**COMMITTEE SUMMARY**

**RESEARCH STUDY TITLE**: Food As Medicine Everyday Research (FAMER): Evaluating physiological changes associated with a shift toward a whole-foods diet

**PRINCIPAL INVESTIGATOR**: Kim Tippens

**DATE OF REVIEW**: 9/16/14 **IRB NUMBER**: 091614

**NEXT SCHEDULED IRB MEETING DATE**: 10/21/14

This is a summary of the IRB review, recommendations, actions, and decisions. When resubmitting documents, please 1) Indicate on this Committee Summary how each IRB concern has been addressed 2) Use track changes to show revisions in all relevant documents.

For questions regarding this summary, please contact IRB Chair, Liz Sutherland, ND at 503-552-1817.

Thank you for submitting this important study, which has the potential to educate and support participants in making better lifestyle choices. The IRB has voted unanimously to approve this study contingent upon the resolution of the issues described below.

**GENERAL**

Please do a close reading of all submitted documents to ensure abbreviations (such as hsCRP, hs-CRP, CRP-hs) appear consistently throughout and that every time study outcomes are listed, the list is complete. For example, serum carotenoids are first mentioned in the IRQ under Data Analysis Plan even though outcomes are described in earlier sections; lipids are mentioned in the abstract but not in the study hypothesis or Specific Aims (and please define which lipid parameters). Also the terms diabetes and prediabetes often seem to be used interchangeably. Please address this inconsistency.

**PROTOCOL**

The IRB asks that the PI check with NCNM's Legal Counsel (if she has not already done so) regarding the liability issues in this study. Considering the class size, the presence of heat, hot liquids, knives, and the possibility of a participant inadvertently injuring another participant in this crowded setting, the IRB is not certain that NCNM would not be (or even should not be) liable to cover any medical costs incurred.

- Please provide information about the safety standards and equipment in the kitchens of the two non-NCNM study sites.
- The liability status of the two non-NCNM study sites should be made explicit in the consent document.
- Consider holding a meeting that orients participants to the kitchens they'll be working in.

**Inclusion/Exclusion Criteria**

Please expand the exclusion criteria and address the following issues:

- CRP measurements may be affected by many factors including aspirin, cox-2 inhibitors, infection, liver disease, and inflammatory diseases, such as SLE or rheumatoid arthritis.
- Lipid measurements may be affected by fish oil supplements
- What about gluten intolerance or celiac disease?
- Pregnancy is mentioned as an exclusion criterion, but no plan is provided as to what would happen should a participant become pregnant.
- The list of exclusions based on medications is incomplete. The list of medications that have an impact on blood glucose is extensive. What about anti-seizure medications? Does corticosteroid medications include inhaled, intranasal steroids?

**Research Design and Methods:**

- Please provide specific parameters for how prediabetes and at risk for prediabetes are defined. Some information is given in the telephone screening script but is absent from key documents such as the IRQ.

- The IRB has some concerns over the choice of outcome measures. We assume in some instances that cost and the challenges of off-site specimen handling factored into these decisions but we would like clarification. Please note the IRB's questions are not intended as criticism of study design. They are a request to the PI to provide more information in all relevant documents about the thinking that went into the selection of outcome measures based on 1) IRB concerns for appropriate use of participant time, given the availability of more specific tests that would likely yield more accurate data; and 2) the perceived softness of these outcomes with regard to the weight of participant risk. Specifically:
    - Please provide a citation for the serum carotenoids test. It strikes the IRB as an odd outcome measure in a study that does not include more substantial risk measurements.
    - Fasting blood glucose and fasting insulin seem like obvious outcome measures for a study such as this. Did specimen handling constraints influence the PI's decision not to include these tests? Please provide more information.
    - Along the same lines, please help the IRB understand why a non-specific marker (hs-CRP) is the primary outcome measure rather than HBA1C
- In clinical practice, there are known risks to major dietary change, even when an individual is moving from a presumably poor diet to a supposedly better one. The IRB has heard reports of a patient with type 2 diabetes who developed an intestinal obstruction within one week of going on a diet similar to the one encouraged in this study. It is possible that participants with IBS or gastroparesis would not do well on this diet, or that it could lead to the worsening of iron or B12 deficiency symptoms. Please provide an indication that these risks are taken into account in the study design, as well as listing the major risks of significant dietary change in the consent and other relevant documents.
- How are blood samples transported from the two off-site study locations to the lab?
- The blood draw is not always described as fasting. Please ensure consistency in all documents and specifically, this needs to be explicit (and what fasting means) in the telephone screening script, reminder telephone scripts, and the consent, especially given that the consent meeting is also when the first blood draw takes place.
- It is good practice to collect vitals during the fasting blood draws. Will this happen?
- Who will perform the blood draws?
- The IRB understands that juice is usually given after fasting blood draws but it is inconsistent with the study principles. Can a healthier alternative be provided?
- The IRB would like to know why no food frequency questionnaire or adherence data are collected at 12 months.

