UNIVERSITY OF CALIFORNIA, SAN DIEGO
CONSENT TO PARTICIPATE IN RESEARCH

1. Study Title and Number

Title: The Impacts of Multivitamin and Mineral Supplementation on cellular Metabolism and Healthy Aging
Study # 812601

2. Principal Investigator

Anthony Molina, PhD

3. Principal Investigator Phone Number, Research Team Number, and Emergency Contact Number

Anthony Molina, PhD (858) 246-5930
Research Team (858) 534-9315

4. Study is funded by:

Haleon

5. Study Overview

This research study is being conducted to determine the impact of multivitamin and mineral (MVM) supplementation on biological factors associated with healthy aging.

We are inviting you to participate in a research study because you are between 40 and 60 years old and are willing and interested in participating in a study involving MVM supplementation.

This form explains the research so that you may make an informed decision about participating.

- Research is voluntary - whether or not you participate is your decision. You can discuss your decision with others (such as family, friends, or another doctor).
- You can say yes and decide to change your mind later.
- If you say no, we will not hold your decision against you.
- You can say no even if the person inviting you is part of your healthcare team.
- Your decision will not affect your health care or other benefits you may be entitled to.
- Please ask the study doctor or study team questions about anything that is not clear, and feel free to ask questions and mention concerns before, during, and after the research.
- You may consult with friends, family, a personal doctor, or anyone else before deciding whether or not to be in the study.
- You will be given a copy of this consent form and the Participant's Bill of Rights.

The purpose of this research study is to study the impact of multivitamin use on biological factors associated with healthy aging. In this study, we will be testing two new Centrum Multivitamin products. Multivitamin and mineral (MVM) dietary supplements have been used to support general health and nutritional status for years, particularly in older adults who are more susceptible to nutritional deficiencies due to factors such as reduced appetite, body changes and use of multiple medications. Observational studies consistently demonstrated that older adults show higher rates of nutritional deficiencies, and that MVM supplementation may reduce these burdens. This study will help scientists understand how multivitamin supplements can support heathy aging in mid-life adults, a key time to make positive changes to your health.

If you wish to enroll in this study, you will first undergo several procedures to determine if you are eligible for the study. If you are eligible, you will be assigned to receive one of two study supplements or the placebo (an inactive substance) over a period of 12 weeks. Over the course of the study, you will visit our study site at the Exercise and Physical Activity Resource Center (EPARC) on the UCSD campus 5 times over 16 weeks (including today) for physical examinations, blood tests and other procedures designed to monitor your safety and measure the effect of the supplement or placebo. The initial visit will last up to 2 hours, and the follow-ups will be approximately 30 minutes each. Additionally, you will be asked to fill out weekly digital surveys with questions about your mood, quality of life, sleep habits, and adherence to the protocol.

The most common risks or discomforts of this study are discomfort from the blood draw. The most serious risks include the risk of loss of confidentiality. Although rare, it is possible that this might occur. A complete listing of possible risks and discomforts associated with this study can be found in Section 9 of this document.

We cannot promise any benefit to you from your participation in this research. The alternative to being in this study is to not participate.

More detailed information about this research study is provided below.

6. Whom can I talk to if I have questions?

If during your participation in the study you have questions or concerns, or if you think the research has hurt you, contact the research team at the numbers listed in Section 3 on the first page of this form. You should not agree to participate in this study until the research team has answered any questions you have about the study, including information contained in this form.

If before or during your participation in the study you have questions about your rights as a research participant, or you want to talk to someone outside the research team, please contact:

UC San Diego Office of IRB Administration at 858-246-4777 or irb@ucsd.edu

7. How many people will take part?

150 people will be enrolled. The research will include people who have participated in other UC San Diego studies.

8. What happens if I take part in the research?

Throughout this form the term “MVM” is used, and it refers to Multivitamin and Mineral. These are meant to supplement your diet with some essential vitamins and minerals you may not be getting from the food you eat.

As you read this form, ask questions if something is not clear.

Here is what will happen to you if you agree to be in this study:

Initial Screening:
Duration: 2 hours

- Informed consent
- Diet history questionnaire – you will be asked questions about the foods you eat

- Physical activity questionnaire – you will be asked about the types of physical activities you engage in.
- Provide an activity monitor that you will be asked to wear around your waist at home for 14 days following your appointment – this will collect information on your movement (steps and intensity)
- Randomization - You will be randomized into one of 3 (three) study groups described below.

