Document Coversheet

Study Title: Investigating the Impact of Moringa Oleifera Leaf Supplementation on Growth, Nutrition, Lactation, and Inflammation in Kenyan Breastfeeding Mothers and Children

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	4/10/2023
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PROTOCOL TYPE (VERSION 4)

Which IRB

◉ Medical ○ NonMedical

Protocol Process Type

○ Exemption
◉ Expedited (Must be risk level 1)
○ Full

IMPORTANT NOTE: You will not be able to change your selections for "Which IRB" and "Protocol Process Type" after saving this section. If you select the wrong IRB or Protocol Process Type, you may need to create a new application.

See below for guidance on these options, or refer to ORI's "Getting Started" page. Please contact the Office of Research Integrity (ORI) at 859-257-9428 with any questions prior to saving your selections.

Which IRB

The **Medical IRB** reviews research from the Colleges of:

- Dentistry
- Health Sciences
- Medicine
- Nursing
- Pharmacy and Health Sciences
- and Public Health.

The **Nonmedical IRB** reviews research from the Colleges of:

- Agriculture
- Arts and Sciences
- Business and Economics
- Communication and Information
- Design; Education
- Fine Arts
- Law
- and Social Work

Note: Studies that involve administration of drugs, testing safety or effectiveness of medical devices, or invasive medical procedures must be reviewed by the **Medical IRB** regardless of the college from which the application originates.

Which Protocol Process Type

Under federal regulations, the IRB can process an application to conduct research involving human subjects in one of three ways:

- by exemption certification
- by expedited review.
- by full review;

The investigator makes the preliminary determination of the type of review for which a study is eligible. Please refer to ORI's "Getting Started" page for more information about which activities are eligible for each type of review.

The revised Common Rule expanded exemption certification category 4 for certain secondary research with identifiable information or biospecimens. The regulations no longer require the information or biospecimens to be existing. For more information see the Exemption Categories Tool.

PROJECT INFORMATION

0 unresolved comment(s)

Title of Project: (Use the exact title listed in the grant/contract application, if applicable).
If your research investigates any aspect of COVID-19, please include "COVID19" at the beginning of your Project Title and Short Title

Investigating the impact of Moringa oleifera leaf supplementation on growth, nutrition, and inflammation in Kenya: an acceptability and pilot RCT

Short Title Description
Please use a few key words to easily identify your study - this text will be displayed in the Dashboard listing for your study.

Moringa Kenya Pilot

Anticipated Ending Date of Research Project: 12/30/2022

Maximum number of human subjects (or records/specimens to be reviewed) 104

After approval, will the study be open to enrollment of new subjects or new data/specimen collection? ○ Yes ◉ No

SUBJECT DEMOGRAPHICS **0 unresolved comment(s)**

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 0 to 99 years

Study Population:

Describe the characteristics of the subject population, including age range, gender, ethnic background and health status. Identify the criteria for inclusion and exclusion.

Provide the following information:

- A description of the subject selection criteria and rationale for selection in terms of the scientific objectives and proposed study design;
- A compelling rationale for proposed exclusion of any sex/gender or racial/ethnic group;
- Justification for the inclusion of vulnerable groups such as children, prisoners, adults with impaired consent capacity, or others who may be vulnerable to coercion or undue influence.

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

Phase A) Acceptability
Inclusion lactating women 18 years or over, children 6-59 months.
Exclusion inability to feed orally
We anticipate enrolling 10 adults including lactating women and 10 children. All participants will be Kenyan and residing in the region of Kisumu.
Phase B) Pilot RCT
Inclusion criteria: lactating women of at least 18 years of age and their exclusively breastfed infants within 30 days of delivery with informed consent. Children 6-59 months who are orally feeding with caregiver informed consent.
Exclusion criteria: regular maternal consumption of moringa in the month prior to study enrollment, receipt and consumption of food supplementation program, or inability to feed orally; for infant, significant congenital disease, inability to feed orally. For child: inability to feed orally or refusal to eat porridge (>3 days consecutively).
We anticipate enrolling up to 50 mother-infant dyads in each of two arms and 50 children in each of two arms.
We propose starting enrollment as soon as all ethical approvals obtained, personnel hired, and study supplies obtained; there is no additional sample composition of subjects. This study targets women and infants as breastfeeding infants have the potential to receive the greatest benefit from moringa leaf supplementation to their lactating mothers.

Attachments

Indicate the targeted/planned enrollment of the following members of minority groups and their subpopulations. Possible demographic sources: Census Regional Analyst Edition, Kentucky Race/Ethnic Table, Kentucky Population Data.
(Please note: The IRB will expect this information to be reported at Continuation Review time for Pre-2019 FDA-regulated Expedited review and Full review applications):

Participant Demographics

	Cisgender Man	Cisgender Woman	TGNB/TGE	Unknown/Not Reported
American Indian/Alaskan Native:	0	0		
Asian:	0	0		
Black/African American:	0	0		
Latinx:	0	0		
Native Hawaiian/Pacific Islander:	0	0		
White:	0	0		
American Arab/Middle Eastern/North African:				
Indigenous People Around the World:				
More than One Race:				
Unknown or Not Reported:	200	300		

If unknown, please explain why:

all are Kenyan in Kisumu, Western Kenya. Acceptability will focus on lactating mothers and children; Intervention will focus on lactating mothers and their infants and

also children if funding extended. Therefore the majority of participants will be female.

Indicate the categories of subjects and controls to be included in the study. You may be required to complete additional forms depending on the subject categories which apply to your research. If the study does not involve direct intervention or direct interaction with subjects, (e.g., record-review research, outcomes registries), do not check populations which the research does not specifically target. For example: a large record review of a diverse population may incidentally include a prisoner or an international citizen, but you should not check those categories if the focus of the study has nothing to do with that status.

Check All That Apply (at least one item must be selected)

- ☑ Children (individuals under age 18)
- ☐ Wards of the State (Children)
- ☐ Emancipated Minors
- ☐ Students
- ☐ College of Medicine Students
- ☐ UK Medical Center Residents or House Officers
- ☐ Impaired Consent Capacity Adults
- ☑ Pregnant Women/Neonates/Fetal Material
- ☐ Prisoners
- ☑ Non-English Speaking (translated long or short form)
- ☑ International Citizens
- ☐ Normal Volunteers
- ☐ Military Personnel and/or DoD Civilian Employees
- ☐ Patients
- ☐ Appalachian Population

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

- Children/Emancipated Minors
- Students as Subjects
- Prisoners
- Impaired Consent Capacity Adults
- Economically or Educationally Disadvantaged Persons

Other Resources:

- UKMC Residents or House Officers [see requirement of GME]
- Non-English Speaking [see also the E-IRB Research Description section on this same topic]
- International Citizens [DoD SOP may apply]
- Military Personnel and/or DoD Civilian Employees

Assessment of the potential recruitment of subjects with impaired consent capacity (or likelihood):

☐ Check this box if your study does NOT involve direct intervention or direct interaction with subjects (e.g., record-review research, secondary data analysis). If there is no direct intervention/interaction you will not need to answer the impaired consent capacity questions.

Does this study focus on adult subjects with any conditions that present a high *likelihood* of impaired consent capacity or *fluctuations* in consent capacity? (see examples below)

○ Yes ◉ No

If Yes and you are not filing for exemption certification, go to "Form T", complete the form, and attach it using the button below.

Examples of such conditions include:

- Traumatic brain injury or acquired brain injury
- Severe depressive disorders or Bipolar disorders
- Schizophrenia or other mental disorders that involve serious cognitive disturbances
- Stroke
- Developmental disabilities
- Degenerative dementias
- CNS cancers and other cancers with possible CNS involvement
- Late stage Parkinson's Disease
- Late stage persistent substance dependence
- Ischemic heart disease
- HIV/AIDS
- COPD
- Renal insufficiency
- Diabetes
- Autoimmune or inflammatory disorders
- Chronic non-malignant pain disorders
- Drug effects
- Other acute medical crises

Attachments

SUBJECT CHILDREN

0 unresolved comment(s)

SECTION 1. Risk Level

Complete this section and include it with your IRB application submission. *In Kentucky, a child is an individual less than 18 years of age unless the individual is legally emancipated.*

Note: the explanation(s) you are being asked to provide in Section 1 correlate(s) to the risk level you selected in the Risk Level section.

Minimal risk means that the probability and magnitude of the harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life *of a healthy child* or during the performance of routine physical or psychological exams or tests.

FOR FDA REGULATED RESEARCH: Based on the 2013 FDA final rule Subpart D, a placebo control arm of a clinical trial must be approved under either Risk Category 1, Risk Category 3], or Risk Category 4]. FDA does not consider administration of a placebo to offer a prospect of direct benefit to an individual subject under Subpart D, Risk Category 2 [21 CFR 50.52].

Not involve greater than minimal risk.

In the Risk Level section of the IRB Application you indicated your research does not involve greater than minimal risk.

A. Explain why your research does not involve greater than minimal risk:

Risks are: discomfort and bleeding or bruising from capillary stick. Infants and children receive this as a routine physical test in their lifetimes. This is is a routine test for newborn screening at birth and again for blood sugar checks if blood sugars are low and again for hemoglobin assessment between 12-24 months of age.

Additional risks are bloating and/or diarrhea from the consumption of moringa or the placebo; both contain a lot of soluble fiber.

Additional risks are not liking the taste of moringa or placebo.

SECTION 2. Assessment and Evaluation of the Risks

For details, refer to the UK IRB's Policy on Children in Research.

A. Provide justification for the participation of children as research subjects in your study.

We are investigating the effect to their infants of moringa oleifera leaf supplementation to breastfeeding mothers. Infants are thus required participants

B. Has this research been conducted in adults? ◉ Yes ○ No

If yes, is there any indication that the proposed research would benefit, or at least not be harmful to children?

Multiple generations of traditional use of moringa oleifera by adults, children, animals; many studies utilizing moringa oleifera leaf with no significant safety concern to breastfeeding mother or children

C. Indicate how many children you propose to enroll in the study: 320

Note: Whenever possible, involve the fewest number of children necessary to obtain statistically significant data which will contribute to a meaningful analysis relative to the purpose of the study.

Justify this number:

In the United States as an example of a mostly well-resourced population, stunting prevalence in children under five years is 3.5% (UNICEF data from last census 2016).(44) In comparison, in a 2019 cross-sectional survey of Pamoja CBO recipient population in Kisumu (unpublished data, Pamoja CBO 2019) stunting prevalence is 25% in children <5 years. This is comparable to the most recent national level Kenyan data of the region that contains Kisumu (Nyanza region) from the 2014 Kenyan National Demographic Health Survey showing a stunting prevalence of 24.9% in children <5 years of age.(45) We hypothesize that we will see a 75% reduction in stunting prevalence (<-2 LAZ) at 3 months of age in children with moringa-supplemented breastmilk versus controls. We think that moringa supplementation will

increase breastmilk volumes thus increasing infant growth and may lead to improved intestinal health leading to increased absorption of nutrients consumed. Thus, we estimate a change from estimated 25% stunting prevalence to 6.5% stunting; in comparison, this is still double the prevalence of stunting in children under five years in the United States (3.5% UNICEF data 2016). At 80% power, this would require a sample size of 82 infants in each arm. Due to concern for loss to follow up and a possibility of a smaller effect than estimated, we aim to recruit 100 infants in each arm if external funding is obtained. That is 200 infants. We also estimate 50 children 6-59 months in each arm, that is 100 children. We also estimate 10-20 children trying moringa and placebo for the acceptability study. That is a total of 320 children.

D. Check all that apply:

- ☐ My research involves children 6 years of age or older.
- ☑ My research involves children under 6 years of age.

Indicate how assent will be solicited by selecting all that apply:

Assent will be solicited from: ○ All Children ○ Sub-group of children ○ None of the children

I am requesting waiver of the requirement for assent from: ○ All Children ○ Sub-group of children ○ N/A

Indicate justification for waiving assent for these children: (Check all that apply)

- ☐ 1. The intervention or prospect involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the child/children and is available only in the context of the research.
- ☐ 2. The children are not capable of providing assent based on the age, maturity, or psychological state.
- ☐ 3. The capability of the children is so limited that they cannot reasonably be consulted
- ☐ 4. Other (explain)

** If you checked question 3, please explain:

** If you checked question 4, please explain:

E. Unless you are requesting a waiver of the requirement for assent for ALL children, you must answer “yes” to at least one of the following two statements.

Note: All assent forms or scripts must be attached to the “Informed Consent" section of this application. Be sure to save your responses in this section first.

For Children 6-11:
Assent will be obtained verbally. I have attached an assent script for obtaining verbal assent for IRB review.

○ Yes ◉ No

For Children 12-17:
The children will document assent by signing an assent form, or provide assent verbally if approved by the IRB, depending on the circumstances outlined in the application. I have attached an assent form or script for IRB review.

