Document Coversheet

Study Title: The Pediatric Oncology Interventional Nutrition Therapy (POINT) Trial

Institution/Site:	University of Kentucky
Document (Approval/Update) Date:	8/8/2023
NCT Number:	NCT06175273
IRB Number	89377
Coversheet created:	6/26/2026

Statistical Analysis

Data analysis was conducted using SPSS Statistics Version 31 (IBM Corp., Armonk, NY). Given the pilot nature of this randomized controlled trial (N=17), the primary focus was on estimating effect sizes and assessing feasibility trends alongside hypothesis testing. However, given the small sample sizes and distributional characteristics of the data, emphasis was placed on examining associations among change scores. Changes in weight and muscle parameters from baseline to follow-up (3 and 6 months) were summarized as mean change ± standard deviation and analyzed using paired Wilcoxon signed-rank tests. Spearman's rank-order correlations were used to examine associations between biomarkers and anthropometric measures. Analyses were conducted across two frameworks: (1) cross-sectional correlations using all available measurements across participants over time and (2) longitudinal associations using change scores defined as follow-up (3-and 6- month) values minus baseline values. Pairwise complete-case deletion was applied for each correlation calculation. The sample sizes for each test are provided alongside the corresponding correlation coefficients and p-values. Demographic data are reported as mean ± SD or median (IQR). Significance was determined as $p < 0.05$.

IRB Approval
8/8/2023
IRB # 89377
IRB2

PROTOCOL TYPE (VERSION 4)

Which IRB

◉ Medical ○ NonMedical

Protocol Process Type

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

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

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

Which IRB

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

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

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

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

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

Which Protocol Process Type

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

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

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

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

PROJECT INFORMATION

0 unresolved comment(s)

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

The Pediatric Oncology Interventional Nutrition Therapy (POINT) Trial: A Pilot Study

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

POINT trail

Anticipated Ending Date of Research Project: 6/30/2025

Maximum number of human subjects (or records/specimens to be reviewed) 45

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

PI CONTACT INFORMATION

0 unresolved comment(s)

Principal Investigator (PI) role for E-IRB access
The PI is the individual holding primary responsibility on the research project with the following permissions on the E-IRB application:

1. Read;
2. write/edit;
3. receive communications; and
4. submit to the IRB (IR, CR, MR, Other Review*).

If research is being submitted to or supported by an extramural funding agency such as NIH, a private foundation or a pharmaceutical/manufacturing company, the PI listed on the grant application or the drug protocol must be listed as PI here.

Please fill in any blank fields with the appropriate contact information (gray shaded fields are not editable). Required fields left blank will be highlighted in pink after you click "Save".

To change home and work addresses, go to myUK and update using the Employee Self Service (ESS) portal. If name has changed, the individual with the name change will need to submit a 'Name Change Form' to the Human Resources Benefits Office for entering into SAP. The new name will need to be associated with the individual's Link Blue ID in SAP before the change is reflected in E-IRB. Contact the HR Benefits Office for additional information.

The Principal Investigator's (PI) contact information is filled in automatically based on who logged in to create the application.

If you are not the Principal Investigator, do NOT add yourself as study personnel.
To change the PI contact information on an application in Researcher edit status:

- click "Change Principal Investigator";
- search for the PI's name using the search feature;
- click "Select" by the name of the Principal Investigator, then "Save Contact Information".

  You will automatically be added as study personnel with editing permissions to continue editing the application.

Change Principal Investigator:

First Name:	Corey	Room# & Bldg:	204 Funlkhouset Building
Last Name:	Hawes	Speed Sort#:	405060054
Middle Name	Joseph		
Department:	Physician Based Clinics - MG…	Dept Code:	MG100
PI's Employee/Student ID#:	10348127	Rank:	
PI's Telephone #:	8593237230	Degree:	DCN, RD, CSO, CSNC, LD
PI's e-mail address:	cjhawe2@uky.edu	PI's FAX Number:	
PI is R.N.	○ Yes ◉ No	HSP Trained:	Yes
		HSP Trained Date:	12/21/2020
		RCR Trained:	Yes

Do you, the PI, have a significant financial interest related to your responsibilities at the University of Kentucky (that requires disclosure per the UK administrative regulation 7:2)?

○ Yes ◉ No

RISK LEVEL

0 unresolved comment(s)

Indicate which of the categories listed below accurately describes this protocol

- ○ (Risk Level 1) Not greater than minimal risk
- ◉ (Risk Level 2) Greater than minimal risk, but presenting the prospect of direct benefit to individual subjects
- ○ (Risk Level 3) Greater than minimal risk, no prospect of direct benefit to individual subjects, but likely to yield generalizable knowledge about the subject's disorder or condition.
- ○ (Risk Level 4) Research not otherwise approvable which presents an opportunity to understand, prevent, or alleviate a serious problem affecting the health or welfare of subjects.

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

Refer to UK's guidance document on assessing the research risk for additional information.

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

Age level of human subjects: (i.e., 6 mths.; 2yrs., etc..) 2 to 18

Study Population:

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

Provide the following information:

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

Please consider these resources:
NIH Diversity Policy
FDA Diversity Guidance

The subject population is 2-18-year-old children with a new diagnosis of pediatric cancer, without any exclusion criteria on gender, race, or ethnic background. The only exclusion criteria are those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, or use of medications that are orexigenic or anorectic.
We are including children because the present study addresses nutrition interventions within the pediatric cancer realm.
In Kentucky, 22% of children typically present to UKHC with leukemia, 20% with brain tumors, 16% with lymphoma, 13% with epithelial tumors, 6% with germ cell tumors, 5% with soft tissue sarcomas, 5% with nervous system tumors, 5% with bone tumors, 3% renal tumors, 2% with retinoblastoma, 2% with hepatic tumors, and 1% unspecified or other tumors.

Attachments

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

Participant Demographics

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

If unknown, please explain why:

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

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

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

ADDITIONAL INFORMATION:

Please visit the IRB Survival Handbook for more information on:

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

Other Resources:

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

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

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

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

○ Yes ◉ No

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

Examples of such conditions include:

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

Attachments

SUBJECT CHILDREN

0 unresolved comment(s)

SECTION 1. Risk Level

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

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

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

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

Is greater than minimal risk

In the Risk Level section of the IRB Application you indicated your research is greater than minimal risk, but presenting the prospect of direct benefit to individual subjects.

A. Explain why your research involves greater than minimal risk but presents the prospect of direct benefit to the individual subjects:

The greater than minimal risk is due to the potential for discomfort or stress during a feeding tube placement or the potential for adverse side effects from medications. These interventions, however, do provide direct benefits to the patient by improving their nutritional status and overall clinical outcomes. Additionally, this patient population is at high risk for receiving these interventions due to medical necessity even if not enrolled in this study.

B. Justify the risk(s) by explaining the anticipated benefit to the subjects:

They will have improved nutritional status, which in turn improves the subjects' overall outcomes from cancer therapy. Additionally can reduce the risk of cancer therapy complications including malnutrition rates, infection rates, and hospital length of stays.

C. Explain how the relation of the anticipated benefit to the risk is at least as favorable to the subjects as that presented by available alternative approaches:

The alternative approaches are treating them medically which include the same nutrition interventions. The main difference between medical treatment and these intervention options is that they are not randomized. Otherwise, the alternative approaches are the exact same options.

SECTION 2. Assessment and Evaluation of the Risks

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

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

The study population is pediatric cancer.

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

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

C. Indicate how many children you propose to enroll in the study: 45

Note: Whenever possible, involve the fewest number of children necessary to obtain statistically significant data which will contribute to a

meaningful analysis relative to the purpose of the study.

Justify this number:	This is on average how many new diagnoses the DanceBlue Pediatric Hematology/Oncology Clinic receives each year and the budget for a potential grant from CCTS.

D. Check all that apply:

- [x] My research involves children 6 years of age or older.
- [x] My research involves children under 6 years of age.

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

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

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

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

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

** If you checked question 3, please explain:

** If you checked question 4, please explain:

We currently don't assent the children during their cancer treatment protocols and only consent the patients. So plan to only consent to stay consistent.

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

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

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

○ Yes ◉ No

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

○ Yes ◉ No

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

N/A

G. Describe how parental permission will be obtained.

All Parents/guardians of the child subject will be required to sign an approved IRB consent form prior to participation. All procedures included in the study will be explained in detail (including approximate time commitment) to subjects and parents/guardians prior to consent signing. We have previously used pictures of children performing the techniques required in this study to explain the testing methods and what will be required of both the pediatric participants and their parents/guardians. We have found that reading through the consent form with the subject and parent/guardian in conjunction with showing these pictures is very helpful in assuring that both the child and parent/guardian have a clear understanding of the study procedures and requirements. We plan to use this method during our consenting/assenting process for this study. The original signed consent form will be appropriately filed for review at any time during the study duration to ensure the confidentiality of the data collected. All subjects and parents/guardians will receive a copy of the signed consent/assent forms.