**Initial Visit**

- Investigators must double check a participant's BMI at this visit. As it currently stands, only the participant's word during the telephone screening is when this important information is gathered.
- The IRB suggests participants are asked to bring their medications and supplements with them for more accurate data collection

**Non-NCNM Data Collection Form**

No FWA numbers are provided but nothing is checked in the list of contingencies in the event of no FWA number.

**Recruitment**

- Recruitment posters need to be more explicit about the term prediabetes and the exclusion criteria
- The IRB understands recruitment will occur at each site, but what steps are in place in case participant numbers are not equal among the study sites?
- There seems some possibility that the recruitment strategy at Mt. Olivet will allow for participation in classes but not the study. How will this be avoided?
- Please define passive and active recruitment

**Incentives:** The payment schedule and total are unclear. Please provide information about the total amount in the IRQ and protocol documents, and include payment schedule information in the timeline table in the consent.

**IRQ**

- Funding information is fuzzy. Please clarify that this study is funded by a foundation within an industry.
- Please provide a brief definition of whole foods tailored to your study population that you will use when communicating on this topic with participants.

- The USDA recommendations for a whole-foods, plant-based diet are not significantly different from the study diet. Please consider either omitting comparisons with the USDA or being more explicit about how the recommendations differ
- **Please ensure all modifications required in this committee summary are reflected in the IRQ.**

**CONSENT/HIPAA AUTHORIZATION**

- The consent needs to explain the participant will be withdrawn from the study if they miss three classes.
- Describe the location where blood draws will take place

**Section: What is the study about?**

- Please do not use the abbreviation Dx
- Move the 2nd paragraph, "The purpose of the study……." to be the first paragraph in this section. Inclusions/Exclusions becomes the second 'paragraph.'
- Under Inclusions, Pre-diabetes or at risk: This needs parentheses and a definition that includes items on the diabetes assessment tool, weight, BMI, high cholesterol, etc. So the phrase in parentheses might read, "For example, information on your weight, cholesterol, …. "

**Section: What will happen during the study?**

- The study schedule table contains terminology such as "outcome visit" that is not meaningful to participants. Please reword.
- The section titles below the table should be changed to match the language used in the table so that the participant can easily map the fuller descriptions of what will happen at each visit with the timeline.
- Data collection is not a useful term for participants. Please make the paragraph titles more friendly. The content of the paragraph can explain that data will be collected.
- It isn't clear whether the Baseline visit on week 1 will include a FAMER class. If not, the baseline visit may need to be called just that, instead of week 1. Then the classes can begin on week 1 for consistency.
- The table needs to include the classes
- Please add the payment schedule
- Data collection visit 1 (Baseline visit) the IRB suggests asking participants to bring their supplements and medications with them for more accurate data collection
- BMI needs to be measured at the consent meeting

**Section: Will I be paid**…..?

- Unclear. Will the participant receive $20 following the baseline visit, or following the first FRAMER class? It seems like it is after class 1 and class 12. The same confusion for the $80. Insert '6 month and 12 month' for clarity.
- Typo: Bob's Red **Mill,** not meal

**Section: Are there any risks?**

- Expand this section based on IRB concerns mentioned above
- Typo: third paragraph, first sentence: participation in **a** cooking class

**Section: Are there any benefits?**

- Free meals are a benefit
- Typo: Third sentence: "…education class with **hands**-on cooking

End of form: delete the last sentence in parentheses, regarding the signature of a parent or legal guardian.

