MetroHealth

Date: Wednesday, June 19, 2019 9:27:54 AM
View: 01-00 Study Information

Print Close

1.0 Study Information:

1.1

*** Short Title:** Targeted Breast Milk Fortification

The Short Title Should be the sponsor protocol number. If there is no sponsor protocol, then enter 3-5 words or numbers that capture the important study characteristics and help identify the study.

1.2 *** Full Title of Research Project:**
Targeted fortification of human breast milk and adjustment of TPN for Very Low Birth Weight infants to optimize growth and nutrition using Miris mid infrared human milk analyzer

Enter the Full Title of the study.

1.3

Principal Investigator: Sharon Groh-Wargo

HSR Certification Status: Certified **HSR Certification Expiration Date:** 9/1/2019 ;

COI Expire Date: 10/27/2019 ; **COI Yes or No:** Yes ; **COI Management Plan:** Yes ; **PI Non-Compliance:**

The PI must be a MetroHealth Staff person or have privileges to practice at MHS. The PI must assume full responsibility for the conduct of the study.

1.4

Key Personnel:

	Name	CREC Status	CREC Expiration	COI	COI Expire	Management Plan?	Study Roles	Employer Name	Non-Compliance
View	Stacey Ramey	Certified	6/26/2021	no	9/14/2019		eIRB Notification Recipient Responsible Investigator (Resident PI one RI required) Obtaining Informed Consent DRA (only one)	The MetroHealth System	
View	Stephanie Merlino	Certified	6/1/2022	no	5/13/2020		Obtaining Informed Consent Co-investigator	The MetroHealth System	
View	Mathavan Sivarajah	Certified	12/17/2021	no	5/6/2020		Obtaining Informed Consent	The MetroHealth System	

Add additional Staff as needed.

Update to add Study Roles

If using Epic, add role of DRA to one person

1.5 **Type of Research:**
Other

1.6 If "Other" Type of Research Please Explain:
Randomized clinical research study

View: 01-01 Study Information

1.1 Study Information:

1.7 * Department-What Department approvals are required?
Name
Pediatrics

1.9

Definitions to keep in mind when selecting the degree of risk:

<u>Minimal Risk</u> is defined in 45CFR46 and in FDA regulations 21CFR50.3 as:
Minimal risk means that the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.

Select most appropriate one.

*** Degree of Risk: (This is the investigator's assessment of the risks involved in the research which will informed the IRB Decision but which will not automatically be accepted. The Board is the final arbiter of risk. The risk level will be set by the IRB staff at the time of approval.)**

Name

- ○ Risk
- ◉ **Not Greater Than Minimal Risk**

1.10 * Type of IRB Review Requested:
Full Board

Select one. If you select Exempt or Expedited you will be taken to that section when you hit continue.

View: 01-02 Study Information

1.2 Study Information:

1.11 Will you require access to Epic to conduct this study? ◉ **Yes** ○ No

If you answer this question yes you will need to identify a Designated Records Administrator <u>one person only</u>.

*****The DRA's employee number must be listed on their registration form.*****

Please add the role of "DRA" to one study staff member on page 1 of the application.

1.12 Is the Principal Investigator a resident or trainee?

Please check yes or no.

○ Yes ◉ **No**

NOTE: Residents, Fellows, and non-MHS Personnel cannot be listed as the Principal Investigator

View: 01-03 Study Information

1.3 Study Information:

1.13

*** Will CRU Be Used:**
Yes *If you answer yes to this question this application will be sent to the CRU for review after departmental review and before it is submitted to the IRB.*

Will the CRU be used?

1.14

*** Has this research protocol ever been submitted to another CASE affiliated IRB (i.e. UH, CCF, VA or CASE)?**
No

If this study has been reviewed at another CASE affiliated IRB you should answer yes.

1.15

If yes, was it:

Select one from drop down menu.

1.16 **Please supply the following information: At which institution was it approved? If it was disapproved, why was it disapproved?**

What institutions have approved this study. If it has been disapproved, please give a brief explanation of why study was disapproved.

Please attach the Approval letter/letters from other IRBs (i.e. UH, CCF, VA or CASE):

Name	Description
There are no items to display	

1.17

Please attach approval letter/letters.

View: CRU 01-01 Application

Please Note: If you are using the CRU you must adhere to the following New NIH Public Access Policy:

Please review the information provied by theis link regarding enforcement of the NIH Public Access Policy that will begin on April 1, 2013. The most recent changes to the NIH Public Policy are explained in the attached Power point presentation from the NIH (January 15, 2013) and the attached MS-Word document, "Manuscript Submission to PubMed Central for a PMCID".

All studies that utilize the MetroHealth CRU resources (space, nursing, lab, bionutrition) that are non-industry funded, are required be NIH Public Access Policy compliant by obtaining a PMCID number. The PMCID number is an separate index from the PMID - the PMCID number indexes the entire publication while the PMID indexes the abstract, only. In addition to the PMCID number, investigators are required to post their publications on 'My Bibliography' and link their publications to grant numbers.

Attention to this policy is important because the NIH will halt the process of renewals, re-submissions and certain progress reports if relevant publications are non-compliant with the PMCID number and My Bibliography. Continued use and funding of the CRU may be jeopardized if appropriate publications are not fully compliant.

In addition, please ensure that studies utilizing the CRU also acknowledge the CTSC grant in their publications and cite the CTSC grant number, **UL1TR000439**. This is a NEW NIH CTSC grant number that went into effect on June 1, 2012. The acknowledgment and grant number can also be found by going to the Cleveland CTSC website acknowledgments page. (This page also has information about the NIH Public Access Policy.)

Thank you in advance for ensuring that all publications from studies utilizing CRU resources (that are not-industry supported) are compliant with these requirements as soon as possible.

1.00 CRU Application [*Since you have indicated in your application that you want to utilize the resources of the CRU Please complete the following pages of the IRB Application. Hit the continue button to move from page to page in that way you will be able to take advantage of the built in branching logic to complete your CRU application.]*

1.01 **Is this an HIV/AIDS Project:** ○ Yes ◉ **No**

HIV/AIDS?

1.02

Are you currently Funded by NIH? ○ Yes ◉ **No**

If yes please add grant or contract number.

1.03

Would you like to conduct your study on the CRU?

◉ **Yes** ○ No

Yes or No

1.04

What is your eRA Commons Name?

eRA Commons Name required for all non- industry studies

1.05

Anticipated Start Date:
5/20/2019

Anticipated Date Study to Begin (1st Patient)

Anticipated End Date:
3/31/2021

Anticipated End Date

1.06 **Approximate Inpatient Days Per Subject:**
90

Enter approximate numbers

Approximate Outpatient Visits Per Subject:
0

1.07 *After August 2010 this is a read only copy of the paper CRU Resource Application:*

Old CRU Application forms

Name	Version
There are no items to display	

1.08 **These are your target enrollment numbers for the ethic and racial categories below:**

Enter anticipated numbers for this protocol

Ethnic Category

	Sex/Gender		
Ethnic Category	Females	Males	**Total**
Hispanic or Latino	5	5	10
Not Hispanic or Latino	25	25	50
Ethnic Category Total of All Subjects	30	30	60

Racial Category

	Females	Males	**Total**
American Indian/Alaska Native	0	0	0
Asian	1	1	2
Native Hawaiian or Other Pacific Islander	0	0	0
Black or African American	17	17	34
White	12	12	24

Racial Categories Total of all Subjects	30	30	60

View: CRU 01-02 CRU Resource Needs

2.00 CRU: Resource Needs

Hospital Lab Tests: ○ Yes ◉ **No**

Hospital Lab Tests = CRU draws blood and send it to Hospital Lab or forwards blood already drawn to Hospital Lab

Human Performance Lab Tests and Measurements:
◉ **Yes** ○ No

Human Performance Lab Tests and Measurements

Research Nutrition Services: ◉ **Yes** ○ No

Research Nutrition Services

CRU Laboratory Services: ○ Yes ◉ **No**

Core Laboratory Services (7:00 am to 5:30 pm, weekdays)

Use of CRU Facilities or Equipment Only: ○ Yes ◉ **No**

Use of CRU Faciities or Equipment Only

Nursing Resources: ◉ **Yes** ○ No

Use CRU Nurses

Spanish Translation Services: ○ Yes ◉ **No**

Translation is the rendering of a written text in one language in a comparable written text in another language

Spanish Interpertation Services: ○ Yes ◉ **No**

Interpreting is the oral rendering of spoken or signed communication from one language into another.

View: CRU 01-03 CRU Nursing Resources

1.03 CRU: Nursing Resources

3.01
CRU Nursing Visits:

Please Add Each Visit

	Title	Visit #	Visit Length	Admissions	Comments
View	Targeted breast milk fortification	1	60 Minutes	no	CRU will obtain PEAPOD prior to discharge

View: CRU 01-06 Human Performance Lab Tests and Measurements

1.06 CRU: Human Performance Lab Tests and Measurementes

6.01 **Exercise Training:** ○ Yes ◉ **No** — *Answer Yes or No*

6.02 **Exercise Training Description:** — *Describe the exercise training*

How many times per week

6.03 **Exercise Training # Times/Week:**

Answer Yes or No

6.04 **Treadmill:** ○ Yes ◉ **No**

6.05 **Treadmill Description:** — *Description of treadmill exercises*

6.06 **Ergocycle:** ○ Yes ◉ **No** — *Answer Yes or No*

6.07 **Ergocycle Description:** — *Describe the use of the ergocycle*

6.08 **Other Activities:** ○ Yes ◉ **No** — *Answer Yes or No*

6.09 **Description of Other Activities:** — *Describe "Other" activities*

View: CRU 01-07 Research Nutrition Services

7.00 CRU: Research Nutrition Services

7.01 **Research Measurements:** ○ Yes ◉ **No** — *Answer Yes or No*

7.02 **BIA:** ○ Yes ○ No — *Answer Yes or No*

7.03 **BIA Measurements Per Subject:** — *Enter # of measurements*

7.04 **Anthropometry:** ◉ **Yes** ○ No — *Answer Yes or No*

7.05 **Anthropometry Measurements Per Subject:** — *Enter # of measurements*
1

7.06 **Indirect Calorimetry:** ○ Yes ◉ **No** — *Answer Yes or No*

7.07 **Indirect Calorimetry Number Per Subject:** — *Enter # of measurements*

7.08 **Weigh Backs:** ○ Yes ◉ **No** — *Answer Yes or No*

7.09	**Weigh Backs Number:**	*Enter #*
7.10	**Other Research Measurements:**	*Describe other measurements*
7.11	**Bionutrition Services:** ○ Yes ◉ **No**	*Answer Yes or No*
7.12	**Nutrition Assessment Or Counseling:** ○ Yes ◉ **No**	*Answer Yes or No*
7.13	**Food Record Analysis:** ○ Yes ◉ **No**	*Answer Yes or No*
7.14	**Food Frequency Questionnaire:** ○ Yes ◉ **No**	*Answer Yes or No*
7.15	**Research Diet Or Menu Development:** ○ Yes ◉ **No**	*Answer Yes or No*
7.16	**Research Diet Or Menu Development Description:**	*Describe diet or menu developement*
7.17	**Other Bionutrition Services:**	*Describe other Bionutrition services*
7.18	**Research Meal Services:** ○ Yes ◉ **No**	*Answer Yes or No*
7.19	**Research Meal Service Type of Meal:** Type of Meal Number Of Meals Per Subject Other There are no items to display	*Click add and answer the questions contained on the form.*

View: CRU 01-09 Additional Notes or Requests

1.09 CRU: Additional Notes or Requests

9.01

If you have any additional notes or requests from the Clinical Research Unit that have not been covered, please describe them here:

View: 01-04 Study Information

1.4 Study Information

These Questions are specifically about the adequacy of resources, are there the necessary resources to complete this study? There are two questions which focus on nursing resources. If this research will require the use of nursing resources then the Nursing Resources Form found on the IRB Home Page under forms and templates will need to be completed and attached to this research application.

1.18	**Can you assure the IRB that there are adequate numbers of qualified staff to conduct this research?** ◉ **Yes** ○ No	*Please answer yes or no. This is an assurance to the IRB.*
1.19	**How will the investigator ensure that persons assisting with the research were adequately informed about the protocol and their research-related duties and functions and requirements for maintaining the confidentiality of all data?** **Regular meetings will be held to update all co-investigators and study staff about the interventions planned and outcomes measured.**	*i.e. investigator meeting, formal protocol review with PI, monitor, sponsor.*
1.20	**Will the PI and study staff have sufficient time to conduct and complete the research?** ◉ **Yes** ○ No	*Please answer yes or no. This is an assurance to the IRB.*
1.21	**What facilities are available to conduct the research? Are they adequate? Please describe.** Study personnel are health care professionals working in the Neonatal Intensive Care Unit (NICU) at Metrohealth and have access to the study population. A space has been designated in NICU which will function as the milk lab for mixing the	*Please describe the facilities, i.e. lab, procedure room, chemo treatment room.*

milk. Analysis of the human milk will be done in the lab at Metrohealth using the Miris human milk analyzer.

Nursing Resources:

1.22 **Is this study using MetroHealth staff nurse time or labor ? (i.e. giving medcations, teaching, or additional documentation)**

This is in addition to the time of the study/research nurse.

○ Yes ◉ **No**

1.23 **Attach Nursing Resources Form here:**

Click here for Nursing Resources form

Open the form, Complete the form and save it to your files then attach it to the study by hitting the browse file and selecting the file and hitting OK.