○ Yes ◉ No

F. Explain how study personnel will evaluate dissent (e.g., behaviors that would indicate the child does not want to participate such as moving away, certain facial expressions, head movements, etc.). If your study involves only children under 6 years of age, enter “N/A” below.

N/A

G. Describe how parental permission will be obtained.

Mothers will be approached for consent by a member of the research team. The study will be described and explained to them in their native language. The content of the informed consent will be read to the mothers if necessary. The mothers will receive a copy of the consent and will be encourage to ask questions they may have, the research personnel will ask the mother questions to make sure that she has a clear understanding of the research study. Written or verbal consent for illiteracy will be obtained from the enrolled mother for her and/or her child's participation.

I have attached a parental permission form for IRB review. ○ Yes ◉ No

Parental permission forms must be attached in the “Informed Consent" section of this application. Be sure to save your responses in this section first.

Note that for Risk Category 3 or Risk Category 4 where research involves more than minimal risk without the prospect of direct benefit to the individual child, the permissions of both parents is required unless one parent is deceased, unknown, incompetent, or not reasonably available OR or only one parent has legal responsibility for the care and custody of the child.)

I am requesting

☐ The permission of both parents unless one parent is deceased, unknown, incompetent, or not reasonably available or when only one parent has legal responsibility for the care and custody of the child. **(required for Risk Category 3 or Category 4 Research).**

☑ The permission of one parent even if the other parent is alive, known, competent, reasonably available, and shares legal responsibility for the care and custody of the child. **(permitted for Risk Category 1 or Category 2 Research).**

☐ Waiver of the requirement for signatures on parental permission forms. (Complete the “Request for Waiver of Signatures” questions in the in the Informed Consent/Assent Process/Waivers Section)

☐ Waiver of the requirement for parental permission.

Note: Parental/guardian permission cannot be waived for FDA regulated studies that are greater than minimal risk (Risk Categories 2-4).

Parental Permission Waiver Options

○ Complete the "Request for Waiver of Informed Consent Process” questions in the Informed Consent/Assent Process/Waivers Section.

○ Justify that the research study is designed for conditions or for a subject population for which parental or guardian permission is not a reasonable request (e.g., abused children):

Justify:

H. Describe how study personnel will ensure that a parent is present when the child participates in any research activities.
Note: If the nature of the research is such that it is not appropriate to have a parent present (e.g., research into sensitive personal issues, physical examinations of teenagers, etc.), explain why.

Measurements of infants including capillary stick or stool collection will be done only in presence of mother or designated caregiver.

I. Describe the study personnel expertise for dealing with children at the ages included and whether they are knowledgeable and sensitive to the physical and psychological needs of the children and their families. Explain how the facility in which the research will be conducted is appropriate in relation to environment and/or equipment accommodating to children.

Capillary stick will be performed by a trained study staff member. Stool collection will be performed by the parent or by the same staff member. Anthropometry (measuring weight, length, arm circumference) will be performed by study personnel trained in the proper measurement of infants.

J. If applicable, provide additional information that may support your request to involve children in research.

N/A

SECTION 3. Wards of the State

If you need to activate this section:

- go to the Subject Demographics section;
- select “Wards of State (Children)” in the categories of subjects and controls to be included in your study;
- save that section.

A. 45 CFR 46.409(a)

Please indicate which category describes your research proposal:

- ○ Research is related to subjects’ status as ward of the state.
- ○ Research is conducted in schools, hospitals, or similar setting(s) in which the majority of children involved in the study are NOT wards.

B. 45 CFR 46.409(b)

Federal regulations state that an advocate must be appointed in circumstances where investigators enroll wards of the state for research studies which are greater than minimal risk **specifically risk category 3 or 4**. Please answer the following questions:

a) Will the advocate serve in addition to a guardian or in loco parents?

○ Yes ○ No

b) Check the applicable item:

- ○ Each child will have their own advocate.
- ○ One advocate will serve for all children enrolled in the study.
- ○ N/A

c) Explain why the advocate has the background and experience to serve as an advocate for the study.

d) Federal regulations state that an advocate cannot be associated with the study, investigator or organization. Please provide assurances that the advocate does not meet any of the criteria listed above.

SECTION 4. Children Located Outside the State of Kentucky

Does your study involve children outside the state of Kentucky? ● Yes ○ No

Provide information regarding the state definition of legally authorized representative, child, or guardian, as applicable to the research and to the federal definitions. [If the research is to be conducted in more than one state outside of Kentucky, provide this information for each state.]:

This research will be done in Kisumu, Kenya. We will also obtain ethical approval in Kenya.

Guidance on Consent and/or Authorization by a Legally Authorized Representative
Consistent with Kentucky health care decision statutes for choosing a legally authorized representative for children, the following responsible parties in the order of priority listed shall be authorized to make research participation decisions on behalf of the child: (a) the judicially-appointed guardian of the person, if the guardian has been appointed and if the decisions to be made under the consent are within the scope of the guardianship; (b) the parent of the child.

Definitions
For definitions of “child/children”, emancipated individuals, “legally authorized representative”, “guardian”, “assent”, and “permission”, see the ORI/IRB Informed Consent Standard Operating Procedures (SOP).

PREGNANT WOMEN/NEONATES/FETUSES

0 unresolved comment(s)

For studies involving pregnant women, human fetuses and/or neonates, check the option that best fits your research, then address the questions and requests for information.

☐ **Section 1: Research Involving Pregnant Women or Fetuses**

Research Involving Pregnant Women or Fetuses

A. Explain why the proposed research is scientifically appropriate, including descriptions of any pre-clinical studies on pregnant animals and any clinical studies on non-pregnant women that have been conducted and have provided data for assessing potential risks to pregnant women and fetuses.

B. Select the option that best describes the anticipated risk to the fetus:

- ○ Not greater than minimal; or
- ○ Greater than minimal risk and the risk to the fetus is caused solely by interventions or procedures that hold out the prospect of direct benefit for the woman or the fetus.

C. Provide a rationale for anticipated risk:

D. Explain why any risk is the least possible for achieving the objectives of the research:

E. Select the options that apply:

○ Yes ○ No 1) This research holds out the prospect of direct benefit to the pregnant woman.

○ Yes ○ No 2) This research holds out the prospect of a direct benefit both to the pregnant woman and the fetus; or

○ Yes ○ No 3) This research does not hold out the prospect of direct benefit for the woman or the fetus, but the risk to the fetus is not greater than minimal and the purpose of the research is the development of important biomedical knowledge that cannot be obtained by any other means.

If "Yes" to any of these three questions, informed consent must be obtained from the pregnant woman or her legally authorized representative, but consent from the father is not required. The informed consent process should include a clear explanation regarding the reasonably foreseeable impact of the research on the fetus.

○ Yes ○ No 4) This research holds out the prospect of a direct benefit solely to the fetus.

If "Yes", informed consent must be obtained from the pregnant woman AND the father. The informed consent process should include a clear explanation regarding the reasonably foreseeable impact of the research on the fetus. NOTE: The father's informed consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity, or the pregnancy resulted from rape or incest.

○ Yes ○ No 5) This research will involve individuals under the age of 18 who are pregnant and are not considered emancipated minors.

If "Yes", assent from the pregnant child and permission from her parent or legal guardian must be obtained.

○ Yes ○ No 6) Will there be any inducements, monetary or otherwise, offered to terminate a pregnancy?

○ Yes ○ No 7) Will individuals performing research procedures have any part in any decisions as to the timing, method, or procedures used to terminate a pregnancy?

○ Yes ○ No 8) Will individuals performing research procedures have any part in determining the viability of a fetus?

☑ **Section 2. Research Involving Neonates**

Research Involving Neonates

A. Viable Neonates - A neonate, after delivery, that has been determined to be viable may be included in research only to the extent permitted by and in accordance with the requirement of 45 CFR 46 Subpart A and Subpart D.

◉ Yes ○ No Does your research involve viable neonates?

If yes, you will need to complete the Children subsection before submitting this application (if the Children subsection is not visible, go to the "Subject Demographics" section, checkmark "Children", and save).

B. Neonates of Uncertain Viability AND Nonviable Neonates - Until it has been ascertained whether or not a neonate is viable, a neonate may not be involved in research covered by 45 CFR 46 Subpart B unless the IRB determines that certain conditions are met. Your responses to the following will help the IRB determine whether the conditions are met.

Explain why the proposed research is scientifically appropriate and provide a description of any pre-clinical and clinical studies that have been conducted which provide data for assessing potential risks to neonates.
If not applicable, please enter "N/A".

only mothers will receive the intervention. Studies show increased breastmilk yield and improvement in breastmillk vitamin A levels and anti-inflammatory components with moringa leaf supplementation.

○ Yes ◉ No Will individuals engaged in the research have any part in determining the viability of a neonate?

C. Neonates of Uncertain Viability - Additional Requirements - Select the option that applies to your research.

☑ Not Applicable

○ The research holds out the prospect of enhancing the probability of survival of the neonate to the point of viability, **AND** any risk is the least possible for achieving that objective.

○ The research has the main purpose of the development of important biomedical knowledge, which cannot be obtained by other means **AND** there will be no added risk to the neonate resulting from the research.

Explain the procedures that will be used to obtain legally effective informed consent of either parent of the neonate.

NOTE: If neither parent is able to consent because of unavailability, incompetence, or temporary incapacity, the legally effective informed consent of either parent's legally authorized representative will be obtained. **These procedures must ensure that each individual providing informed consent will be fully informed regarding the reasonably foreseeable impact of the research on the neonate. The father's informed consent need not be obtained if he is unable to consent because of unavailability, incompetence, or temporary incapacity or the pregnancy resulted from rape or incest.**

D. Nonviable Neonates – Additional Requirements - After delivery, a nonviable neonate may not be involved in research covered by 45 CFR 46 Subpart B unless the IRB determines that the following additional conditions are met.

☑ Not Applicable

○ Yes ○ No 1) Will the vital functions of the neonate be artificially maintained?

If "Yes", please explain:

Yes No 2) Does the research include procedures to terminate the heartbeat or respiration of the neonate?

Yes No 3) Will there be any added risk to the neonate resulting from this research?

If "Yes", please explain:

Yes No 4) Is the sole purpose of the research for the development of important biomedical knowledge that cannot be obtained by other means?

If "Yes", please explain:

5) Explain the procedures that will be used to obtain legally effective informed consent of both parents of the neonate.

Note: *If either parent is unable to consent because of unavailability, incompetence, or temporary incapacity, the informed consent of one parent of a nonviable neonate will suffice. The consent of the father need not be obtained if the pregnancy resulted from rape or incest. The consent of a legally authorized representative of either or both of the parents of a nonviable neonate will not suffice.* ***These procedures must ensure that each individual providing informed consent will be fully informed regarding the reasonably foreseeable impact of the research on the neonate.***

☐ **Section 3. Research Involving After Delivery, The Placenta, The Dead Fetus, Or Fetal Material**

Research Involving After Delivery, The Placenta, The Dead Fetus, Or Fetal Material

A. This research proposes to use the following: (Check all that apply)

- ☐ Placenta
- ☐ The Dead Fetus
- ☐ Macerated Fetal Material
- ☐ Cells Excised from Dead Fetus
- ☐ Tissue Excised from Dead Fetus
- ☐ Organs Excised from Dead Fetus
- ☐ Other

If 'Other' Describe:

NOTE: The use of any of the above must be conducted in accordance with any applicable Federal, State, or local laws, regulations, and institutional policies regarding such activities.

B. Yes No Will any information associated with the material identified above be recorded for research purposes in such a manner that living individuals can be identified, directly or through identifiers linked to those individuals?

If "Yes", provide a rationale for the recording of identifiable information [Note: those individuals are considered to be research subjects and all pertinent human subject regulations are applicable to their participation.]:

☐ **Section 4. Research Not Otherwise Approvable Which Presents an Opportunity to Understand, Prevent, or Alleviate a Serious Problem**

Affecting the Health or Welfare of Pregnant Women, Human Fetuses, or Neonates

If the study is Department of Health and Human Services (HHS) funded, or funding by HHS is sought, review by the Secretary of HHS and posting in the Federal Register for public comments and review is required. If this category is applicable, the Office of Research Integrity will prepare and submit a report of IRB review to the appropriate HHS institutional official.

Select all that apply:

- ☐ Neonates
- ☐ Pregnant Women
- ☐ Fetal Material

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

For creating your informed consent attachment(s), please download the most up-to-date version listed in "All Templates" under the APPLICATION LINKS menu on the left, and edit to match your research project.