1. **Centrum MVM "GOLD" Blend:**
   - 17-ingredient blend of vitamins and minerals
   - 1 pill per day for 12 weeks (84 pills total)
2. **Centrum MVM "US CORE" Blend:**
   - 22-ingredient blend of vitamins and minerals
   - 1 pill per day for 12 weeks (84 pills total)
3. **Placebo:**
   - 1 pill per day for 12 weeks (84 pills total)

Randomization means that you are put into a group by chance. It is like drawing straws. Neither you nor the researchers choose which group you will be in. You will have a 33% chance of being placed in a specific group.

Throughout the study, neither you nor the researchers will know which group you are in.

In this study, you might receive a placebo. A placebo is a pill that looks like the study supplement but has no active ingredients in it. A placebo is often used in research studies so that the doctor and you do not know your study group. The study is done this way because knowing whether you are getting the study supplement or placebo can change the results of the study. In case of an emergency, we can find out if you are getting the placebo or the supplement.

A fasted blood sample will be collected at each of the 4 in-person visits. Please do not eat or drink anything but water for 8-10 hours before your scheduled visit.

Baseline Visit 1 (2 weeks after the initial screening visit):

Duration: 30 minutes

- A blood sample will be drawn (approximately 4 tablespoons) by a licensed phlebotomist via venipuncture in your arm.
- We will gather vital information including resting blood pressure, resting heart rate, birthdate, height, and weight.
- Your grip strength will be assessed
- You will complete an exercise test, during which you will walk or run on a treadmill until you reach voluntary exhaustion while wearing a mask that collects all your expired air.
- An X-ray scan called DXA (Dual-energy X-ray Absorptiometry) to measure your body composition.
- We will collect your activity monitor
- You will receive a 12-week supply of study supplement that you are randomly assigned to.

Visit 2 (4 weeks after the initial screening visit):
Duration: 30 minutes

- A blood sample will be drawn (approximately 4 tablespoons) by a licensed phlebotomist via venipuncture in your arm.

- We will gather vital information including resting blood pressure, resting heart rate, height, and weight.
- Your grip strength will be assessed.
- You will complete a graded exercise test, during which you will walk or run on a treadmill until you reach voluntary exhaustion while wearing a mask that collects all your expired air.

Visit 3 (14 weeks) after the initial screening visit:

Duration: 30 minutes

- We will provide an activity monitor that you will be asked to wear around your waist at home for 14 days following your appointment.
- A blood sample will be drawn (approximately 4 tablespoons) by a licensed phlebotomist via venipuncture in your arm.
- We will gather vital information including resting blood pressure, resting heart rate, height, and weight.
- Your grip strength will be assessed.
- You will complete a graded exercise test, during which you will walk or run on a treadmill until you reach voluntary exhaustion while wearing a mask that collects all your expired air.
- An X-ray scan called DXA (Dual-energy X-ray Absorptiometry) to measure your body composition.

Visit 4 (16 weeks) after the initial screening visit:

Duration: 30 minutes

- A blood sample will be drawn (approximately 4 tablespoons) by a licensed phlebotomist via venipuncture in your arm.
- We will gather vital information including resting blood pressure, resting heart rate, height, and weight.
- Your grip strength will be assessed.
- You will complete a graded exercise test, during which you will walk or run on a treadmill until you reach voluntary exhaustion while wearing a mask that collects all your expired air.
- We will collect your activity monitor.

Weekly Survey
You will be emailed a link to a weekly survey about diet, mental well-being, quality of life, sleep, and adherence to supplement schedule. The surveys can be completed using a computer, tablet, or smartphone

Additional Requirements
We ask that you pause any other supplements that you normally use for the duration of the study, which may last up to 4 months. After randomization, you may receive no supplement (placebo), or supplement at a dose which may not be the same formulation as the one you normally use. As a result, you may not have the same effect as your usual supplement(s).

As with any supplements, the components may affect a baby, before or after the baby is born. As a result, those able to become pregnant should not be in this study if they are:

- pregnant,
- breast-feeding, or

- trying to become pregnant.

If you become pregnant or think you might be pregnant during study, you must inform the Study PI immediately and discontinue the study.