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

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

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

child.)

I am requesting

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

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

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

☐ Waiver of the requirement for parental permission.

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

Parental Permission Waiver Options

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

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

Justify:

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

The research activities will occur either within the DanceBlue clinic itself or during admission to the hospital. Parents are present during these visits and we will conduct the research activities at that time.

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

The study personnel all work within the clinic of study, DanceBlue Pediatric Hematology/Oncology Clinic, and serve as clinicians on the patient's care team as the oncologist, pharmacist, or dietitian. The team has been well-trained in the management of pediatric populations.

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

N/A

SECTION 3. Wards of the State

If you need to activate this section:

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

A. 45 CFR 46.409(a)

Please indicate which category describes your research proposal:

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

B. 45 CFR 46.409(b)

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

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

○ Yes ○ No

b) Check the applicable item:

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

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

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

SECTION 4. Children Located Outside the State of Kentucky

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

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

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

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

INFORMED CONSENT/ASSENT PROCESS/WAIVER

0 unresolved comment(s)

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

Additional Resources:

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

Consent/Assent Tips:

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

How to Get the Section Check Mark

1. You must:

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

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

Check All That Apply

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

Attachments

Attach Type	File Name
Assent Form	CLEAN Assent.pdf
Assent Form	CLEAN Verbal Assent Script.pdf
Informed Consent/Parental Permission	CLEAN Adult Consent .pdf
Informed Consent/Parental Permission	CLEAN Informed Consent .pdf
InformedConsent-Highlighted/Tracked_Changes	Informed Consent .pdf

InformedConsent-Highlighted/Tracked_Changes	Assent.pdf
InformedConsent-Highlighted/Tracked_Changes	Adult Consent.pdf
InformedConsent-Highlighted/Tracked_Changes	Verbal Assent Script.pdf

Informed Consent Process:

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

- the circumstances under which consent will be sought and obtained
- the timing of the consent process (including any waiting period between providing information and obtaining consent)
- who will seek consent
- how you will minimize the possibility of coercion or undue influence
- the method used for documenting consent
- if applicable, who is authorized to provide permission or consent on behalf of the subject
- if applicable, specific instruments or techniques to assess and confirm potential subjects' understanding of the information

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

Special considerations may include:

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

Consent will be attained after diagnosis and agreement to enroll on the study. The consent will be sought during the first week of a newly diagnosed cancer patient. Consent will be obtained by either the PI or Co-investigators.
Subjects will be able to contact the Office of Research Integrity with any complaints they may have about the study. The principal investigator or any study personnel will be available to discuss any complaints or concerns related to the project.

☐ Request for Waiver of Informed Consent Process

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

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

SECTION 1.

Check the appropriate item:

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

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

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

SECTION 2.

Explain how each condition applies to your research.

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

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

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

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

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

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

Request for Waiver of Signatures

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

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

Select the option below that best fits your study.

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

Option 1

Describe how your study meets these criteria:

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

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

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

Option 2

Describe how your study meets these criteria:

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

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

Option 3

Describe how your study meets these criteria:

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

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

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

STUDY PERSONNEL **0 unresolved comment(s)**

Do you have study personnel who will be assisting with the research?
After selecting 'Yes' or 'No' you must click the 'Save Study Personnel Information' button.

◉ Yes ○ No

Manage Study Personnel

Identify other study personnel assisting in research project:

- The individual listed as PI in the 'PI Contact Information' section should NOT be added to this section.
- If the research is required for a University of Kentucky academic program, the faculty advisor is also considered study personnel and should be listed below. ***Residents and students who are PI's are encouraged to designate the faculty advisor or at least one other individual as a contact with an editor role (DP).***
- Role: DP = Editor (individual can view, navigate, and edit the application for any review phase (IR, CR/FR, MR) or 'Other Review", and submit Other Reviews on behalf of the PI.)
- Role: SP = Reader (individual can view and navigate through the currently approved application only.)

To add an individual via the below feature:

- Search for personnel;
- Click "select" by the listing for the person you want to add;
- For each person, specify responsibility in the project, whether authorized to obtain informed consent, AND denote who should receive E-IRB notifications (contact status).

NOTE: Study personnel must complete human subject protection (HSP) and Responsible Conduct of Research (RCR) training before implementing any research procedures. For information about training requirements for study personnel, visit UK's HSP FAQ page, the RCR Getting Started page, or contact ORI at 859-257-9428. If you have documentation of current HSP training other than that acquired through UK CITI, you may submit it to ORI (HSPTrainingSupport@uky.edu) for credit.

Study personnel assisting in research project:

Last Name	First Name	Responsibility In Project	Role	AC	Contact	Degree	StatusFlag	(HSP)	(HSP)Date	(RCR)	Removed?	Last Updated	SFI
Harrington	Amanda	Co-Investigator	DP	Y	N	MD	P	Y	05/31/2022	Y	N	07/07/2023	N
Zavitz	Kelly	Sub-Investigator	DP	Y	N	PharmD, BCPPS	P	Y	01/06/2021	Y	N	07/17/2023	N

RESEARCH DESCRIPTION

0 unresolved comment(s)

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

Pro Tips:

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

Background

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

Nearly 60% of pediatric patients diagnosed with cancer develop malnutrition[1] caused by a combination of disease burden, side effects of chemotherapy, and the intensity of cancer treatment.[2] These patients are known to have an increased risk of infection, treatment-related toxicity, inferior clinical outcomes, and increased risk of mortality.[3-5] Malnutrition may progress to cancer cachexia, characterized by anorexia, increased inflammation, decreased fat, and decreased muscle mass with subsequent weight loss, which is associated with decreased overall survival.[1 3 4 6 7]
Interventions to mitigate weight loss and support growth and development in the pediatric cancer population include medical nutrition therapy (MNT) counseling, oral nutrition supplements (ONS), appetite stimulants, and nutrition support in the form of enteral (EN) or parenteral nutrition (PN). [8-10] Clinical judgment is used to implement these interventions as there are no clinical guidelines for nutrition interventions among the pediatric cancer population. ONSs and counseling are frequently the first-line intervention used to improve both weight status and calorie/protein intake.[7-10] These interventions have demonstrated improvements in weight status in both the general pediatric population and adult oncology population, but lack data in the pediatric oncology setting.[8-10] Although ONS have shown to be efficacious, there are concerns with compliance due to palatability, frequency of consumption, and access to ONS.[11] Additionally, there are situations in which the combination of oral intakes and ONS are not enough to sustain adequate weight status, which may lead to the prescribing of appetite stimulants or more invasive interventions like nutrition support.
Appetite stimulants like megestrol acetate (MA), cyproheptadine (CPH), and dronabinol have also been successful in enhancing oral intakes and weight status in the general pediatric and adult populations; however,[12] most pediatric oncology literature discuss MA and CPH with a growing interest in dronabinol.[12-17] Lastly, when appetite stimulants are ineffective and oral intake inadequate, a more invasive intervention such as EN and/or PN has been shown to be effective.[18]
Although EN is utilized as a last resort due to the invasive nature of feeding tube placement, it has demonstrated effectiveness in the improvement of chemotherapy-related weight loss among multiple malignancy types.[19] Of note, prophylactic feeding tubes have not been shown to be of benefit.[20] Current guidelines suggest starting enteral nutrition when patients are severely malnourished with a BMI for age <5th percentile for age, when the z-score is less than –1, or when patients have lost 10% of their diagnosis body weight.[21] Although nutritional intervention has a role in weight improvement, there is minimal data on how it affects body composition. Adiposity has been shown to increase with the use of appetite stimulants, however, compositional changes due to ONS or EN interventions have not been well characterized in the literature.[22] By directly monitoring composition changes prospectively, this novel study will be able to interpret how each intervention may support a pediatric oncology patient's lean muscle mass and its effect on adipose tissue. The wide array of primary literature supporting treatment-related changes of increased adiposity and reduced lean body mass in pediatric cancer patients have been noted to not only increase risk of obesity in adulthood, but also the risk for cancer relapse, worsening overall survival rates, and increased rate of comorbidities such as ischemic heart disease, hypertension, and pancreatic, colon, or breast cancer.[23-26]