**TELEPHONE SCREENING**

- Clarify inclusion/exclusion criteria
- Explain blood draws are fasting and what that means

**STUDY AD**

Recruitment posters need to be more explicit about both the term prediabetes and the exclusion criteria.

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**COMMITTEE DECISION: _ _X__ INITIAL ____ CONTINUING _ _ RE-REVIEW**

1. **_X__** Contingent approval based on receipt of the described changes. The described changes must be submitted to the IRB for review before approval will be given
2. ___ Defer approval for the described reasons
3. ___ Reject submission for the described reasons

9/19/2014

**Elizabeth Sutherland, ND**
**IRB Chair**

**Date**

**Response to Contingent Approval**

**Research Study Title:** Food As Medicine Everyday Research (FAMER): Evaluating physiological changes associated with a shift toward a whole-foods diet
**Principal Investigator:** Kimberly M. Tippens, ND, MSAOM, MPH
**Clinical Investigator:** Andrew Erlandsen, ND
**Date of Review:** 9/16/14
**Date of Response:** 10/30/14
**IRB Number:** 091614

**GENERAL**
Thank you for your careful review of the FAMER protocol and accompanying documents. The research team greatly appreciates the effort and feedback from the IRB. All documents have been revised as suggested, with special attention paid to editing and formatting to improve consistency of language and readability. Specific changes are outlined below, in response to the requests of the IRB.

**PROTOCOL**
*The IRB asks that the PI check with NCNM's Legal Counsel (if she has not already done so) regarding the liability issues in this study.*

The Principal Investigator has communicated with NCNM's legal counsel regarding the study design and wording on the consent form. Legal counsel (Ronald J. Freidman) suggested revisions to the consent form language in multiple areas, including the signatures statements.

- *Please provide information about the safety standards and equipment in the kitchens of the two non-NCNM study sites.*
  - The non-NCNM study sites include the Banks Community United Methodist Church and the Mt. Olivet Baptist Church community kitchens.

- *The liability status of the two non-NCNM study sites should be made explicit in the consent document.*
  - The original submitted consent form has been reviewed by the NCNM legal team and revised according to their specific recommendations. The included language has been approved by legal counsel.

- *Consider holding a meeting that orients participants to the kitchens they'll be working in.*
  - Thank you for your attention to this important detail. The FAME/ECO groups have a set of kitchen safety standards that have been used for several sessions. These written standards are included with the revised application, and provide an outline for the verbal safety training that is conducted with facilitators and as part of the introductory session for each FAME class (week 1).
  - The Introductory (week 1) FAME class always includes a general orientation session which includes kitchen safety and knife etiquette. The investigators have included the outline for this training with the revised documents. We apologize for neglecting to

include this with the original submission. A description of the week 1 visit has been revised in the protocol on page 11, and to the consent form on page 4, and details about risks associated with participation in FAME classes have been added to the consent form on page 6.

**Inclusion/Exclusion Criteria**

Please expand the exclusion criteria and address the following issues:

