparation before each visit will require no more than 1 hour.

5. Can I stop being in the study?

You may leave the study at any time. If you decide to stop participating in the study, there will be no penalty to you, and you will not lose any benefits to which you are otherwise entitled. Your decision will not affect your future relationship with The Ohio State University.

6. What risks, side effects or discomforts can I expect from being in the study?

The physical risks associated with this study are believed to be low. There are no known side effects of the diet in this study. The beverages contain black raspberries, or products approved by the FDA for use in foods and found in beverages such as Kool-Aid™. The beverages may cause temporary discoloration of teeth; short-term gastrointestinal side effects, such as diarrhea; and there is a small chance of an allergic reaction. Symptoms of an allergic reaction include throat tightness; itching or tingling mouth; skin rashes, such as hives or eczema; itchy skin; wheezing; cough; congestion; nausea; stomach pains; vomiting; diarrhea; dizziness; lightheadedness. There is a reported association between red food dye and hyperactivity in some children. The dose used in this study has been demonstrated to be safe in previous human research.

The nasal swab can result in minimal bleeding and irritation that resolves in 1-2 days. Risks of blood draws may include lightheadedness or fainting, as well as localized pain, bleeding/bruising, swelling, or infection at the blood collection site.

Though it is a food product, the effect of these beverages on an embryo or fetus is currently unknown. You cannot take part in this study if you are pregnant or breast-feeding a child. You must agree not to become pregnant while you are in this study.

Research using your specimens will include measuring your RNA (transcriptome sequencing), which could potentially identify you. However, no genetic test results will be shared with you, released to your physician or be included as part of your medical record.

7. What benefits can I expect from being in the study?

You may not benefit directly from participating in this study, as the benefits of the berry products are still being investigated and modest at best over such a short period of time. Rather, the greatest benefits likely will be to scientific research and the greater public with regards to information about berry products' effects on the microbiome, inflammation and lung cancer risk.

8. What other choices do I have if I do not take part in the study?

You may choose not to participate without penalty or loss of benefits to which you are otherwise entitled.

9. What are the costs of taking part in this study?

All study-related procedures and tests will be performed at no cost to you. This includes paid parking at each of your four study visits.

10. Will I be paid for taking part in this study?

Yes, you will receive a \$50 in Amazon or Walmart gift cards for completing each visit (Week 0, 4, 6, 10). In total, you will earn \$200.

By law, payments to participants are considered taxable income

11. What happens if I am injured because I took part in this study?

If you suffer an injury from participating in this study, you should notify the researcher or study doctor immediately, who will determine if you should obtain medical treatment at The Ohio State University Wexner Medical Center.

The cost for this treatment will be billed to you or your medical or hospital insurance. The Ohio State University has no funds set aside for the payment of health care expenses for this study.

12. What are my rights if I take part in this study?

If you choose to participate in the study, you may discontinue participation at any time without penalty or loss of benefits. By signing this form, you do not give up any personal legal rights you may have as a participant in this study.

You will be provided with any new information that develops during the course of the research that may affect your decision whether or not to continue participation in the study.

You may refuse to participate in this study without penalty or loss of benefits to which you are otherwise entitled.

An Institutional Review Board responsible for human subject research at The Ohio State University reviewed this research project and found it to be acceptable, according to applicable state and federal regulations and University policies designed to protect the rights and welfare of research participants.

13. Will my de-identified information and bio-specimens be used or shared for future research?

Yes, de-identified data will be made publicly available upon publication to support the reproducibility of the published analyses.

14. Will my study-related information be kept confidential?

Efforts will be made to keep your study-related information confidential. However, there may be circumstances where this information must be released. For example, personal information regarding your participation in this study may be disclosed if required by state law.

Also, your records may be reviewed by the following groups (as applicable to the research):

- Office for Human Research Protections or other federal, state, or international regulatory agencies;
- U.S. Food and Drug Administration;
- The Ohio State University Institutional Review Board or Office of Responsible Research Practices;
- The sponsor supporting the study, their agents or study monitors; and
- Your insurance company (if charges are billed to insurance).

We will work to make sure that no one sees your survey responses without approval. But, because we are using the Internet, there is a chance that someone could access your online responses without permission. In some cases, this information could be used to identify you. Your data will be protected with a code to reduce the risk that other people can view the responses.

The NIH has issued a Certificate of Confidentiality for this study. This Certificate provides extra protection for you and your study information, documents, or samples (blood, tissue, etc.). The Certificates are issued so that we cannot be required to disclose any identifiable, sensitive information collected about you as a part of this study in a lawsuit or legal proceeding. We are also prevented from releasing your study information without your consent. This is a layer of protection over and above the already existing protections in place for you and your information, documents, or samples.