Click here for the MHS Policy

View: 04-00 Scientific Review

4.0 Scientific Review:

All Studies need a Science Review. Has your study been reviewed by any of the following?

4.1 **Please Check all that Appy to this study so that the IRB may make a determination if there needs to be further scientific review:**

Select all that apply. Note FDA Approval does not equal science review.

	Review Type
☐	Initiated and sponsored by industry under an IND, IDE, HDE, or 510K exemption issued by the FDA for which no scientific integrity concerns were identified during the FDA review process
☐	Trial initiated and sponsored by industry that has undergone a scientific merit review by the sponsoring agency, but is not being conducted under an IND, IDE, HDE, or 510K exemption
☐	Sponsored by a Cooperative Group
☐	Proposed research has been awarded funding by a federal agency
☐	Peer reviewed by a federal funding agency and received a favorable funding score
☐	Peer reviewed by a federal funding agency with the acknowledgment of scientific merits, but not likely to be funded for reasons unrelated to scientific merit
☐	Sponsored by a foundation or a private agency that requires a separate scientific merit review process at the sponsoring agency
☑	**No Science Review**

4.2 **Do any of the following apply to your study? Please check all that apply:**

Check all that apply your answers will assist the IRB in deciding if further science review is necessary.

Additional Reasons Why Science Review May Be Required
Investigator-initiated study

4.3 **Does this study require review by the Biosafety Committee?**

All studies involving vaccines, potentially hazardous

No

materials or genetic research must go to the biosafety committee at CASE.

4.4 Does this study require review by the Radiation safety committee? No

If a study involves more than routine exposure to radiation on the part of subjects the study must go to the radiation safety committee.

4.5 Does this study require Review by the Nursing Committee?
No

The nursing committee must review all studies where the PI is a nurse, and all studies which have as the primary objective to contribute to nursing knowledgebase, and/or have implications for nursing practice.

View: 05-00 Funding Information I

5.0 Funding Information I:

All Research Projects must have an identified funding source!

5.1
Is this research externally funded? No

Check one

Research can be both externally and internally funded so you can answer yes to both 5.1 and 5.6.

5.2 Types Of External Funding:
Check all that apply.

Name
There are no items to display

5.3 If other, external funding please explain:

If other please describe.

5.4 Sponsor Information:

Please supply this information as your application can not be processed without it.

Name Sponsor/Agency | Address | Telephone | FAX | Contact Person
There are no items to display

5.5
Have you received and/or submitted a Notice of Award or Contract?
No

Select one from drop down menu.

Attach notice of award.

If yes, attach your Notice of Award letter here (not your grant):

Name | Version
There are no items to display

View: 05-01 Funding Information II

5.1 Funding Information II

5.6

Is Research Internally Funded (internal funding is any MetroHealth System or MetroHealth Foundation funds):

Check one, research can be both externally and internally funded so you can answer yes to both 5.1 and 5.6.

◉ ***Yes*** ○ *No*

5.7 Internal Funding Sources List:
Check all the apply.

Internal Funding Source
Department Operating Budget

5.8
If a MetroHealth Foundation funds or any MetroHealth

Check yes or no.

System funds are being used, has department approval been received?

(●) **Yes** ( ) No

5.9 **If a MetroHealth Foundation funds or any MetroHealth System funds are being used indicate the Account Number:**

Please enter the account number if this applies.

5.10 * **Are there current Conflict of Interest Forms for all Key Personnel? [It is the responsibility of the Principal Investigator to ascertain this information and check this box.]**

(●) **Yes** ( ) No

This question is not asking if there are COI forms for all Key Personnel it is asking if all Key Personnel have current COI forms so that any SFI is reported and can be dealt with if a management plan is need or reporting to NIH is required.

In order to submit a new protocol all COI Forms for key personnel and investigators must be current = provide up to date information.

5.11 **Please check below any Conflicts of Interest (Financial) you as Principal Investigator or your study staff [Co-Investigator, Coordinators, Other Study Staff] may have on this Study:**

Potential Conflict of Interest

None of the above options apply and there are no other financial conflicts of interest in the conduct of this research.

This question pertains to this study and is not a general question. Check all that apply.

You and/or your study staff will need to file a Conflict of Interest Disclosure Form annually.

If anyone working on this study has a Conflict of Interest or a perceived conflict. This information will need to be included in the consent form i.e. company is paying MHS to do this study.

5.12 **Please attach a copy of your grant application here:**

Name	Description

There are no items to display

You must attach a copy of your grant application here (i.e. NIH Grant Application).

You have the option to attach a copy of the budget, clinical trial account authorization form, contract and Approval letter(s) now or you can email them to your grants management specialist in the RABO office.

Copies of all RABO forms are available at:

http://www.metrohealthresearch.org/raboforms.html

View: 06-00 Performance Site Information

6.0 Performance Site Information:

6.1 **At what sites will the study team be performing this research, (please enter information about all non-MHS sites in 5.2):**

Name

The MetroHealth System

Select all that apply. If you select other please enter information about that site in question 6.2.

If this study is being done at MetroHealth where is it being done give the physical location (i.e. 8B, ED, Broadway, Old Brooklyn, PICU, Cath Lab):

MetroHealth Main Campus- NICU and CRU

Where is the research going to be done? What physical location on

the Main campus or the community health centers?

6.2 Please provide information about other external sites here:

Name of Site | Address | Telephone Number

There are no items to display

Please enter contact information. Please include name of facility, address and department.

6.3 If you are doing this research at an external site does this site have an IRB?

○ Yes ○ No

Select yes or no.

6.4 If the External Site has an IRB will that IRB defer review to the MHS IRB?

○ Yes ○ No

This only applies if there is no IRB or if there is a legal agreement between institutions permitting a reciprocal review, i.e. CASE.

6.5 Attach letter from external site agreeing to permit the MHS to review this protocol:

Name | Description

There are no items to display

Attach letter.

6.6 Has the external site granted permission for the research to be conducted?

○ Yes ○ No

This applies to sites where there is no IRB and the investigator must get a letter from the site that gives permission to conduct the research at the site.

6.7 Attach letter from external site granting permission for the research to be conducted:

Name | Description

There are no items to display

Attach letter of support.

View: 06-01 Performance Site Information

6.1 Performance Site Information

6.8 Is MHS the lead institution of a multi-site study? ○ Yes ◉ **No**

Please answer yes or no.

6.9 If yes, is there a plan to communicate information obtained through research that might be relevant to the protection of human subjects, including a plan to provide the IRB with information on unanticipated events, interim results, and protocol modifications.

○ **Yes** ◉ **No**

Please answer yes or no.

6.10 Please give a detailed explanation of the above plan:

This plan must give the IRB enough information to decide if the plan is appropriate and adequate.

6.11 Will the Principal Investigator conduct this study at any location outside the United States of America?

○ Yes ◉ **No**

Answer these questions only if there are research sites outside the USA.

6.12 Country, City, and address:

Country | Address of Research Facility

There are no items to display

Give country and location.

View: 07-00 Research Objectives and Background

7.0 Research Objectives and Background:

7.1 * **ABSTRACT: Please give the IRB a 500 word Abstract that contains the specific objectives of the study.**

This is your abstract also known as a synopsis from an industry sponsored study. Please limit to 500 words.

Breast feeding is the preferred method of feeding in newborns and breast milk is the safest form of enteral nutrition for premature infants. The American Academy of Pediatrics' policy statement recommends exclusive breast feeding for 6 months, and until 12 months as complimentary foods are introduced. Premature infants have difficulty achieving this recommendation due to multiple barriers created by the neonatal intensive care unit (NICU). One of these barriers is the increased caloric and nutrient requirements, compared to term infants, making it necessary to add fortification to maternal breast milk. Despite these barriers, breast milk has the potential to be the most beneficial for premature, critically ill infants. Preterm infants fed human milk, compared to those fed formula, have a decreased risk for necrotizing enterocolitis, sudden infant death syndrome (SIDS), respiratory syncytial virus (RSV) bronchiolitis, respiratory infections, and many other childhood conditions. There is variability in macronutrient and caloric content of breast milk between mothers, making it difficult to accurately quantify the nutritional content the breast milk is providing. The protein content varies by postnatal age, and the fat content varies temporally during a feed. Currently calculations use a standard value for caloric density and macronutrient content of breast milk, which is a reported average, but not necessarily specific to each individual mother.

Human milk analysis has been used to address this variability. The Miris Human Milk Analyzer (HMA) is a mid-infrared analyzer and has been evaluated in many studies. It measures the macronutrient content of breast milk, providing values for protein, fat, carbohydrates, and calculated calories. By having this information available, the fortification added to breast milk can be tailored specifically to each mother's breast milk composition to meet each neonate's nutritional needs, and optimize growth. As of December 2018, the Miris HMA has obtained FDA approval in the United States.

This will be a prospective randomized control study of preterm infants less than 1500 grams [very low birth weight (VLBW)] receiving human milk (maternal or donor) will be included. The control group will receive adjustment of total parenteral nutrition (TPN) per NICU guidelines as enteral feedings are advanced followed by standard fortification of human milk. The intervention group will have TPN (protein and lipids) adjusted based on analysis of human milk as feedings are advanced to provide goal 4g/kg/day of protein and 100-130 kcal/kg/day followed by targeted fortification of breast milk based on human milk analysis to continue to provide 4 g/kg/day of protein and 100-130 kcal/kg/day for once full feeds are achieved. The primary aim of this study is to evaluate the growth, anthropometric measurements, and body composition, to see if targeted fortification improves neonatal growth. By optimizing neonatal growth and nutrition there is potential to also have an impact on other morbidities and long term neurodevelopmental outcomes.

7.2 * **What are the specific aims of this study i.e. what are the question(s) this research intends to answer? Provide at a maximum 3 primary and 3 secondary aims.**

This is your Hypothesis also know as your aims (NIH) or safety and efficacy aims (industry). Please list no more than 3 primary and 3 secondary clearly label these aims primary and secondary.

The aim of this study is to demonstrate improved growth and body composition in VLBW infants by using human milk analysis as a tool to guide when adjusting TPN and lipids followed by targeted fortification of breast milk at full feeds to provide 4g/kg/day of protein 100-130 kcal/kg/day, compared to those who receive standard management of TPN per guidelines and standard fortification.

The primary outcome measured will be body composition measurement 4 weeks after achieving full feeds with targeted fortification, or at NICU discharge, whichever comes first.

Secondary outcome variables:

1) Weight gain velocity

2) Anthropometric measurements including weight, length, head circumference, and mid upper arm circumference or skinfold thickness

7.3 **Please provide a summary of the present knowledge relevant to the research and make citation to any applicable scientific literature:**

This is your literature search and bibliography. Also known as

Background and significance (NIH) or Introductory Section from industry sponsored trial.

Breast feeding is the preferred method of feeding in newborns and breast milk is the safest form of enteral nutrition for premature infants. The American Academy of Pediatrics' policy statement recommends exclusive breast feeding for 6 months, and until 12 months as complimentary foods are introduced [1]. Premature infants have difficulty achieving this recommendation due to multiple barriers created by the neonatal intensive care unit (NICU). One of these barriers is the increased caloric and nutrient requirements, compared to term infants, making it necessary to add fortification to maternal breast milk [5]. Despite these barriers, breast milk has the potential to be the most beneficial for premature, critically ill neonates. Preterm infants fed human milk, compared to those fed formula, have a decreased risk for necrotizing enterocolitis, SIDS, RSV bronchiolitis, respiratory infections, and many other childhood conditions [1]. The variability in macronutrient and caloric content of breast milk makes it difficult to accurately quantify the nutritional content the breast milk is providing. The protein content varies by postnatal age, and the fat content varies temporally during a feed[2]. Human milk analysis has been used to address this variability. The Miris Human Milk Analyzer (HMA) is a mid-infrared analyzer and has been evaluated in many studies[3]. It measures the macronutrient content of breast milk, providing values for protein, fat, carbohydrates, and calculated calories. By having this information available, the fortification added to breast milk can be tailored specifically to each mother's breast milk composition, and each neonate's nutritional needs [4]. As of December 2018, the Miris HMA has obtained FDA approval in the United States.

1. American Academy of Pediatrics Section on Breastfeeding: Breastfeeding and the use of human milk. Pediatrics 2012, 129(3):e827-841.
2. Martin, C., Ling, P., & Blackburn, G. (2016). Review of Infant Feeding: Key Features of Breast Milk and Infant Formula. Nutrients, 8(5), 279. doi:10.3390/nu8050279
3. Fusch, G., Kwan, C., Kotrri, G., & Fusch, C. (2017). "Bed Side" Human Milk Analysis in the Neonatal Intensive Care Unit. Clinics in Perinatology, 44(1), 209-267. doi:10.1016/j.clp.2016.11.001
4. Miris. Our Solution. 2019. Available at https://mirissolutions.com/solution. Accessed March 8, 2019.
5. Tudehope, D. I. (2013). Human Milk and the Nutritional Needs of Preterm Infants. The Journal of Pediatrics, 162(3). doi:10.1016/j.jpeds.2012.11.049

7.4 Option to Upload Documents related to question 7.3:

If it is easier to attach your response to question 7.3 please do so here. Please limit to three pages.

Name	Description
There are no items to display	

View: 08-00 Methods and Procedures I

8.0 Methods and Procedures I:

8.1 Will this research involve the following Social-Behavioral Procedures:

Check all that apply.

Name
None of the Above Social-Behavioral Procedures Apply to this Study

8.2 Will this research involved any of the following Medical Procedures/Considerations:

Check all that apply.