Biobank
Blood will be stored indefintely in Dr. Molina's Geroscience Biobank laboratory. All identifying information will be removed before sample storage, and all identifiers will be kept separately.

9. What are the risks and possible discomforts?

Participation in this study may involve risks or discomforts. These include the following:

Risks of MVM Supplementation
MVM supplements are generally considered safe with recommended use. Some potential risks on the product information page include:

- There is enough iron in the package to seriously harm a child. Close container tightly and keep out of reach of children; if taken accidentally, call a doctor immediately.
- Beta carotene should not be taken by smokers and those exposed to asbestos.
- Mega doses of Vitamin C may contribute to oxalate kidney stones and kidney diseases; it may also interfere with blood sugar test as it gives a false result.

Risks of Blood Draw
As with all blood draws, participants may experience temporary pain, bruising, bleeding and a small risk of infection or fainting or dizziness during the collection process. Only trained staff will be responsible for the collection of blood samples.

Risks of Muscle and Exercise Tests
The participant may experience muscle fatigue and soreness due to the exercise tests performed in the study. The graded difficulty levels of the assessments are designed to probe an individual's true capacity; thus, there is a small risk of loss of balance during the graded exercise task. Trained research staff will be present at all times.

Risk of radiation exposure
The total amount of radiation exposure for the DXA scan is less than what you would get from one year of natural exposure in the San Diego area. To minimize exposure to radiation with the DXA scan, scans will only be conducted by highly skilled technologists certified by the state of California. Pregnant women will not be scanned.

Risks of Interviews/Questionnaires/Quality of Life Assessments that Discuss Sensitive Issues
Some of the questions we will ask you are personal. You may feel embarrassed or stressed. You may ask to see the questions before deciding whether or not to take part in this study.
Re-Identification
There may be a small risk of re-identification of your samples if the security of the identification documents is breached. We will ensure the proper storage and security of all samples and identification documents.

Risk of Loss of Confidentiality

There is also a risk that information about you could be released to an unauthorized party. All of the research information will be kept separate from your identifiable information, such as your name and birthdate.

10. How will information about me be protected?

While we cannot guarantee complete confidentiality, we will limit access to information about you. Only people who have a need to review your information, documents, or specimens will have access. These people might include:

- Members of the research team and other staff or representatives of UCSD whose work is related to the research or to protecting your rights and safety.
- Representatives of Federal and other regulatory agencies who make sure the study is done properly and that your rights and safety are protected.

Study information will be labeled with a code instead of your name or other information that can easily identify you. The record linking your identifying information (name, address, etc.) and the code will be kept separate from the rest of the study information.

The results of this study may be published once the study is completed. However, we will keep your name and other identifying information confidential. Although your participation will be 16 weeks, we expect this study for all participants will be completed in 2 years. This is only an estimate and the actual time to complete the study may be longer or shorter depending on a number of factors. If you decide later that you do not want the specimens collected from you to be used for future research, you may tell this to the study coordinator who will use their best efforts to stop any additional studies. However, in some cases, such as if your specimens have already been tested, the data from these tests are no longer linked to your identity and cannot be removed from the research database.

11. Will I need to pay to participate in the research?

There will be no cost to you for participating in this study. The MVM supplement will be supplied at no cost while you take part in this study.

12. What if I agree to participate, but change my mind later?

You can stop participating at any time for any reason, and it will not be held against you. Your choice will not affect any treatment relationship you have with healthcare providers at UC San Diego Health or any services you receive from them. No matter what you decide, there will be no penalty to you. You will not lose medical care or any legal rights.

If you stop early, please contact us immediately. We will ask you to return the remaining pills and complete a final questionnaire about your sleep and diet. If you stop participating, the study information, including blood samples that have been collected before the date and time you give notification, will still be used for the purposes of this study.

In addition, the study doctor may stop the study or take you out of the study at any time, even if you would like to continue. This could happen because it may be in your best medical interest, or you do not follow the instructions given to you by the study personnel.

13. What will happen to information and/or biospecimens collected from me?

The data and/or specimens we collect as a part of this study will be stored in a biobank and may be used to answer other research questions. If we do so, we will remove all identifiable information before use. Once identifiers have been removed, we will not ask for your consent for the use of your data and/or specimens.

Biospecimens (such as blood, tissue, or saliva) collected from you for this study and/or information obtained from your biospecimens may be used in this research or other research, and shared with other organizations. You will not share in any commercial value or profit derived from the use of your biospecimens and/or information obtained from them.