However, these protections do not apply in some situations. For example, we may have to release your information if a law requires us to do so, the Agency that is funding this study requests the information, or if the FDA tells us to release this information. We may also use your information to conduct other scientific research as allowed by federal regulations.

Study information that has health implications may be placed in your medical record where authorized employees may see the information. Further, authorized requests for your records (medical record release for continuity of care) may result in research-related information being released.

Please talk to your study team, or contact the Office of Responsible Research Practices at 614-688-8641, if you have questions.

A description of this clinical trial will be available on <http://www.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.

**15. HIPAA AUTHORIZATION TO USE AND DISCLOSE INFORMATION FOR
RESEARCH PURPOSES**

I. What information may be used and given to others?

- Past and present medical records;
- Research records;
- Records about phone calls made as part of this research;
- Records about your study visits;
- Information that includes personal identifiers, such as your name, or a number associated with you as an individual;
- Information gathered for this research about:
 - HIV / AIDS
 - Hepatitis infection
 - Sexually transmitted diseases
 - Other reportable infectious diseases
 - Physical exams
 - Laboratory, x-ray, and other test results
 - Diaries and questionnaires
 - The diagnosis and treatment of a mental health condition

II. Who may use and give out information about you?

Researchers and study staff.

III. Who might get this information?

- Authorized Ohio State University staff not involved in the study may be aware that you are participating in a research study and have access to your information;
- If this study is related to your medical care, your study-related information may be placed in your permanent hospital, clinic, or physician's office record;

IV. Your information may be given to:

- The U.S. Food and Drug Administration (FDA), Department of Health and Human Services (DHHS) agencies, and other federal and state entities;
- Governmental agencies in other countries;
- Governmental agencies to whom certain diseases (reportable diseases) must be reported; and
- The Ohio State University units involved in managing and approving the research study including the Office of Research and the Office of Responsible Research Practices.

V. Why will this information be used and/or given to others?

- To do the research;
- To study the results; and
- To make sure that the research was done right.

VI. When will my permission end?

There is no date at which your permission ends. Your information will be used indefinitely. This is because the information used and created during the study may be analyzed for many years, and it is not possible to know when this will be complete.

VII. May I withdraw or revoke (cancel) my permission?

Yes. Your authorization will be good for the time period indicated above unless you change your mind and revoke it in writing. 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 researchers. If you withdraw your permission, you will not be able to stay in this study. When you withdraw your permission, no new health information identifying you will be gathered after that date. Information that has already been gathered may still be used and given to others.

VIII. What if I decide not to give permission to use and give out my health information?

Then you will not be able to be in this research study and receive research-related treatment. However, if you are being treated as a patient here, you will still be able to receive care.

IX. Is my health information protected after it has been given to others?

There is a risk that your information will be given to others without your permission. Any information that is shared may no longer be protected by federal privacy rules.

X. May I review or copy my information?

Signing this authorization also means that you may not be able to see or copy your study-related information until the study is completed.

16. Who can answer my questions about the study?

For questions, concerns, or complaints about the study, or if you feel you have been harmed as a result of study participation, you may contact **Dr. Marisa Bittoni at (614) 398-1032.**

For questions related to your privacy rights under HIPAA or related to this research authorization, please contact **Kathleen Ojala at (614) 293-6482 or Kathleen.Ojala@osumc.edu**

For questions about your rights as a participant in this study or to discuss other study-related concerns or complaints with someone who is not part of the research team, you may contact **the Office of Responsible Research Practices at 1-800-678-6251.**

If you are injured as a result of participating in this study or for questions about a study-related injury, you may contact **Dr. Steve Clinton at 614-293-2886.**

Signing the consent form

I have read (or someone has read to me) this form and I am aware that I am being asked to participate in a research study. I have had the opportunity to ask questions and have had them answered to my satisfaction. I voluntarily agree to participate in this study.

I am not giving up any legal rights by signing this form. I will be given a copy of this combined consent and HIPAA research authorization form.

Printed name of participant

Signature of participant

Date and time AM/PM

Printed name of person authorized to consent for
participant (when applicable)

Signature of person authorized to consent for participant
(when applicable)

Relationship to the participant Date and time AM/PM

Investigator/Research Staff

I have explained the research to the participant or his/her representative before requesting the signature(s) above. There are no blanks in this document. A copy of this form has been given to the participant or his/her representative.

Printed name of person obtaining consent

Signature of person obtaining consent

Date and time AM/PM

Witness(es) - *May be left blank if not required by the IRB*

Printed name of witness

Signature of witness

Date and time AM/PM

Printed name of witness

Signature of witness

Date and time AM/PM