Name
Study of Human Biological Materials (i.e. Urine Collection)
Study of Existing Data
Medical Tests, Comparisons, Evaluations
Special/prescribed diets
Anthropomorphic Measurments

8.3 Identify Data Collection types for this study:

Check all that apply.

Note if you are doing, recordings, Video-Recording/Photographs then subjects will need to sign the MetroHealth Audio-Video Consent form. See the IRB Forms and Templates.

Name
Chart Review - Prospective
Anthropomorphic evaluations

View: 08-01 Methods and Procedures II

8.1 Methods and Procedures II:

8.4 *** Please specify in detail the methods and procedures that are involved in this research:**

If this field is not completed your protocol will not be reviewed. Do not enter N/A. Please describe what methods and procedures will be involved in this research.

In the NICU, there is a feeding protocol in place for all infants that is based on their birth weight. All infants less than 1500 grams at birth are placed on starter total parenteral nutrition, and delayed initiation of enteral feeds determined by birth weight. The standard feeding protocol is as follows:

Maternal breast milk (MBM) is preferentially used, or donor breast milk (DBM) if maternal milk is unavailable and the mother has consented to the use of donor breast milk.

Infants <750 grams are nil per os (nothing by mouth, or NPO) for 10 days followed by initiation of priming feed of 0.5 ml every 2 hours for 10 days, after which feeds are increased by 0.5 ml/feed every other day until they reach 100 ml/kg/day. They then increase by 10 ml/kg/day until they reach full feeds of 150 ml/kg/day.
Infants with birth weight 750-1000 grams are NPO for 7 days followed by initiation of priming feed of 1 ml every 2 hours for 7 days, after which feeds are increased by 0.5 ml/feed daily until they reach 100 ml/kg/day. They then increase by 10 ml/kg/day until they reach full feeds of 150 ml/kg/day.
Infants with birth weight 1001-1250 grams are NPO for 4 days followed by initiation of priming feeds of 1.5 ml every 2 hours for 4 days, after which feeds are increased by 1 ml/feed every other day until 100 ml/kg/day. They then increase by 10 ml/kg/day until they reach full feeds of 150 ml/kg/day.
Infants with birth weight 1251-1500 grams are NPO for 1 day followed by priming feeds of 2 ml for 2 days, after which they increase by 20 ml/kg/day until they reach full feeds of 150 ml/kg/day.
Once enteral feeds reach 50 ml/kg/day MBM is fortified with 1 packet of human milk fortifier for every 50 ml of breast milk. Then at 75 ml/kg/day MBM is fortified with 1 packet of human milk fortifier for every 25 ml of breast milk.
As enteral feedings are advance the total parenteral nutrition is gradually decreased. The control group will have TPN and SMOF lipid adjusted per NICU guidelines and standard practice until full enteral feeds are achieved. The protein provided in TPN is adjusted based on volume being given and what will fit inside the TPN due to concentration, and lipids are usually decreased by 50% when the enteral nutrition is providing 75 ml/kg/day, and then discontinued with enteral nutrition is providing 100 ml/kg/day. The intervention group will have protein content of the TPN and SMOF lipid adjusted dependent on the breast milk composition- goal 4g/kg/day protein, 100-130kcal/kg/day.
This study will be a randomized control trial with 2 arms. Patients will be randomized to either the control group (standard fortification) or intervention group (targeted fortification) in a 1:1 allocation ratio. Twins will be considered as one and allocated to the same group. Allocation group will be stratified to four groups according to birth weight: <750g, 751-1000g, 1001-1250g, 1251-1500g. This stratification is based upon our NICU feeding guideline, and will ensure that enrolled infants will receive comparable nutrition progression (e.g. NPO days, days of trophic feeds) throughout the study period. The allocation will be concealed in a sequentially numbered, opaque, sealed envelope, that will be opened after consent is obtained. After randomization, the groups will not be blinded to the investigators or caregivers.

All VLBW infants whose mothers consent to provide breast milk and participate in the study will be included. In the control group, breast milk will be fortified per protocol as listed above and TPN weaned per NICU guideline. The intervention group will receive standard fortification with additional added liquid protein to provide 4 g/kg/day and microlipid to provide 100-130 kcal/kg/day once 100 ml/kg/day of enteral feeds are achieved. Once the infants reach goal enteral feeds of 150ml/kg/day they will continue on the standard or targeted fortification for 4 weeks.

The mothers will provide breast milk when they come to visit their infant in the NICU. They will have access to a pump while visiting in the NICU and lactation consultant will help to arrange for a pump to use at home. They will be provided containers to collect breast milk at home to bring in when they visit their baby in the NICU. Once weekly the mother will collect the previous 24 hours supply of breast milk, which will be homogenized and a sample taken for analysis. The sample will then be analyzed for composition using the Miris human milk analyzer for the carbohydrate, fat, and protein content and caloric density. The remainder of

the milk will be stored as a batch and labelled to feed the infant when he/she is ready.
In the NICU a work area has been identified which has a sink, storage area, and work surface. The work surface will be cleansed with a sterilization cloth, followed by handwashing and then retrieving the milk from the refrigerator using universal precautions. The 24 hour supply will be mixed into one clean mixing bottle large enough to accommodate the entire 24 hours supply. It will be homogenized by inverting the bottle 10 times. A 10 ml aliquot of the sample will be transferred into a container labeled with subject number and taken for analysis. The remainder of the milk will be repackaged into containers and labeled as one batch. The Miris human milk analyzer is a mid infrared that reports the amount of energy absorbed at each wavelength. The amount of fat (grams), lactose (grams), total protein (grams), true protein (grams), and energy (kcal) per 100 ml will be reported. The milk will be then fortified per protocol (control group), or with targeted fortification (intervention group) as described above.
In the NICU infants are weighed on a daily basis, as clinical condition allows; weekly head circumference, length, and either flank skin fold or mid upper arm circumference (dependent on weight). As standard of care infants <1500 g at birth have a PEAPOD measurement prior to discharge to evaluate body composition. The measurements will be performed by nursing staff on routine basis and will not be blinded to the group assignment, as the bedside nurse will also likely be assisting in preparing the feeds for the infant. The Peapod assessment is performed by CRU staff as standard of care for these patients prior to discharge, they will be blinded to the group assignment but the NICU staff (nursing, nurse practitioner, or fellow) accompanying the patient to the measurement will not be blinded.

8.5 Does this study only involve the use of existing/retrospective data/specimens?
No

Check yes or no.

8.6 Describe in <u>detail</u> the study design also known as the experimental flow. Include all study procedures a subject will go through, in order of sequence and timing, including frequency of visits, duration of visits, length of subject participation etc. *Please Note this needs to be written for an educated person who is not an expert in the field, do not exceed 300 words*:

This is also known as NIH Experimental Procedure section or Clinical Trial Procedure/Experimental Flow section. Do not just attach documents in response to this question you must do a study design summary for IRB Review.

- Infants with birth weight <1500g born at MetroHealth will be identified and are eligible for this study if they meet inclusion and exclusion criteria. Mothers of these infants will be approached for recruitment and included if they consent to participate
- As standard NICU procedure these infants will be started on total parenteral nutrition (TPN) with SMOF lipids, and delayed initiation of enteral feeds determined by birth weight and NICU guideline
- The infant will be randomized to the standard fortification group (control) or targeted fortification group (intervention).
o Standard fortification group (control)
Breast milk will be fortified standard with Similac Human Milk Fortifier 1 packet: 50 ml breast milk at 50ml/kg/day enteral feeds, then 1 packet:25 ml breast milk at 75 ml/kg/day
As feedings are advanced to goal of 150 ml/kg/day, the TPN and SMOF lipids will be decreased per standard management and NICU guidelines
o Targeted fortification group (intervention)
Breast milk will be fortified standard with Similac Human Milk Fortifier 1 packet: 50 ml breast milk at 50ml/kg/day enteral feeds, then 1 packet:25 ml breast milk at 75 ml/kg/day
During this time, as the volume decreases, the TPN and SMOF lipids will be optimized to provide a goal of 4 g/kg/day of protein, and 100-130kcal/kg/day
At 100 ml/kg/day of enteral feeds additional liquid protein and/or microlipids will be added to the breast milk to provide goal of 4 g/kg/day of protein and 100-130 kcal/kg/day. This will be determined by analysis of the milk and reported composition.
They will continue targeted fortification for 4 weeks after achieving full feeds of 150 ml/kg/day
- Breast milk analysis will occur on a weekly basis immediately after birth for all infants enrolled in the study.
- Mothers collect a 24hr supply of breast milk once per week, from which a study team member will obtain a 10 ml representative sample for analysis. The 24hr collection of breast milk will be mixed into a clean container that can accommodate the entire volume. It will be homogenized and a 10 ml sample removed for

analysis. The remaining breast milk will be repackaged and placed back into the refrigerator in the NICU.
- After analysis, the milk for the following 1 week will be labeled and batched together
- For donor breast milk, each 'lot' will be analyzed and labeled for future use
- Analysis will take place at MetroHealth in the lab, using the Miris human milk analyzer. The amount of fat (grams), lactose (grams), total protein (grams), true protein (grams), and energy (kcal) per 100 ml will be reported and used for calculations.
- Infants will have birth measurements obtained, daily weight, weekly anthropometric measurements, and body composition measurement prior to discharge. The measurements will take a few minutes to obtain on routine basis per NICU protocol. The Peapod (body composition) measurement will take approximately 20 minutes total traveling from the NICU to CRU and back, but the actual assessment takes 2-3 minutes. This will be done with the infant is medically stable and approaching discharge.

The subjects will be in the study from time of consent to 4 weeks following the achievement of full enteral feedings, which may range from 6 weeks to 12 weeks depending on the birth weight and the clinical status of the infant. The smallest babies will take the longest to increase to full feeds due to the slow feeding protocol.

8.7 Please attach study design/subject visit schedule here:

If you have an electronic schedule of study visits and/or procedures please attach here.

Name	Description
There are no items to display	

View: 09-00 Inclusion/Exclusion Criteria

9.0 Inclusion/Exclusion Criteria:

9.1 What are the inclusion criteria? Put this information in bullet form:

Please list inclusion criteria.

Premature infants <1500 g
Mother consenting to provide breast milk or use of donor breast milk

9.2 What are exclusion criteria? Put this information in bullet form:

Please list exclusion criteria.

Infants with major congenital malformations
Infants with medical conditions precluding them from having breast milk
Mothers with medical conditions that preclude them form providing breast milk
Insufficient breast milk supply
Refusal of donor breast milk

9.3 How will subject eligibility be determined and by whom?

Please describe in detail.

The principal investigator and co-investigators will determine subject eligibility based on birth weight, inclusion, and exclusion criteria.

9.4 Will you exclude women and minorities, or persons under 21 from enrollment?

Check yes or no.

No

9.5 If yes, which groups are you excluding? Provide justification for your decision.

List groups to be excluded then provide justification.

9.6 Attach Documents:

If you are unable to fit your answers in the text boxes provided please attach as a word document.

Name	Description
There are no items to display	

View: 10-00 Risk/Benefits

10.0 Assessment of Risk I:

10.1 Identify and distinguish between those procedures that are standard versus those that are experimental. Include the frequency and duration of each activity and the total length of subject participation:

Please distinguish between those procedures that are standard versus those that are experimental. Describe in detail all experimental procedures.

Standard procedures: Pumping and providing expressed breast milk, documentation of baby demographics, weekly anthropometric measurements, PEAPOD prior to discharge, Metrohealth standard feeding protocol.

Experimental procedure: Weekly analysis of small aliquot of breast milk with Miris mid infrared human milk analyzer, targeted fortification of breast milk to achieve protein goal of 4g/kg/day and calories 100-130 kcal/kg/day, fortification of breast milk specifically for each mother/infant.

Deviation from standard Metrohealth NICU practice: collection of 24 hour supply of breast milk, analysis of breast milk content, targeted individualized addition of protein and fat. All other procedures are the standard of practice in NICU.

The measurements will take a few minutes to obtain on routine basis per NICU protocol. The Peapod (body composition) measurement will take approximately 20 minutes total traveling from the NICU to CRU and back, but the actual assessment takes 2-3 minutes. This will be done with the infant is medically stable and approaching discharge. Analysis of the breast milk will take approximately 20 minutes per sample, including the time to prepare the sample for analysis and analysis using the Miris human milk analyzer.

The subjects will be in the study from time of consent to 4 weeks following the achievement of full enteral feedings, which may range from 6 weeks to 12 weeks depending on the birth weight and the clinical status of the infant. The smallest babies will take the longest to increase to full feeds due to the slow feeding protocol.

10.2 Describe any therapeutic alternatives to the research that may exist. How are they different from those procedures that subjects would normally undergo?
Therapeutic alternative is standard fortification of breast milk per protocol. This uses reported average protein and caloric content of breast milk and adds standard amounts of fortifier. Content of breast milk is variable between mothers and has wide range. They also have the option to not participate in the study and receive standard NICU management.

Describe any therapeutic alternatives. Can subjects receive this drug or device outside of a research study?

10.3 What are the outcome variables and how will they be analyzed? What are the statistical and analytical methods that will be used? *Note this section can be copied from the NIH Grant Application or from the Statistical and Analytical Methods section of the industry trial protocol.*
The outcome variables are the anthropometric measurements including daily weight; weekly length, head circumference, skin fold thickness or mid upper arm circumference; and PEAPOD body composition measurements prior to discharge.