- *CRP measurements may be affected by many factors including aspirin, cox-2 inhibitors, infection, liver disease, and inflammatory diseases, such as SLE or rheumatoid arthritis.*
  - In response to the IRB's comments about the target population, the exclusion criteria have been updated to include inflammatory bowel conditions and an enhanced list of medications that may affect CRP levels. Since this is a Pre-post study, we will note in the participant Health History Form of autoimmune disease, but not exclude them specifically.
- *Lipid measurements may be affected by fish oil supplements*
  - When we review participants' supplements during the first visit, we will ask that they keep their regimen consistent if possible throughout the study. We will add to that no new initiation of fish oils should occur during the 12-week FAME portion of the study.
- *What about gluten intolerance or celiac disease?*
  - The majority of the FAME recipes are gluten free. In past classes, the physician leaders prepare gluten free version of recipes upon request for participants with gluten intolerances. However, none of the community kitchens are designated as gluten free kitchens. As such, we have added celiac disease as an exclusion criterion.
- *Pregnancy is mentioned as an exclusion criterion, but no plan is provided as to what would happen should a participant become pregnant.*
  - Blood levels of CRP rise during a healthy pregnancy, and can be a marker of preeclampsia and other disorders if extremely elevated. We are not likely to see extreme elevations associated with complications of pregnancy among women who become pregnant during our 12-week intervention. However, we will ask participants during their follow-up visits if there have been any changes to their health, including becoming pregnant. Women who become pregnant will be excluded from the study after the 12-week intervention, and will not participate in the two follow-up visits.
- *The list of exclusions based on medications is incomplete. The list of medications that have an impact on blood glucose is extensive. What about anti-seizure medications? Does corticosteroid medications include inhaled, intranasal steroids?*
  - Since the proposed study included pre-post evaluation of changes in blood markers within subjects, we will not need to exclude every medication which may be have an effect of CRP or lipids.

- The following specific medications have been added to the list of excluded medications: antidiabetic: *sulfonylureas, metformin, glinides, alpha-glucosidase inhibitors, thiazolidinediones (TZDs), DDP-4 inhibitors, and GLP-1 analogues*, lipid lowering medications: statins (Atorvastatin (Lipitor), Fluvastatin (Lescol), Lovastatin (Mevacor), Pitavastatin (Livalo), Pravastatin (Pravachol), Rosuvastatin (Crestor)Simvastatin (Zocor), bile acid resins (Questran, Colestid, Lopid), fibrates (Atromid, Tricor, Lopid), nicotinic acid (Nicolar, Niaspan), and corticosteroid medications (inhaled or intranasal): *flunisolide, fluticasone, Triamcinolone, Beclomethasone, and budesonide*
- We do not expect to control the medications and supplements that participants take for the duration of their 12-month involvement in this pilot community-based study. A detailed medication and supplement form is included with the baseline visit in order to capture medications that participants may be taking, which have effects on the measured biomarkers, but are not listed as exclusion criteria. This medication form will be reviewed with participants at the outcome visit and at each follow-up visit, so that changes can be documented.

**Research Design and Methods:**

The investigators have made a few noteworthy changes in order to streamline data collection and address some of the IRB concerns. The number of venous blood draws has been reduced, and several measures will now be collected using blood spot tests from ZRT Laboratory. This will allow do the inclusion of insulin measurement, and fasting glucose will be measured using glucometers at each site. Serum carotenoids will still require venous blood draw, but will only be conducted among the participants who attend classes at Charlee's Kitchen at NCNM. Finally, the investigators have added the FAME Assessment Survey to the baseline and week12 study visits. Further details are provided below.

- *Please provide specific parameters for how prediabetes and at risk for prediabetes are defined. Some information is given in the telephone screening script but is absent from key documents such as the IRQ.*
  - A clear definition of prediabetes has been added to the protocol, telephone screening script, and consent form.
  - We have clarified the risk test in the IRQ with a clear definition of prediabetes, and ensured that this information is consistent across all documents.

- *The IRB has some concerns over the choice of outcome measures.*
  - Insulin and glucose: Specimen handling and budgetary constraints did greatly influence our original design and data collection strategy. However, this revised protocol includes the use of blood spot tests for all measures apart from carotenoids. We will now be able to collect fasting levels of hemoglobin A1c, hs-CRP, lipids, and insulin with a single drop of blood. We have also added a separate test for fasting blood glucose, which will collected with a second drop of blood using glucometers.
  - Carotenoids: Section D.5 of the protocol includes several citations for measurement of serum carotenoids. In summary, carotenoids are a class of organic pigments found in plants that serve as biomarkers of fruit and vegetable intake. These potent antioxidants

have protective effects on cardiovascular disease, especially when taken in their naturally occurring form. The rationale for this exploratory measure has been expanded on page 10 of the protocol.