This gap in evidence leaves clinicians without adequate guidance to appropriately treat nutritional deficits in the pediatric oncology population. This project will assess changes in muscle status across cancer therapy and will analyze the impact of nutritional interventions on changes in body composition. As described, weight loss can impact outcomes such as infection, treatment-related toxicity, clinical outcomes, and increased risk of mortality. Consequently, increases in adipose deposition, which can occur with nutrition interventions, also can lead to worse outcomes including increased risk of relapse, event-free survival, and obesity. Additionally, this risk of pediatric obesity can also increase the risk of obesity-related complications such as cardiovascular disease, diabetes, renal disease, and obesity-related adult secondary cancers. The proposed study can inform clinicians on the optimal nutritional interventions to not only reduce rates of malnutrition but also optimize body composition to aid in preventing increased adipose deposition while maximizing muscle mass development. Moreover, there are no biomarkers that have been identified as reliable markers of nutritional status or clinical outcomes. The proposed study will also assess inflammatory markers (IL-6 and C-reactive protein), markers of muscle mass (cystatin-C), adiposity markers (leptin and lipid profiles), and vitamin D which has been found to be deficient in the obese population and have vitamin D receptors found on nearly all cells including muscle cells. These biomarkers, combined with ultrasound measurements, can provide light on how nutrition interventions affect body composition and outcomes in this population. When the proposed aims of the study are achieved, clinical guidelines to optimize pediatric cancer nutrition can be developed. Additionally, we can provide patients with appropriate nutrition interventions at the right time to optimize cancer outcomes and provide nutrition interventions that promote ideal body composition. This may also improve long-term survivorship outcomes by reducing cancer-related and obesity-related comorbidities like cardiovascular disease, diabetes, arthritis, kidney disease, etc

Objectives

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

The goal of the proposed research is to determine changes in body composition, weight status, and nutritional status between common nutrition interventions including oral nutrition supplements (ONS), appetite stimulants, and enteral nutrition (EN) among pediatric cancer patients. A secondary goal of this research is to utilize the findings to develop clinical nutrition guidelines for this patient population. The specific objective of the research proposed is to solve the lack of evidence to adequately treat nutritional deficits in the pediatric oncology population. Without this data, there is a lack of clinical consistency in the initiation and selection of appropriate nutrition interventions to provide a more definitive pathway of care. This study can help formulate a clinical guideline for this patient population before, during, and after treatment.

Study Design

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

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

Randomized control trial. All participants enrolled will receive ‘standard of care’ medical nutrition therapy (MNT) counseling at diagnosis for following a high-protein/high-calorie diet. If any of the qualified participants lose >10% of the diagnosis weight, he/she will be randomized to receive (1) oral nutrition supplements, (2) age-appropriate appetite stimulants, or (3) enteral nutrition via a feeding tube.

Attachments

Subject Recruitment Methods & Advertising

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

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

For additional information on recruiting and advertising:

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

Recruitment will occur after the initial diagnosis of a pediatric cancer in the Kentucky Children’s Hospital. The first contact with potential subjects will be conducted by someone who has a prior treatment relationship. The study design, objectives, procedures, time commitment, and risks will be explained to the subjects and parents/guardians. If both the subject and parent/guardians agree to participate then we will proceed by obtaining the appropriate required consent/assent as approved by the University of Kentucky Office of Research Integrity. No advertisement for this study will occur.

Attachments

Research Procedures

Describe how the research will be conducted.

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

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

We plan to enroll a minimum of 45 subjects between the ages of 2-18 years old, over the course of one year, including males and females of all ethnicities. Other exclusion criteria include those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, use of medications that are orexigenic or anorectic, past medical history of schizophrenia, and current use of any forms of marijuana. We believe this is a non-biased recruitment process whereby the participants will be enrolled under the following parameters: the subject must be a newly diagnosed pediatric patient with cancer who will actively receive chemotherapy at UK Healthcare's Kentucky Children's Hospital (KCH) and will maintain an established relationship with the Pediatric Oncologist (Amanda Harrington; study PI) and Pediatric Oncology Dietitian (Corey Hawes; study Co-PI).
All those that enroll will have a baseline ultrasound and biomarkers taken at enrollment. Participants will also receive 'standard of care' medical nutrition therapy (MNT) counseling at diagnosis for following a high protein/high-calorie diet. If any of the enrolled participants lose >10% of the diagnosis weight, he/she will be randomized to receive (1) oral nutrition supplements, (2) age-appropriate appetite stimulants, or (3) enteral nutrition via a feeding tube. At the point of randomization, participants will receive another ultrasound and biomarkers. Those randomized will then receive additional ultrasounds and biomarkers at 1 month and 3 months after randomization (Figure 1). The remaining patients that have either weight maintenance or weight gain, will be utilized as a comparator group and will receive an ultrasound at 3 months and 6 months from enrollment/diagnosis. Each group will have a goal of at least 10 patients per group.
Those receiving ONS will be prescribed a standard ONS (1.0 kcal per mL) that will meet a minimum of 50% of estimated energy needs to promote weight gain but allow for continued regular dietary intakes. The ONS will be prescribed as 8oz (240mL) per dose at least once a day, but up to six times per day depending on estimated nutrient needs. Those receiving age-appropriate appetite stimulants will be provided either cyproheptadine or dronabinol. Subjects will be given cyproheptadine if they fall between the ages of 2-12 years of age and dronabinol if they are >12 years of age or older. Table 1 summarizes the medication dosage forms, initial and dose titration options, and precautions/contraindications of each appetite stimulant. Medication adjustments will be made within 2-4 weeks of initiation due to the variable peak effect times, and chemotherapy treatment plans dictating clinic follow-up. Those randomized to EN will have a feeding tube placed and started on tube feeds via a designated pump for overnight feeds, meeting at least 50% of estimated energy needs to allow for continued regular dietary intakes during the day. After placement of a feeding tube, an abdominal x-ray will be obtained per hospital policy to confirm appropriate placement of feeding tube prior to use to ensure safety of using said feeding tube.
Baseline demographics will be collected, including gender, age, diagnosis, QMLT ultrasound measurement, subjective global assessment (SGA) malnutrition risk, pediatric z-scores, and activity levels. The team will assess the subjects' nutritional intake, body composition via QMLT ultrasound, mid-upper arm circumference, pediatric z-scores (weight, length, and body mass index), biomarkers (leptin, IL-6, Lipid profiles, Cystatin-C, Vitamin D, and C-reactive protein), compliance and tolerance to nutrition intervention, physical activity, and clinical outcomes (rates of infection, number of hospital days for non-chemotherapy administration, number of clinic visits for non-chemotherapy administration, chemotherapy toxicity CTCAE grade, rate or relapse, and 1-year survival rates) at multiple time points throughout the study. Nutritional assessment will involve a 24-hour food recall which will be performed at diagnosis, randomization, and then every 1-2 weeks once randomized to an intervention. Weight loss and pediatric z-scores (weight-for-age, length-for-age, and BMI-for-age) will be assessed every 1-2 weeks throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then at 1 month and 3 months after randomization (or when weight lost is regained). Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, 1 month, and 3 months after randomization.

Standard of care for patients are to receive MNT education at diagnosis. For those that lose weight, standard of care is to receive the nutrition interventions listed above (oral nutrition supplements, appetite stimulants, or enteral nutrition via feeding tube). The standard of care is to generally go from a least invasive to a more invasive approach. The research components of this study include being randomized to a nutrition intervention rather than a non-validated step-wise approach, the ultrasound measurements, and the biomarkers. These components are not considered standard of care and are research procedures.

Baseline demographics will be collected, including gender, age, diagnosis, QMLT ultrasound measurement, subjective global assessment (SGA) malnutrition risk, pediatric z-scores, and activity levels. The team will assess the subjects' nutritional intake, body composition via QMLT ultrasound, mid-upper arm circumference, pediatric z-scores (weight, length, and body mass index), biomarkers (leptin, IL-6, Lipid profiles, Cystatin-C, Vitamin D, and C-reactive protein), compliance and tolerance to nutrition intervention, physical activity, and clinical outcomes (rates of infection, number of hospital days for non-chemotherapy administration, number of clinic visits for non-chemotherapy administration, chemotherapy toxicity CTCAE grade, rate or relapse, and 1-year survival rates) at multiple time

points throughout the study. Nutritional assessment will involve a 24-hour food recall which will be performed at diagnosis, randomization, and then every 1-2 weeks once randomized to an intervention. Weight loss and pediatric z-scores (weight-for-age, length-for-age, and BMI-for-age) will be assessed every 1-2 weeks throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella, a total of 4 ultrasounds will be conducted during the study. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then every 1-2 weeks for up to 8 weeks after randomization. Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, and weeks 4 and 8 after randomization. Additionally, measurements of resource utilization will be measured such as the number of hospital days for non-chemotherapy-related problems, the number of sick visits to the clinic, dietitian visits, infections, and rates of relapse or overall survival. Biomarkers will be drawn when the children are in the clinic for chemotherapy or lab work. They will already have their central venous line accessed by a qualified clinic RN and labs will be drawn at that time to ensure no extra harm to the patient. Additionally, all patients will have EMLA cream used to numb the area prior to having a clinic RN who is trained in accessing ports and has accessed the ports during previous clinic visits and will continue to do so throughout therapy.