Our primary outcome is body composition, as measured by air displacement plethysmography (PEAPod). As standardized assessment of body composition is relatively new in the preterm infant population, we are using clinical judgment to determine that a difference in fat free mass z-score (from data from Norris T, 2019) of 0.5 is clinically significant. To detect a difference at alpha a=0.05 with 80% power, 25 infants per group are required. This is a realistic goal for clinical enrollment, due to the historical MetroHealth NICU census composition. According to the census at MetroHealth, the total number of infants with birth weight less than 1500 g for 2016 was 81 infants, and in 2017 was 84 infants.

Define outcomes and describe data analysis, please include a power calculation.

10.4 If the above requested information does not fit in the text box please attach a word document here:

Name	Description
There are no items to display	

If the requested information does not fit in the text box please attach a word document.

View: 10-01 Risk/Benefits

10.1 Assessment of Risk II:

10.5 List and quantitate the risks involved for each experimental procedure in bullet form. Identify risks as common (greater than 10%) uncommon (greater than 1% up to and including 10 %) rare (1% or less). This must match the risks listed in the Consent Form:
Targeted fortification- rare, some babies may have elevated BUN which is routinely monitored in the NICU, or rare, feeding intolerance

There is also risk of breach of confidentiality, but this is rare. Data will be stored securely, only key study investigators will have access to data, and it will be deidentified and only the PI will have access to the key.

Select all that apply.

The probability and magnitude of harm or discomfort anticipated in the

research are no greater than those ordinarily encountered daily during routine care while admitted to NICU.

10.6 *Describe in enough detail for the IRB to assess safety.*

Are there defined stopping rules? (•) **Yes** ( ) No

What are the stopping rules for the study? What are the conditions under which a subject will be withdrawn from the study for safety reasons, i.e. disease progression?
Intolerance to fortification, excessive emesis or recurrent, otherwise unexplained, abdominal distention.

What findings, events, or conditions would require a research subject to be removed from the study? (i.e. disease progression)
Clinical worsening, acute decompensation of infant precluding them from receiving enteral feeds.
If a patient become acutely ill and significantly decompensates they may be removed from the study. Ex: sepsis, abdominal distention, blood in the stool, respiratory failure with increasing need for respiratory support. If a patient becomes comfort-care only and no longer receiving enteral feeds they may also be removed from the study.

10.7 **What Category of risk will study participants be exposed too?** *Should be consistent with risks listed in the Consent Form.*

Name
Privacy
Other

10.8 **If Other listed above please specify:**
Infants will need to leave the NICU for PEAPOD body composition measurement. This will be done once they are determined to be medically stable and ready for discharge.

A text box is provided for further explanation.

A text box is provided for further explanation.

10.9 **Describe the availability of medical or psychological services that participants might require as a consequence of participation in this the research:**
The participants will have medical services available in the NICU at their disposal during the entirety of involvement in the study. Every effort will be made to obtain resources to support mother's pumping activities and providing of breast milk- pumping room with breast pumps and supplies, lactation services, nutrition services.

10.10 **Describe in detail any measures in place to minimize or protect against the exposure of study subjects to these risks:** *Discuss any provisions for intervention in the event of an Adverse Event i.e. stopping rules.*
Infants will be transferred to the research unit in an open crib one hour after his/her regular feed. they will be placed on a warmer while heart rate, respiratory rate, and pulse ox will be monitored continuously. The entirety of the assessment will take about 20 minutes. After the PEAPOD is completed the infant will be transferred back to the NICU.

Data will be stored in a secure location to protect confidentiality.

10.11 **Please add any documents related to the above questions:** *If your answers to the above questions are too long for the space provided please attach them here.*

Name	Description
There are no items to display	

View: 10-02 Risk/Benefits

10.2 Benefits:

10.12 **Describe the potential benefits to the subject as a result of participating in this research. If there is no direct benefit to subjects please state that as well: *Note: payment or compensation to subjects for participation is not to be considered a potential benefit.*** *Describe potential benefits to the study subjects.*
Receiving targeted fortification may result in improved growth and body composition with more lean body mass. Improved neonatal growth may have

impact on improved long term medical outcomes, with decreased susceptibility to infections, and also neurodevelopmental outcomes.

10.13 **Describe the potential benefits to society as result of this research:**
Care of premature infants has a large financial and emotional impact on parents and society, even after discharge from the NICU. They are high risk patients that may require frequent readmissions to the hospital with illnesses. Optimizing growth and nutrition of premature infants is associated with decreased morbidity and improved outcomes.

If a significant difference can be shown in the study group, having a milk analyzer in all NICUs and targeted fortification of breast milk to provide optimal nutrition can become standard of care. This has the potential to reduce the burden on the health care systems taking care of these patients.

Describe potential benefits to society.

10.14 **What is the risk/benefit ratio of the research?**
In this research, infants are given additional protein and fat targeted to their mother's breast milk composition and their nutritional needs, which alone does not have any potential risk. The benefit of improved growth is significant with overall improved medical and neurodevelopmental outcomes. Potential benefits outweigh the risk of participation.

Discuss why the risks are reasonable in relation to the anticipated benefits.

10.15 **Attach Documents:**

Name	Description
There are no items to display	

Attach documents here.

View: 11-00 Study Participant Information I

11.0 Study Participant Information I:

11.1 **How will the Principal Investigator assure he/she has access to a population that would allow recruitment of the required number of study participants (i.e. prep for research):**
Based on MetroHealth Medical Center NICU statistics, there are approximately 80 babies weighing less than 1500 grams admitted every ear.

The accrual numbers in 11.2 represent mother/baby couples.

How does the PI know he/she has the required number of subjects?

Please give the total #of subjects to be enrolled at all sites and anticipated subjects to be enrolled at MHS.

11.2

Anticipated number of subjects (all sites): [enter a number]
60

Anticipated number of subjects to be enrolled at MHS: [enter a number]
60

Anticipated number of potential subjects to be approached: [enter a number]
60

11.3 **If this is a multi-site study, how many sites will there be? [enter a number]**

How many total sites?

11.4 **Subject Characteristics:**

Subject Population Categories
Inpatients

Check all that apply

11.5 **Subject Source:**

Subject Source Characteristics
Other

Check all that apply

11.6 **If "other" list above in either 11.4 or 11.5 please describe:** *If applicable please describe.*
Infants delivered at MHMC with birth weight less than 1500 grams on admission to NICU.

View: 12-00 Study Participant Information II

12.0 Study Participant Information II:

12.1 **Select age range of study participants:** *Check all that apply.*

Subject Age Range
0 - 6
12 - 17
18 - 64

12.2 *Check yes or no.*

* Will the study enroll vulnerable subject groups?
Yes

* Will you be enrolling Children?
(•) **Yes** ( ) No

* Will you be enrolling Pregnant Women and/or Fetuses?
( ) Yes (•) **No**

* Will you be enrolling decisionally impaired subjects?
( ) Yes (•) **No**

* Will you be enrolling Prisoners? ( ) Yes (•) **No**

12.3 **Please identify any vulnerable populations participating in the study:** *Check all that apply.*

Vulnerable Populations
Poor / Uninsured
Minors - Children under 18
Employees
Students
Minorities

12.4 **If you selected "other" above please describe:** *Please describe other.*

12.5 **If you are going to enroll <u>any</u> vulnerable populations please describe the safeguards you will put in place to protect these vulnerable Populations.** *Please enter a detailed plan.*
Informed consent will be obtained from the mother prior to enrollment of the premature infant. They will be informed that participation in the study is optional and their decision will not impact the medical care that the infant receives.

View: Supplemental Review Form for Research with Children I

Supplemental Review Form for Research with Children I:

Federal regulations require the IRB to provide additional protections for children involved as subjects in research. There are four categories of permissible research that involve children [45 CFR 46.404, 46.405, 46.406, or 46.407]. **Please complete each section as it applies to your research. Each question must be fully answered, or your study will be returned and IRB review will be delayed.**

ASSESSING RISKS AND BENEFITS

When assessing risks and benefits, consider the variability in health status of the subjects to be enrolled, their medical experiences, and the extent to which the research procedures will be a burden to the subjects in the context of their daily lives and/or routine medical care. Be sensitive to how a procedure that generally entails little to no physical or psychosocial risks may affect someone with limited (or no) understanding of the situation. Procedures that usually present no more than minimal risk to a healthy child include: physical exam, ultrasound, urinalysis, obtaining a small amount of blood, EEGs, allergy scratch

tests, minor changes in diet or daily routine, and/or the use of standard psychological or educational tests. The assessment of the probability and magnitude of the risk, however, may be different in sick children and may vary depending on the diseases or conditions the subjects may have.

Minimal Risk: As defined in the regulations 45 CFR 46.102(i), "*minimal risk*" means the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests."

Answer 1, 2, 3, or 4 below if applicable:

1. Is this Pediatric Research not involving greater than minimal risk (see definition above) [45 CFR 46.404]:
(●) **Yes** ( ) No

Explain Why you think this study is not greater than minimal risk:
We will be fortifying breast milk with protein and fat to provide individualized nutrition based on human milk analysis to meet nutritional goals and optimize premature infants growth. We will be using liquid protein and microlipids which are approved for neonatal use. Optimizing nutrition will potentially have a beneficial effet on growth, medical, and developmental outcomes.
No medications or other potential harmful substances are given. The probability and magnitude of harm or discomfort anticipated in the research are not greater than those ordinarily encountered in daily life or during routine care in the NICU.

****

2. Is this Pediatric Research involving greater than minimal risk but presenting the prospect of direct benefit to individual subjects [45 CFR 46.405]. Answer all questions below. ( ) Yes (●) **No**

Explain why you think the procedures or interventions are of greater than minimal risk:

Describe the anticipated or possible health benefits, and explain why you think the study interventions or procedures hold out the prospect of direct benefit to each individual subject:

Explain why you think the risk to subjects is justified by the anticipated benefit:

Explain why you think the risk/benefit ratio is at least as favorable to the subjects as that presented by available alternative approaches:

****

3. Research involving greater than minimal risk and no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition. [45 CFR 46.406]. Answer all questions below:
( ) Yes (●) **No**

Explain why you think the interventions or procedures represent no more than a minor increase over minimal risk:

Explain why you think the interventions or procedures present experiences to subjects that are reasonably commensurate with those inherent in their actual or expected medical, dental, psychological, social, or educational situations:

Explain why you think the interventions or procedures are likely to yield generalizable knowledge about the subjects' disorder or condition that is of vital importance for the understanding or amelioration of the subjects' disorder or condition:

****

4. Is this Pediatric research that is, not otherwise approvable that presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of children [45 CFR 46.407]. This category includes research that does not meet the criteria for any of the above three risk/benefit categories. Research in this category represents more than a minor increase over minimal risk and no prospect of direct benefit to subjects.

○ Yes ◉ **No**

Explain why you think the research presents a reasonable opportunity to further the understanding, prevention, or alleviation of a serious problem affecting the health or welfare of children:

NOTE: This kind of research requires review by the Secretary of DHHS, after consultation witha panel of experts in pertinent disciplines, and public review and comment. Contact the Manager and Chair of the MHS IRB at 216-778-2077, if you believe your research falls into this category.

View: Supplemental Review Form for Research with Children II

Supplemental Review Form for Research with Children II:

SECTION 2: PERMISSION OF PARENTS/GUARDIANS AND ASSENT OF CHILDREN

*INSTRUCTIONS: Check **all** that apply and answer the related questions.*

5.

Permission of Parents or Guardian (check one below)

☐ The permission of both parents or a guardian(s) will be sought 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 categories 45CFR.406 & 407 see questions [3] and [4]).

or

☑ The permission of only one parent will be sought (acceptable for categories 45CFR46. 404 & 405 see questions [1] and [2]).

6.

Assent of Children (check one below)

☑ The assent of each child who is capable of providing assent based on age, maturity, and psychological state will be sought.

or

☑ The assent of each child will not be sought because the capability of all of the children in this study population is so limited that they cannot reasonably be consulted.

Explain why the capacity is so limited, e.g., age, maturity and/or psychological state:
Age- premature infants, from birth until hospital discharge approximately 3-4months old

or

☐ The assent of each child will not be sought because the intervention or procedure involved in the research holds out a prospect of direct benefit that is important to the health or well-being of the children and is available only in the context of the research.

Explain what the direct benefit may be and why it is only available in the context of the research:

NOTE: Ohio law generally permits individuals to consent for their own medical care at age 18, but limited exceptions permit individuals to consent at an earlier age to certain treatments. Consult the MHS Policy I-34 on the MIV.

View: 13-00 Recruitment I

13.0 Recruitment I:

All external advertisements (for radio, print media or TV) must be approved by MHS Communications Department prior to submission to the IRB so the IRB can see the final advertisement or script. All Advertisements on the MIV or On Hold messaging must be approved by the IRB before they are placed. You may not advertise a study which is not approved by the IRB. Please note that all studies which have a contract which an external sponsor must have that contract signed before any advertising can be done.

13.1 **Recruitment Methods/Sources:** *Check all that apply.*

Name
None

13.2 **If "Other" checked in 13.1 please explain:** *Please explain what other means.*

13.3 **Describe in detail all recruitment strategies for each subject group (as listed in Section 11.0) selected for this research:** *Please describe recruitment strategies in detail.*

Recruitment is from all deliveries at MHMC with birth weight less than 1500 grams. The NICU admission log will be consulted. Mothers of infants fulfilling the inclusion criteria will be approached and informed consent will be obtained for enrollment into the study. Mothers will be approached while in labor and delivery once they are stable or when they visit the infant in the NICU and able to comprehend the informed consent process.

