Informed Consent for NCT03750968

Lutein & Zeaxanthin in Pregnancy – Carotenoid Supplementation during Pregnancy: Ocular and Systemic Effects

The following pages contain the most up to date version of the informed consent that was approved by the IRB for this study. It was approved with our 2021-2022 annual renewal. Consent approval date: 12 January 2022.

Consent and Authorization Document

for Minimal Risk Research

Study Title: Lutein & Zeaxanthin in Pregnancy (L-ZIP) - Carotenoid Supplementation During Pregnancy: Ocular and Systemic Effects

Study Doctors:

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CONCISE SUMMARY

You are being asked to take part in a research study because you are receiving prenatal care and planning to deliver your baby at the University of Utah. It is your choice whether to be in the study or not. You will get standard medical care for your pregnancy even if you decide not to join the study.

The purpose of the study is to find out if prenatal supplements containing lutein and zeaxanthin are more beneficial to pregnant mothers and their infants than prenatal supplements without lutein and zeaxanthin.

The study will last throughout your pregnancy and will finish after the delivery of your baby. You will either be assigned to a treatment group that takes a softgel containing carotenoids (lutein and zeaxanthin) and safflower oil or an identical looking softgel that contains only safflower oil. Both groups will also receive a Prenatal Multi + DHA capsule. You have a 50/50 chance of being assigned to either group. Everyone in the study gets standard medical care for their pregnancy, including prenatal vitamins, in addition to getting the study supplement.

We will ask you to complete 4 study visits, which will include being seen at the OB clinic and the Moran Eye Center. At each visit we will collect a blood sample from you, take photos of the inside of your eyes and do a skin scan. For the final study visit (when your baby is 0 – 2 weeks old) we will collect a sample of umbilical cord blood after delivery and a blood sample from you. We will take photos of both your and your baby's eyes and do the skin scan on you and your baby. All of the study procedures are described in more detail later in this document.

The risks of being in the study are very similar to standard medical care for you and your baby. You may receive useful information about the health of your eyes and your baby's eyes. It's also possible the study supplement could help you or your baby. The risks and benefits are described in more detail later in this document. If you think you want to be in the study, you should read the rest of this document and discuss it with the study team.

BACKGROUND

Before you decide it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether you want to volunteer to take part in this study.

WHY IS THIS STUDY IMPORTANT?

The macula is an oval-shaped colored area near the center of the retina of the human eye. Because the macula is yellow in color, it absorbs excess blue and ultraviolet light and acts as a natural sunblock for this area of the retina. The yellow color is caused by the carotenoids lutein and zeaxanthin. Carotenoids are taken up from the diet where they exist in particularly high concentrations in green leafy vegetables and orange-yellow fruits. There is some evidence that these carotenoids protect the macula from some types of macular degeneration.

Researchers have recently shown that the macular pigment is detectable immediately after birth, correlates with zeaxanthin levels in the blood of the infant and the mother, and progressively increases through the first seven years of life. This suggests that the macular carotenoids play functional and protective roles throughout our lives and may be particularly important during infant visual development.

Pregnant women worldwide take prenatal supplements; but most prenatal supplementation guidelines are not yet supported by clinical research. Lutein and zeaxanthin are certified by the FDA as "Generally Recognized As Safe" in a variety of human supplements, including infant formulas and prenatal supplements.

The last trimester of pregnancy is when the mother transfers some of her carotenoid stores to the developing infant through the placenta, potentially putting her at risk for depletion of carotenoids.

Researchers don't know for sure what happens to mothers' carotenoid levels in the blood throughout pregnancy and no research has been done before about macular pigment levels in the eye during pregnancy. Some, but not all, studies report lower blood carotenoid levels in pregnant women. Some researchers have reported that mothers who did not take lutein or zeaxanthin supplements during pregnancy had about a 20% reduction of carotenoids in the skin at the time of delivery when compared to non-pregnant adults who were not taking supplements.

The main goal of this study is to measure the carotenoid levels of mothers during pregnancy and to determine if taking supplements prevents carotenoid depletion in mothers.

STUDY PROCEDURES

This study will involve a study visit during each trimester of your pregnancy and a final study visit after your baby is born, for a total of 4 study visits. If you agree to take part in this study (and your obstetrician approves) we will ask you to sign this consent form and review your health history to make sure you qualify to be in the study.