Attachments

Attach Type	File Name
ResearchProcedures	Table 1.docx
ResearchProcedures	Randomization Tree.pdf

Data Collection & Research Materials

In this section, please provide the following:

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

Data will be collected utilizing blood samples, vital signs from the clinic visits, and bedside ultrasound machines in the clinic. Any nutrition intakes, activity recalls, or quality of life measures will be obtained during interviews within the clinic visit. Additionally, measurements of resource utilization will be measured such as number of hospital days for non-chemotherapy related problems, number of sick visits to clinic, dietitian visits, infections, and rates of relapse or overall survival.

Attachments

Attach Type	File Name
DataCollection	PROMIS activity tool.pdf
DataCollection	24-hour Dietary Recall Form.pdf

Resources

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

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

All study personnel resides within the Pediatric Hem/Onc team. The ultrasound machine is a bedside US machine that is housed and owned by the clinic. All technological needs such as computers are also available within the clinic. The testing personnel will include the PI and Co-PIs. All personnel have been trained to perform specific testing required in this study and are experienced in working with pediatric populations. It is not anticipated that the subjects will require psychological, social, or medical services as a direct result of study participation.
The nurses that are involved with the blood draws are only providing clinical services, as they are clinic nurses within the Pediatric Hem/Onc clinic who are trained in accessing port-a-caths, and are not considered study personnel per the guidance document from ORI.

Potential Risks & Benefits

Risks

- Describe any potential risks – including physical, psychological, social, legal, ability to re-identify subjects, or other risks. Assess the seriousness and likelihood of each risk.
- Which risks may affect a subject's willingness to participate in the study?

- Describe likely adverse effects of drugs, biologics, devices or procedures participants may encounter while in the study.
- *Qualitative research* - describe ethical issues that could arise while conducting research in the field and strategies you may use to handle those situations.
- Describe any steps to mitigate these risks.

Benefits

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

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

Risks associated with this study are greater than minimal but presenting the prospect of direct benefit to individual subjects. There is a risk of discomfort with the feeding tube placement, side effects from medication, and small radiation exposure due to abdominal x-ray to confirm location of feeding tube placement. Additional feeding tube risks include dislodgement requiring replacement, sore throat, nosebleeds, and sinusitis. Considering these aforementioned risks, the experimental situation will be closely monitored in order to reduce any risks. The risk of the blood sampling procedure includes localized bruising, bleeding, and infection. However, with careful standardized sterile techniques with qualified and trained pediatric cancer clinic registered nurses, these risks are all minimized. There is always a chance that any medical treatment can harm your child. The research treatments/procedures in this study are no different. In addition to risks described in this consent, your child may experience a previously unknown risk or side effect.
The risk of side effects from appetite stimulants (cyproheptadine and dronabinol) are also a possibility.
o Dronabinol (Marinol)
Common side effects: abdominal pain, nausea, vomiting, dizziness, euphoria, paranoid reaction, somnolence, thinking abnormalities
Uncommon side effects: palpitations, tachycardia, facial flush, amnesia, anxiety, confusion, hallucinations, depersonalization, abnormal weakness, and loss of coordination.
o Cyproheptadine (Periactin)
Common side effects: tiredness, sleepiness, dizziness, hypotension, and dryness of nose/throat.
Uncommon side effects: nervousness, excitation, tremor, hallucinations, rash, tachycardia, epigastric distress, anorexia, nausea, vomiting, diarrhea, and constipation.

Available Alternative Opportunities/Treatments

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

If patients wish to not participate in the study, they will be treated equally based on clinical and medical status which may still include the use of oral nutrition supplements, appetite stimulants, and feeding tube as nutritional status dictates.

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Records, Privacy, and Confidentiality

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

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

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

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

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

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

The specimens will be stored in a -80 freezer within CCTS.
Researchers will take careful steps to keep the information confidential. We will remove the child's name or other direct identifiers from

their information. We will label the child's information with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the children.
Researchers will store the identifiable information or samples, in a locked freezer and password-protected database. Researchers will remove the child's name or other direct identifiers from the child's information or samples. We will label the child's information or samples with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the child. Any remaining information and samples will be destroyed. In addition, it may be possible to destroy the code that links the child's information and specimen samples.

UK IRB policies state that IRB-related research records must be retained for a minimum of 6 years after study closure. Do you confirm that you will retain all IRB-related records for a minimum of 6 years after study closure?

◉ Yes ○ No

Payment

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

As a patient incentive, the patient will receive 40$ if they are randomized to a nutrition intervention.

Costs to Subjects

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

Services that are not covered by the study or sponsor are patient care supplies including any copay for oral nutrition supplements, appetite stimulants, or enteral nutrition for the feeding tube. Often times, these items are covered by nutrition programs including Women, Infant, and Child (WIC) program or insurance providers. If the participant gets hurt or sick while taking part of this study, the medical care will not be covered by this study. We also will not cove any wages lost to seek medical treatment. The participant will have to use their health insurance to cover additional costs.

Data and Safety Monitoring

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

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

This study will include the following data safety monitoring plan: All subject eligibility will be determined at the time of recruitment and verified at the time of initial testing. This will include a review of the demographic data, and various baseline measurements. The data will be entered and verified by approved study personnel weekly. Any 'paper copied documentation' will be stored in a locked file cabinet in the Peds Hem/Onc Clinic. All procedures will be conducted by trained personnel serving as significant personnel of this protocol. In the case that an adverse event does occur, we will report this information to the Medical IRB as soon as possible.

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

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

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

The researchers would like to store, use, and share the blood samples for future research. The stored blood samples to learn more about pediatric cancer and obesity, body composition, or research additional nutrition-related questions.

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

○ Yes ◉ No

Non-English Speaking Subjects or Subjects from a Foreign Culture

Recruitment and Consent:

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

Cultural and Language Consultants:

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

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

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

Local Requirements:

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

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

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

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

HIV/AIDS Research

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

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

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

PI-Sponsored FDA-Regulated Research

Is this an investigator-initiated study that:

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

PI-Sponsored FDA-Regulated Research

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

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

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

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

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

Attachments

HIPAA

0 unresolved comment(s)

Is HIPAA applicable? ◉ Yes ○ No

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

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

☐ HIPAA De-identification Certification Form

☑ HIPAA Waiver of Authorization

Attachments

Attach Type	File Name
HighlightedChanges	IRB HIPPA Waiver.pdf
Waiver	CLEAN IRB HIPPA Waiver.pdf

STUDY DRUG INFORMATION

0 unresolved comment(s)

The term drug may include:

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

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

◉ Yes ○ No

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

LIST EACH DRUG INVOLVED IN STUDY IN THE SPACE BELOW

Drug Name:

Cyproheptadine & Dronabinol

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

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

☐ Investigational Drug Service (IDS) UK Hospital

Other Location:

Chandler Retail Pharmacy

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

○ Yes ◉ No

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

IND Submitted/Held by:

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

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

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

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

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

Complete and attach the required Study Drug Form picking "Study Drug Form" for the document type. Any applicable drug documentation (e.g., Investigator Brochure; approved labeling; publication; FDA correspondence, etc.) should be attached using "Other Drug Documentation" for the document type.

Attachments

Attach Type	File Name
Other Drug Documentation	Cyproheptadine tablet PI.pdf
Other Drug Documentation	Dronabinol cap PI.pdf
Study Drug Form	e-IRB Cyproheptadine Form.pdf
Study Drug Form	e-IRB Dronabinol Form.pdf

STUDY DEVICE INFORMATION

0 unresolved comment(s)

A DEVICE may be a:

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

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

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

○ Yes ◉ No

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

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

LIST EACH DEVICE BEING TESTED IN STUDY IN THE SPACE BELOW

Device Name:

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

○ Yes ○ No

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

IDE/HDE Submitted/Held by:

Sponsor: ☐ Held By:

Investigator: ☐ Held By:

Other: ☐ Held By:

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

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

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

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

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

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

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

Attachments

RESEARCH SITES

0 unresolved comment(s)

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

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

UK Sites

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

Schools/Education Institutions

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

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

Other Medical Facilities

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

- [ ] Correctional Facilities
- [ ] Home Health Agencies
- [ ] International Sites

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

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

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

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

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

Attachments

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

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

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

RESEARCH ATTRIBUTES

0 unresolved comment(s)

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

☐ Not applicable

Check All That Apply

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

FUNDING/SUPPORT

0 unresolved comment(s)

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

☐ Not applicable

Check All That Apply

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

Other:

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

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

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

The University of Kentucky Center for Clinical and Translational Science - Maternal and Pediatric Research Alliance (MaPRA) Pilot Award

Add Related Grants

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

Add Related Grants

Grant/Contract Attachments

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

○ Yes ◉ No

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

DOD SOP Attachments

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

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

Assurance/Certification Attachments

OTHER REVIEW COMMITTEES

0 unresolved comment(s)

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

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

◉ Yes ○ No

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

Additional Information

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

Attachments

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

ADDITIONAL INFORMATION/MATERIALS

0 unresolved comment(s)

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

Approval Letter Details:

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

Additional Materials:

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

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

Protocol/Other Attachments

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

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

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

SIGNATURES (ASSURANCES)

0 unresolved comment(s)

Introduction

All IRB applications require additional assurances by a Department Chairperson or equivalent (DA), and when applicable, a Faculty Advisor or equivalent (FA). This signifies the acceptance of certain responsibilities and that the science is meritorious and deserving of conduct in humans. The person assigned as DA *should not* also be listed in the Study Personnel section, and the individual assigned as FA *should* be listed in the Study Personnel section.