13.4 **What measures will be taken during the recruitment process to safeguard against the potential coercion or appearance of coercion of human subjects, particularly vulnerable subject groups?** *Please give an explanation of safeguards to be used.*

Mothers will be given ample time to read and review the informed consent and discuss with close family and friends. They will also be told that participation in the study is not required and it will not impact their care.

13.5 **Incentives to Subjects: Will subjects receive any incentives (payments, free service, gifts, etc.) for participation in the research?** *This information must mirror the consent form language.*

No

13.6 **If yes, please describe these incentives and how they will be disbursed:** ***Note: payment or compensation to subjects for participation is not to be considered a potential benefit.*** *Describe incentives, if they are to be pro-rated based on visits completed please give that information. This information must mirror consent form language.*

13.7 **Please attach copies of all recruitment/advertising materials and verbal scripts:** *Attach copies of all recruitment and advertising materials.*

Name	Version
There are no items to display	

View: 13-01 Recruitment II

13.1 Recruitment II:

13.8 **Expense to Subjects: Will subjects incur any expenses as a result of participation in the study or will they be billed for any study-related procedures?** *Check yes or no, make sure this information is in the consent.*

No

13.9 **If yes, please describe the expenses or charges that subjects will be assessed:** *Please provide information regarding expenses to subjects and add information to consent.*

13.10 **Compensation For Injury: If applicable, will funding be available to compensate subjects for injuries sustained as a result of participation in** *Check yes or no, make sure this information is in the consent.*

this research?
No

13.11 Who will cover the costs related to any injuries sustained due to participation in the study?

Please describe in detail. Examples subjects or their insurance company, study sponsor.

View: 14-00 Data Collection

14.0 Data Collection:

14.1

A. What type of data will you be collecting as part of this research?

Existing data must be in place or on the shelf prior to the submission of the research protocol to the IRB.

Prospective data is collected in real time.

Will you collect existing data?

or

Will you collect prospective data?
○ Yes ○ No

or

Will you collect both existing and prospective data? ◉ **Yes** ○ No

***Definitions:* Data are considered to be existing data only if they were in place or "on the shelf" prior to the submission of the research protocol to the IRB. Data are considered prospective if they are created and collected as part of the research i.e. from surveys, questionnaires.**

Tell the IRB why you are collecting this data i.e. to verify inclusion criteria.

B. Why are you collecting this data?

What will be the purpose of collecting and/or reviewing the data (new data or existing data).
After intervention of targeted fortification vs standard fortification anthropometric measurements and body composition will be measured. Daily weight; weekly length, head circumference, skinfold thickness or mid upper arm circumference; and PEAPOD body composition prior to discharge. These will be measured to evaluate growth parameters of infants receiving individualized targeted fortification to meet nutritional goals vs standard fortification.

14.2

If you are collecting existing data:

Specify the types of existing data you will use in this study.

Specify the type(s) of existing data sources you will use (medical records, school records, publicly available records, existing database). If you are collecting data from an exisitng database and that database contains PHI, you must provide the IRB Approval letter (attach to Section 27.00 Additional Documents).
We will use medical records for mother and baby to obtain demographics.

Time frame i.e. last 10 years or from 1990-2000.

What is the timeframe of the existing data you wish to review? (i.e. 2000-2006)
Any time before study enrollment.

14.3

If you are collecting prospective data:

Where or how will the data be obtained? (i.e. surveys, questionnaires, psychological tests)
NICU admission log and electronic medical records. Milk samples will be analyzed in the lab at MHMC using the Miris human milk analyzer. PEAPOD body composition measurements will be done at the CRU.

Where will data be obtained? i.e. survey.

14.4

How will the data you collect be identified?

Types of Data Identification:

Please select how your subject data will be identified.

Name
Deidentified/Confidential- Data will be linked to subject(s) via a code or indirect identifier (i.e. study IDs or numbers)

14.5 Will the information collected from these records be linked to any research subjects by identifiers? (i.e. name, MRN#, DOB)

Will your data be linked to subjects?

(●) **Yes** ( ) No

Please answer questions about the security of the data in section 15.00

14.6 If subject data will be deindentified using a code will there be a link or a key? Please describe. Who will have the key and where will the key be kept?

Explain how Data will be linked.

Each patient in the database will be assigned a sequential subject number. Medical record number will be in the key only, not I the database. The key will be kept in REDCap and the deidentified data will be kept on a secure MHS network drive. Only the PI and coinvestigator will have access to the key.

Under the HIPAA Regulations, deidentified key codes must be stores separately from data & must not be kept on paper, but electronically. The MetroHealth Research Informatics Support should be contacted at REDcap@metrohealth.org for assistance. They will assist personnel in developing a key in MetroHealth REDcap database. They can also assist with training & development for your study. REDcap is a free database provided in part by the Case CTSA.

14.7 Data Collection Form(s):

Add data collection forms and CRFs.

Name	Version
data sheet HMA revised.xlsx | History	0.01

View: 15-00 Data Security I

15.0 Data Security I:

It is imperative that the IRB is proactive and consistent in protecting all research data containing Protected Health Information(PHI).

15.1 * Are the records for this study (some or all) electronic? (●) **Yes** ( ) **No**

What is Protected Health Information? The Privacy Rule protects certain information that covered entities use and disclose. This information is called protected health information (PHI), which is generally individually identifiable health information that is transmitted by, or maintained in, electronic media or any other form or medium. This information must relate to 1) the past, present, or future physical or mental health, or condition of an individual; 2) provision of health care to an individual; or 3) payment for the provision of health care to an individual. If the information identifies or provides a reasonable basis to believe it can be used to identify an individual, it is considered individually identifiable health information.

The following questions must be answered when submitting a new protocol.

15.2 * Are you collecting PHI? (●) **Yes** ( ) No

15.3 Is any PHI going to be stored as paper files? ( ) Yes (●) **No**

15.4 Is any PHI going to be stored in an electronic file format? (i.e. access, excel) (●) **Yes** ( ) **No**

15.5 Is your data being stored on a laptop computer? ( ) Yes (●) **No**

15.6 Will you be using RedCap to store your data? (●) **Yes** ( ) **No**

Which RedCap Database will you be using?

Name

Name

MetroHealth

15.7 Are you planning to store your data using a portable storage device?(i.e. jump drive, external hard drive, cd) ○ Yes ◉ **No**

Per current MetroHealth Policy PHI may not be stored on portable electronic devices.

15.8 Are there any circumstances under which you would want to remove data from MHS? (i.e. take data home to work on it) Give details below. Please note identified data can't be removed from MHS unless there is permission granted in the HIPAA Authorization. If you are unsure about what is identified data please consult the IRB staff. If you feel you will need access to your data when you are off campus you should ask the MHS IT Department located in Rammelkamp room R 134 about VPN access.

○ Yes ◉ **No**

If you answered yes to question 15.8, please explain?

15.9 **Where will the records pertaining to this research be stored? (give the actual physical location of the paper records i.e building name and room number); and/or the secure network drive where the data is being stored.**

State the exact physical location of paper files and the network drive for electronic files.

Records will be stored electronically on the shared secure network drive of the MetroHealth network.

REDCap(Research ElectronicData Capture) is a secure, web application designed to support data capture for research studies, providing user-friendly web-based case report forms, real-time data entry validation (e.g. for data types and range checks), audit trails and a de-identified data export mechanism to common statistical packages (SPSS, SAS, Stata, R/S-Plus). The system was developed by a multi-institutional consortium which includes The MetroHealth Medical Center and was initiated at Vanderbilt University. The database is hosted at the MetroHealth Datacenter. The system is protected behind a login and The MetroHealth Firewall. There is an audit trail tracking all logins and activities in the database. Data collection is customized for each study or clinical trial based on a study-specific data dictionary defined by the research team with guidance from the REDCap administrator.

15.10 **How will these records be secured (we are refering to both paper records and electronic records)? Examples for electronic records (i.e. secure drive, password protected documents, encrypted jump drive). Examples for paper records, must be double locked (i.e. locked office and locked file cabinet or a locked file box inside a locked cabinet).**

i.e. locked cabinet, locked room.

Records will be stored electronically on the shared secure network drive of the MetroHealth network, which will require a password to retrieve which only the study team will have access to. Only the study team will have access to REDcap, which will require a password to access.

15.11 **Who will have access to the data?**

Give name and title exclude study staff who are MHS employees.

Principal investigator and co-investigators listed.

Please Note: All study documents must be retained for a minimum of four years after study completion (even when no subjects have been enrolled), twenty-two years if study involves children or pregnant women. Records for device studies must not be assigned a destruction date until the FDA approval status is determined, at which point records will be retained according to the scheme above (minimum of four or twenty-two years as appropriate). Under HIPAA regulations you must keep a record of all medical records where you looked at or recorded PHI (without a HIPAA Authorization) for 6 years (i.e. prep for research).

MHS Record Retention Policy VII-4

15.12 **How long will you keep the records pertaining to this research? Where will these records be stored after the study has been completed?**

Check the MHS Record retention policy for guidance.

Records will be kept for 22 years after the end of the study in a password protected secure MHS drive.

15.13 **Where, when, and how will the information be destroyed?**
The electronic records will be deleted in consultation with IS 22 years after study completion.

*Please Note: There are EPA regulations surrounding the destruction of CDs, DVDs, Floppy discs and other portable storage media. If you want to destroy these types of media please contact Ron Wallace in Environmental Services at 778-4776.

You must have a plan for data destruction.

View: 15-01 Data Security II

15.1 Data Security II:

15.14 **Who (non-study staff) will have access to the records? Give name and title of individuals. Where an individual's name is not known give title i.e. monitor from CRO.**
NA

List all those not study staff who will see and have access to data.

15.15 **Will data be transmitted to the sponsor?** ○ Yes ◉ **No**

Are you sending CRFs to sponsor?

15.16 **If yes, describe what data will be sent to the sponsor and the provisions that have been made for preservation of confidentiality in the transmission of data to the sponsor:**

Please describe i.e. will you be using encryption software?

15.17 **Will the data from this research project be transmitted to anyone other than the sponsor?** ○ Yes ◉ **No**

Check yes or no.

15.18 **If yes, to whom will this data be transmitted?**

Please describe organization or individual.

15.19 **Describe the data that will be sent to entities other than the sponsor and what provisions have been made for the preservation of confidentiality:**

Please describe data, and confidentiality provisions.

View: 16-00 Request for a Partial Waiver of HIPAA Authorization

16.00 Request For a Partial Wavier of HIPAA Authorization

An IRB, under certain circumstances, may allow researchers to forgo obtaining an authorization; this is called a waiver of authorization. A waiver of authorization may be full or partial:

- full waiver: an IRB waives the requirement for authorization for all uses of PHI for a particular research protocol (see Section 16.01 Request for a Waiver of HIPAA Authorization);
- partial waiver: an IRB waives the requirement for an authorization only for some uses of PHI for a particular research protocol. Researchers are required to obtain subjects' Research Authorizations after recruiting and enrolling subjects via a partial waiver and prior to creating or using PHI during research procedures.

Partial Waiver for Preparatory for Research Activities:
According to HHS guidance on the Privacy Rule the preparatory to research provision permits covered entities to use or disclose protected health information for purposes preparatory to research, such as to aid study recruitment. **However, the provision at 45 CFR 164.512(i)(1)(ii) does not permit the researcher to remove protected health information from the covered entity's site.** *As such, a researcher who is an employee or a member of the covered entity's workforce could use protected health information to contact prospective research subjects.* The preparatory research provision would allow such a researcher to identify prospective research participants for purposes of seeking their Authorization to use or disclose protected health information for a research study.

Under the preparatory to research provision, a covered entity may permit a researcher who works for that covered entity to use PHI for purposes preparatory to research. A covered entity may also permit, as a disclosure of PHI, a researcher who is not a workforce

member of that covered entity to review PHI (within that covered entity) for purposes preparatory to research.

16.1 *Check yes or no.*

Are you requesting a Partial Waiver of HIPAA Authorization? ◉ **Yes** ○ No

Why are you requesting a Partial Waiver?

16.2 *Check yes or no.*

Is the purpose of the Partial Waiver Recruitment (including screening of Medical Records)?

◉ **Yes** ○ No

Is the purpose of the Partial Waiver to request access to PHI for Non-MetroHealth personnel?

○ Yes ◉ **No**

16.3 Will the use of Protected Health Information (PHI) involve more than minimal risk to the privacy of the patients? *Check yes or no.*

○ Yes ◉ **No**

16.4 *Check true or false.*

The IRB as part of it's review of this request must have certain reassurances that Patient Privacy will be protected, please respond to the following questions true or false.