Additional Resources:

- Informed Consent/Assent Website
- Waiver of Consent vs. Waiver of Signatures
- Sample Repository/Registry/Bank Consent Template

Consent/Assent Tips:

- If you have multiple consent documents, be sure to upload each individually (not all in a combined file).
- If another site is serving as the IRB for the project, attach the form as a “Reliance Consent Form” so the document will not receive a UK IRB approval stamp; the reviewing IRB will need to stamp the consent forms.
- Changes to consent documents (e.g., informed consent form, assent form, cover letter, etc...) should be reflected in a 'tracked changes' version and uploaded separately with the Document Type "Highlighted Changes".
- It is very important that only the documents you wish to have approved by the IRB are attached; DELETE OUTDATED FILES -- previously *approved* versions will still be available in Protocol History.
- Attachments that are assigned a Document Type to which an IRB approval stamp applies will be considered the version(s) to be used for enrolling subjects once IRB approval has been issued.
  Document Types that do NOT get an IRB approval stamp are:
  - "Highlighted Changes",
  - "Phone Script", and
  - "Reliance Consent Form",
  - "Sponsor's Sample Consent Form".

How to Get the Section Check Mark

1. You must:

   a) provide a response in the text box below describing how investigators will obtain consent/assent, and
   b) check the box for at least one of the consent items and/or check mark one of the waivers

2. If applicable attach each corresponding document(s) **as a PDF**.
3. If you no longer need a consent document approved (e.g., closed to enrollment), or, the consent document submitted does not need a stamp for enrolling subjects (e.g., umbrella study, or sub-study), only select "Stamped Consent Doc(s) Not Needed".
4. After making your selection(s) be sure to scroll to the bottom of this section and SAVE your work!

Check All That Apply

- ☐ Informed Consent Form (and/or Parental Permission Form and/or translated short form)
- ☐ Assent Form
- ☐ Cover Letter (for survey/questionnaire research)
- ☐ Phone Script
- ☐ Informed Consent/HIPAA Combined Form
- ☐ Debriefing and/or Permission to Use Data Form
- ☐ Reliance Consent Form
- ☐ Sponsor's sample consent form for Dept. of Health and Human Services (DHHS)-approved protocol
- ☑ Stamped Consent Doc(s) Not Needed

Attachments

Informed Consent Process:

Using active voice, describe how investigators will obtain consent/assent. Include:

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)

- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

Note: all individuals authorized to obtain informed consent should be designated as such in the E-IRB "Study Personnel" section of this application.

Special considerations may include:

- Obtaining consent/assent for special populations such as children, prisoners, or people with impaired decisional capacity
- *Research Involving Emancipated Individuals*
  If you plan to enroll some or all prospective subjects as emancipated, consult with UK legal counsel **prior to submitting this application to the IRB**. Include research legal counsel's recommendations in the "Additional Information" section as a separate document.
- *Research Involving Non-English Speaking Subjects*
  For information on inclusion of non-English speaking subjects, or subjects from a foreign culture, see IRB Application Instructions for Recruiting Non-English Speaking Participants or Participants from a Foreign Culture.
- *Research Repositories*
  If the purpose of this submission is to establish a research repository describe the informed consent process. For guidance regarding consent issues, process approaches, and sample language see the Sample Repository/Registry/Bank Consent Template.

Informed caregiver consent is required for this study. English is the first official language of Kenya followed by Swahili and Luo. Informed consent will be provided in all three languages. In the case of illiteracy, verbal consent with fingerprint or mark by pen will be obtained. Non-English versions of the informed consent will undergo approval by Amref Health in Kenya ESRC from whom we have applied for local ethical approval for this study.
Any complaints can be directed to study personnel and will be brought to the attention of the PI at weekly meetings or immediately if the situation requires. Any complaints can also be directed to the Kenyan IRB (Amref) or to the University of Kentucky Institutional Review Board (only if unable to reach Kenyan IRB). The contact information that all participants will receive for Amref is:
The Research Officer, Amref Health Africa in Kenya
Wilson Airport, Lang'ata Road
Office Tel: +254 20 6994000
Mobile No: 0795746777
Fax: +254 20 606340
P.O Box 30125-00100
Nairobi, Kenya

☐ Request for Waiver of Informed Consent Process

If you are requesting IRB approval to waive the requirement for the informed consent process, or to alter some or all of the elements of informed consent, complete, Section 1 and Section 2 below.

Note: The IRB does not approve waiver or alteration of the consent process for greater than minimal risk research, except for planned emergency/acute care research as provided under FDA regulations. Contact ORI for regulations that apply to single emergency use waiver or acute care research waiver (859-257-9428).

SECTION 1.

Check the appropriate item:

☐ I am requesting a waiver of the requirement for the informed consent process.

☐ I am requesting an alteration of the informed consent process.

If you checked the box for this item, describe which elements of consent will be altered and/or omitted, and justify the alteration.

SECTION 2.

Explain how each condition applies to your research.

a) The research involves no more than minimal risk to the subject.

b) The rights and welfare of subjects will not be adversely affected.

c) The research could not practicably be carried out without the requested waiver or alteration.

d) Whenever possible, the subjects or legally authorized representatives will be provided with additional pertinent information after they have participated in the study.

e) If the research involves using or accessing identifiable private information or identifiable biospecimens, the research could not practicably be carried out without using such information or biospecimens in an identifiable format.

- Private information/specimens are “identifiable” if the investigator may ascertain the identity of the subject or if identifiers are associated with the information (e.g., medical records). This could be any of the 18 HIPAA identifiers including dates of service.
- If not using identifiable private information or identifiable biospecimens, insert N/A below.

☐ Request for Waiver of Signatures

If you are requesting IRB approval to waive the requirement for signatures on informed consent forms, **your research activities must fit into one of three regulatory options**:

1. The only record linking the participant and the research would be the consent document, and the principal risk would be potential harm resulting from a breach of confidentiality (e.g., a study that involves participants who use illegal drugs).
2. The research presents no more than minimal risk to the participant and involves no procedures for which written consent is normally required outside of the research context (e.g., a cover letter on a survey, or a phone script).
3. The participant (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm, the research presents no more than minimal risk to the subject, and there is an appropriate alternative mechanism for documenting that informed consent was obtained.

Select the option below that best fits your study.

*If the IRB approves a waiver of signatures, participants must still be provided oral or written information about the study. To ensure you include required elements in your consent document, use the **Cover Letter Template** as a guide. There is an English and a Spanish version.*

○ **Option 1**

Describe how your study meets these criteria:

a) The only record linking the participant and the research would be the consent document:

b) The principal risk would be potential harm resulting from a breach of confidentiality (i.e., a study that involves subjects who use illegal drugs).

Under this option, each participant (or legally authorized representative) must be asked whether (s)he wants to sign a consent document; if the participant agrees to sign a consent document, only an IRB approved version should be used.

○ **Option 2**

Describe how your study meets these criteria:

a) The research presents no more than minimal risk to the participant:

b) Involves no procedures for which written consent is normally required outside of the research context (i.e. a cover letter on a survey, or a phone script):

○ **Option 3**

Describe how your study meets these criteria:

a) The subject (or legally authorized representative) is a member of a distinct cultural group or community in which signing forms is not the norm.

b) The research presents no more than minimal risk to the subject.

c) There is an appropriate alternative mechanism for documenting that informed consent was obtained.

RESEARCH DESCRIPTION

0 unresolved comment(s)

You may attach a sponsor's protocol pages in the "Additional Information" section and refer to them where necessary in the Research Description. However, each prompt that applies to your study should contain at least a summary paragraph.

Pro Tips:

- **Save your work often to avoid losing data.**
- **Use one of the attachment buttons in this section or under the Additional Information section to include supplemental information with your application. During the document upload process, you will be able to provide a brief description of the attachment.**

Background

Include a brief review of existing literature in the area of your research. You should identify gaps in knowledge that should be addressed and explain how your research will address those gaps or contribute to existing knowledge in this area. For interventional research, search PubMed and ClinicalTrials.gov for duplicative ongoing and completed trials with same condition and intervention(s).

Background and Significance. Childhood undernutrition (low weight for age, low height for age, low weight for height, or micronutrient deficiencies) contributes up to 45% of deaths globally in children under five years and negatively impacts individual and societal health by impairment of long-term health, cognitive capacity, productivity and wage-earning force. Identification of effective, locally available, low-cost, and readily scalable interventions for its prevention remains elusive. Undernutrition may begin in utero due to maternal undernutrition and micronutrient deficiencies. After birth, poor nutrient intake, frequent infectious disease, and poor intestinal health lead to ongoing impaired growth and psychomotor-cognitive development. Intestinal inflammation and reduced gut integrity from chronic exposure to intestinal pathogens leads to Environmental Enteric Dysfunction or EED (aka "tropical sprue"). Large-scale research has increasingly established the role of intestinal inflammation and a leaky gut in stunting, reduced efficacy of oral vaccines, reduced absorption of nutrients, intestinal dysbiosis, and increased morbidity and mortality in childhood undernutrition.
Early intervention within the first 1000 days of life from conception to 24 months may mitigate or reverse the adverse impact of undernutrition and its associated complications. Interventions after 24 months are additionally important to prevent or reverse worsening undernutrition. Potential targets include improving breastmilk quality and quantity for exclusively-breastfeeding infants, increasing the nutrient density of complementary foods for infants and children over 6 months of age, and optimizing intestinal and systemic inflammation to improve nutrient absorption and reduce nutritional needs in all age groups. Accessible and practical interventions that address multiple determinants of undernutrition in regions with high prevalence of maternal and child undernutrition such as the western Kenyan state of Kisumu are a priority.
Moringa oleifera (moringa) is a drought-resistant, rapidly growing, and extremely nutrient dense tree suitable to household- or community-level cultivation in many regions with high rates of childhood and maternal undernutrition. Moringa leaves are a promising local resource to supplement existing low-quality diets with high concentration of complete protein (30g/100g dried leaf), iron (97.9 mcg/g dried leaf), Vitamin A precursors (17.6-39.6mg/100g dried leaf) as well as B vitamins, calcium, and many other essential nutrients and fiber at very low cost. In addition, medicinal claims under investigation demonstrate antimicrobial properties and impacts on metabolism and inflammation including reduced intestinal inflammation in models of colitis. Veterinary and agricultural data have long shown improved lactation, growth, reduced infection, and increased litter yields in animals; however, human studies have been limited in scope, consistency, and quality for this and for the evaluation of micronutrient changes. Limited clinical research shows increased vitamin A levels in infants supplemented directly with low dose (5g) moringa leaf powder with mixed impact on iron levels; adult studies suggest improvements in iron deficiency anemia with differing doses of high dose daily but not weekly moringa leaf powder supplementation. Animal studies examining Moringa leaf supplementation and its impact on breastmilk antioxidants show improved antioxidant catalase activity and vitamin C concentration and decreased marker of fatty acid oxidation malondialdehyde in 25% moringa leaf supplementation to ewes compared to standard alfalfa hay diet in addition to increased milk yield. Dairy cows supplemented with 6% moringa leaves show increased milk fat content and improved unsaturated fatty acid concentration with no changes in protein content. Human studies assessing changes in breastmilk composition with moringa supplementation are not available.
Relevance to Kisumu, Kenya: Our target subjects of Kisumu, Kenya are a rural population with poor water, sanitation, hygiene, high rates of undernutrition and limited access to health resources. They have low Dietary Diversity (availability of adequate varied food groups) leading to additional micronutrient deficiencies. They are mostly subsistence farmers who are not universally acquainted with moringa cultivation or consumption, however we have recently completed a study in Kisumu that shows excellent acceptance and uptake of moringa intensive leaf cultivation and a positive attitude to dried leaf powder consumption (Waterman and Mbullo, manuscript in progress 2020). The wider Kisumu population is the target area of our partner Pamoja Community Based Organization (Pamoja, executive director Patrick Mbullo), which spans three districts in the region of Kisumu comprising some of the highest-needs populations in Kenya. In a 2019 baseline survey of 469 0-59 month old children within Pamoja's catchment area, 25% were stunted, 8% wasted, and 13% underweight (unpublished data, personal communication from Patrick Mbullo). Micronutrient deficiencies are not specifically defined in this population, however an estimated 69% of children under five years in Kenya are iron deficient and 20-39% are estimated to have vitamin A deficiency. Targeting undernutrition in a cost-effective manner is crucially needed in this region; our study will work with the infrastructure and trust of Pamoja and the communities it serves by testing acceptability of moringa leaf consumption in staple food of grain porridge, acceptability of placebo, and conducting a pilot of moringa leaf consumption and its effect on childhood growth, nutrition, and intestinal and systemic inflammation.
Safety: No trial of moringa leaf consumption in children or lactating women has shown significant adverse effects. Cultures all over the world and across centuries have used moringa leaf as food and medicine without reported ill effect at traditional doses. Seed, root, or leaf extract are not the intervention used in this study. They concentrate the biochemically active plant isothiocyanates and phytosterols

and have medicinal effects and may potential toxic effects at extremely high doses. Moringa leaf powder has not yet been shown to interact with HIV medications, and preclinical studies even raise the possibility of improvements in immune function for HIV affected individuals. However unlikely, any serious and unexpected adverse event will be reported to the IRB according to current protocol.
Innovation. Studies to date on the effects of moringa in diabetes and anemia and animal studies that examine the utility of moringa for increased milk and litter yield are of small scale, however high quality large-scale placebo or case-controlled clinical trials to define the impact on infants of moringa leaf powder consumption by breastfeeding mothers are lacking. Moringa has a traditional and agricultural history of use as a galactagogue; despite this and its incorporation into products such as Mother's Milk Tea© and placement on NIH LactMed Lactation Database, this property has not been studied in large clinical trials nor in populations dependent on breastmilk such as in Kisumu. This study will improve and add to existing knowledge of moringa's effect on human breastmilk and will provide novel information on the effect of moringa supplementation to lactating mothers on their infant's intestinal inflammation and health. Further understanding of the acceptability of moringa leaf in a staple food of porridge and more the effect of moringa supplementation on infant and childhood growth, nutrition, and intestinal and systemic inflammation may translate in the future to the cultivation of moringa at the community or household level as an effective resource for the improvement of childhood undernutrition.
Ethical Approval: We have obtained Reliance agreement with University of California, Davis. We will obtain ethical approval from Amref Health Africa Ethics and Scientific Review Committee (application submitted).