14. What are my responsibilities if I take part in this research?

If you take part in this research, you will be responsible for communicating with the study team, following the supplement administration schedule, completing at-home virtual surveys that will be delivered via email and can be completed on a computer or phone, and going to study follow up appointments.

You will be responsible for advising the study team if you begin using any new medications at any point during the study period.

15. Will I be compensated for participating in the research?

We will provide you with $40 for the screening visit whether or not you agree to take part in this research, $40 for the Baseline Visit 1 (2 weeks later), $50 for Visit 2, $60 for Visit 3, $60 for Visit 4, and $5 weekly for completing the digital surveys. We will not reimburse you for any out-of-pocket expenses related to your participation, such as fuel costs. However, if you need transportation to and from each scheduled research visit, a study team member will reserve a ride for you through UCSD's Lyft on-demand ride service from your home to the appointment and from your appointment to your home. If you elect to use your own car to drive to the in-person study visits, you can park in a designated spot for participants outside the EPARC building. These parking spots are only for in-person visits to the EPARC facility. There is no charge to park in these spaces for those specific appointments.

16. What else is important for me to know?

If you are injured as a direct result of participation in this research, the University of California will provide any medical care you need to treat those injuries. The University will not provide any other form of compensation to you if you are injured. You may call the Office of IRB Administration at 858-246-4777 or irb@ucsd.edu for more information about this, to inquire about your rights as a research participant, or to report research-related problems. A description of this clinical trial will be available on 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 Web site at any time.

17. Additional Choices to Consider

The study team would like your permission to contact you about participating in future studies. You may still join this study even if you do not permit future contact. You may also change your mind about this choice. Please initial your choice below:

_____YES, you may contact me

_____NO, you may NOT contact me

UNIVERSITY OF CALIFORNIA, SAN DIEGO

CONSENT TO PARTICIPATE IN RESEARCH

Signature Block for Adults Able to Provide Consent

Participant

I have received a copy of this consent document and a copy of the "Experimental Participant's Bill of Rights" to keep. I agree to participate in the research described in this form.

Printed Name of Participant

Signature of Participant Date

Person Obtaining Consent

I document that:

- *I (or another member of the research team) have fully explained this research to the participant.*
- *I have personally evaluated the participant's understanding of the research and obtained their voluntary agreement.*

Printed Name of Person Obtaining Consent

Signature of Person Obtaining Consent Date

Witness (if applicable)

I document that the information in this form (and any other written information) was accurately explained to the participant. The participant appears to have understood and freely given consent to join the research.

Printed Name of Witness

Signature of Witness Date

UNIVERSITY OF CALIFORNIA, SAN DIEGO

CONSENT TO PARTICIPATE IN RESEARCH

Experimental Participant's Bill of Rights

Every individual asked to participate in a research study has the right to be:

1. Informed about the nature and purpose of the study.

2. Provided an explanation of the procedures to be followed in the research study, and whether any of the drugs, devices, or procedures is different from what would be used in standard practice.

3. Given a description of any side effects, discomforts, or risks that you can reasonably expect to occur during the study.

4. Informed about any benefits that would reasonably be expected from the participation in the study, if applicable.

5. Informed about of any alternative procedures, drugs, or devices that might be helpful, and their risks and benefits compared to the proposed procedures, drugs or devices.

6. Told of the types of medical treatment, if any, available if complications should arise.

7. Provided an opportunity to ask any questions concerning the research study both before agreeing to participate and at any time during the course of the study.

8. Informed that individuals can refuse to participate in the research study. Participation is voluntary. Research participants may refuse to answer any question or discontinue their involvement at any time without penalty or loss of benefits to which they might otherwise be entitled. Their decision will not affect their right to receive the care they would receive if they were not in the experiment.

9. Provided a copy of the signed and dated written consent form and a copy of this form.

10. Given the opportunity to freely decide whether or not to consent to the research study without any force, coercion, or undue influence.

If you have any concerns or questions regarding the research study, contact the researchers listed at the top of the consent form.

If you are unable to reach a member of the research team and have general questions, or you have concerns or complaints about the research study, research team, or questions about your rights as a research participant, please contact:

- UC San Diego Office of IRB Administration at irb@ucsd.edu or 858-246-4777