1.) The PHI will be used solely to facilitate the research protocol as an aid to study recruitment or to expand the research study. The waiver would allow identification of prospective research participants for the purpose of seeking authorization to use or disclose PHI for a research study. Essentially, PHI will be used to identify and contact potential research participants. Only contact and screening information (race, age, medications, diagnosis, and primary physician) will be recorded, and no information will leave the premises of MetroHealth Medical Center. The information will not be disclosed outside the research group for this study. ◉ **True** ○ False

2.) Information about potential subjects who are not interested in participating will be destroyed after the patient declines enrollment. The information of patients choosing to participate will be further used to schedule an appointment. As soon as the research staff sees the participant, a full authorization will be obtained to collect, use and disclose PHI for the remainder of the study. ◉ **True** ○ False

3.) The PHI will not be reused or disclosed. Because the PHI belongs to individuals who are not yet in the study, oversight provisions do not apply. After subjects are formally enrolled, an authorization will be in effect and the waiver will no longer apply. ◉ **True** ○ False

16.5 If you did not answer true to all three parts of question 16.4 please explain: *Please explain your response to any statement where you have entered false.*

16.6 Please give a detailed explanation as to why this research activity cannot be practicably conducted without a Partial Waiver or without access to PHI: Prospective study subjects from the inborn deliveries at MHMC will be identified based on inclusion criteria, evaluated with access to PHI. *Example: our study population has xxx disease and we rely on the EMR information to identify and contact potential subjects.*

16.7 Who will have access to PHI? Please list below: *Add the names of persons who will have access to PHI.*

Name	Employer	Department	Employer Name
Sharon Groh-Wargo	MHS	Pediatrics	The MetroHealth System
Stephanie Merlino	MetroHealth	Neonatal	The MetroHealth System
Stacey Ramey	MetroHealth	Pediatrics, Neonatology	The MetroHealth System

16.8 *Check yes or no.*

Are you or anyone who assists you Non-MetroHealth Personnel? ○ Yes ◉ **No**

**Note all Non-MetroHealth Personnel have to go through employee orientation, have a security clearance and Epic training before they can access the MetroHealth*

EMR. Also all all Non-MetroHealth Personnel must work under the control of a member of the MetroHealth Staff.

If you filed a Prep for research form with IT and RABO please attach it here.

If you have previously completed an MHS **Prep for Research form** add that form here:

Partial Wavier Memos completed prior to 11/26/2010 will populate here.

Name Version
There are no items to display

Old Memos Requesting Partial Waivers (prior to 11/26/2010):

There are no items to display

View: 16-01 Request for a HIPAA Waiver of Authorization

16.1 Request For a HIPAA Waiver of Authorization:

16.9 *Check yes or no.*

Are you requesting a Waiver of HIPAA Authorization?
No

Check one, if you check no then hit continue and go to the next page.

If you are requesting a Waiver In order for the IRB to Grant a Waiver you must answer questions 16.10-16.16

16.10 Disclosure of Protected Health Information (PHI) will not involve more than minimal risk to the privacy of the patients/subjects: *Check true or false.*

16.11 What is the plan to protect patient/subject identifiers from improper use and disclosure? *i.e. This unique identifier will be used on the data collection form. Only the PI will have access to the key linking the unique identifier to patient/subject names.*

16.12 What is the plan to destroy the identifiers at the earliest opportunity consistent with the conduct of the research? *i.e. The unique identifier key will be retained in Red Cap and will be destroyed two years after the study ends.*

16.13 Will PHI be reused or disclosed to others: *Check yes or no.*

16.14 Please complete the following: Data will only be used to analyze... *i.e. Data will only be used to analyze...*

16.15 Describe why this research can not be conducted without a waiver: *i.e because many of the subjects who participate in this treatment are dead or have transferred to other treatment modalities, or are transient. To obtain HIPAA Authorization from these individuals would be a greater risk to their loss of privacy.*

16.16 Describe why this research could not be conducted without access to and use of PHI: *i.e. It would not be possible to determine linkages between .....and clinical outcomes without the use of PHI.*

View: 16-02 HIPAA II

16.2 HIPAA II:

16.11 *Check all that apply, your answers will help the IRB to determine if your data is a limited data set.*

Which of the following identifiers about subjects will be collected for this study?

Name
2. Telephone Numbers
8. Names or Initials
16. Medical record or prescription numbers
21. Dates (except year) related to an individual (birth date, admission date, discharge date, date of death)

*These Questions deal with the collection of data and data use agreements. If you are **not** receiving data or sending data out to another entity this does not apply to you. If you have a signed contract with a sponsor or are in a cooperative group that has a signed agreement with MHS this does not apply to you. Data use agreements specify the conditions under which data can be shared between MHS and other organizations or individuals.*

16.12 **If you have selected only numbers 4, 5, 6, or 22 in question number 16.11 your research is considered to use a limited data set. If either of the following conditions apply, you will need to obtain a Data Use Agreement and complete a waiver of authorization or obtain a HIPAA authorization from the subjects. (check one):**
Name
There are no items to display

Check one, please read carefully if you are not receiving data or sending data out to another entity this does not apply to you, move on to 16.14. If you have a contract with a sponsor or you are in a cooperative group that has a signed agreement with MHS this does not apply to you. In all other cases please contact the MHS Legal Department with questions about data use agreements.

16.13 **Attach a copy of the Data Use Agreement:**
Name Description
There are no items to display

Attach Data Use Agreement.

View: 16-03 HIPAA III

16.3 HIPAA III:

16.14 **If any other unique identifying number, characteristic or code is selected, please specify:**
NA

Please specify this question refers back to the list of 22 identifiers.

16.15 **If a link to an identifier will be used (i.e. code numbers) is selected, please describe the coding mechanism that will be used:**
As patients are enrolled into the study they will be assigned a study number. Only the study staff will have access to the key.

Describe the coding mechanism.

16.16 **Will a certificate of Confidentiality be obtained for this study?** No

Check yes or no.

16.17 **If yes, please attach a copy the Certificate of Confidentiality:**
Name Version
There are no items to display

Attach a copy of the Certificate of Confidentiality.

16.18 **Describe how you will protect the privacy of participants. Describe specifically how you will gather information from or about them. *Please note while confidentiality concerns data, privacy concerns people. Example People may be uncomfortable answering questions about their employer in an open cubicle, so investigators may arrange for a more private location.***
When approaching parents and speaking to them, the study staff will ensure that this is done within a private location in NICU.
Patients will be assigned a study number. The key will be kept in a private,

Please note while confidentiality concerns data, privacy concerns people.

secure location, that only the study staff will have access to.

View: 17-00 Waiver of Informed Consent

17.0 Request for a Waiver or Alteration of Informed Consent:

17.1 *Answer yes or no.*

Are you requesting a Waiver of Consent [45 CFR 46.116(d)] OR a Waiver of Documentation of Consent [45 CFR 46.117 (c)].
No

If no hit continue button and you will go to the next page.

If yes please Note:

Note: Waivers of consent are not applicable if the research is subject to FDA regulations, except the following.

FDA Exception from general requirements:

1. Emergency Ues: Waivers of Informed Consent in FDA-regulated studies are permissible in case of life-threatening situations, inability to communicate, not sufficient time and no alternative method, even if research presents more than minimal risk [21CFR50.23];
2. Planned Emergency Research: If the study satisfies the requirements under 21CFR50.24 "Exception from Informed Consent Requirements for Emergency Research."

17.2 *Check true or false.*

Waiver of Consent: If you are requesting a waiver of consent, please provide the justification and address each of the following points for the IRB's consideration:

Note: practicably does not mean it would be inconvenient.

This research study involves no more than minimal risk:

The waiver will not adversely affect the rights and welfare of the subjects:

This research could not practicably be carried out without a waiver:

Whenever appropriate, the subjects will be provided with additional pertinent information after participation:
○ Yes ○ No

17.3 *Please explain in detail.*

Please explain your answers to the above questions (You must provide the IRB with enough information to make a decision):

An IRB may **waive the requirement to obtain a *signed* consent form** for some or all subjects if it finds either of the conditions below. In cases in which the documentation requirement is waived, the IRB may require the investigator to provide subjects with a written statement regarding the research.

17.4 *Check true or false.*

(1) The only record linking the subject and the research would be the consent document and the principal risk would be potential harm resulting from a breach of confidentiality. Each subject will be asked whether the subject wants documentation linking the subject with the research, and the subject's wishes will govern; OR

Check yes or no.

17.5

(2) The research presents no more than minimal risk of harm to subjects and involves no procedures for which written consent is normally required outside of the research context.

○ Yes ○ No

17.6 **If you are requesting any Alteration to the standard consent form/process (written long form consent is the standard) please provide a detailed explanation or plan.**

Example of an alteration: verbal consent.

View: 17-01 Informed Consent Process I

17.1 Informed Consent Process I:

17.7 **Who will be approached to obtain consent/assent:**

Check all that apply.

Consent Method
Subjects will be asked to sign a study consent form after receiving a complete explanation of the study.
Parents/Legal Guardian will be asked for permission after receiving a complete explanation of the study.

Idendtify all Staff obtaining consent on page 1 question 1.4 by selecting the corresponding role.

17.8 **Subject Comprehension: What measures will be taken to ensure that subjects fully understand the nature of their involvement in the research?**

Please give brief explaination.

Note to Investigator:

To address issues of comprehension on the part of the participant or representative, and who is involved in obtaining consent, the answers to following questions should be addressed:

1.) Once a potential participant is identified, what process is followed to inform the subject of the study prior to obtaining a signature on the informed consent form?

a. Who introduces the study to the potential subject?

b. Who reviews the informed consent document in depth?

c. Do you require the potential participant to have another person present during the presentation of the study?

2.) Who answers the questions presented by the potential participant and/or family?

3.) What method is used to determine if the potential participant fully understands the study, what is required from them, risk and benefits, and their rights as a participant?

4.) Is the principal investigator usually present during the presentation of the informed consent?

Potential mothers will be approached by a study team member and a detailed explanation of the study will be given to them. A copy of the informed consent will be given to the mother. they will be allowed time to read over the consent and discuss it with family or close friends. they will be asked if they fully understand the study, risk and benefits, what is required of them, and their rights as a participant. One of the co-investigators will be present. The consent form will be in English and it will be ensured that the participant understands English and can read English.

17.9 **Capacity to Consent: How will capacity to consent be assessed? *This question is to be addressed for all subjects not just those with limited decision making capacity. Identify who will make this assessment? Suggested language....all subjects will be awake, alert and oriented, be able to read etc. It is important to address issues like ability to read and understand information in the consent.***

How will you determine capacity to consent?

All subjects will be spoken to in English and it will be ensured that they understand, speak, and can read the language. They will be approached with they are awake, alert, and oriented and out of the effect of any sedating medications given during delivery.

17.10 **Attach a description of the Consent Process: Explain the process of obtaining consent from subjects. Under what settings and conditions will consent be obtained? What will be the timing/waiting period? What measures will be taken to ensure that subjects will make decisions independently?** *Note to Investigator: The "informed consent process" should include sufficient time for the participant to review and consider participating with the assistance of family members, research partners or representative if necessary. Other items to consider regarding time / waiting periods are: Is the potential participant given a copy of the consent form to read prior to the discussion of the study? Is it presented in person or mailed (where they can review it in the privacy of their own home)? How much time elapses between the presentation of the study and informed consent form and the actual signing of the form? The answers to these questions will ensure the PI has considered this component of the process and will reassure the IRB that the PI is allowing adequate time for the participant to make an informed decision and minimize the possibility of coercion or undue influence.*

Attach a plan for consenting subjects. This must give detail about the consent process.

Name	Description
Consent Process | History	

17.11 **Parental Permission and Youth Assent: Complete this question only if enrolling minors. How will parental permission and youth assent (if applicable) be obtained?**

Mothers of premature infants involved in the study will be approached and informed consent will be obtained. If the mothers are minor, the guardian of the mother will be approached for informed consent.

Give details of assent process and assent form.

View: 17-02 Informed Consent Process II

17.2 Informed Consent Process II:

17.12 **What method will be used to document the consent process (i.e. a note in EPIC)? Not how you will get consent only how you will document consent has been obtained, i.e chart note, note in study file.**

A note in Epic EMR, note in study file

i.e chart note, note in study file.

17.13 **What type of Informed Consent will be used in this study? (check all that apply):**

Consent Type
Written/Signed Consent by Subject
Written/Signed Permission by Parent/Guardian

Check all that apply

A non-return cover memo applies to a study in which you are sending out a questionnaire with a memo or letter that informs participants about the study but does not need to be signed and returned. If they complete and return the questionnaire they have given consent.

17.14 **If other, please specify:**

If other, please give specifics.

****Attach all consent forms (Informed Consent, Genetic Consent and HIPAA) here:****

17.15 Please attach a copy of each Informed Consent form(s) and HIPAA Authorization you are using for this study:

Attach Consent form(s) and HIPAA Authorization here

Name	Version
HMA ICF & HIPAA 6 17 tracked changes .docx	0.01
HMA ICF & HIPAA 6 18 clean.docx	0.02

17.16

Will non-English speaking subjects be enrolled?

Check one

○ Yes ◉ No Clear

If the answer to 17.17 is no we will not be enrolling non-English speaking subjects then tell the IRB why not?

Please give the IRB an explanation as to why non-English speaking subjects will not be enrolled.

Study staff only knows English

17.17 If non-English speaking subjects will be enrolled please provide information about the person(s) obtaining consent (what language they will speak)and how you will deal with written translation(s):

Provide information about translating consents and having interpertative services available for consent.

View: 18-00 Data Safety Monitoring I

Section 18.0 Data Safety Monitoring Plan

DATA AND SAFETY MONITORING PLAN GUIDE

WHEN DO YOU HAVE TO COMPLETE A DATA SAFETY MONITORING PLAN?

FOR THE IRB- **All interventional studies that are greater than minimal risk should have a Data Safety Monitoring Plan. The IRB reserves the right to require a Data Safety Monitoring Plan for any study.**

Archived IRB Data Plans - prior to 9/28/2010

FOR THE CRU- **ALL CRU PROTOCOLS [Recent NIH guidelines stipulate that all protocols that involve human subjects, a signed consent form and are conducted on, or use the resources of, the CTSA Clinical Research Unit - MHMC (CRU) are required to have a Data and Safety Monitoring Plan (DSM Plan).]**

What is a Data and Safety Monitoring Plan (DSM Plan)?