Objectives

List your research objectives. Please include a summary of intended research objectives in the box below.

Hypothesis and Aims:
Moringa leaf supplementation in porridge and placebo in porridge will be acceptable to lactating mothers and 6-59 month old children.
Three months of high dose Moringa leaf supplementation to breastfeeding mothers of neonates in Kisumu, Kenya will lead to improved infant growth and nutrition compared to controls.
Aim 1: Determine acceptability, composition, and preference of consumption of moringa and placebo in porridge.
Aim 2: Test the hypothesis that three months of daily moringa leaf supplementation to breastfeeding mothers for infants and to children 6-59 months for themselves will improve childhood growth and nutritional status via measurements of growth, Vitamin A, and iron deficiency.
Aim 3: Assess mechanisms of improved infant and childhood growth and nutritional status as defined by 1) improved intestinal health using biomarkers of Environmental Enteric Dysfunction and prevalence of diarrhea, and 2) improved breastmilk volume and composition.

Study Design

Describe and explain the study design (e.g., observational, secondary analysis, single/double blind, parallel, crossover, deception, etc.).

- *Clinical Research*: Indicate whether subjects will be randomized and whether subjects will receive any placebo.
- *Community-Based Participatory Research*: If you are conducting community-based participatory research (CBPR), describe strategies for involvement of community members in the design and implementation of the study, and dissemination of results from the study.
- *Qualitative research*: Indicate ranges where flexibility is needed, if a fixed interview transcript is not available, describe interview topics including the most sensitive potential questions.
- *Research Repositories*: If the purpose of this submission is to establish a Research Repository (bank, registry) and the material you plan to collect is already available from a commercial supplier, clinical lab, or established IRB approved research repository, provide scientific justification for establishing an additional repository collecting duplicate material. Describe the repository design and operating procedures. For relevant information to include, see the UK Research Biospecimen Bank Guidance or the UK Research Registry Guidance.

We will implement:
A) a short acceptability study of acceptability, adherence, and preference for moringa dried leaf consumption and placebo consumption in porridge. Selection will be from lactating women 18 years and over and children 6-59 months; subjects will come from our target region of Kisumu.

B) a pilot placebo-controlled RCT of mother-infant dyads and their children 6-59 months who present for first postnatal check to two high volume rural maternal and child health centers in Kisumu, Kenya.

Inclusion criteria: lactating women of at least 18 years of age and their exclusively breastfed infants within 30 days of delivery with informed consent. Children 6-59 months of age who are eating food.
Exclusion criteria: regular maternal consumption of moringa, receipt and consumption of food supplementation program, or inability to feed orally; for infant, significant congenital disease, inability to feed orally. For mother or child: inability to orally feed or complete refusal (>3 days) to eat moringa or placebo porridge.
Sample size: 100 infant-mother pairs in each arm (n=400 participants total). 100 children in each arm (n=200)
Intervention:
Mothers: 20g moringa leaf powder vs. placebo in the staple food of porridge consumed daily for three months.Children: 10g moringa leaf powder vs. placebo in porridge consumed daily for three months. Moringa dose will be determined by the upper limit of acceptability in Phase A.

Data collection:
Monthly anthropometrics for mother, infant, and child. These include infant weight, length and maternal and child weight, height/length, and mid-upper arm circumference.
Enrollment and exit quantitative surveys including but not limited to Food Frequency Questionnaire from which we will calculate Dietary

Diversity Score.
Mother, infant and child finger or finger/ heel stick for hemoglobin and capillary blood collection at study enrollment and exit.
Mother, infant and child feces collection at study enrollment and exit.
Daily recording by parent in provided diary of daily moringa percent consumption, incidence of diarrhea, diagnosis by health professional of medical condition in mother, infant, or child.
Lactating Women:
24 hour volume of breastmilk at study enrollment and exit
Breastmilk sample collection (est. 5ml) at study enrollment and exit

We would like to complete one more anthropometric measurement (weight and length) of enrolled infants in the next few months; this is 8-12 months from study start.

Attachments

Subject Recruitment Methods & Advertising

Describe how the study team will identify and recruit subjects. Please consider the following items and provide additional information as needed so that the IRB can follow each step of the recruitment process.

- How will the study team identify potential participants?
- Who will first contact the potential subjects, and how?
- Will you use advertisements? If so, how will you distribute those?
- How and where will the research team meet with potential participants?
- If applicable, describe proposed outreach programs for recruiting women, minorities, or disparate populations.
- How you will minimize undue influence in recruitment?
- Attach copies of all recruiting and advertising materials (emails, verbal scripts, flyers, posts, messages, etc.).

For additional information on recruiting and advertising:

- IRB Application Instructions - Advertisements
- PI Guide to Identification and Recruitment of Human Subjects for Research

Phase A)
We will recruit adults and children from communities in the population of Pamoja Community Based Organization.
Phase B)
We will recruit mothers and their infants and children 6-59 months at two regional health centers. At the regional health center, mothers arrive for their postnatal visits with their babies and for well child checks. With regional health center approval, study personnel will approach potentially eligible mothers and provide face-to-face informed consent by written and verbal means. The study personnel will speak in the mother's language (English, Swahili, or Luo). Mother will provide consent for herself and her eligible infant and child. The study personnel will clearly communicate that we are not her medical care team, and that the potential study participant may choose not to enroll and that this will not affect her or her infant or child's medical care in any way.
no advertising

Attachments

Research Procedures

Describe how the research will be conducted.

- What experience will study participants have?
- What will study participants be expected to do?
- How long will the study last?
- Outline the schedule and timing of study procedures.
- Provide visit-by-visit listing of all procedures that will take place.
- Identify all procedures that will be carried out with each group of participants.
- Describe deception and debrief procedures if deception is involved.

Differentiate between procedures that involve standard/routine clinical care and those that will be performed specifically for this research project. List medications that are explicitly forbidden or permitted during study participation.

Phase A)
Participants will be offered unlabelled variations of porridge with moringa and/or with placebo. Participants will eat the portion. Utilizing standard questionnaires, participants will verbally or by writing rate their preferences and opinions of these variations in regards to acceptability, palatability, and adherence of each variation of porridge.
Phase B)
Participants regularly receive postnatal appointments at their health center for routine child check with health center staff. During this visit, our trained study personnel will enroll the participants and separately perform anthropometrics (weight, height or length, mid upper-arm circumference), collect blood, fecal, and breatsmilk sample, and distribute study supplies. At monthly visits (month 1, 2, exit visit at month 3), followup will occur at the participant's study site. At these visits, study staff will perform anthropometrics, review porridge and/or moringa consumed, review parental diary, distribute study supplies, and at end visit will again collect blood, fecal, and breastmilk samples as applicable. Compliance with porridge-moringa ratio will be assessed by review of parent recorded amount consumed in the diary and direct visualization of percentage of porridge and leaf powder remaining prior to distribution. This will occur via verbal recall for parents identifying as illiterate.
Biological samples of mothers, infants and children (blood by heel stick or finger stick and stool) will be collected by trained study personnel at the presenting health center on enrollment and exit (3 months). Hemoglobin will be assessed by Hemoccue© utilizing a capillary (heel or finger) stick with direct readout. Capillary blood by heel or finger stick will be transferred to special paper and dried appropriately to create Dried Blood Spots by a standardized process and/or stored in aliquot containers. Fecal collection will occur on the day of monthly presentation to the health center, or kits and instructions will be given to caregivers and the stool collected by study personnel in the participant's village. Hemoglobin will be recorded to the nearest 0.1 g/dL by Hemoccue©. Stool, breastmilk, andblood samples will be immediately chilled and transported to Kenya Medical Research Institute Lab (KEMRI) in Kisumu, processed, and stored at -80 degree C freezers until transport. Samples will then be shipped on dry ice to the University of Kentucky or to the contracted laboratory for analysis. Breastmilk will be transported to Eurofin Laboratories or the laboratory of analysis. Breastmilk volume will be performed at enrollment and exit by 24 hour breastmilk volume pumped by hand pump that we supply and measured with the milk subsequently fed to the infant.

We would like to complete one more anthropometric measurement (weight and length) of enrolled infants in the next few months; this is 8-12 months from study start. This would entail calling previously consented participants, asking them to come to the sub-county hospital, ensuring they agree to and sign the modified informed consent, and performing length and weight in the same method as previously and recording this is Redcap as previously done. We would provide the reimbursement of 500 kenyan shillings, ~ 5USD.

Attachments

Data Collection & Research Materials

In this section, please provide the following:

- Describe all sources or methods for obtaining research materials about or from living individuals (such as specimens, records, surveys, interviews, participant observation, etc.), and explain why this information is needed to conduct the study.
- For each source or method described, please list or attach all data to be collected (such as genetic information, interview scripts, survey tools, data collection forms for existing data, etc.).
- If you will conduct a record or chart review, list the beginning and end dates of the records you will view.

Aim 1: Determine acceptability, composition, and preference of consumption of moringa and placebo in porridge.
Subjects will provide their ratings of taste, texture, visual appearance, palatability.

Aim 2: Test the hypothesis that three months of daily moringa leaf supplementation to breastfeeding mothers will improve infant or to children will improve their own nutritional status via measurements of infant growth, vitamin A, and iron deficiency
Anthropometric Measurements: Weight, height (mothers and children 24 months and older), length (infants and children less than 24 months), head circumference (infants), and mid upper-arm circumference (mothers and children) will be measured by trained study personnel monthly.
Weight: Women will be measured clothed without footwear alone and while holding unclothed infants. Infant weight will be determined by subtracting mother's weight. Children will be measured without clothes except for underwear. The mean of three consecutive measurements will be recorded to the nearest 10g. The scales will be calibrated monthly.
Length/Height: Recumbent length will be measured by a sliding infantometer for infants and children up to 24 months and standing

stadiometer in adult women or children 24 months and older without footwear or headgear. The mean of three consecutive measurements will be recorded to the nearest 0.1cm.
Mid-Upper Arm Circumference (MUAC): MUAC for mothers and children will be measured with a standard WHO-issued tape by measuring midpoint between the relaxed elbow and top part of shoulder then taking a measurement of the circumference of the bent arm at that point. The mean of three consecutive measurements will be recorded to the nearest 0.1 cm.
Head circumference: A standard measuring tape will be extended from the broadest part of forehead to the broadest part of the back of the head for infants. A mean of three consecutive measurements will be recorded to the nearest 0.1cm.
Standardization: For infants and children, weight for age, weight for length/height, and length/height for age will be compared to WHO standard deviation tables or Z scores and assigned their Z score. Wasting is low weight for length/height; stunting is low length/height for age; underweight is low weight for age. These are all measures of undernutrition. Mild undernutrition is defined for any of those parameters as <-1 to and including <-2; moderate undernutrition is <-2 to and including -3; severe undernutrition is <-3. Infants or children with Severe Acute Malnutrition defined as severe wasting (weight or length for height <-3), and/or the presence of nutritional edema will be referred to the nearest nutritional rehabilitation center for treatment as per standard WHO protocol. For mothers, Body Mass Index will be calculated (weight / height squared in metric units) and MUAC recorded.
Quality Control: Participants will be consecutively measured by the same instruments. The study coordinator will perform monthly quality control assessing variance between measurers for all measurements in order to ensure consistent measurement. Retraining and observed measurement will occur for any inconsistencies. Patients who do not arrive for their monthly visits will be contacted to remind them if contact information is available, and then visited at home if unable to come to the health center.
Vitamin A: serum retinol binding protein will survey infant vitamin A levels as an efficient measure of vitamin A at the individual level. (46,47) Other assays of vitamin A are more informative at the population level. Measurement of the systemic inflammatory marker CRP (C-reactive protein) will allow for assessment of Vitamin A with and without correction for inflammation.
Iron: low hemoglobin is a proxy of childhood iron deficiency utilized internationally by UNICEF in LMIC. Iron levels can be measured via their transporters and intermediate forms. Calculation of a transferrin receptor-ferritin index from ferritin and soluble transferrin receptor will lessen the impact of fluctuations in ferritin from inflammation.(48,49)

Aim 3: Assess mechanisms of improved infant or child growth and nutritional status as defined by improved infant intestinal health using biomarkers of Environmental Enteric Dysfunction and prevalence of diarrhea
Sample collection: Baseline and exit visit collection of stool samples, prevalence of diarrhea
Intestinal health measurements: Markers of environmental enteric dysfunction (fecal neopterin, myeloperoxidase, alpha-1- antitrypsin), and prevalence of maternal and infant acute diarrheal illness (>3 watery stools in 24 hours). The rationale for this choice of biomarkers comes from the largest study of markers of environmental enteric dysfunction to date, the MAL-ED cohort, that determined that fecal neopterin, myeloperoxidase, and alpha-1-antiryptsin provide the most sensitive measures of intestinal inflammation and integrity in breastfeeding infants.(50,51) MAL-ED additionally established improved performance of these fecal markers over the previous standard of urine lactulose:mannitol ratio to assess intestinal integrity. These assays will be completed at the UK Biomarker Analysis Laboratory with send-out as needed to UK approved facilities. The impact on intestinal health may also be visible in mothers directly consuming moringa. For this reason, we are collecting maternal stool and analyzing it for the same markers of EED as well as for fecal calprotectin as a measure of intestinal inflammation. In addition to more directly quantifying moringa's impact on intestinal health, icreased maternal intestinal integrity may lead to improved nutrition and impact her breastmilk quality or quantity.