If you qualify, you will be assigned to either the Carotenoid Group or the Control Group. You will have an equal chance of being assigned to either group. Neither you nor the study team will know which type of supplement you are receiving.

The Carotenoid Group will receive a commercially available prenatal vitamin plus a softgel containing lutein, zeaxanthin and safflower oil. The Control Group will receive the same prenatal vitamin plus a softgel containing only safflower oil.

Below is the schedule of study procedures we will ask you to complete. A description of the procedures follows.

	Screening/ Baseline	**Maternal Supplementation**		
Visit:	**1st Trimester**	**T2**	**T3**	**Birth**
Timeframe:	Before week 14 of pregnancy	Week 22-26 of pregnancy	Week 37-39 of pregnancy	Week 0-2 after delivery
Informed Consent	X			
Randomization	X			
Maternal visual acuity and contrast sensitivity	X	X	X	X
Maternal diet questionnaire	X	X	X	X
Dilated eye examination	X			
Maternal serum carotenoids	X	X	X	X
Maternal macular pigment imaging	X	X	X	X
Maternal skin carotenoids	X	X	X	X
Dispense prenatal supplement & do pill counts	X	X	X	X
Infant cord blood carotenoids				X
Infant macular pigment imaging				X
Infant foveal imaging (sdOCT)				X
Infant skin carotenoids				X

- **Maternal visual acuity and contrast sensitivity** – We will check your vision by testing how well you can see letters on a chart.
- **Maternal diet questionnaire** – At each study visit we will ask you to complete a food questionnaire.
- **Dilated eye examination** – One of your eyes will be chosen as the "study eye". We will dilate your study eye to examine the inside. We will also check your eye pressure.
- **Maternal serum carotenoids** – We will collect a blood sample (5.0 mL or about 1 teaspoon) from you to test your level of carotenoids. Whenever possible the blood samples for this study will be taken at the same time you are having your blood drawn for your routine prenatal blood work so you don't have to have another needle stick.
- **Maternal macular pigment imaging** – We will use a specialized camera (similar to cameras used to take routine pictures of the inside of your eye) to measure the amount of carotenoids you have in your macula. The macula is the area of keenest vision in the eye. This camera uses a software program that is not yet FDA approved and is used for research purposes only.
- **Maternal skin carotenoids** – We will measure the carotenoid levels in your skin with a scanner that uses a painless blue laser light for exposure of the skin and a photodetector for scattered light. We will ask you to hold the palm of your hand against a small optical module for less than a minute to take a reading. This scanner is not FDA approved and is used for research purposes only.

  Dr. Bernstein, the principal investigator, has a significant financial interest in this technology, as determined by the University of Utah conflict of interest policy. If you require more information regarding the financial arrangements described in this paragraph, you should discuss the matter with the investigator, Dr. Bernstein, who can be reached at 801-581-4069; or you may contact the Conflict of Interest Office at 801-587-3232.
- **Dispense prenatal supplement and do pill counts** – At each visit we will give you a 3 month supply of prenatal supplements with instructions to take one capsule and one softgel daily. We will ask you to bring your supplement bottles with you to your study visits. At your final study visit we will give you your final 3 month supply of prenatal supplements.
- **Infant cord blood carotenoids** – Cord blood is routinely collected for all deliveries at the University of Utah. For this study, we will collect about ¼ teaspoon from your baby's umbilical cord at the time of delivery. This sample will be used to measure the amount of carotenoids in your baby's blood.
- **Infant macular pigment imaging and foveal imaging (sdOCT)** –We will take pictures of the inside of your baby's eyes. Your baby's eyes will need to be dilated for these pictures. A lid speculum to hold the eyelids and proparacaine drops to numb the eye may be used if necessary during the imaging.
- **Infant skin carotenoids** – We will measure your baby's carotenoid levels in the skin by scanning the sole of his/her foot.

Optional Specimen Collection and Banking

1. We would like to collect a sample of placenta tissue at the time of delivery and put it in a tissue bank so that other researchers can use it in the future. Normally the placenta is discarded after delivery. The future research done on your placenta sample will help us learn more about how carotenoids are transferred from mothers to their infants.

2. We would like to collect a saliva sample from you and put it in a tissue bank so that other researchers can use it in the future. The future research done on this sample will help us learn more about the genetics of carotenoid metabolism enzymes. This sample can be collected at any time during the study.