A DSM Plan is a prospectively defined strategy to assess the assumptions made in the trial design while the study is in progress. Its main purpose is to ensure the safety of participants in clinical research studies and the validity and integrity of research data collection. A properly designed DSM Plan improves the scientific quality and yield from a clinical trial and the protection of human subjects.

The DSM Plan needs to address the nature of the safety monitoring and who will be conducting that monitoring. It may be reasonable for a single individual to perform the monitoring in a small trial with minimal/low risk while a local independent or an external data and safety monitoring board (DSMB) may be required for more complex/high risk trials.

Key elements to be incorporated in a DSM Plan

- **Assessment of risks and monitoring level**
- **Safety contact: Who is responsible?**
- **Safety monitoring: Who will do it? How often?**
- **Informed consent process; consistency with the protocol**
- **Data collection process**
- **Adverse Events Monitoring: Anticipated and unanticipated**
  - **Description of anticipated adverse events**
  - **Grading and attribution method**
  - **Reporting of unanticipated adverse events**
  - **Plans for periodic reporting**
  - **Impact on termination of subjects from the study and study closure**

Step 1 - only for Investigators Using the CRU:

1.A Is your protocol approved and supported by the Ireland Cancer Center? ○ Yes ◉ **No**

If Yes - The Comprehensive Cancer Center Data and Safety Moniotoring Plan for Clinical Trials is on file. Proceed to Step 5.1.B If No, Proceed and complete Steps 2-5

****

Step 2 - all Investigators - Provide Information in order to determine the level of safety monitoring required

2.A List all data collection types and study procedures (this information will pull from Section 8 Methods and Procedures questions 8.1, 8.2, 8.3)

Data Collection types:

Name
Chart Review - Prospective
Anthropomorphic evaluations

Social-Behavioral Procedures:

Name
None of the Above Social-Behavioral Procedures Apply to this Study

Medical Procedures:

Name
Study of Human Biological Materials (i.e. Urine Collection)
Study of Existing Data
Medical Tests, Comparisons, Evaluations
Special/prescribed diets
Anthropomorphic Measurments

****

You must select the risk level Please read the information below, check the applicable boxes and select an appropriate risk level.

Level I: Minimal and Low Risk Studies (examples of studies that are minimal and low risk studies)

Types of Studies:

Name
Anthropomorphic evaluations

Level II: Moderate Risk Studies (examples of studies with populations, drugs, and procedures that are moderate risk)

Types of Studies:

Name
Child Population

Level III: High Risk Studies (examples of diagnostic procedures and drugs or device studies which are high risk)

Types of Studies:

Name
There are no items to display

2.B If you do not see your study procedures on the above list please add in the procedures being done for research purposes:

Add additional risk(s):

Procedure	DSMB Risk

There are no items to display

Select the Appropriate Level of Risk for this study based on the criteria above:

Level of Risk:
Risk Level I Mimimal and Low Risk Studies

Now Select the appropriate Level of Monitoring and give your justification:

2.C Rank Level of Monitoring (select one by checking the box)

Minimal/Low/Moderate Levels of Monitoring ☑

Justification for selecting Minimal/Low/Moderate Level of Monitoring Required:
We are not introducing a new drug. We are only adjusting the amount of protein and fat given to premature infants based on the analysis of their mother's breast milk composition in the intervention group. Outcomes measured are growth parameters and anthropometric measurements when infants are clinically stable. The harm anticipated is no higher than those encountered in daily life or during care in the NICU, therefore only needing low level monitoring.

High Level of Monitoring ☐

Justification for selecting Risk High Level of Monitoring:

View: 18-01 Data Safety Monitoring II

18.01 Data Safety Monitoring II

A designee will perform the safety monitoring:
○ Yes ◉ **No**

Identify the designee [provide contact information]:

A medical monitor or independent individual/safety officer will be performing the safety assessments.
◉ **Yes** ○ No

Identify who will be performing the safety assessments [provide contact information]:
Dr. John Moore
Professor of Pediatrics and Reproductive Biology
Case Western Reserve University School of Medicine
Director of the Division of Neonatology
MetroHealth Medical Center
2500 MetroHealth Drive
Cleveland OH 44109
Tel: 216-778-5946
email: Jmoore@metrohealth.org

Has a Data Safety Monitoring Board or Committee been established for this study?
○ Yes ◉ **No**

Identify these members by name, title and qualifications. How often will the DSMB meet? How frequently will the DSMB report it's findings?) data prior to 9/28/2010 read only.

If there is a DSMB or DSMC is it a nationally constituted Data and Safety Monitoring Committee? ○ Yes ○ No

Please enter the Name of Contact or Chair, Address and Phone or E-Mail:

Is there a locally constituted Data and Safety Monitoring Committee or Board that will perform the safety monitoring. Specify composition and responsibilities in the box below. *Note: Board Members should not have conflicts with this study or with study personnel.* ○ Yes ◉ **No**

Names of Members of Local DSMB [provide contact information]:

3.B.1 Description of anticipated adverse events. Pulled from question 10.5.

Targeted fortification- rare, some babies may have elevated BUN which is routinely monitored in the NICU, or rare, feeding intolerance

There is also risk of breach of confidentiality, but this is rare. Data will be stored securely, only key study investigators will have access to data, and it will be deidentified and only the PI will have access to the key.

The probability and magnitude of harm or discomfort anticipated in the research are no greater than those ordinarily encountered daily during routine care while admitted to NICU.

Additional Comments on anticipated adverse events:

3.B.2 Safety data/procedure used to preform evaluation:

Data to be evaluated:

Name
There are no items to display

Who will evaluate safety data:

Frequency of Monitoring:

Name
6 Months

3.C. Grading method and attribution for adverse event reporting:

Grading method and attribution for adverse event reporting

The PI must identify what scale will be used to grade adverse events (AEs) and indicate his/her attribution/assessment of the relationship between the adverse event and the protocol/intervention. Each protocol may have a unique approach to grading adverse events and the PI should consult the parent protocol and/or funding source for specific grading scales. Suggested guidelines for the grading of adverse events are available below:

Example A: ***Cancer Therapy Evaluation Program (CTEP) Common Toxicity Criteria (CTC II) available for viewing at http://ctep.info.nih.gov (see "Reporting Guidelines, Common Toxicity Criteria")***

Example B: Common grading scale

0 No adverse event or within normal limits or not clinical significant
1 Mild AE, did not require treatment
2 Moderate AE, resolved with treatment
3 Severe AE, resulted in inability to carry on normal activities and required professional medical attention
4 Life threatening or disabling AE
5 Fatal AE

3.C.1 Identify the scale to be used to Grade AEs in this study:

CRU Safety Scale:

Name
There are no items to display

3.C.2 Identify the attribution scale to be used in this study:

CRU Attribution Scale:

Name
There are no items to display

3.D. Population being studied: (populated from your answers to Sections 11.00 and 12.00)

Vulnerable subject groups? Yes

Children? Yes

Decisionally Impaired Subjects? No

Pregnant Women and/or Fetuses? No

Will you be enrolling Prisoners? No

Other Populations being studied:

Vulnerable Populations
Poor / Uninsured
Minors - Children under 18
Employees
Students
Minorities

**** Note More Frequent monitoring intervals may be needed for vulnerable populations.***

4.A. Plan for Adverse Event Reporting:

All Reportable Events (Anticipated and Unanticipated events) from this protocol must be submitted using the MHA eIRB Reportable event form in a timely maner consistent with MHS IRB SOPs.

In addition to the MHS IRB adverse events and Uanticipated problems will be reported to:

Reporting Institutions (check all that apply):

Name
There are no items to display

If other has been selected above please specify:

4.B Stopping Rules or Conditions under which Subjects can be removed from the Study [this information is from Section 10.01 of the Protocol Risks/Benefits Questions

Are there defined Stopping Rules? Yes

What are the stopping rules for the study? Intolerance to fortification, excessive emesis or recurrent, otherwise unexplained, abdominal distention.

What findings, events, or conditions would require a research subject to be removed from the study? (i.e. disease progression)
Clinical worsening, acute decompensation of infant precluding them from receiving enteral feeds.
If a patient become acutely ill and significantly decompensates they may be removed from the study. Ex: sepsis, abdominal distention, blood in the stool, respiratory failure with increasing need for respiratory support. If a patient becomes comfort-care only and no longer receiving enteral feeds they may also be removed from the study.

4.D. Additional Information (if Applicable):

Provide any other information relevant to the data and safety monitoring plan that was not already incorporated into this form.

Attach A copy of your Data Safety Monitoring Plan or other relevant information related to this form:

Name	Version
There are no items to display	

View: 19-00 Use of Human Biological Materials In Research I

19.0 Use of Human Biological Materials In Research I:

19.1 *Check yes or no.*

Will Human Biological Materials be collected as part of this study? (i.e. blood, tissue, fluids and substances etc.)
Yes

If no, hit continue and you will be taken to the next page.

19.2 **Will the storage or transportation of study materials place anyone at a health risk? In other words, are these biohazardous materials? Will they put the staff collecting them or transporting them at risk?** *Check yes or no.*
No

19.3 **If yes, please explain:** *Please explain the risks. Above*

and beyond universal precautions.

19.4 **Will information from the materials be stored in an electronic database?** Yes

Check yes or no.

19.5 **If yes, list the database(s) where the information from the materials will be stored and who will have access to them:**
The data collected will be stored in the shared secure drive of MHMC secure network and will be accessible only to the study team and will be password protected. REDCap will also be used to store study data. REDCap (Research Electronic Data Capture) is a secure, web application designed to support data capture for research studies.

List the database(s) and who will have access to them.

19.6 **Human Biological Material Destruction: please describe the plan for materials destruction (when, where, how and by whom):**
After study completion the breast milk will be disposed of by study personnel in the lab in a sanitary waste drain. After rinsing, the sample vials will be disposed of in a standard garbage dumpster.

Give the destruction plan i.e. shipped back to sponsor for destruction at end of study, incinerated by Browning Ferris 3 months after study ends.

19.7 **Storage of Human Biological Materials: please describe where, how and for how long the materials will be stored:**
Once weekly the previous 24 hour breast milk sample that is provided by the mothers will be mixed properly and a small aliquot will be collected. The samples will be put into sample vials and stored in the refrigerator in the NICU along with the remainder of the mother's breast milk supply. Each sample will then be taken to the lab at Metrohealth with a unique ID and analyzed in the lab.

Physical storage of materials where will it be, how will it be stored and for how long.

View: 19-01 Use of Human Biological Materials in Research II

19.1 Use of Human Biological Materials In Research II:

19.8 **Does this research involve human cell/lines and/or products that are made from human biological materials?** ○ Yes ◉ **No**

Check Yes or No.

If yes, please explain:

Please explain.

19.9 **Will Human Biological Materials (tissue, blood or salavia) be collected in this study for genetic research?**
No

Check Yes or No.

If Yes, please provide additional discussion of the genetic testing components including who will conduct the tests:

19.10 **If yes, can subject(s) decide not to participate in the genetic research and still participate in the study?**

Check Yes or No.

Please submit the appropriate genetic consent/tissue storage form and attached at 17.15
A template for this form can be found on the IRB Home Page. Note: if tissue storage is mandatory for participation in a study the subject consent must be included in the body of the consent form; if it is not mandatory it can be included as a separate page at the end of the consent form.

19.11 **Will NIH Genome-Wide Association Studies (GWAS) be conducted?** ○ Yes ◉ **No**

Check Yes or No.

19.12 **Will you be sending samples/data to the NIH GWAS?** ○ **Yes** ◉ **No**

Check Yes or No.

19.13 **Will you be using sample/data obtained frm the NIH GWAS?** ○ Yes ◉ **No**

Check Yes or No.

19.14 Please provide justification for using NIH GWAS:

Please explain.

If this is a GWAS study you will need to submit a **Patient Information Sheet (add at 17.16)**. This sheet should summarize the Genetic research component of this study and tell the subjects where their biological materials will be sent, what analysis they will undergo, who will have control of them and for how long and who to contact if they want to withdraw their permission. It must be clear to subjects that these samples will not be housed at MHS nor will the MHS Investigator retain control over them.

View: 20-00 Drug Information I

20.0 Drug Information I:

20.1

If you check no and hit continue you will go to the next page.

* **Does this study involve drugs?** No

If you are doing a drug study you may be required by law to register that study at Clinical Trials.gov Section 113 of the FDA Modernization Act mandates registration with ClinicalTrials.gov of investigational new drug efficacy trials for serious diseases or conditions. For more information click on the link below:
http://prsinfo.clinicaltrials.gov/registering.pdf

If you answer no and hit continue you will go to the next section.

Does this study involve:

Is the study drug(s) FDA approved for this indication? ○ Yes ○ No

Does this study involve use of a Placebo? ○ Yes ○ No

Does this study have a drug washout period? ○ Yes ○ No

Do you have an IND? ○ Yes ○ No

If yes please give the IND: (include a copy of the FDA approval letter at 20.4)

Who is the sponsor or holder of the IND?

Does this study have an IND exemption? (include a copy of the FDA exemption letter at 20.4) ○ Yes ○ No

20.2 Fill in an entry for all drugs that will be used in the study:

Please give a complete list.

Drug Name	FDA Approved (yes, no)	IND Number	Supplied By
There are no items to display			

20.3 Manufacturer (name, address):

Answer only if produced commercially.

20.4 Attach a copy of:
1.) Investigator Brochure and/or Package Insert
2. FDA Form 1571 Investigational new Drug Application Form
3.) FDA Form 1572 Statement of the Investigator Form
4.) FDA Correspondence (i.e. FDA Approval Letter for IND, FDA Exemption letter)

Attach the IB, 1572 and 1571 here.