Aim 3: Assess mechanisms of improved infant growth and nutritional status of infants as defined by improved breastmilk volume and composition including Vitamin A precursors and antioxidants.
Sample collection: At exit, maternal breastmilk.
Breastmilk measurements: Volume (24 hour pre and post-breastfeeding infant weights), vitamin A and its precursors (retinols), antioxidants (catalase, Vitamin E, lactoferrin), and nutritional profile (fatty acid profile and protein analysis). Measures of breastmilk volume include assessment of 24 hour breast pumping or hand expression or weighing the infant before and after feeding for 24 hours.(52–56). Breastmilk contains a wide variety of nutrients necessary for growth and multiple bioactive compounds that can dramatically affect infant health by modifying inflammation. Breastmilk components vary according to time from birth as well as maternal nutritional status, dietary intake, and disease states. Compounds that act to modify inflammation include vitamins and their precursors such as Vitamin A, retinols, and Vitamin E, as well as catalase, lactoferrin, and certain fatty acids.(57–59) All assays will be completed in Eurofin Laboratories. Due to the likelihood of moringa to improve any pre-existing maternal vitamin A or iron deficiency and this, in turn, affecting the composition of breastmilk (most notably in vitamin A precursors), we will also collect maternal blood for vitamin analysis.

Attachments

Attach Type	File Name
DataCollection	Data Collection. Table 1 and 2 Timeline and Outcome measures.docx
DataCollection	Data Collection Tools Moringa BF Kisumu.xlsx

Resources

Describe the availability of the resources and adequacy of the facilities that you will use to perform the research. Such resources may include:

- Staffing and personnel, in terms of availability, number, expertise, and experience;
- Computer or other technological resources, mobile or otherwise, required or created during the conduct of the research;
- Psychological, social, or medical services, including equipment needed to protect subjects, medical monitoring, ancillary care, or counseling or social support services that may be required because of research participation;
- Resources for communication with subjects, such as language translation/interpretation services.

This is a single-site project led by Dr. Suzanna Attia with local collaboration from Mr. Patrick Mbullo (see below). Dr. Attia will supervise

the study via virtual technology and will provide training and monthly quality checks with study personnel. Mr. Mbullo will be on-site in Kisumu and will perform day to day site supervision. Kenya has a long history of research and has developed research infrastructure including in Kisumu. Trained, experienced study coordinators from Kenya will coordinate and perform the study. We will utilize laptops with secure passwords in the field and work computers with secure passwords. Dried blood spots, capillary blood samples, and fecal samples will be transferred to the performing laboratory / storage facility. This will be updated with final logistics once arranged. We will receive ethical approval and guidance from Amref Health in Kenya ESRC. This project is funded through the K01 award from NIH NCCIH/Fogarty International Center to Coinvestigator Dr. Carrie Waterman at the University of California, Davis. From this grant, University of Kentucky will receive a contract to cover lab analyses done at the University of Kentucky. UK will not receive any direct funding or subawards. We have obtained Reliance agreement with UC, Davis. Coinvestigator Mr. Patrick Mbullo is a PhD Anthropology Candidate and Executive Director of Pamoja Community Based Organization in Kisumu. Pamoja has worked for decades on improving health outcomes in HIV/AIDS and maternal and child health in the region of our research. Mr. Mbullo and Pamoja will provide cultural and logistical guidance to ensure that our study is culturally sensitive in its approach. Statistical design and analysis is done with the assistance of UK Biostatistician Dr. Aric Schadler.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?
- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

- Describe potential direct benefits to study participants – including diagnostic or therapeutic, physical, psychological or emotional, learning benefits. This cannot include incentives or payments.
- State if there are no direct benefits.
- Describe potential benefits to society and/or general knowledge to be gained.

Describe why potential benefits are reasonable in relation to potential risks. If applicable, justify why risks to vulnerable subjects are reasonable to potential benefits.

Moringa has been eaten by many cultures around the world for many generations. Moringa leaf is safe to eat. Moringa has been used traditionally to help stop pregnancy; although the true effect on pregnancy is unknown and in the first three months after giving birth, pregnancy is extremely unlikely, moringa will be stopped for any women reporting pregnancy.
It is possible that participants like the taste of moringa porridge or non-moringa (placebo) porridge. It is possible that moringa will cause unreported gastrointestinal side effects such as increased stool frequency due to its high fiber content. Moringa eaten at high amounts can help control high blood sugar. We do not know exactly how much is needed to do that, but we know that it has never been shown to cause low blood sugar. Moringa has been studied with some HIV medicine (nevirapine, an antiretroviral) and does not stop the medicine from working. We do not know if moringa does or does not affect all medications. There is a rare risk that eating moringa can change how well the subject's medicines work for any disease. We will ask subjects' caregivers to collect feces and to wash their hands in soap and water after collection to stay clean. If the caregiver does not wash her or his hands well, there is a risk of oral-fecal transmitted diseases. This is a similar risk to changing diapers.
We will provide practices to maintain confidentiality, however breach of confidentiality is a risk.
We do not know if the subject will experience any benefit from taking part in this study. However, some studies have shown improvement in micronutrient deficiencies when eating moringa every day. The subject will also benefit from receiving flour to make porridge every day for three months even if if moringa is not consumed (placebo). We will not offer money in this study. Although we don't know all the benefits, information learned from this study may help other moms, babies, and children in the future. The risks as described above are minimal and outweighed by the potential current and future benefits.

Available Alternative Opportunities/Treatments

Describe alternative treatments or opportunities that might be available to those who choose not to participate in the study, and which offer the subject equal or greater advantages. If applicable, this should include a discussion of the current standard of care treatment(s).

There are no alternative treatments.

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Records, Privacy, and Confidentiality

Specify where the data and/or specimens will be stored and how the researcher will ensure the privacy and confidentiality of both. Specify who will have access to the data/specimens and why they need access.

Describe how data will be managed after the study is complete:

- If data/specimens will be maintained, specify whether identifiers will be removed from the maintained information/material.
- If identifiers will not be removed, provide justification for retaining them and describe how you will protect confidentiality.
- If the data/specimens will be destroyed, verify that this will not violate retention policies and will adhere to applicable facility requirements.

If this study will use de-identified data from another source, describe what measures will be taken to ensure that subject identifiers are not given to the investigator.

If applicable, describe procedures for sharing data/specimens with collaborators not affiliated with UK.

For additional considerations:
Return of Research Results or Incidental Research Findings
HIPAA policies
FERPA policies
Procedures for Transfer agreements
Information regarding multi-site studies
NIH Genomic Data Sharing (GDS) Policy
Digital Data

The investigative team maintains the right to keep, preserve, use and dispose of the findings of this investigation. Investigational records from this study will be maintained in a confidential manner; subject names will not be associated with any published results. Initial data collection will be done by study personnel on password-protected computers. These computers will be stored in locked offices at the Pamoja headquarters. Data will be immediately coded and stored in REDCap on the central servers at Kentucky Children's Hospital and used for analysis. Individual data collection will be password protected and only the research staff and investigator will have access to those files. Any PHI will be securely protected and stored separately from the data, in the locked office (Leader 207) of Mr. Patrick Mbullo and then Dr. Suzanna Attia. Paper containing PHI will be disposed of once the information is coded and no longer necessary for obtaining the required study information in a manner which meets HIPAA compliance and approved by the University of Kentucky Medical Center. In the event of publication of finding, all information to be presented in the literature will not breach confidentiality and participants will remain anonymous.
Steps will be taken to assure confidentiality. De-identified patient data will be stored in REDCap on password-protected devices in the field and transferred to the PI with storage on the central servers at Kentucky Children's Hospital for analysis. We have worked with our information security officials at UK to ensure safe transmission of data. Individual data collection will be password protected and only the research staff and investigator will have access to those files. Codes will be used and PHI will be securely protected and stored separately from the data, in the locked offices of Dr. Suzanna Attia (Leader 207) locally and/or of Mr. Patrick Mbullo in Kisumu, Kenya. Paper containing PHI will be disposed of once the information is coded and no longer necessary for obtaining the required study information in a manner which meets ethical approval. In the event of publication, all information to be presented in the literature will not breach confidentiality and participants will remain anonymous.
Safety: No trial of moringa leaf consumption in children or lactating women has shown significant adverse effects. Cultures all over the world and across centuries have used moringa leaf as food and medicine without reported ill effect at traditional doses. Seed, root, or leaf extract are not the intervention used in this study. They concentrate the biochemically active plant isothiocyanates and phytosterols and have medicinal effects and may potential toxic effects at extremely high doses. Moringa leaf powder has not yet been shown to interact with HIV medications, and preclinical studies even raise the possibility of improvements in immune function for HIV affected individuals. However unlikely, any serious and unexpected adverse event will be reported to the IRB according to current protocol.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Do you confirm that you will retain all IRB-related records for a minimum of 6 years after study closure?
◉ Yes ○ No

Payment

Describe the incentives (monetary or other) being offered to subjects for their participation. If monetary compensation is offered, indicate the amount and describe the terms and schedule of payment. Please review this guidance for more information on payments to subjects, including restrictions and expectations.

We will reimburse transportation to the subcounty hospital up to a maximum of 5USD/500 Kenyan Shillings. We will offer potential benefit from moringa leaf supplementation. We will offer free grain flour to prepare porridge, which is a staple food in Kisumu.

Costs to Subjects

Include a list of services and/or tests that will not be paid for by the sponsor and/or the study (e.g., MRI, HIV). Keep in mind that a subject will not know what is “standard” – and thus not covered by the sponsor/study – unless you tell them.

There are no additional costs to subjects. They will be seen in the regional health clinic when they come for their regularly scheduled medical visit or in their home. In the case of unexpected travel to meet a study personnel (for example to drop off a specimen or obtain measurements with missed Health Center appointment), then we will reimburse transportation up to a maximum of 5USD/500 Kenyan Shillings. We do not anticipate research related injury care.

Data and Safety Monitoring

The IRB requires review and approval of data and safety monitoring plans for greater than minimal risk research or NIH-funded/FDA-regulated clinical investigations.

- If you are conducting greater than minimal risk research, or your clinical investigation is NIH-funded, describe your Data and Safety Monitoring Plan (DSMP). Click here for additional guidance on developing a Data and Safety Monitoring Plan.
- If this is a non-sponsored investigator-initiated protocol considered greater than minimal risk research, and if you are planning on using a Data and Safety Monitoring Board (DSMB) as part of your DSMP, click here for additional guidance for information to include with your IRB application.

The PI and research team will meet weekly to every two weeks discuss progress and any concerns regarding safety, logistics, or enrollment. Adverse events will be reported to the PI who will communicate with each IRB if unanticipated significant reactions are observed. Prompt report (serious) adverse events will be reported to each IRB involved in this project (Amref in Kenya, UC Davis, UK) in a timely manner, and non serious adverse events will be reported upon continuation or annual review.

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Future Use and Sharing of Material (e.g., Data/Specimens/Information)

If the material collected for this study will be used by members of the research team or shared with other researchers for future studies, please address the following:

- list the biological specimens and/or information that will be kept
- briefly describe the types, categories and/or purposes of the future research
- describe any risks of the additional use
- describe privacy/confidentiality protections that will be put into place
- describe the period of time specimens/information may be used
- describe procedures for sharing specimens/information with secondary researchers
- describe the process for, and limitations to, withdrawal of specimens/data

Unidentified biological specimens and data may be used for secondary analysis with no additional risks to participants, no risks to privacy or confidentiality, and with applicable ethical review in place.