For a list of responsibilities reflected by signing the Assurance Statement, refer to "What does the Department Chairperson's Assurance Statement on the IRB application mean?"

For a detailed illustration of how to complete this section, please review the short online video tutorial "Signatures (Assurance) Section - How to Complete." Otherwise, follow the steps below.

Required Signatures:

First Name	Last Name	Role	Department	Date Signed	
John	D'Orazio	Department Authorization	Pediatrics - Hematology/Oncology	07/25/2023 12:40 PM	View/Sign
Corey	Hawes	Principal Investigator	Physician Based Clinics	07/25/2023 11:30 AM	View/Sign
Amanda	Harrington	Other Signee	Pediatrics - Hematology/Oncology	07/26/2023 09:40 AM	View/Sign

Department Authorization

☑ This is to certify that I have reviewed this research protocol and that I attest to the scientific validity and importance of this study; to the qualifications of the investigator(s) to conduct the project and their time available for the project; that facilities, equipment, and personnel are adequate to conduct the research; and that continued guidance will be provided as appropriate. When the principal investigator assumes a sponsor function, the investigator has been notified of the additional regulatory requirements of the sponsor and by signing the principal investigator Assurance Statement, confirms he/she can comply with them.

*If the Principal Investigator is also the Chairperson of the department, the Vice Chairperson or equivalent should complete the "Department Authorization".

**IF APPLICABLE FOR RELIANCE: I attest that the principal investigator has been notified of the regulatory requirements of both the Reviewing and Relying IRBs, according to the information provided in the E-IRB application. The attached Reliance Assurance Statement, signed by the principal investigator, confirms that he/she can comply with both sets of IRB requirements.

Principal Investigator's Assurance Statement

I understand the University of Kentucky's policies concerning research involving human subjects and I agree:

1. To comply with all IRB policies, decisions, conditions, and requirements;
2. To accept responsibility for the scientific and ethical conduct of this research study;
3. To obtain prior approval from the Institutional Review Board before amending or altering the research protocol or implementing changes in the approved consent/assent form;
4. To report to the IRB in accord with IRB/IBC policy, any adverse event(s) and/or unanticipated problem(s) involving risks to subjects;
5. To complete, on request by the IRB for Full and Expedited studies, the Continuation/Final Review Forms;
6. To notify the Office of Sponsored Projects Administration (OSPA) and/or the IRB (when applicable) of the development of any financial interest not already disclosed;
7. Each individual listed as study personnel in this application has received the mandatory human research protections

education (e.g., CITI);
8. Each individual listed as study personnel in this application possesses the necessary experience for conducting research activities in the role described for this research study.
9. To recognize and accept additional regulatory responsibilities if serving as both a sponsor and investigator for FDA regulated research.

☑ Furthermore, by checking this box, I also attest that:

- I have appropriate facilities and resources for conducting the study;
- I am aware of and take full responsibility for the accuracy of all materials submitted to the IRB for review;
- If applying for an exemption, I also certify that the only involvement of human subjects in this research study will be in the categories specified in the Protocol Type: Exemption Categories section.
- If applying for an Abbreviated Application (AA) to rely on an external IRB, I understand that certain items above (1, 3, 4, 7-8) may not apply, or may be altered due to external institutional/IRB policies. I document my agreement with the Principal Investigator Reliance Assurance Statement by digitally signing this application.

*You will be able to "sign" your assurance after you have sent your application for signatures (use Submission section). Please notify the personnel required for signing your IRB application after sending for signatures. Once all signatures have been recorded, you will need to return to this section to submit your application to ORI.

Other Signee's Assurance Statement

☑ This is to certify, that at the request of the Principal Investigator (PI), I have reviewed this research protocol and agree it is appropriate per departmental/college policy and/or procedures and I will support the PI as needed.

SUBMISSION INFORMATION

0 unresolved comment(s)

Each Section/Subsection in the menu on the left must have a checkmark beside it (except this Submission section) indicating the Section/Subsection has been completed. Otherwise your submission for IRB review and approval cannot be sent to the Office of Research Integrity/IRB.

If applicable, remember to update the Approval Letter Details text box under the Additional Information section

If your materials require review at a convened IRB meeting which you will be asked to attend, it will be scheduled on the next available agenda and you will receive a message to notify you of the date.

If you are making a change to an attachment, you need to delete the attachment, upload a highlighted version that contains the changes (use Document Type of "Highlighted Changes"), and a version that contains the changes without any highlights (use the appropriate Document Type for the item(s)). Do **not** delete approved attachments that are still in use.

Your protocol has been submitted.

Download all

	Document Type	File Loaded	Document Description	File Size	Modified By	Mod Date
	ApprovalLetter	ApprovalLetter.pdf		0.079	pkma223	9/8/2023 1:28:10 PM
	Stamped Consent Form	CLEAN Informed Consent .pdf		0.339	pkma223	9/8/2023 1:28:10 PM
	Stamped Consent Form	CLEAN Verbal Assent Script.pdf		0.056	pkma223	9/8/2023 1:28:09 PM
	Stamped Consent Form	CLEAN Assent.pdf		0.068	pkma223	9/8/2023 1:28:09 PM
	Stamped Consent Form	CLEAN Adult Consent .pdf		0.338	pkma223	9/8/2023 1:28:09 PM
	Informed ConsentParental Permission	CLEAN Informed Consent .pdf	Informed Consent ICF	0.337	cjhawe2	9/8/2023 12:37:26 PM
	InformedConsent_HighlightedChanges	Informed Consent .pdf	Informed Consent	0.363	cjhawe2	9/8/2023 12:37:09 PM
	Assent	CLEAN Assent.pdf	Assent 12-17 ICF	0.067	cjhawe2	9/8/2023 12:36:58 PM
	InformedConsent_HighlightedChanges	Assent.pdf	Assent 12-17	0.069	cjhawe2	9/8/2023 12:36:43 PM
	Informed ConsentParental Permission	CLEAN Adult Consent .pdf	Adult Consent ICF	0.337	cjhawe2	9/8/2023 12:36:26 PM
	InformedConsent_HighlightedChanges	Adult Consent.pdf	Adult Consent	0.351	cjhawe2	9/8/2023 12:36:09 PM
	Assent	CLEAN Verbal Assent Script.pdf	Verbal Assent 6-11 ICF	0.056	cjhawe2	9/6/2023 3:43:13 PM
	Waiver	CLEAN IRB HIPPA Waiver.pdf	IRB Waiver ICF	0.098	cjhawe2	9/6/2023 3:41:35 PM
	HighlightedChanges	IRB HIPPA Waiver.pdf		0.077	cjhawe2	9/6/2023 3:35:23 PM
	InformedConsent_HighlightedChanges	Verbal Assent Script.pdf	Verbal assent	0.066	cjhawe2	8/28/2023 4:17:06 PM
	AdditionInfoConsiderations	Revision Letter 2 for EIRB 89377.pdf	Additional Revisions (minor)	0.102	pkma223	8/28/2023 10:15:31 AM
	StudyDrug	e-IRB Dronabinol Form.pdf		0.515	cjhawe2	8/15/2023 1:19:54 PM
	AdditionInfoConsiderations	89377 Hawes RL.pdf	Revision Letter - minor revisions	0.226	pkma223	8/11/2023 8:25:14 AM
	DataCollection	24-hour Dietary Recall Form.pdf	Data collection document - diet	0.182	pkma223	7/28/2023 3:32:50 PM
	DataCollection	PROMIS activity tool.pdf	data collection	0.122	pkma223	7/28/2023 3:32:02 PM
	ResearchProcedures	Randomization Tree.pdf	Randomization Tree	0.082	cjhawe2	7/25/2023 10:54:30 AM
	OtherDrugDocumentation	Dronabinol cap PI.pdf		0.430	kgl222	7/18/2023 5:25:50 PM
	OtherDrugDocumentation	Cyproheptadine tablet PI.pdf		0.246	kgl222	7/18/2023 5:25:39 PM
	StudyDrug	e-IRB Cyproheptadine Form.pdf		0.747	kgl222	7/18/2023 5:24:59 PM
	ResearchProcedures	Table 1.docx	Table 1	0.013	cjhawe2	7/7/2023 3:21:32 PM