Name	Description
There are no items to display	

View: 21-00 Medical Device Information I rev

21.0 Medical Device Information I:

Definition of a Medical Device:

An instrument, implement, machine, contrivance, implant, in vitro reagent, or other similar or related article, including a component part, or accessory which is

- Intended for use in the diagnosis of disease or other conditions, or in the cure, mitigation, treatment or prevention of disease in man or other animals.
- Intended to affect the structure or any function of the body of man or other animals, and which does not achieve any of its primary intended purposes through chemical action within or on the body of man or other animals and which is not dependent upon being metabolized for the achievement of any of its primary intended purposes.

In short any health care product that does not achieve its primary intended purposes by chemical action or by being metabolized. Medical devices include, among other things, surgical lasers, wheelchairs, sutures, pacemakers, vascular grafts, intraocular lenses, and orthopedic pins. Medical devices also include diagnostic aids such as reagents and test kits for *in vitro* diagnosis (IVD) of disease and other medical conditions such as pregnancy.

21.1 *Answer yes or no.*

Is this a Medical Device Study? Yes

If you are doing a device study you may be required by law to register that study at Clinical Trials.gov Section 113 of the FDA Modernization Act mandates registration with ClinicalTrials.gov of investigational new device efficacy trials for serious diseases or conditions. For more information click on the link below:

http://prsinfo.clinicaltrials.gov/registering.pdf

If you answer no and hit continue you will go to the next section.

21.2 **Medical Device Generic Name:** *Give generic name.*
Breast milk macronutrients test system

21.3 **Medical Device Brand Name:** *Give brand name.*
Miris Human Milk Analyzer

21.4 **Medicare Code Number:**

As stated in regulations 21 CFR 812.3(m), a device may be considered a, Significant Risk Device, if it meets any of the following criteria and a determination is made by the IRB that the device presents a potential for serious risk to the health, safety or welfare of a subject.

21.5 *Check one*

Is this device intended as an implant? No

21.6 **Is device to be used in supporting or sustaining human life?** No *Check one*

21.7 **Is the device for use of substantial importance in diagnosing, curing, mitigating, or treating disease or otherwise preventing impairment of human health?** *Check one*
No

21.8 **Does this device present a potential for serious risk to the health, safety, or welfare of a subject?** *Check one*
No

21.9 **If you answered NO to all the above, or if an initial risk assessment has determined that this is a non-significant risk device (21CFR 812.3), attach the appropriate documentation for this justification:** *Attach justification.*

Name	Description
MIRIS FDA.pdf | History	

21.10 What is the regulatory status of the study device?
FDA Class II Device

Provide information on the regulatory status of the device.

21.11 What is the long term plan for device management once the study closes?
Once the study closes the device will remain in the lab at MetroHealth for future clinical and research use.

Provide information such as how you will communicate important information to subject; plan for maintenance/repairs; contact information besides the PI.

View: 21-01 Medical Device Information II

21.1 Medical Device Information II:

21.12 What is the FDA Approval date?
12/21/2018

Please give date.

21.13 What is the Premarket Approval (PMA)number?

Please give number.

21.14 What is the Premarket Notification (510K) number?

Please give number.

21.15
What is the Investigational Device Exemption (IDE) number?

Who is the sponsor or holder of the IDE?

Please give IDE number if applicable.

21.16 What is the Humanitarian Device Exemption (HDE) number?

Please give HDE number if applicable.

21.17 Has this medical device ever been used in animals?
No

Check one

21.18 If yes, please give a brief summary of the results of studies involving animals:

Give a brief summary or attach one below at 22.16.

21.19 Please attach supporting documents:

Name	Description

Miris Manual | History

Give a brief summary.

View: 21-02 Medical Device Information III

21.2 Medical Device Information III:

21.20 Has this medical device ever been used in humans? Yes

Check yes or no.

21.21 If yes, please give a brief summary of the results from studies involving humans:
This device has been used extensively in Sweden in the NICU to analyze mother's breast milk. This information is used to individualize fortification to meet each infant's nutritional needs.

Give a brief summary.

21.22 Please list all research personnel authorized to use the study device:

Name	Employer	Department	Employer Name
Sharon Groh-Wargo	MHS	Pediatrics	The MetroHealth System
Stephanie Merlino	MetroHealth	Neonatal	The MetroHealth System
Stacey Ramey	MetroHealth	Pediatrics, Neonatology	The MetroHealth System

List all research personnel authorized to use study device.

21.23 How will this medical device be used in research?
We will perform weekly analysis of breast milk, for the infants in the targeted fortification group will have the milk fortified to meet their nutritional needs.

The intended use of the Miris human milk analyzer: to quantitatively measure the concentration of fat, protein, carbohydrate, total solids, and energy in human milk. These measurements will be used to aid in the nutritional management of the infants included in this study.

Give a brief description.

21.24 Please list all possible complications:
Inaccurate measurement of macronutrients of breast milk is a risk, and inappropriate fortification may be a complication. This will be minimized by

List all complications.

following the device manual instructions, testing control samples provided by the manufacturer to evaluate for accuracy as instructed by the manufacturer, and carefully calculating and adjusting each neonates nutritional needs based on the result.

21.25 **Please list all precautions, warnings, and contraindications:**
The device will only be used for analysis of human milk. If the mother has inadequate supply to provide a sample for analysis then the human milk analysis will not occur. The device will be used as instructed by the user manual and all safety monitoring protocol will be followed.

List all precautions, warnings and contraindications.

View: 21-03 Medical Device IV

21.03 Medical Device IV

INVESTIGATOR'S RESPONSIBILITY FOR CONTROL OF THE INVESTIGATIONAL DEVICES:
To protect the rights, safety and welfare of research participants the investigator must ensure control and accountability of all devices used in conjunction with clinical research protocols. To make certain that investigational devices are used only on research participant's who have signed the informed consent form specific for the device and IDE number.

Please check these boxes

21.26 ☑ The device will not be used on a research participant until FDA(when FDA regulated investigational device is being studied) and IRB approval has been obtained and the research participant has signed an informed consent document.

21.27 ☑ The informed consent document will inform the research participants that their names and information will be shared with the device company for tracking purposes.

21.28 ☑ The investigation will be conducted in accordance with the signed agreement with the sponsor, the investigational plan, and all applicable laws and regulations.

21.29 ☑ The device will be used only in accordance with the MHS IRB approved protocol.

21.30 ☑ The Investigator is thoroughly familiar with the appropriate use of the investigational device, as described in the protocol, in the product information, and in other information sources provided by the sponsor.

21.31 ☑ All persons assisting with the trial are adequately informed about the protocol and the investigational product(s).

21.32 ☑ Devices will be properly maintained and cleaned.

21.33 ☑ Research participants will receive adequate instructions about the investigational device to assure their safe participation in a research study.

21.34 **Any investigational devices used in conjunction with an investigational protocol must be kept in a locked and secured area. Access to investigational devices must be limited to personnel designated by the Principal Investigator. Please describe How you will secure the investigational devices to be used in this study and who will have access to them.**
The analyzer will be kept in the lab at MetroHealth. Only the study personnel will have access to the key to the lab.

21.35 **Attach copies of device logs, see examples of logs on the IRB Home Page in the IRB Guidelines Section under MHS Medical Device Guidelines :**

Name	Version
There are no items to display	

View: 22-00 Clinical Trials Registration

22.0 Clinical Trials Registration:

Note: Phase 2 - 4 trials of drugs and biologics (controlled clinical investigations other than Phase 1 investigations of a product subject to FDA regulation) AND trials of devices (controlled trials with health outcomes, other than small feasibility studies and pediatric post-marketing surveillance) must be registered per the Food and Drug Administration Act of 2007; NIH encourages registration of all trials, regardless of whether required under applicable law.

How are study protocols submitted to ClinicalTrials.gov?
The FDA Guidance Document (March 2002) (http://www.fda.gov/cder/guidance/4856fnl.htm) describes the submission criteria. The NLM has developed the Protocol Registration System (PRS), a Web-based tool for submitting information to ClinicalTrials.gov. Study sponsors or their representatives may register online to apply for a PRS account (http://prsinfo.clinicaltrials.gov/).

22.1 Has this trial been registered on www.clinicaltrials.gov?
○ Yes ◉ **No**
Web link to clinical trails website.

22.2 If **Yes**, who registered the trial?(i.e. sponsor, investigator)
Please respond

22.3 Please provide ClinicalTrials.gov Identifier (i.e. NCT00391872)
The sponsor can provide you with this information or you can look it up on the website.

22.4 If **No**, are there plans to register the study? ○ Yes ◉ **No**
If you answer No you must provide an reason why this study will not be registered.

22.5 If the answer to 22.4 is **No**, provide and explanation:
This is a research study that is using a medical device with FDA approval.
Provide a response if the answer to 22.4 is No.

View: 23-00 Interview/Focus Groups

23.0 Interview/Focus Groups:

23.1 **Does this study involve Interviews/Focus Groups?** No
Answer yes or no.

If you answer no and hit continue you will go to the next page.

23.2 **Attach copies of any scripts/or questions that will be used to guide the interview focus/groups:**
Attach scripts or questions.

Name	Version
There are no items to display	

23.3 **Idendtify all Staff conducting interviews on page 1 question 1.4 by selecting the correct role.**

23.4 **Is there any specific training or qualifications needed to conduct the interviews/focus groups?**
Describe training and/or qualifications.

View: 24-00 Psychological Testing

24.0 Psychological Testing:

24.1 **Does this study involve Psychological testing?** No
Answer yes or no.

If you answer no and hit continue you will go to the next page.

24.2 **First Please list all Psychological Tests that will be given:**
First please list the test(s)/measures to be used.

24.3 **Attach copies of all psychological test(s)/measures that will be used for this study:** *Second attach copies of all test(s)/measures.*

Name Version

There are no items to display

24.4 **Is there any necessary training or licenses required of those administering the psychological testing?** *Describe any training or licenses required to administer test(s).*

Idendtify all Staff Administering tests on page 1 question 1.4 by selecting the correct role.

View: 25-00 Surveys/Questionnaires

25.0 Surveys/Questionnaires:

25.1 **Does this study involve Surveys/Questionnaires?** No *Answer yes or no.*

If you answer no and hit continue you will go to the next section.

25.2 **Please attach all questionnaires and/or surveys to be used in this study:** *Attach survey(s)/questionnaire(s).*

Name Version

There are no items to display

25.3 **Idendtify all Staff conducting Surveys on page 1 question 1.4 by selecting the correct role.**

View: 26-00 Deception

26.0 Deception:

Deception is a research methodology. When deception is used in research the subject is not told, or is misled, about the true purpose of the research, such as in certain studies of group processes, contextual influences on cognition, etc.

26.1 **Does this study involve the use of deception as a study design method for the research?** *Deception is defined as intentionally misleading or withholding information about the nature of the experiment.*

No

If you checked no then hit the continue button and you will be taken to the next page.

26.2 **Describe in detail the nature of the deception and explain why this is necessary for the research:** *Please describe the nature of the deception.*

26.3 **State how, when and by whom the research subjects will be debriefed:** *Briefly describe your plan to debrief subjects.*

View: 27-00 Additional Documents

27.0 Additional Documents:

27.1 **Are there any additional study documents you wish to attach to this application?** *Attach any additional study documents i.e protocols supplied by sponsor.*

Name Version

There are no items to display

View: The End

To Finalize this application you must do two things:

1.) As a final step you should click on Hide/Show Errors on the top of this page. If there are any required fields in the Application you have omitted they will show up in red. If you click on each item you will be taken to that page of the application so you can

complete the question.

Note: Unless all named Co-investigators have agreed to participate you will not be able to submit your study. Co-Investigators have to press the Co-Investigators agree to participate button. You can send them an email message tellng them to do this by pressing

Notify Co-Investigators of Need to Agree to Participate. The minute you have selected your Co-Investigators you can press this button it is not advisable to wait until you have completed the application as it may hold up your submission.

When all error messages are gone then...

2.) Click Finish

Please click on the "Finish" button to finalize and exit the Study application. Doing so will **NOT** submit the application for review.

3.) The PI must press the Submit Study button (when they are ready to submit to the IRB)

Please note that a submission may only be forwarded to the IRB by the Principal Investigator. To do this, the Principal Investigator must push **" Submit Study"** in the blue area on the left hand side of the page under **My Activities**. Only the PI will have this button it will not be visible to any other study team members.

You can track the ongoing status of your submission by logging into the study workspace. On the top left hand side of the page in the light blue area there will be a box labeled with the **Current State** of your study.

Please contact the IRB with any questions or concerns. When calling the IRB Office Please direct your questions to the IRB staff named as the "Owner" of your study.

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Stacey Ramey

Study Role:

Name
Responsible Investigator (Resident PI one RI required)
DRA (only one)
Obtaining Informed Consent
eIRB Notification Recipient

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Stephanie Merlino

Study Role:

Name
Co-investigator
Obtaining Informed Consent

View: CCF Key Personnel Questions View
* **Name of Key Personnel Working on Study:** Mathavan Sivarajah

Study Role:

Name
Obtaining Informed Consent

View: CRU DSMP Data Collection Simple View
Name: Anthropomorphic evaluations
Level of Risk: Minimal and Low Risk Studies
Type: Data Collection
View: CRU DSMP Data Collection Simple View
Name: Child Population
Level of Risk: Moderate Risk Studies
Type: Study Population