Are you recruiting or expect to enroll **Non-English Speaking Subjects or Subjects from a Foreign Culture**? (does not include short form use for incidentally encountered non-English subjects)

(•) Yes ( ) No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

Describe how information about the study will be communicated to potential subjects appropriate for their culture, and if necessary, how new information about the research may be relayed to subjects during the study.
When recruiting Non-English-speaking subjects, provide a consent document in the subject's primary language. After saving this section, attach both the English and translated consent documents in the "Informed Consent" section.

Cultural and Language Consultants:

The PI is required to identify someone who is willing to serve as the cultural consultant to the IRB.

- This person should be familiar with the culture of the subject population and/or be able to verify that translated documents are the equivalent of the English version of documents submitted.
- The consultant should not be involved with the study or have any interest in its IRB approval.
- Please include the name, address, telephone number, and email of the person who agrees to be the cultural consultant for your study.
- ORI staff will facilitate the review process with your consultant. Please do not ask them to review your protocol separately.

For more details, see the IRB Application Instructions on Research Involving Non-English Speaking Subjects or Subjects from a Foreign Culture.

Local Requirements:

If you will conduct research at an international location, identify and describe:

- relevant local regulations
- data privacy regulations
- applicable laws
- ethics review requirements for human subject protection

Please provide links or sources where possible. If the project has been or will be reviewed by a local ethics review board, attach a copy in the “Additional Information/Materials” section. You may also consult the current edition of the International Compilation of Human Research Standards

This study takes place in Kisumu, Kenya. The official languages of this region are English and Swahili. Luo is a tertiary language. Our informed consent has been translated into Swahili and Luo. Study personnel will be able to communicate with the participant in her preferred language of the three. In case of illiteracy, the consent will occur verbally. We will use telephone and in-person communication to relay any new information during the study period. Mr. Mbullo will assure that all study procedures are culturally sensitive.

Does your study involve **HIV/AIDS research and/or screening for other reportable diseases (e.g., Hepatitis C, etc…)**?
○ Yes ◉ No

HIV/AIDS Research

If you have questions about what constitutes a reportable disease and/or condition in the state of Kentucky, see ORI's summary sheet: "Reporting Requirements for Diseases and Conditions in Kentucky" [PDF].

HIV/AIDS Research: There are additional IRB requirements for designing and implementing the research and for obtaining informed consent. Describe additional safeguards to minimize risk to subjects in the space provided below.

For additional information, visit the online IRB Survival Handbook to download a copy of the "Medical IRB's requirements for Protection of Human Subjects in Research Involving HIV Testing" [D65.0000] [PDF], and visit the Office for Human Research Protections web site for statements on AIDS research, or contact the Office of Research Integrity at 859-257-9428.

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

1) involves testing a Nonsignificant Risk (NSR) Device, or
2) is being conducted under an investigator-held Investigational New Drug (IND) or Investigational Device Exemption (IDE)?
○ Yes ◉ No

PI-Sponsored FDA-Regulated Research

If the answer above is yes, then the investigator assumes the regulatory responsibilities of both the investigator and sponsor. The Office of Research Integrity provides a summary list of sponsor IND regulatory requirements for drug trials [PDF], IDE regulatory requirements for SR device trials [PDF], and abbreviated regulatory requirements for NSR device trials [PDF]. For detailed descriptions see FDA Responsibilities for Device Study Sponsors or FDA Responsibilities for IND Drug Study Sponsor-Investigators.

- Describe the experience/knowledge/training (if any) of the investigator serving as a sponsor (e.g., previously held an IND/IDE); and
- Indicate if any sponsor obligations have been transferred to a commercial sponsor, contract research organization (CRO), contract monitor, or other entity (provide details or attach FDA 1571).

IRB policy requires mandatory training for all investigators who are also FDA-regulated sponsors (see Sponsor-Investigator FAQs). A sponsor-investigator must complete the applicable Office of Research Integrity web based training, (drug or device) before final IRB approval is granted.

Has the sponsor-investigator completed the mandatory PI-sponsor training prior to this submission?
○ Yes ○ No

If the sponsor-investigator has completed equivalent sponsor-investigator training, submit documentation of the content for the IRB's consideration.

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ○ Yes ◉ No

(Visit ORI's Health Insurance Portability and Accountability Act (HIPAA) web page to determine if your research falls under the HIPAA Privacy Regulation.)

If yes, check below all that apply and attach the applicable document(s):

- ☐ HIPAA De-identification Certification Form
- ☐ HIPAA Waiver of Authorization

Attachments

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

- FDA approved drugs,
- unapproved use of approved drugs,
- investigational drugs or biologics,
- other compounds or products intended to affect structure or function of the body, and/or
- complementary and alternative medicine products such as dietary supplements, substances generally recognized as safe (GRAS) when used to diagnose, cure mitigate, treat or prevent disease, or clinical studies of e-cigarettes examining a potential therapeutic purpose.

Does this protocol involve a drug including an FDA approved drug; unapproved use of an FDA approved drug; and/or an investigational drug?

○ Yes ◉ No

If yes, complete the questions below. Additional study drug guidance.

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Note: Inpatient studies are required by Hospital Policy to utilize Investigational Drug Service (IDS) pharmacies (Oncology or Non-Oncology). Use of IDS is highly recommended, but optional for outpatient studies. Outpatient studies not using IDS services are subject to periodic inspection by the IDS for compliance with drug accountability good clinical practices.

Indicate where study drug(s) will be housed and managed:

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Is the study being conducted under a valid Investigational New Drug (IND) application?

○ Yes ○ No

If Yes, list IND #(s) and complete the following:

IND Submitted/Held by:

Sponsor: ☐	Held By:	
Investigator: ☐	Held By:	
Other: ☐	Held By:	

☐ Checkmark if the study is being conducted under FDA's Expanded Access Program (e.g., Treatment IND) or if this is an Individual Patient Expanded Access IND (FDA Form 3926).

FDA's Expanded Access Program Information for Individual Patient Expanded Access INDs, and attach the following:

- FDA Form 3926;
- FDA expanded access approval or correspondence;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Expanded Access SOP.

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any

applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

- component, part, accessory;
- assay, reagent, or in-vitro diagnostic device;
- software, digital health, or mobile medical app;
- other instrument if intended to affect the structure or function of the body, diagnose, cure, mitigate, treat or prevent disease; or
- a homemade device developed by an investigator or other non-commercial entity and not approved for marketing by FDA.

For additional information, helpful resources, and definitions, see ORI's Use of Any Device Being Tested in Research web page.

Does this protocol involve testing (collecting safety or efficacy data) of a medical device including an FDA approved device, unapproved use of an approved device, humanitarian use device, and/or an investigational device?

○ Yes ◉ No

[Note: If a marketed device(s) is only being used to elicit or measure a physiologic response or clinical outcome, AND, NO data will be collected on or about the device itself, you may answer “no” above, save and exit this section, (Examples: a chemo drug study uses an MRI to measure tumor growth but does NOT assess how effective the MRI is at making the measurement; an exercise study uses a heart monitor to measure athletic performance but no safety or efficacy information will be collected about the device itself, nor will the data collected be used for comparative purposes against any other similar device).]

If you answered yes above, please complete the following questions.

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

Is the study being conducted under a valid Investigational Device Exemption (IDE), Humanitarian Device Exemption (HDE) or Compassionate Use?

○ Yes ○ No

If Yes, complete the following:
IDE or HDE #(s)

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

☐ Check if this is a Treatment IDE or Compassionate Use under the Food and Drug Administration (FDA) Expanded Access program.

For Individual or Small Group Expanded Access, see FDA's Early Expanded Access Program Information, and attach the following:

- FDA expanded access approval or sponsor’s authorization;
- An independent assessment from an uninvolved physician, if available;
- Confirmation of agreement from manufacturer or entity authorized to provide access to the product.

For guidance and reporting requirements at the conclusion of treatment see the Medical Device SOP.

Does the intended use of any research device being tested (not clinically observed) in this study meet the regulatory definition of Significant Risk (SR) device?

- Yes. Device(s) as used in this study presents a potential for serious risk to the health, safety, or welfare of a subject and (1) is intended as an implant; or (2) is used in supporting or sustaining human life; or (3) is of substantial importance in diagnosing, curing, mitigating or treating disease, or otherwise prevents impairment of human health; or (4) otherwise presents a potential for serious risk to the health, safety, or welfare of a subject.
- No. All devices, as used in this study do not present a potential for serious risk to the health, safety, or welfare of subjects/participants.

Complete and attach the required Study Device Form, picking the "Study Device Form" for the document type. Any applicable device documentation (e.g., Manufacturer information; patient information packet; approved labeling; FDA correspondence, etc.) should be attached using "Other Device Documentation" for the document type.

Attachments

RESEARCH SITES

0 unresolved comment(s)

To complete this section, ensure the responses are accurate then click "SAVE".

A) Check all the applicable sites listed below at which the research will be conducted. If none apply, you do not need to check any boxes.

UK Sites

- ☐ UK Classroom(s)/Lab(s)
- ☐ UK Clinics in Lexington
- ☐ UK Clinics outside of Lexington
- ☐ UK Healthcare Good Samaritan Hospital
- ☐ UK Hospital

Schools/Education Institutions

- ☐ Fayette Co. School Systems *
- ☐ Other State/Regional School Systems
- ☐ Institutions of Higher Education (other than UK)

***Fayette Co. School systems, as well as other non-UK sites, have additional requirements that must be addressed. See ORI's IRB Application Instructions - Off-site Research web page for details.**

Other Medical Facilities

- ☐ Bluegrass Regional Mental Health Retardation Board
- ☐ Cardinal Hill Hospital
- ☐ Eastern State Hospital
- ☐ Norton Healthcare
- ☐ Nursing Homes
- ☐ Shriner's Children's Hospital
- ☐ Veterans Affairs Medical Center
- ☑ Other Hospitals and Med. Centers

- ☐ Correctional Facilities
- ☐ Home Health Agencies
- ☐ International Sites

Research activities conducted at performance sites that are not owned or operated by the University of Kentucky, at sites that are geographically separate from UK, or at sites that do not fall under the UK IRB's authority, are subject to special procedures for coordination of research review. Additional information is required (see IRB Application Instructions - Off-Site Research web page), including:

- A letter of support and local context is required from non-UK sites. See *Letters of Support and Local Context* on the IRB Application Instructions - Off-Site Research web page for more information.
- Supportive documentation, including letters of support, can be attached below.
- NOTE: If the non-UK sites or non-UK personnel are engaged in the research, there are additional federal and university requirements which need to be completed for their participation. For instance, the other site(s) may need to complete their own IRB review, or a cooperative review arrangement may need to be established with non-UK

sites.
- Questions about the participation of non-UK sites/personnel should be discussed with the ORI staff at (859) 257-9428.

List all other non-UK owned/operated locations where the research will be conducted:

This research will be performed in two regional Maternal and Child Health Centers within the region of Kisumu, Kenya. I attach the SMART Reliance agreement with University of California, Davis, as Coinvestigator Carrie Waterman, who is funding the study, is based there.

Describe the role of any non-UK site(s) or non-UK personnel who will be participating in your research.

Attachments

Attach Type	File Name
-IRB Approval (non-UK)	58219 Attia Fully Executed SMART IRB LOA template with signatures 10.15.20.pdf
-IRB Approval (non-UK)	UK Relying Site Form when UK Reviews.pdf
-IRB Approval (non-UK)	UK Communications Plan Form UK reviews.docx

B) Is this a multi-site study for which **you are the lead investigator or UK is the lead site**? ○ Yes ◉ No

If YES, describe the plan for the management of reporting unanticipated problems, noncompliance, and submission of protocol modifications and interim results from the non-UK sites:

C) If your research involves collaboration with any sites and/or personnel outside the University of Kentucky, then it is considered multisite research and IRB reliance issues will need to be addressed. This may include national multi-center trials as well local studies involving sites/personnel external to UK. If you would like to request that the University of Kentucky IRB (UK IRB) serve as the lead IRB for your study, or if you would like the UK IRB to defer review to another IRB, please contact the IRBReliance@uky.edu.

RESEARCH ATTRIBUTES

0 unresolved comment(s)

Indicate the items below that apply to your research. Depending on the items applicable to your research, you may be required to complete additional forms or meet additional requirements. Contact the ORI (859-257-9428) if you have questions about additional requirements.