Protocol Changes

Click link to sort Changed Date

HIPAA HIPAADeIdentificationCertForm changed by pkma223 on 9/7/2023 9:16:34 AM
~~Y~~N

Informed Consent AssentForm changed by cjhawe2 on 8/25/2023 10:20:39 PM
~~N~~Y

Informed Consent InformedConsentParentalPermission changed by cjhawe2 on 8/25/2023 10:20:39 PM
~~N~~Y

Other Review Committees MCC changed by cjhawe2 on 8/15/2023 1:12:50 PM
Y

Other Review Committees ResearchFallUnderPurview changed by cjhawe2 on 8/15/2023 1:12:50 PM
~~N~~Y

Project Information ProjectEndDate changed by cjhawe2 on 8/15/2023 2:13:30 PM
~~1/1~~6/30/202~~4~~5 12:00:00 AM

Project Information SubjectCount changed by cjhawe2 on 8/15/2023 2:13:30 PM
~~70~~45

Research Description CostsToSubjects changed by cjhawe2 on 8/15/2023 2:12:32 PM
Services that are not covered by the study or sponsor are patient care supplies including any copay for oral nutrition supplements, appetite stimulants, or enteral nutrition for the feeding tube. Often times, these items are covered by nutrition programs including Women, Infant, and Child (WIC) program or insurance providers. If the participant gets hurt or sick while taking part of this study, the medical care will not be covered by this study. We also will not cove any wages lost to seek medical treatment. The participant will have to use their health insurance to cover additional costs.

Research Description FutureUseAndSharing changed by cjhawe2 on 8/15/2023 2:10:27 PM
~~N/A~~The researchers would like to store, use, and share the blood samples for future research. The stored blood samples to learn more about pediatric cancer and obesity, body composition, or research additional nutrition-related questions.

Research Description PotentialRisks changed by cjhawe2 on 8/28/2023 3:09:01 PM
Risks associated with this study are greater than minimal but presenting the prospect of direct benefit to individual subjects. There is a risk of discomfort with the feeding tube placement, side effects from medication, and small radiation exposure due to abdominal x-ray to confirm location of feeding tube placement. Additional feeding tube risks include dislodgement requiring replacement, sore throat, nosebleeds, and sinusitis. Considering these aforementioned risks, the experimental situation will be closely monitored in order to reduce any risks. The risk of the blood sampling procedure includes localized bruising, bleeding, and infection. However, with careful standardized sterile techniques with qualified and trained pediatric cancer clinic registered nurses, these risks are all minimized. There is always a chance that any medical treatment can harm your child. The research treatments/procedures in this study are no different. In addition to risks described in this consent, your child may experience a previously unknown risk or side effect. ¶
The risk of side effects from appetite stimulants (cyproheptadine and dronabinol) are also a possibility. ¶
o Dronabinol (Marinol) ¶
~~?~~ Common side effects: abdominal pain, nausea, vomiting, dizziness, euphoria, paranoid reaction, somnolence, thinking abnormalities ¶
~~?~~ Uncommon side effects: palpitations, tachycardia, facial flush, amnesia, anxiety, confusion, hallucinations, depersonalization, abnormal weakness, and loss of coordination. ¶
o Cyproheptadine (Periactin) ¶
~~?~~ Common side effects: tiredness, sleepiness, dizziness, hypotension, and dryness of nose/throat. ¶
~~?~~ Uncommon side effects: nervousness, excitation, tremor, hallucinations, rash, tachycardia, epigastric distress, anorexia, nausea, vomiting, diarrhea, and constipation.

Research Description PotentialRisks changed by cjhawe2 on 8/15/2023 2:05:53 PM
Risks associated with this study are ~~a grade 1. Body composition measurements pose a mini~~greater than minimal but presenting the prospect of direct benefit to individual subjects. There is a risk of discomfort with the feeding tube placement, side effects from medication, and small ~~risk with the use of ultrasound~~adiation exposure due to abdominal x-ray to confirm location of feeding tube placement. Additional feeding tube risks include dislodgement requiring replacement, sore throat, nosebleeds, and sinusitis. Considering these aforementioned risks, the experimental situation will be closely monitored in order to reduce any risks. The risk of the blood sampling procedure includes localized bruising, bleeding, and infection. However, with careful standardized sterile techniques with qualified and trained pediatric cancer clinic registered nurses, these risks are all minimized. ~~¶~~
~~An additional risk within this study is the potential for a p~~ There is always a chance that any medical treatiment ~~to experience an adverse drug reaction or allergic reaction to either cyproheptadine of dronabinol. Those prescribed cyproheptadine may experience hypotension, tachycardia, hepatic impairment, constipation, fatigue, tremor, diaphoresis, among other things. The D~~can harm your child. The research treatments/procedures in this study are no different. In addition to risks described in this consent, your child may experience a previously unknown risk or side effect. ¶
The risk of side effects from appetite stimulants (cyproheptadine and dronabinol) ar~~m may experience a state of euphoria, dizziness, drowsiness, p~~e also a possibility. ¶
o Dronabinol (Mara~~i~~noi~~a,~~l) ¶
? Common side effects: abdominal pain, nausea~~/~~, vomiting, ~~or more. Due to this risk, those assigned an appetite stimulant will be provided with a medication review of potential side effects along with a step-wise approach of if/when to call the team. There can be some discomfort with placement of a feeding tube, however, all participants will have access to tools to minimize anxiety and stress such as child life specialists during placement. ¶~~
~~Benefits include obtaining data for future stud~~idizziness, euphoria, paranoid reaction, somnolence, thinking abnormalities ¶
? Uncommon side effects: palpitations, tachycardia, facial flush, amnesia, anxiety, confusion, hallucinations, depersonalization, abnormal weakness, and loss of coordination. ¶
o Cyproheptadine (Periactin) ¶
? Common side effects: tiredness, ~~data for patient information regarding body composit~~sleepiness, dizziness, hypotension, and ~~nutrition information. Risks are minimal as patient will already be accessed for clinical treatment within the clinic and will not have labs drawn in addition to~~

