# *Strategies to Augment Ketosis: Optimization of Ketone Delivery(STAK:OK'd)*

## *The Ohio State University*

## *IRB Approval July 26, 2022*

***IRB# 2022H0160***

# The Ohio State University Consent to Participate in Research

| | |
|---|---|
| **Study Title:** | **Strategies to Augment Ketosis: Optimization of Ketone delivery (STAK OK'd)** |
| **Principal Investigator:** | **Jeff Volek PhD, R.D.** |
| **Sponsor:** | Department of Defense (DOD)<br>BHB Therapeutics/ Juvenescence<br>Abbott Laboratories |

- **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.*

This study is intended to evaluate the effects of different dosing measurements for different ketone products in healthy male adults. After giving consent to this study you will schedule 9 testing sessions about 3 days apart. During these sessions you will come into the Physical Activity and Education Services (PAES) building in the morning, having had no food that day and take a study product. Various tests will be administered after ingestion. You will have blood draws to tell us more about your metabolic response to the product. We will draw 56mL per testing day, which is less than 4 tablespoons of blood (~3.8 tbsp). For the entire study, we will draw 504mL of blood, which is roughly ~2.1 cups over 4 weeks.

You will receive finger sticks that tell us your ketone and glucose levels. Your respiratory gas will be assessed using a Parvo Metabolic Cart as you breathe through a face mask and then a handheld breathe analyzer. You will be asked to complete a couple surveys at the beginning and end of each testing session. From the beginning to end of your participation in the study (~4 weeks) you will wear a Continuous Glucose and Ketone Monitor. This will be applied at your first testing session. We expect the full visit experiment to last 4 hours. You will be monitored at all times by research staff.

## 1. Why is this study being done?

This study is being done to identify the preferred ketone supplement type, the ideal ketone supplement dose, and those effects on your body. With the widespread use of ketogenic diets, the research on ketones (a molecule created when fat is broken down in the body) has grown as well. It is now possible to increase blood levels of ketones by consuming them directly instead of restricting carbohydrates or prolonged fasting. When ketones are consumed, they are quickly absorbed and increase blood levels of ketones, even in those not consuming a very low-carbohydrate diet. Since they are so new, very little work has been done to show how ketone supplements affect blood-based changes, heart based changes and tolerability. These findings will be used to help develop future research protocols and drive product development.

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

We will recruit up to 15 healthy and normally-active resistance/endurance trained men from the ages of 20-30 yr that represents typical active-duty military personnel

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

This study will be a single center, randomized study of up to 15 apparently healthy males comparing the effect of an oral ketone supplement in various forms and doses.

If enrolled, you will be randomly assigned using an online random sequence generator (randomization.com) that will generate a list of random number sequences between 1 – 9 that correspond to product/serving code. If you meet all inclusion and none of the exclusion, a staff member will randomize you in the order that you are enrolled. The randomization number will be recorded in your study documentation.