☐ Not applicable

Check All That Apply

	For additional requirements and information:
☐ Academic Degree/Required Research	• Cancer Research (MCC PRMC) • Certificate of Confidentiality (look up "Confidentiality/Privacy...") • CCTS (Center for Clinical and Translational Science)
☐ Alcohol/Drug/Substance Abuse Research	• Clinical Research (look up "What is the definition of....)
☐ Biological Specimen Bank Creation (for sharing)	• Clinical Trial
☐ Cancer Research	• Collection of Biological Specimens for Banking (look up "Specimen/Tissue Collection...")
☐ CCTS-Center for Clinical & Translational Science	• Collection of Biological Specimens (look up "Specimen/Tissue Collection...")
☐ Certificate of Confidentiality	• Community-Based Participatory Research (look up "Community-Engaged...")
☑ Clinical Research	• Data & Safety Monitoring Board (DSMB) *For Medical IRB: Service Request Form for CCTS DSMB
☐ Clinical Trial - Phase 1	
☑ Clinical Trial	• Data & Safety Monitoring Plan • Deception* *For deception research, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Collection of Biological Specimens for internal banking and use (not sharing)	
☐ Community-Based Participatory Research	
☐ Deception	
☐ Educational/Student Records (e.g., GPA, test scores)	
☐ Emergency Use (Single Patient)	• Emergency Use (Single Patient) [attach Emergency Use Checklist] (PDF) • Genetic Research (look up "Specimen/Tissue Collection...") • Gene Transfer • HIV/AIDS Research (look up "Reportable Diseases/Conditions") • Screening for Reportable Diseases [E2.0000] (PDF) • International Research (look up "International & Non-English Speaking") • NIH Genomic Data Sharing (GDS) Policy (PDF) • Planned Emergency Research Involving Waiver of Informed Consent* *For Planned Emergency Research Involving Waiver of Informed Consent, also go to the E-IRB Application Informed Consent section, checkmark and complete "Request for Waiver of Informed Consent Process"
☐ Gene Transfer	
☐ Genetic Research	
☐ GWAS (Genome-Wide Association Study) or NIH Genomic Data Sharing (GDS)	
☐ Human Cells, Tissues, and Cellular and Tissue Based Products	
☐ Individual Expanded Access or Compassionate Use	
☐ International Research	
☐ Planned Emergency Research Involving Exception from Informed Consent	
☐ Recombinant DNA	
☐ Registry or data repository creation	
☐ Stem Cell Research	
☐ Suicide Ideation or Behavior Research	
☐ Survey Research	
☐ Transplants	
☐ Use, storage and disposal of radioactive material and radiation producing devices	• Use, storage and disposal of radioactive material and radiation producing devices
☐ Vaccine Trials	

FUNDING/SUPPORT

0 unresolved comment(s)

If the research is being submitted to, supported by, or conducted in cooperation with an external or internal agency or funding program, indicate below all the categories that apply.

☐ Not applicable

Check All That Apply

☐ Grant application pending
☑ (HHS) Dept. of Health & Human Services
☑ (NIH) National Institutes of Health
☐ (CDC) Centers for Disease Control & Prevention
☐ (HRSA) Health Resources and Services Administration
☐ (SAMHSA) Substance Abuse and Mental Health Services Administration
☐ (DoJ) Department of Justice or Bureau of Prisons
☐ (DoE) Department of Energy
☐ (EPA) Environmental Protection Agency
☐ Federal Agencies Other Than Those Listed Here
☐ Industry (Other than Pharmaceutical Companies)
☐ Internal Grant Program w/ proposal
☐ Internal Grant Program w/o proposal
☐ National Science Foundation
☐ Other Institutions of Higher Education
☐ Pharmaceutical Company
☐ Private Foundation/Association
☐ U.S. Department of Education
☐ State

Other:

Click applicable listing(s) for additional requirements and information:

- (HHS) Dept. of Health & Human Services
- (NIH) National Institutes of Health
- (CDC) Centers for Disease Control & Prevention
- (HRSA) Health Resources & Services Administration
- (SAMHSA) Substance Abuse & Mental Health Services Administration
- Industry (Other than Pharmaceutical Companies) [IRB Fee Info]
- National Science Foundation
- (DoEd) U.S. Department of Education
- (DoJ) Department of Justice or Bureau of Prisons
- (DoE) Department of Energy Summary and Department of Energy Identifiable Information Compliance Checklist
- (EPA) Environmental Protection Agency

Specify the funding source and/or cooperating organization(s) (e.g., National Cancer Institute, Ford Foundation, Eli Lilly & Company, South Western Oncology Group, Bureau of Prisons, etc.):

This research is supported from K01 funds of UC Davis Coinvestigator Carrie Waterman. We are contracted to provide lab analysis. Dr. Attia (IRB Applicant, UK) is the PI and does not require salary support.

Add Related Grants

If applicable, please search for and select the OSPA Account number or Electronic Internal Approval Form (eIAF) # (notif #) associated with this IRB application using the "Add Related Grants" button.
If required by your funding agency, upload your grant using the "Grant/Contract Attachments" button.

Add Related Grants

Grant/Contract Attachments

The research involves use of Department of Defense (DoD) funding, military personnel, DoD facilities, or other DoD resources. (See DoD SOP and DoD Summary for details)

○ Yes ◉ No

Using the “attachments” button (below), attach applicable materials addressing the specific processes described in the DoD SOP.

DOD SOP Attachments

Additional Certification: (If your project is federally funded, your funding agency may request an Assurance/ Certification/Declaration of Exemption form.) Check the following if needed:

☐ Protection of Human Subjects Assurance/Certification/Declaration of Exemption (Formerly Optional Form – 310)

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

If you check any of the below committees, additional materials may be required with your application submission.

Does your research fall under the purview of any of the other review committees listed below? [*If yes, check all that apply and attach applicable materials using the attachment button at the bottom of your screen.*]

○ Yes ◉ No

Additional Information

- ☐ Institutional Biosafety Committee
- ☐ Radiation Safety Committee
- ☐ Radioactive Drug Research Committee
- ☐ Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)
- ☐ Graduate Medical Education Committee (GME)
- ☐ Office of Medical Education (OME)

- Institutional Biosafety Committee (IBC) - Attach required IBC materials
- Radiation Safety Committee (RSC) - For applicability, see instructions and attach form
- Radioactive Drug Research Committee (RDRC)
- Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC)** - Attach MCC PRMC materials, if any, per instructions.
- Office of Medical Education (OME)
- Graduate Medical Education Committee (GME)

Attachments

**** If your study involves cancer research, be sure to select "Cancer Research" in the "Research Attributes" section.** ORI will send your research protocol to the Markey Cancer Center (MCC) Protocol Review and Monitoring Committee (PRMC). The MCC PRMC is responsible for determining whether the study meets the National Cancer Institute (NCI) definition of a clinical trial and for issuing documentation to you (the investigator) which confirms either that PRMC approval has been obtained or that PRMC review is not required. Your IRB application will be processed and reviewed independently from the PRMC review.

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

Do you want specific information inserted into your approval letter? ○ Yes ◉ No

Approval Letter Details:

If you wish to have specific language included in your approval letter (e.g., serial #, internal tracking identifier, etc…), type that language in the box below exactly as it should appear in the letter. The text you enter will automatically appear at the top of all approval letters, identical to how you typed it, until you update it. Don't include instructions or questions to ORI staff as those will appear in your approval letter. **If these details need to be changed for any reason, you are responsible for updating the content of this field.**

Additional Materials:

If you have other materials you would like to include for the IRB's consideration, check all that apply and attach the corresponding documents using the Attachments button below.

- ☐ Detailed protocol
- ☐ Dept. of Health & Human Services (DHHS) approved protocol (such as NIH sponsored Cooperative Group Clinical Trial)
- ☐ Other Documents

Protocol/Other Attachments

Attach Type	File Name
Other	58219 Attia IR22.pdf

NOTE: Instructions for Dept. of Health & Human Services (DHHS)-approved protocol]

If you have password protected documents, that feature should be disabled prior to uploading to ensure access for IRB review.

To view the materials currently attached to your application, click “All Attachments” on the left menu bar.

Statistical Analysis Plan – 58219

Statistical Analysis: Data analyses were performed using SPSS v28 (IBM Corp. 2021) with graphing via SPSS and Prism GraphPad (v9.5.1). Using an intention-to-treat approach, we performed univariate and multivariable analysis for primary and secondary outcomes as change from baseline per individual/group and between groups. We used Pearson's (for normally distributed data) or Spearman's (for non-normally distributed data) correlation to examine relationships between continuous variables, Pearson's chi square and Fisher's exact tests between categorical variables, and independent t-test or Mann-Whitney U test between binary and continuous variables as appropriate. Paired samples t-tests or Wilcoxon matched-paired sign-rank test were used for paired data. Continuous variables are presented here as mean with standard deviation (if normally distributed) as mean ± SD or median with interquartile range (if not normally distributed) as median, IQR, while categorical variables are presented with counts and percentages. An alpha-level of 0.05 was used to determine significance. All enrolled participants who continued study activities through at least the first month were analyzed regardless of loss to follow up.

IRB Approval
8/25/2021
IRB # 58219
IRB6

KEY INFORMATION FOR Moringa leaf supplementation for improved childhood nutrition and decreased intestinal inflammation pilot Randomized Controlled Trial (Phase B)

We are asking you to choose whether or not to volunteer for a research study to help us learn about how *Moringa oleifera* leaf powder may help babies and children grow. Moringa leaf grows on a tree and is dried and made into powder. It has a lot of vitamins and nutrients in it including iron, vitamin A, and protein. These are important nutrients that a lot of moms don't have enough of when they are breastfeeding their babies or that children may not have enough of from their food. Moringa also helps increase milk production so that moms make more milk. We have seen that moringa can make the milk more nutritious and healthier for baby as well as helping mom make more milk. We know that moringa can help increase vitamins in the body for children. Moringa can be grown at home as a bush or tree. We think it will be very useful for communities in Kisumu to grow moringa and eat it, but we don't know how much eating it can help a baby grow when mom eats it every day and breastfeeds baby or when a child its it directly. That is why we are doing this study.
We would like to mix moringa into grain porridge, as grain porridge is an everyday food. We will do a separate study first to understand what type of moringa or moringa replacement (placebo) porridge is acceptable to eat to parents and children in Kisumu. We are asking you and/or your child to eat moringa in porridge every day for three months or eat porridge without moringa every day for three months. We want to see if breastfeeding babies grow better and are healthier if mom is eating moringa. We also want to see if children grow better and are healthier when they eat moringa. We will ask your child to eat moringa every day in porridge for three months to see if your child is healthier than children not eating moringa. We are asking you because you have a breastfeeding baby and your baby born within the last month and/or because you have a child under five years of age who is already eating food. We are asking permission for your breastfeeding baby and/or your child to be a part of this study with you. We are asking permission to take measurements of growth for your baby and/or your child and your growth. We are asking permission to take a sample from a heelstick from your baby or fingerstick from your child and poop from your baby and/or child at the beginning and end of this study. We are asking some of you to allow us to count the volume of breastmilk you make in a day and to take a few very small samples (a few teaspoons) of breastmilk at the beginning and end of the study to help us understand how moringa makes breastmilk better for baby. This page is to give you key information to help you decide whether to participate. We have included detailed information after this page. Ask the research team questions. If you have questions later, the contact information for the research investigator in charge of the study is below.

In Kisumu:
Mr. Patrick Mbullo, Coinvestigator and Executive Director of Pamoja Community Based Organization, +254 725 668711, mbullo@pamojapamoja.org

In the United States:
Dr. Suzanna Attia, Primary Investigatory, University of Kentucky, +1 859 216 1676, Suzanna.Attia@uky.edu

WHAT IS THE STUDY ABOUT AND HOW LONG WILL IT LAST?

By doing this study, we hope to learn about if and how moringa in porridge eaten by moms compared to porridge without moringa may help their breastfeeding babies grow bigger, increase mom's breastmilk, and improve baby's vitamin levels. We also want to know if the baby's intestine is healthier when mom eats moringa. We also want to know how moringa changes breastmilk and whether it makes breastmilk healthier for baby.

We hope to learn if children eating moringa grow bigger than children who do not and if their vitamin levels and intestinal health is better than children who eat porridge without moringa. This study will last approximately four months for you to agree to the study, your or your child to eat moringa every day for three months, and for us to make sure we have the measurements and information we need to understand if the moringa helps.

In order to have enough information to answer our questions about moringa, we will first ask your permission. Once you agree to participate, we will ask for information such as any medical problems you have. We will collect your and baby and/or child's measurements of growth such as height/length, weight, and arm circumference throughout the study. We will also collect fecal samples at the beginning and end of the study. We will also collect a fingerprick or heelstick sample from you and/or your baby or child at the beginning and end of the study. This is the same type of sample done in many countries routinely for newborn screening for diseases or to check blood counts or blood sugar. We will ask some of you who are breastfeeding to collect

breastmilk for 24 hours and measure how much before feeding it to your baby. We will provide the equipment to do this. We will ask some of you who are breastfeeding to give us a small sample--approximately a teaspoon of breastmilk--at the beginning and end of the study. We will ask you to keep track of how much you or your child eats of the porridge every day and whether during the time of the study you or your baby or child has any illness such as diarrhea, fever, or cough.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE TO VOLUNTEER FOR THIS STUDY?