3. We would like to store some of your blood we collect during the study visits and put it in a tissue bank so that other researchers can use it in the future. The future research done on your stored blood sample will help us learn more about the genetics of carotenoid metabolism enzymes.

Your sample(s) will be kept by Dr. Bernstein who manages the tissue bank at the University of Utah. Because the results from future research will not directly affect your health care, you will not receive any results from this part of the research.

Your sample(s) will be coded so that your name is not on the sample. Dr. Bernstein and the University of Utah will keep your name in a separate place so that we can link your sample(s) back to you later if we need to. Your sample(s) may be shared with researchers at the University of Utah and at other institutions. Dr. Bernstein will not give your name to other researchers who want to use your sample(s), but will only give them information like your age, and the carotenoid measurements in your eyes and blood and your baby's eyes and blood.

You can choose to provide any or none of these samples and still participate in the main part of this study. Your choice will have no effect on the care you receive. Please indicate your choices at the end of this consent form.

You can have your sample(s) removed from this tissue bank later. You will need to contact Dr. Bernstein at 801-581-4069.

Blood and tissue samples obtained from you in this research may help in the development of a commercial product by the University of Utah or its research partners. There are no plans to provide financial compensation to you should this occur.

RISKS

- **Carotenoid and Control Supplements –** Both kinds of supplements are within the standard of care you would receive if you were not in the study. They pose no additional risk to you.
- **Visual acuity and contrast sensitivity –** These are routine vision tests and pose no risk to you above your standard medical care.
- **Eye (ophthalmic) imaging –** Light levels projected on the retina during the photographs and macular pigment measurements are well within established safety limits. You may notice a central dark spot in your vision similar to the afterimage generated by a camera flash. This will fade in about 5 minutes. Your infant may experience discomfort during the macular pigment imaging and foveal imaging. You may feel emotional distress when observing your infant undergoing this safe examination.

  Although the photographs of your eye and your baby's eyes are being taken for research purposes only, they will be stored in your medical record at the University of Utah, where we normally keep ophthalmic photographs. Your name and medical record number will be attached to the images. The images will only show the inside of your eye, not your face.
- **Carotenoid skin measurements –** There are no expected risks from the light exposure from the skin measurement. It is important not to look directly at the laser for a long period of time.
- **Blood draws –** Whenever possible the blood samples for this study will be taken at the same time you are having your blood drawn for your routine prenatal blood work. The blood sample from your baby's umbilical cord will be taken at the same time blood is collected for his/her routine care.
- **Eye exams –** The dilation drops used for the exams are considered standard of care for dilated eye exams during pregnancy.
- **Food questionnaires and supplement logs –** recording your diet and supplement intake will take a few minutes of your time, but poses no risk to you.
- **Risks of genetic testing and sample banking** – There is a risk of loss of confidentiality, but procedures are in place to make this highly unlikely.

UNFORESEEABLE RISKS

In addition to the risks listed above, you may experience a previously unknown risk of side effect.

BENEFITS

We cannot promise any direct benefit for taking part in this study. However, you may possibly receive nutritional benefits from taking the supplements. We hope the information we learn from this study will help us provide better care for pregnant mothers and their infants in the future.

ALTERNATIVE PROCEDURES

You do not have to participate in this study in order to receive medical care for you or your infant.

PERSON TO CONTACT
If you have questions, complaints or concerns about this study, or if you feel you have been harmed as a result of participation, please call Dr. Bernstein at 801-581-4069 or Dr. Varner at 801-581-8425. They may be reached during routine business hours Monday through Friday.

Institutional Review Board: Contact the Institutional Review Board (IRB) if you have questions regarding your rights as a research participant. Also, contact the IRB if you have questions, complaints or concerns which you do not feel you can discuss with the investigator. The University of Utah IRB may be reached by phone at (801) 581-3655 or by e-mail at irb@hsc.utah.edu.

Research Participant Advocate: You may also contact the Research Participant Advocate (RPA) by phone at (801) 581-3803 or by email at participant.advocate@hsc.utah.edu.

VOLUNTARY PARTICIPATION
Research studies include only people who choose to take part. You can tell us that you don't want to be in this study. You can start the study and then choose to stop the study later. This will not affect your relationship with the investigator.

COSTS AND COMPENSATION TO PARTICIPANTS
You will be participating in this study while you are being seen for your regular prenatal care. You will be billed the usual charges for your regular care.