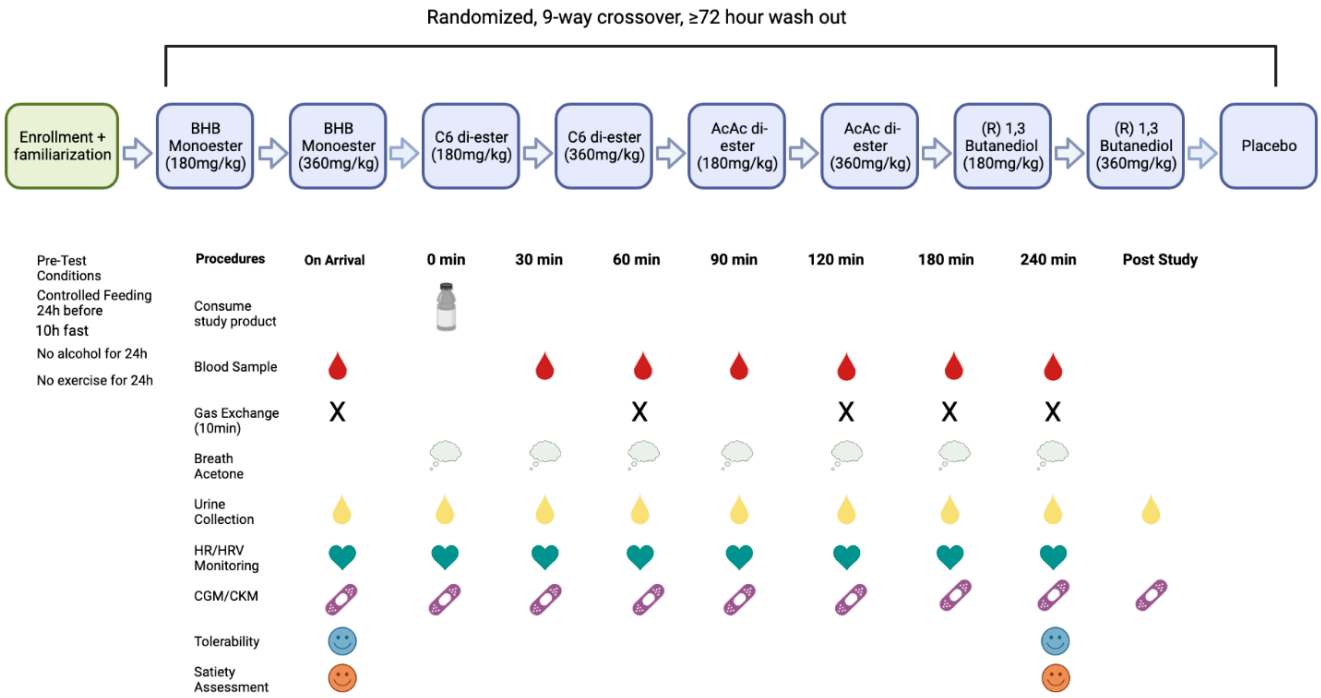


Figure 1. Study Overview

## Study Procedures

| Study Day | Screening | Test Days 1-9 |
|---|---|---|
| Visit to Study Center | X | X |
| Informed consent | X | |
| Medical intake questionnaire, taste screening, diet assessment, anthropometrics[1] | X | |
| Randomization[2] | X | |
| Compliance assessment[3] | | X |
| Consume study product[4] | | X |
| IV Cannulation and whole blood collection[5] | | X |
| Urine collection[6] | | X |
| Respiratory gas analysis[7] | | X |
| Heart rate and HRV monitoring[8] | | X |
| Tolerability assessment[9] | | X |
| Satiety assessment[10] | | X |
| Continuous Ketone Monitor placement/check[11] | | X |

1. Medical intake questionnaire, taste screening diet assessment questionnaire and anthropometric data will include: Lean Body Mass by DXA, BMI, height and weight.
2. Your order of study products will be randomized using a computer randomization generator.

3. Prior to starting each test day, you will be asked to confirm that you meet pre-test criteria, including: fasted >10h, no alcohol for 24h, no exercise for 24h and consumed the provided pre-test food.
4. Study Product will be consumed within +/- 60 minutes of the time established on the first test day. Participants will be provided with a choice of non-caffeinated, non-caloric beverage to remove the bitter taste of the Study Product.
5. IV cannula will be inserted at the start of each Test Day, and removed at the end of each Test Day, Blood samples will be collected according to the schedule in Figure 1. Cannula will be flushed with a small volume of saline after each sample to maintain patency. We will draw 56 mL of blood, per testing day, which is less than 4 table spoons.
6. Prior to consumption of the Study Product, participants will be asked to completely void your bladder. And hydration status will be determined via urine specific gravity (USG) reporting <1.025. Urine passed after the ingestion of the study product will be collected in a plastic container; you will be asked to void their bladder and collect urine at the end of the test day. The volume produced will be recorded at the end of the study and aliquots will be frozen and stored for future analysis.
7. You will breathe into a commercially available handheld breath acetone analyzer according to the schedule in Figure 1. Participants will wear a fitted face mask attached to a metabolic cart for a 10-minute period every 60 minutes.
8. Participants will wear a Bluetooth heart rate monitor chest strap throughout the test day.
9. Participants will complete a Beverage Tolerability Questionnaire prior to Study Product consumption and at the end of the Test Day.
10. Participants will complete a 3-item satiety visual analogue scale prior to Study Product consumption and at the end of the Test Day.
11. Continuous Ketone Monitor will be applied at the start of Test Day 1. The sensor will be checked by the study team at each test day and will be removed and replaced by a fresh sensor at ~2- week intervals during the study. The sensor will be removed at the end of the final test day.