You may wish to volunteer for this study to help us understand if eating moringa when breastfeeding is helpful for breastfeeding babies or if eating moringa as a child is helpful to improve growth and vitamins in the body of the infant or child. This can help your baby if you receive moringa or your child if he or she receives moringa, and it may help other babies and children in the future. You may wish to volunteer for this study to have the chance that your baby will grow better if you receive moringa or your child will grow better if he or she receives moringa. You may wish to volunteer for this study to have porridge provided to you for three months. For a complete description of benefits, refer to the Detailed Consent.

WHAT ARE KEY REASONS YOU MIGHT CHOOSE NOT TO VOLUNTEER FOR THIS STUDY?

You may choose not to volunteer for this study because you do not wish to share your baby's or child's growth and health information with us, or because you do not want your baby or child to provide the heelprick or fingerstick the poop that we need to understand how well moringa is working. For a complete description of risks, refer to the Detailed Consent and/or Appendix.

DO YOU HAVE TO TAKE PART IN THE STUDY?

If you decide to take part in the study, it should be because you really want to volunteer. You will not lose any services, benefits or rights you would normally have if you choose not to volunteer.

WHAT IF YOU HAVE QUESTIONS, SUGGESTIONS OR CONCERNS?

If you have questions, suggestions, or concerns regarding this study or you want to withdraw from the study contact Dr. Suzanna Attia, Principal Investigator of the University of Kentucky, Department of Pediatrics at Suzanna.Attia@uky.edu. In Kenya, you can also contact Mr. Patrick Mbullo, Coinvestigator and Executive Director of Pamoja Community Based Organization, at mbullo@pamojapamoja.org.

If you have any concerns or questions about your rights as a volunteer in this research, contact staff in the University of Kentucky (UK) Office of Research Integrity (ORI) between the business hours of 8am and 5pm EST, Monday-Friday at 859-257-9428 or toll free at 1-866-400-9428.

DETAILED CONSENT:

ARE THERE REASONS WHY YOU WOULD NOT QUALIFY FOR THIS STUDY?

You would not qualify for this study if your baby was born less than 36 weeks of age, your baby was born with a serious problem such as serious heart disease, your baby can not breastfeed, or you can not or will not eat porridge with or without moringa. Your child will not qualify for this meeting if he or she refuses to eat porridge or cannot eat by mouth.

WHERE WILL THE STUDY TAKE PLACE AND WHAT IS THE TOTAL AMOUNT OF TIME INVOLVED?

The research procedures will be conducted at the Maternal and Child health centers of Kombewa Hospital (Seme subcounty) and Chulimbo Hospital (Kisumu West). You will need to come three to four times during the study. This will be at your regular Maternal and Child Health visit or may mean an extra visit. Each of those visits will take about half an hour. We will also ask you to write details down in a diary about how much porridge you or your child ate every day if not all of it, if you or your baby or child is sick, and other details we need to understand how the moringa is working. The total amount of time you will be asked to volunteer for this study is 40 hours over the next 3-4 months.

WHAT WILL YOU BE ASKED TO DO?

We will assign you and/or your child by chance (randomly) to one of two groups. You will be in the group receiving porridge with moringa or you will be in the group receiving porridge without moringa (placebo). You have a 50% chance of being in one of the groups.

We will give you enough porridge and moringa or its replacement for one month for you and/or your child. We will also give you instructions on how to mix it. We will give you a diary to record the amount of moringa or non-moringa porridge you and/or your child eats per day and if you, your baby, and/or child has diarrhea, a cough, or an illness diagnosed by a health professional.

We will take a heelstick or fingerstick from your baby and/or child (a very small and quick poke to the heel or finger to collect a few drops of blood) and collect and freeze poop from your baby and/or child at the beginning and end of the study. We may ask you for a finger poke for a few drops of blood and to collect a small amount of your poop at the beginning and end of the study. We will use this blood and poop to see if eating moringa helps increase vitamins in the blood and helps keep the intestine healthy. We may freeze your blood and/or poop sample(s).

We will measure your weight and height and mid-upper arm circumference and your baby's and/or child's weight and length at the beginning of the study and once a month until the end of the study. We will use this information to see if eating moringa helps mom and baby and/or child grow.

We will ask a few of you from each group to allow us to count your volume of breastmilk in 24 hours by pumping and measuring the breastmilk and recording it in a diary before you feed your baby the breastmilk once a month. We will give you a hand pump to pump the breastmilk and bottle to feed baby in order to do this. We will ask a few of you from each group to allow us to take small samples of breastmilk (about a teaspoon in each sample) at the beginning and end of the study. We will freeze the sample and will test it later to see if the breastmilk is healthier or more nutritious for baby when mom eats moringa.

We will ask you to come to your Maternal and Child Health appointments once a month until the end of the study. If you are not able to provide baby's or child's poop sample or heel or finger stick sample at the visit at the beginning and end of the study, we may give you a container to collect the poop and ask you to meet us at there or at a different location with the poop as soon as you collect it and/or collect the heel or finger stick when we meet you with your baby or child.

WHAT ARE THE POSSIBLE RISKS AND DISCOMFORTS?

There is always a chance that any new food can cause discomfort. The research treatments/procedures in this study are no different. In addition to risks described in this consent, you may experience a previously unknown risk or side effect. Moringa has been eaten by many cultures around the world for many generations. Moringa leaf is safe to eat. Moringa leaf in very high amounts may stop you from making a baby when you are eating it. For that reason, we ask that you stop taking the moringa and tell us if you are pregnant, although this is unlikely to happen in the first three months after giving birth.

It is possible that you will not like the taste of moringa porridge or non-moringa porridge. Moringa eaten at high amounts can help control high blood sugar. We do not know exactly how much is needed to do that, but we know that it will not make your blood sugar go low. Moringa has been studied with some HIV medicine and does not stop the medicine from working. We do not know if moringa does or does not affect all medications. There is a rare risk that eating moringa can change how well your medicines work for any disease.
We will ask you to collect poop and to wash your hands in soap and water after to stay clean. If you do not wash your hands well, you can accidentally eat the poop and get sick from it. We will protect the information that we gather to prevent a problem with confidentiality. We will stop others from taking your personal information, but that is an unlikely risk.

- We will ask your baby and/or your child for a heelstick (baby) or finger stick (child). Potential risks include: soreness, bruising, pain, infection, possible fainting, bleeding.
- We will keep your private information safe. There is a small risk that someone might steal your private information despite our best attempts.

WILL YOU BENEFIT FROM TAKING PART IN THIS STUDY?

We do not know if you, your baby, or child will get any benefit from taking part in this study. However, some people have experienced improvement in vitamins in the body and less inflammation in the body when eating moringa every day. You and/or your child will also benefit from receiving flour to make porridge every day for three months even if you do not receive moringa. We will not offer money in this study. Although we don't know all the benefit, if you take part in this study, information learned may help other moms, babies, and children in the future.

IF YOU DON'T WANT TO TAKE PART IN THE STUDY, ARE THERE OTHER CHOICES?
If you do not want to take part in the study, you can choose not to take part in the study.

WHAT WILL IT COST YOU TO PARTICIPATE?
You will need to pay for your transportation to the Maternal and Child Health Center. We plan to meet you there when you come for your or baby's appointment. We want to avoid that you make extra trips for the study. In some cases, you may need to make an extra trip to the health center. In some cases, we may ask you to meet us somewhere else or we may come to your community to collect breastmilk, poop sample, for example. If we ask you to make an extra trip to somewhere else to meet us, we will reimburse you up to 500 Kenyan Shillings (5USD).

WHO WILL SEE THE INFORMATION THAT YOU GIVE?
When we write about or share the results from the study, we will write about the combined information. We will not collect or share any private information.

We will make every effort to prevent anyone who is not on the research team from knowing that you gave us information, or what that information is. We will protect your information on our computers with passwords on a special database with the REDCap tool and will keep any other information in locked offices. Only the study team will access these records. To ensure the study is conducted properly, officials of the University of Kentucky, the Pamoja Community Based Organization, and University of California, Davis, may look at or copy pertinent portions of records that identify you for your protection. REDCap is a secure, web-based program to capture and store data at the University of Kentucky. We will make every effort to safeguard your data in REDCap. However, given the nature of online surveys, we cannot guarantee the security of data obtained by way of the Internet.

CAN YOU CHOOSE TO WITHDRAW FROM THE STUDY EARLY?
You can choose to leave the study at any time. You will not be treated differently if you decide to stop taking part in the study. If you choose to leave the study early, data collected until that point will remain in the study database and may not be removed.

The investigators conducting the study may need to remove you from the study. You may be removed from the study if:

- you are not able to follow the directions,
- we find that your participation in the study is more risk than benefit to you, or
- the agency paying for the study chooses to stop the study early for a number of scientific reasons.

The porridge and moringa or moringa replacement and/or breastmilk pump if applicable will no longer be provided to you and may not be available for purchase. This may occur for a number of reasons.

ARE YOU PARTICIPATING, OR CAN YOU PARTICIPATE, IN ANOTHER RESEARCH STUDY AT THE SAME TIME AS PARTICIPATING IN THIS ONE?
You may not take part in this study if you are currently involved in another research study that asks you to take additional vitamins or food other than regular vitamins after birth. It is important to let the investigator/your doctor know if you are in another research study. You should discuss this with the investigator/your doctor before you agree to participate in another research study while you are in this study.

WHAT HAPPENS IF YOU GET HURT OR SICK DURING THE STUDY?
If you believe you are hurt or if you get sick because of something that is due to the study, you should call Mr. Mbullo at +254 725 668711 Alternatively, you can call Dr. Suzanna Attia, Principal Investigator, University of Kentucky, United States number +1 859 216 1676. In an emergency, go to the nearest appropriate medical facility. It is important for you to understand that neither the University of Kentucky nor Pamoja CBO has funds set aside to pay for the cost of any care or treatment that might be necessary because you get hurt or sick while taking part in this study. Also, neither the University of Kentucky nor Pamoja will not pay for any wages you may lose if you are harmed by this study. Medical costs related to your care and treatment because of study-related harm will be your responsibility. You do not give up your legal rights by signing this form.

WILL YOU RECEIVE ANY REWARDS FOR TAKING PART IN THIS STUDY?
You will receive porridge and moringa or moringa replacement for taking part in this study. In rare cases, we may provide the money you used to travel to meet us if we asked you to do so and it is out of your way. You may receive a breast milk hand pump and a baby bottle if you are measuring breastmilk volume for 24 hours; not everyone will receive this. If we ask that you meet us in a different location in order to drop off a specimen (poop or breastmilk) or for us to take measurements, then we will reimburse you a maximum of 5 USD / 500 Kenyan Shillings for your transportation costs.

WHAT IF NEW INFORMATION IS LEARNED DURING THE STUDY THAT MIGHT AFFECT YOUR DECISION TO PARTICIPATE?
We will tell you if we learn new information that could change your mind about staying in the study. We may ask you to sign a new consent form if the information is provided to you after you have joined the study.

WILL YOU BE GIVEN INDIVIDUAL RESULTS FROM THE RESEARCH TESTS?
Generally, tests done for research purposes are not meant to provide clinical information. We will not provide you with individual research results.

WILL WE CONTACT YOU WITH INFORMATION ABOUT PARTICIPATING IN FUTURE STUDIES?
The research staff would like to contact you in the future with information about participating in additional studies. If so, it will be limited to a maximum of three times per year.

Do you give your permission to be contacted in the future by Mr. Patrick Mbullo, Dr. Suzanna Attia, Dr. Carrie Waterman, or another study staff regarding your willingness to participate in future research studies?

☐ **Yes** ☐ **No** **Initials**_____

WHAT ELSE DO YOU NEED TO KNOW?
This study is receiving funding from the NIH NCCIH/FIC.

WILL YOUR INFORMATION (OR SPECIMEN SAMPLES) BE USED FOR FUTURE RESEARCH?
All identifiable information (e.g., your name, medical record number, or date of birth) will be removed from the information or samples collected in this study. This means that no link to your identity will be kept. After all identifiers are removed, the information or samples may be used for future research or shared with other researchers without your additional informed consent. Once you give your permission to have your de-identified information or samples stored, they will be available indefinitely and cannot be removed due to the inability to identify them.

INFORMED CONSENT SIGNATURES

This consent includes the following:

- **Key Information Page**
- **Detailed Consent**

You will receive a copy of this consent form after it has been signed.

_____ **Signature of research subject** *or, if applicable, *research subject's legal representative*	_____ **Date**
_____ **Printed name of research subject**	
_____ **Printed name of research subject's legal representative*	
**If applicable, please explain Representative's relationship to subject and include a description of representative's authority to act on behalf of subject:* _____ _____	
_____ Printed name of [authorized] person obtaining informed consent	_____ Date