already being accessed for planned treatmentdryness of nose/throat. ¶
? Uncommon side effects: nervousness, excitation, tremor, hallucinations, rash, tachycardia, epigastric distress, anorexia, nausea, vomiting, diarrhea, and constipation.
Research Description ResearchMaterialsRecordsPrivacy changed by cjhawe2 on 8/15/2023 2:17:30 PM
The specimens will be stored in a -80 freezer within CCTS. ¶
Researchers will take careful steps to keep the information confidential. We will remove the child's name or other direct identifiers from their information. We will label the child's information with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the children. ¶
Researchers will store the identifiable information or samples, in a locked freezer and password-protected database. Researchers will remove the child's name or other direct identifiers from the child's information or samples. We will label the child's information or samples with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the child. Any remaining information and samples will be destroyed. In addition, it may be possible to destroy the code that links the child's information and specimen samples.
Research Description ResearchMaterialsRecordsPrivacy changed by cjhawe2 on 8/15/2023 2:15:55 PM
The specimens will be stored in a -80 freezer within CCTS. ¶
Researchers will take careful steps to keep the information confidential. We will remove the child's name or other direct identifiers from their information. We will label the child's information with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the children. ¶
Researchers will store the identifiable information or samples, in a locked freezer and password-protected database. Researchers will remove the child's name or other direct identifiers from the child's information or samples. We will label the child's information or samples with a code and will store the key separately from the master code list. Only select staff will have access to the list that links the code to the child.
Research Description ResearchProcedures changed by cjhawe2 on 8/15/2023 2:08:04 PM
We plan to enroll a minimum of 45 subjects between the ages of 2-18 years old, over the course of one year, including males and females of all ethnicities. Other exclusion criteria include those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, use of medications that are orexigenic or anorectic, past medical history of schizophrenia, and current use of any forms of marijuana. We believe this is a non-biased recruitment process whereby the participants will be enrolled under the following parameters: the subject must be a newly diagnosed pediatric patient with cancer who will actively receive chemotherapy at UK Healthcare's Kentucky Children's Hospital (KCH) and will maintain an established relationship with the Pediatric Oncologist (Amanda Harrington; study PI) and Pediatric Oncology Dietitian (Corey Hawes; study Co-PI). ¶
All those that enroll will have a baseline ultrasound and biomarkers taken at enrollment. Participants will also receive 'standard of care' medical nutrition therapy (MNT) counseling at diagnosis for following a high protein/high-calorie diet. If any of the enrolled participants lose >10% of the diagnosis weight, he/she will be randomized to receive (1) oral nutrition supplements, (2) age-appropriate appetite stimulants, or (3) enteral nutrition via a feeding tube. At the point of randomization, participants will receive another ultrasound and biomarkers. Those randomized will then receive additional ultrasounds and biomarkers at 1 month and 3 months after randomization (Figure 1). The remaining patients that have either weight maintenance or weight gain, will be utilized as a comparator group and will receive an ultrasound at 3 months and 6 months from enrollment/diagnosis. Each group will have a goal of at least 10 patients per group. ¶
Those receiving ONS will be prescribed a standard ONS (1.0 kcal per mL) that will meet a minimum of 50% of estimated energy needs to promote weight gain but allow for continued regular dietary intakes. The ONS will be prescribed as 8oz (240mL) per dose at least once a day, but up to six times per day depending on estimated nutrient needs. Those receiving age-appropriate appetite stimulants will be provided either cyproheptadine or dronabinol. Subjects will be given cyproheptadine if they fall between the ages of 2-12 years of age and dronabinol if they are >12 years of age or older. Table 1 summarizes the medication dosage forms, initial and dose titration options, and precautions/contraindications of each appetite stimulant. Medication adjustments will be made within 2-4 weeks of initiation due to the variable peak effect times, and chemotherapy treatment plans dictating clinic follow-up. Those randomized to EN will have a feeding tube placed and started on tube feeds via a designated pump for overnight feeds, meeting at least 50% of estimated energy needs to allow for continued regular dietary intakes during the day. After placement of a feeding tube, an abdominal x-ray will be obtained per hospital policy to confirm appropriate placement of feeding tube prior to use to ensure safety of using said feeding tube. ¶
Baseline demographics will be collected, including gender, age, diagnosis, QMLT ultrasound measurement, subjective global assessment (SGA) malnutrition risk, pediatric z-scores, and activity levels. The team will assess the subjects' nutritional intake, body composition via QMLT ultrasound, mid-upper arm circumference, pediatric z-scores (weight, length, and body mass index), biomarkers (leptin, IL-6, Lipid profiles, Cystatin-C, Vitamin D, and C-reactive protein), compliance and tolerance to nutrition intervention, physical activity, and clinical outcomes (rates of infection, number of hospital days for non-chemotherapy administration, number of clinic visits for non-chemotherapy administration, chemotherapy toxicity CTCAE grade, rate or relapse, and 1-year survival rates) at multiple time points throughout the study. Nutritional assessment will involve a 24-hour food recall which will be performed at diagnosis, randomization, and then every 1-2 weeks once randomized to an intervention. Weight loss and pediatric z-scores (weight-for-age, length-for-age, and BMI-for-age) will be assessed every 1-2 weeks throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then at 1 month and 3 months after randomization (or when weight lost is regained). Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, 1 month, and 3 months after randomization. ¶
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Standard of care for patients are to receive MNT education at diagnosis. For those that lose weight, standard of care is to receive the nutrition interventions listed above (oral nutrition supplements, appetite stimulants, or enteral nutrition via feeding tube). The standard of care is to generally go from a least invasive to a more invasive approach. The research components of this study include being randomized to a nutrition intervention rather than a non-validated step-wise approach, the ultrasound measurements, and the biomarkers. These components are not considered standard of care and are research procedures. ¶
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Cystatin-C, Vitamin D, and C-reactive protein), compliance and tolerance to nutrition intervention, physical activity, and clinical outcomes (rates of infection, number of hospital days for non-chemotherapy administration, number of clinic visits for non-chemotherapy administration, chemotherapy toxicity CTCAE grade, rate or relapse, and 1-year survival rates) at multiple time points throughout the study. Nutritional assessment will involve a 24-hour food recall which will be performed at diagnosis, randomization, and then every 1-2 weeks once randomized to an intervention. Weight loss and pediatric z-scores (weight-for-age, length-for-age, and BMI-for-age) will be assessed every 1-2 weeks throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella, a total of 4 ultrasounds will be conducted during the study. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then every 1-2 weeks for up to 8 weeks after randomization. Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, and weeks 4 and 8 after randomization. Additionally, measurements of resource utilization will be measured such as the number of hospital days for non-chemotherapy-related problems, the number of sick visits to the clinic, dietitian visits, infections, and rates of relapse or overall survival. Biomarkers will be drawn when the children are in the clinic for chemotherapy or lab work. They will already have their central venous line accessed by a qualified clinic RN and labs will be drawn at that time to ensure no extra harm to the patient. Additionally, all patients will have EMLA cream used to numb the area prior to having a clinic RN who is trained in accessing ports and has accessed the ports during previous clinic visits and will continue to do so throughout therapy.

Research Description ResearchProcedures changed by cjhawe2 on 8/15/2023 1:22:29 PM

We plan to enroll a minimum of 45 subjects between the ages of 2-18 years old, over the course of one year, including males and females of all ethnicities. Other exclusion criteria include those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, use of medications that are orexigenic or anorectic, past medical history of schizophrenia, and current use of any forms of marijuana. We believe this is a non-biased recruitment process whereby the participants will be enrolled under the following parameters: the subject must be a newly diagnosed pediatric patient with cancer who will actively receive chemotherapy at UK Healthcare's Kentucky Children's Hospital (KCH) and will maintain an established relationship with the Pediatric Oncologist (Amanda Harrington; study PI) and Pediatric Oncology Dietitian (Corey Hawes; study Co-PI). ¶

All those that enroll will have a baseline ultrasound and biomarkers taken at enrollment. Participants will also receive 'standard of care' medical nutrition therapy (MNT) counseling at diagnosis for following a high protein/high-calorie diet. If any of the enrolled participants lose >10% of the diagnosis weight, he/she will be randomized to receive (1) oral nutrition supplements, (2) age-appropriate appetite stimulants, or (3) enteral nutrition via a feeding tube. At the point of randomization, participants will receive another ultrasound and biomarkers. Those randomized will then receive additional ultrasounds and biomarkers at 1 month and 3 months after randomization (Figure 1). The remaining patients that have either weight maintenance or weight gain, will be utilized as a comparator group and will receive an ultrasound at 3 months and 6 months from enrollment/diagnosis. Each group will have a goal of at least 10 patients per group. ¶

Those receiving ONS will be prescribed a standard ONS (1.0 kcal per mL) that will meet a minimum of 50% of estimated energy needs to promote weight gain but allow for continued regular dietary intakes. The ONS will be prescribed as 8oz (240mL) per dose at least once a day, but up to six times per day depending on estimated nutrient needs. Those receiving age-appropriate appetite stimulants will be provided either cyproheptadine or dronabinol. Subjects will be given cyproheptadine if they fall between the ages of 2-12 years of age and dronabinol if they are >12 years of age or older. Table 1 summarizes the medication dosage forms, initial and dose titration options, and precautions/contraindications of each appetite stimulant. Medication adjustments will be made within 2-4 weeks of initiation due to the variable peak effect times, and chemotherapy treatment plans dictating clinic follow-up. Those randomized to EN will have a feeding tube placed and started on tube feeds via a designated pump for overnight feeds, meeting at least 50% of estimated energy needs to allow for continued regular dietary intakes during the day. After placement of a feeding tube, an abdominal x-ray will be obtained per hospital policy to confirm appropriate placement of feeding tube prior to use to ensure safety of using said feeding tube. ¶

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Standard of care for patients are to receive MNT education at diagnosis. For those that lose weight, standard of care is to receive the nutrition interventions listed above (oral nutrition supplements, appetite stimulants, or enteral nutrition via feeding tube). The standard of care is to generally go from a least invasive to a more invasive approach. The research components of this study include being randomized to a nutrition intervention rather than a non-validated step-wise approach, the ultrasound measurements, and the biomarkers. These components are not considered standard of care and are research procedures. ¶

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throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then every 1-2 weeks for up to 8 weeks after randomization. Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, and weeks 4 and 8 after randomization. Additionally, measurements of resource utilization will be measured such as the number of hospital days for non-chemotherapy-related problems, the number of sick visits to the clinic, dietitian visits, infections, and rates of relapse or overall survival. Biomarkers will be drawn when the children are in the clinic for chemotherapy or lab work. They will already have their central venous line accessed by a qualified clinic RN and labs will be drawn at that time to ensure no extra harm to the patient. Additionally, all patients will have EMLA cream used to numb the area prior to having a clinic RN who is trained in accessing ports and has accessed the ports during previous clinic visits and will continue to do so throughout therapy.