You will not be charged to participate in this study. We will supply you with the prenatal supplements free of charge. You will also receive a $25.00 gift card at the first three study visits and a $50.00 gift card at the final study visit (a total of $125.00).

NEW INFORMATION
Sometimes during the course of a research project, new information becomes available about the topic being studied. If this happens, your research doctor will tell you about it and discuss with you whether you want to continue in the study.

AUTHORIZATION FOR USE OF YOUR PROTECTED HEALTH INFORMATION
Signing this document means you allow us, the researchers in this study, and others working with us to use some information about your health for this research study.

This is the information we will use and include in our research records:

- Demographic and identifying information like name, address telephone number, and email address
- Related medical information about you like past medical and ophthalmic history and present conditions, medications and nutritional supplements you are taking, information from eye examinations, information from your prenatal appointments and information from your labor, delivery and baby's birth

- All tests and procedures that will be done in the study

How we will protect and share your information:

- We will do everything we can to keep your information private but we cannot guarantee this. Study information will be kept in a secured manner and electronic records will be password protected. Study information may be stored with other information in your medical record. Other doctors, nurses, and third parties (like insurance companies) may be able to see this information as part of the regular treatment, payment, and health care operations of the hospital. We may also need to disclose information if required by law.

- 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.

- In order to conduct this study and make sure it is conducted as described in this form, the research records may be used and reviewed by others who are working with us on this research:
  - Members of the research team and University of Utah Health Sciences Center;
  - The University of Utah Institutional Review Board (IRB), who reviews research involving people to make sure the study protects your rights;
  - The study sponsor: The National Eye Institute at the National Institutes of Health
  - The Food and Drug Administration, who is authorized to ensure the integrity of the research

- If we share your identifying information with groups outside of University of Utah Health Sciences Center, they may not be required to follow the same federal privacy laws that we follow. They may also share your information again with others not described in this form.

- If you do not want us to use information about your health, you should not be part of this research. If you choose not to participate, you can still receive health care services at University of Utah Health Sciences Center.

What if I decide to Not Participate after I sign the Consent and Authorization Form?
You can tell us anytime that you do not want to be in this study and do not want us to use your health information. You can also tell us in writing. If you change your mind, we will not be able to collect new information about you, and you will be withdrawn from the research study. However, we can continue to use information we have already started to use in our research, as needed to maintain the integrity of the research.

This authorization does not have an expiration date.

CONSENT:

I confirm that I have read this consent and authorization document and have had the opportunity to ask questions. I will be given a signed copy of the consent and authorization form to keep. **I agree to participate in this research study and authorize you to use and disclose health information about me and my infant for this study, as you have explained in this document.**

Optional placenta sample collection and storage: (please initial your choice)

_____ Yes, you have my permission to collect a sample of placenta tissue and store it for future research.

_____ No, I decline the collection of placenta tissue.

Optional saliva sample collection and storage: (please initial your choice)

_____ Yes, I agree to provide a saliva sample and give my permission to the study team to store it for future research.

_____ No, I decline the collection of a saliva sample.

Optional blood sample storage: (please initial your choice)

_____ Yes, the study team has my permission to store a portion of my blood samples from this study and use it for future research.

_____ No, I do not want my any of my blood samples stored for future research.

_____	_____	_____
Participant's Name	Participant's Signature	Date

_____	_____	_____
Name of Person Obtaining Authorization and Consent	Signature of Person Obtaining Authorization and Consent	Date

INTERPRETER STATEMENT: (For Non-English Speaking Participants Only)
I confirm that I was present as an interpreter for the duration of the consent process for this research study. I confirm that I am qualified and have the necessary skills to provide interpretation between the participant's language and English. By signing this form, I confirm that I provided a full and complete interpretation of the exchange between the researcher obtaining consent and the participant, to the best of my ability.

_____	_____	_____
Name of Interpreter	Signature of Interpreter	Date

Permission to Contact You for Future Research

Initial here _____ if you are interested in learning more about carotenoids and how they affect mothers and their infants and give permission to be contacted by Dr. Bernstein or Dr. Varner's study team for future research. By filling out your contact information below, you are providing the following information to the University of Utah for this purpose. **Agreement to be contacted does not obligate you to participate in any study.**

Name: _____

Address: _____

Phone Number: _____

E-mail: _____