Screening Visit: If you meet the initial qualifying criteria you will visit the study center for a screening meeting. You and a member of the research team will meet in a private office to discuss this form. The study will be described in full detail and any questions you have will be answered. If you choose to participate you will be asked to sign the consent form providing written consent to be apart of the study. Even though you have signed the informed consent, you may stop the study at any time.

If you do consent, you will be provided with questionnaires about your diet and medical history. All collected samples and data will be coded to maintain your privacy. We will give you a small volume of Study Product to screen for tolerance of the bitter tasting Study Products. You will complete a DXA scan to assess body composition.

## 4. How long will I be in the study?

The duration of this study is expected to be approximately 4 weeks, which includes consent and screening, and two times per week study testing. Total hours of commitment should be approximately 38 hours. This will include 9 sessions of 4 hours (~36 hours) and a 2-hour consent/screening/baseline testing session.

## 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?

**Ketone Supplements.**

Drinking the supplement beverage could cause some people to have discomfort such as stomach cramps, nausea, vomiting or diarrhea. Additionally, this study is designed to assess palatability and tolerability of the supplement therefore it is possible that you may not like the taste of the product in one or all of the provided forms.

**Continuous Ketone/Glucose Monitor**

The patch application may cause a slight immediate discomfort at the specific stick site. Under normal conditions, there are minimal risks to you when performing application that include: bruising; light-headedness or dizziness due to fear of needles; and infection.

**Blood Draws**

Blood draws will be done via an in-dwelling IV catheter. The insertion of this catheter may cause discomfort at the skin puncture site and a small bruise may develop that may persist for several weeks. Risks of IV cannulation include but not limited to: a) Occasionally: discomfort, bruising and pain at the site of injection. b) Rarely: inflammation of the vein used for injection, phlebitis (vein irritation), metabolic disturbances, and injury. c) Extremely Rare: Severe allergic reaction, anaphylaxis (inability to breathe), infection, cardiac arrest, and death. Venous access for blood draws will be rotated at each testing day to let your veins recover appropriately. We will draw 56mL per testing day, which is less than 4 tablespoons of blood (~3.8 tbsp). For the entire study, we will draw 504mL of blood, which is roughly ~2.1 cups over 4 weeks. Risks are minimized by using sterile disposable needles and gauze and the practice of aseptic (sterile) techniques during the blood draw.

**Body Composition-DXA**

You will be exposed to a very small amount of radiation by the scanner used to measure your body composition. Exposure to any amount of X-ray radiation, no matter how low, may cause abnormal changes in cells. DXA includes exposure to radiation similar to a flight from New York to Los Angeles or 125 times less than the radiation associated with a standard chest x-ray; any exposure to radiation may elevate cancer risk. The total amount of radiation that you will receive in this study is about 0.39 mSv or 39 mrem, and is approximately equivalent to a uniform whole body exposure of 47 days of exposure to natural background radiation. This use involves minimal risk and is necessary to obtain the research information desired.

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

You will receive body composition analysis from your DXA scan. Other than that, there are no potential benefits to being in the study. If there are unusual findings, we will consult with a physician.

## 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. 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).

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 records. 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.

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

Yes, it/they may be used or shared with other researchers without your additional informed consent.

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

There is no cost to you or your insurance company for participating in this research study. There is no cost to you for the food you will be provided.

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

By law, payments to subjects are considered taxable income. $30 will be received for completing each day of testing (9 days), plus enrollment + familiarization day (1 day). If all testing days are completed this will equal to $300.00. Payments will be provided in the form of check at the completion of the study or upon study withdrawal, if occurring prior to final testing day.

## 13. 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.

## 14. 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 subjects 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.

## 15. Who can answer my questions about the study?

For questions, concerns, or complaints about the study you may contact Drs Madison Kackley, 614-247-9650 or Brianna Stubbs, 415-209-2000

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. Jeff Volek 614-688-1701**.

## 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 form**.**

| | |
|---|---|
| **Printed name of participant** | **Signature of participant** |
| | **AM/PM** |
| | **Date and time** |
| **Printed name of person authorized to consent for participant (when applicable)** | **Signature of person authorized to consent for participant (when applicable)** |
| | **AM/PM** |
| **Relationship to the participant** | **Date and time** |

## 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** |
| | **AM/PM** |
| | **Date and time** |

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

| | |
|---|---|
| **Printed name of witness** | **Signature of witness** |
| | **AM/PM** |
| | **Date and time** |
| **Printed name of witness** | **Signature of witness** |
| | **AM/PM** |
| | **Date and time** |