Research Description ResearchProcedures changed by cjhawe2 on 8/15/2023 1:16:31 PM

We plan to enroll a minimum of 45 subjects between the ages of 2-18 years old, over the course of one year, including males and females of all ethnicities. Other exclusion criteria include those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, use of medications that are orexigenic or anorectic, past medical history of schizophrenia, and current use of any forms of marijuana. We believe this is a non-biased recruitment process whereby the participants will be enrolled under the following parameters: the subject must be a newly diagnosed pediatric patient with cancer who will actively receive chemotherapy at UK Healthcare's Kentucky Children's Hospital (KCH) and will maintain an established relationship with the Pediatric Oncologist (Amanda Harrington; study PI) and Pediatric Oncology Dietitian (Corey Hawes; study Co-PI). ¶

All those that enroll will have a baseline ultrasound and biomarkers taken at enrollment. Participants will also receive 'standard of care' medical nutrition therapy (MNT) counseling at diagnosis for following a high protein/high-calorie diet. If any of the enrolled participants lose >10% of the diagnosis weight, he/she will be randomized to receive (1) oral nutrition supplements, (2) age-appropriate appetite stimulants, or (3) enteral nutrition via a feeding tube. At the point of randomization, participants will receive another ultrasound and biomarkers. Those randomized will then receive additional ultrasounds and biomarkers at 1 month and 3 months after randomization (Figure 1). The remaining patients that have either weight maintenance or weight gain, will be utilized as a comparator group and will receive an ultrasound at 3 months and 6 months from enrollment/diagnosis. Each group will have a goal of at least 10 patients per group. ¶

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Baseline demographics will be collected, including gender, age, diagnosis, QMLT ultrasound measurement, subjective global assessment (SGA) malnutrition risk, pediatric z-scores, and activity levels. The team will assess the subjects' nutritional intake, body composition via QMLT ultrasound, mid-upper arm circumference, pediatric z-scores (weight, length, and body mass index), biomarkers (leptin, IL-6, Lipid profiles, Cystatin-C, Vitamin D, and C-reactive protein), compliance and tolerance to nutrition intervention, physical activity, and clinical outcomes (rates of infection, number of hospital days for non-chemotherapy administration, number of clinic visits for non-chemotherapy administration, chemotherapy toxicity CTCAE grade, rate or relapse, and 1-year survival rates) at multiple time points throughout the study. Nutritional assessment will involve a 24-hour food recall which will be performed at diagnosis, randomization, and then every 1-2 weeks once randomized to an intervention. Weight loss and pediatric z-scores (weight-for-age, length-for-age, and BMI-for-age) will be assessed every 1-2 weeks throughout the study enrollment. Ultrasound assessment will be of the QMLT by measuring at the midpoint between the ASIS and the upper pole of the patella. The measurements will be taken bilaterally, three times, and averaged together for the final measurement. Ultrasound assessment will occur at enrollment when weight loss criteria are met for randomization, and then at 1 month and 3 months after randomization (or when weight lost is regained). Pediatric physical activity will be assessed every 1-2 weeks in combination with ultrasound measurements. Adherence and adverse effects to medications, tube feeds, or oral nutrition supplements will be assessed at each clinic visit. Biomarkers will be analyzed at randomization, 1 month, and 3 months after randomization. ¶

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Standard of care for patients are to receive MNT education at diagnosis. For those that lose weight, standard of care is to receive the nutrition interventions listed above (oral nutrition supplements, appetite stimulants, or enteral nutrition via feeding tube). The standard of care is to generally go from a least invasive to a more invasive approach. The research components of this study include being randomized to a nutrition intervention rather than a non-validated step-wise approach, the ultrasound measurements, and the biomarkers. These components are not considered standard of care and are research procedures. ¶

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of hospital days for non-chemotherapy-related problems, the number of sick visits to the clinic, dietitian visits, infections, and rates of relapse or overall survival. Biomarkers will be drawn when the children are in the clinic for chemotherapy or lab work. They will already have their central venous line accessed by a qualified clinic RN and labs will be drawn at that time to ensure no extra harm to the patient. Additionally, all patients will have EMLA cream used to numb the area prior to having a clinic RN who is trained in accessing ports and has accessed the ports during previous clinic visits and will continue to do so throughout therapy.

Research Description Resources changed by cjhawe2 on 8/15/2023 1:26:00 PM

All study personnel resides within the Pediatric Hem/Onc team. The ultrasound machine is a bedside US machine that is housed and owned by the clinic. All technological needs such as computers are also available within the clinic. The testing personnel will include the PI and Co-PIs. All personnel have been trained to perform specific testing required in this study and are experienced in working with pediatric populations. It is not anticipated that the subjects will require psychological, social, or medical services as a direct result of study participation. ¶

The nurses that are involved with the blood draws are only providing clinical services, as they are clinic nurses within the Pediatric Hem/Onc clinic who are trained in accessing port-a-caths, and are not considered study personnel per the guidance document from ORI.

Research Description SubjectRecruitmentMethods changed by cjhawe2 on 8/15/2023 2:06:58 PM

Recruitment will occur after the initial diagnosis of a pediatric cancer in the Kentucky Children's Hospital. The first contact with potential subjects will be conducted by someone who has a prior treatment relationship. The study design, objectives, procedures, time commitment, and risks will be explained to the subjects and parents/guardians. If both the subject and parent/guardians agree to participate then we will proceed by obtaining the appropriate required consent/assent as approved by the University of Kentucky Office of Research Integrity. No advertisement for this study will occur.

Subject Demographics IfUnknownExplain changed by cjhawe2 on 9/8/2023 12:00:33 PM

~~Unknown as the participants have not been diagnosed with cancer prior to enrollment. The majority of our diagnoses are among Caucasians in our demographic area but are not exclusive.~~

Subject Demographics IfUnknownExplain changed by cjhawe2 on 8/15/2023 1:23:58 PM

Unknown as the participants have not been diagnosed with cancer prior to enrollment. The majority of our diagnoses are among Caucasians in our demographic area but are not exclusive.

Subject Demographics StudyPopulation changed by cjhawe2 on 9/8/2023 12:05:03 PM

The subject population is 2-18-year-old children with a new diagnosis of pediatric cancer, without any exclusion criteria on gender, race, or ethnic background. The only exclusion criteria are those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, or use of medications that are orexigenic or anorectic. ¶

We are including children because the present study addresses nutrition interventions within the pediatric cancer realm. ¶

In ~~g~~Keneral, ~~the majority of patients will be pediatric patients with leukemia or lymphoma. Other medical conditions studied will include sarcomas and other solid~~tucky, 22% of children typically present to UKHC with leukemia, 20% with brain tumors, 16% with lymphoma, 13% with epithelial tumors, 6% with germ cell tumors, 5% with soft tissue sarcomas, 5% with nervous system tumors, 5% with bone tumors, 3% renal tumors, 2% with retinoblastoma, 2% with hepatic tumors, and 1% unspecified or other tumors.

Subject Demographics StudyPopulation changed by cjhawe2 on 9/6/2023 3:34:04 PM

The subject population ~~are~~is 2-18-year-old children with a new diagnosis of pediatric cancer, without any exclusion criteria on gender, race, or ethnic background. The only exclusion criteria are those who at cancer diagnosis have current enteral nutrition use, oral nutrition supplement use, or use of medications that are orexigenic or anorectic. ¶

We are including children because the present study ~~is~~ address~~inges~~ nutrition interventions within the pediatric cancer realm. ¶

In general, the majority of patients will be pediatric patients with leukemia or lymphoma. Other medical conditions studied will include sarcomas and other solid tumors.

Subject Demographics WhiteCaucasianMale changed by cjhawe2 on 8/15/2023 1:23:58 PM

~~-4~~

Study Personnel Changes:

No Changes

There are no recorded changes to study personnel.

Subject Demographics Comment by Paul Martin - ORI to IRB/PI on 9/8/2023 11:28:51 AM
-Please add more specific subject demographics which should be available for this population. For example, X percent of children in KY typically present to UKHC with X disease. Please also remove the language in the unknown box below the participant demographic table.

Research Description Comment by Paul Martin - ORI to IRB/PI on 8/11/2023 8:24:31 AM
SEE REVISION LETTER VIA ALL ATTACHMENTS

Informed Consent Comment by Paul Martin - ORI to IRB/PI on 9/8/2023 11:29:36 AM
- Please change the "DRs" title to state Amanda Harrington, MD and Corey Hawes, Doctor of Clinical Nutrition within all assent and consent forms.

*Please keep all tracked changes since the IRB meeting.

Informed Consent Comment by Paul Martin - ORI to IRB/PI on 9/6/2023 3:13:01 PM
-Please update the consent form to put all references (credentials) after the person's name. Several locations in the document have Dr. before the person's name. *Please keep all tracked changes on the consent form since the IRB meeting.

-Please update the subject demographic tab to insert the expected demographics of the medical conditions being studied as the information is likely available and can be predicted.

-Please re-upload the waiver of authorization using the HIPAA tab location for uploading and using a "document type" selection that will not receive an IRB stamp.