- hs-CRP: The proposed study includes a 12-week intervention and observation period with follow-up visits at six and 12 months after baseline. Twelve weeks is not long enough to capture significant changes in hemoglobin A1c, and this pilot community-based study is not powered to detect differences in HbA1c at 12 weeks. Based on previous research conducted at Helfgott along with published literature, we expect that hs-CRP is more sensitive to diet changes. As such, we have powered our study to detect difference in hs-CRP at 12-weeks.

- *In clinical practice, there are known risks to major dietary change, even when an individual is moving from a presumably poor diet to a supposedly better one. The IRB has heard reports of a patient with type 2 diabetes who developed an intestinal obstruction within one week of going on a diet similar to the one encouraged in this study. It is possible those participants with IBS or gastroparesis would not do well on this diet, or that it could lead to the worsening of iron or B12 deficiency symptoms. Please provide an indication that these risks are taken into account in the study design, as well as listing the major risks of significant dietary change in the consent and other relevant documents.*
  - We appreciate the reviewer's consideration of these issues. The investigators have not found evidence in the scientific literature to suggest that an educational intervention promoting increased consumption of whole foods and eating fewer processed foods poses risk to an individual's health. The proposed study does not include a major dietary change intervention. This is an educational intervention where participants eat one meal together each week, as opposed to a feeding study with significant abrupt changes to one's personal eating pattern.
  - Participants will have only one meal per week provided for them. The diet that is promoted is one low in processed foods and high in plant-based foods. However, the diet is not vegan or vegetarian, and healthy meat options are discussed throughout the curriculum. As such, we do not expect this diet to significantly lower vitamin B12 levels.
  - This study will not include type 2 diabetics, as it is one of our exclusion criteria. Active inflammatory bowel disease is also an exclusion criterion for participation.

- *How are blood samples transported from the two off-site study locations to the lab?*
  - The study design has been modified to include blood spot cards and test strips for collection of blood samples at community sites.
  - Venous blood draws for measurement of serum carotenoids will only occur at the Helfgott Research Institute with the Charlee's Kitchen subgroup (approximately 20 people). All phlebotomy will occur in the Helfgott clinic room and processed in the Helfgott lab before transport to Craft laboratory.
  - Blood spot cards will be mailed back to ZRT Laboratory for analysis according to their specified protocol.

- *The blood draw is not always described as fasting. Please ensure consistency in all documents.*

- All blood samples will be collected in fasting individuals. This language has been made consistent throughout all study documents.

- *It is good practice to collect vitals during the fasting blood draws. Will this happen?*
  - Blood pressure will be collected prior to venous blood draws.

- *Who will perform the blood draws?*
  - Phlebotomy and finger sticks will be performed by licensed naturopathic physicians that are NCNM faculty/staff or trained naturopathic students under the supervision of naturopathic physicians. Dr. Erlandsen and Dr. Tippens will lead all data collection.

- *The IRB understands that juice is usually given after fasting blood draws but it is inconsistent with the study principles. Can a healthier alternative be provided?*
  - Participants will be informed that healthy snacks will be provided. Whole grain crackers, trail mix, and non-artificially sweetened fruit/vegetable juice will be provided during data collection visits. In addition, participants will be advised during scheduling to bring a snack for them to consume after their fasting blood draw.

- *The IRB would like to know why no food frequency questionnaire or adherence data are collected at 12 months.*
  - Thank you for pointing out this oversight. An additional FFQ measurement has been added during the 12-month follow-up visit.

**Initial Visit**

- *Investigators must double check a participant's BMI at this visit. As it currently stands, only the participant's word during the telephone screening is when this important information is gathered.*
  - Participants' height and weight will be measured at the baseline visit. Weight will be measured at each subsequent data collection visit for calculation of BMI.

- *The IRB suggests participants are asked to bring their medications and supplements with them for more accurate data collection*
  - Since there is no medication or supplement intervention in this study, we are not concerned about specific doses of meds/supplements, or with screening for potential interactions with our intervention.
  - We agree that bringing medications and supplements would increase accuracy of data collection. However, this will be very time consuming if done for everyone. During the telephone screening and enrollment, we will ask participants to prepare a list of medications and supplements to review with study staff at the baseline visit. They are also welcome to bring medications and supplements with them if they need help preparing the list. The med/supplement list will be reviewed with participants at each subsequent visit, and changes will be noted. These changes will be considered when assessing changes in biomarkers.

**Non-NCNM Data Collection Form**

*No FWA numbers are provided but nothing is checked in the list of contingencies in the event of no FWA number.*

- While there are two community locations for cooking classes, there will be no non-NCNM staff interacting with study participants for research purposes. We believe that the non-NCNM data collection form is not actually relevant for this study, and has therefore been removed from the application.

**Recruitment**

- *Recruitment posters need to be more explicit about the term prediabetes and the exclusion criteria*
  - The recruitment posters have been revised to include more details about the inclusions and exclusions for participation in the study.
- *The IRB understands recruitment will occur at each site, but what steps are in place in case participant numbers are not equal among the study sites?*
  - The sites will not be compared to one another in any analyses. As such, the class sizes do not need to be equal at each site.
  - If we are unable to fill each location with at least 10 participants, we will consider combining classes and adding an additional class during Spring quarter.
- *There seems some possibility that the recruitment strategy at Mt. Olivet will allow for participation in classes but not the study. How will this be avoided?*
  - There will only be research classes held at the named locations during the Winter quarter. Participants who wish to take the regular FAME class but do not qualify for the research study will be put on a list to be contacted for future FAME classes. Language has been added to the phone script for people to opt-in to being contacted for future FAME classes.
- *Please define passive and active recruitment*
  - Passive recruitment refers to posting flyers in community locations near our class sites and placing advertisement in local newspapers. In addition, advertisements will be posted on the NCNM research site, and linked to an online registration form.
  - Active recruitment methods include engaging community partners to "spread the word" about the research study to their constituents. Our key community partners are the Pastor and church leaders at Mt. Olivet and the store owner at the banks Thriftway, who has had a long standing relationship with the NCNM Food as Medicine Institute.

**Incentives**

- *The payment schedule and total are unclear. Please provide information about the total amount in the IRQ and protocol documents, and include payment schedule information in the timeline table in the consent.*
    - The payment schedule has been clarified in the protocol, telephone screening script, and consent form.

**IRQ**

- Funding information is fuzzy. Please clarify that this study is funded by a foundation within an industry.
    - The language in the IRQ and consent form has been clarified to specify that this study is funded by a donation from Bob and Charlee Moore to the Food as Medicine Institute at NCNM.
- Please provide a brief definition of whole foods tailored to your study population that you will use when communicating on this topic with participants.
    - The FAME curriculum promotes a whole food based diet that focuses on whole, unrefined, or minimally processed foods, this includes fruits, vegetables, legumes, nuts, seeds, whole grains, fish, and meat.
- The USDA recommendations for a whole-foods, plant-based diet are not significantly different from the study diet. Please consider either omitting comparisons with the USDA or being more explicit about how the recommendations differ
    - All comparisons to the USDA recommendations have been deleted.
- **Please ensure all modifications required in this committee summary are reflected in the IRQ.**

**CONSENT/HIPAA AUTHORIZATION**

All suggested edits and revisions have been made, and are noted with track changes on the attached revised consent form. Revisions noted in red were made by the study investigators. Revisions in blue were additionally suggested by legal counsel.

**TELEPHONE SCREENING**

All suggested edits and revisions have been made, and are noted with track changes on the attached revised telephone screening form.

**STUDY AD**

Recruitment posters have been modified as suggested. Revised versions are included with this resubmission.

Thank you for your careful review of the FAMER protocol. Please contact me if there are additional questions concerns related to this application.

Best regards,

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