Attachment 5B:

NCI PEDIATRIC CENTRAL IRB (CIRB) APPLICATION FOR TREATMENT STUDIES

OMB#: 0925 – xxxx **Expiry Date: xx/xx/xxxx**

STATEMENT OF CONFIDENTIALITY

Collection of this information is authorized under 42 USC 285a. Completion of this form is required as per the NCI CIRB Standard Operations Procedures based on 45 CFR 46.103 (b) (4). If you choose not to complete this form, you will not be able to participate in the CIRB. Data collected as part of the NCI CIRB review is private and protected by law. Under the provisions of Section 301d of the Public Health Service Act, no information that could permit identification of a participating individual may be released. All such information will be kept private under the Privacy Act and will be presented only in statistical or summary form.

NOTIFICATION TO RESPONDENT OF ESTIMATED BURDEN

Public reporting burden for this collection of information is estimated to average 2 hours per response, including the time for reviewing instructions, searching existing data sources, gathering and maintaining the data needed, and completing and reviewing the collection of information. **An agency may not conduct or sponsor, and a person is not required to respond to, a collection of information unless it displays a currently valid OMB control number.** Send comments regarding this burden estimate or any other aspect of this collection of information, including suggestions for reducing this burden, to: NIH, Project Clearance Branch, 6705 Rockledge Drive, MSC 7974, Bethesda, MD 20892-7974, ATTN: PRA (0925-xxxx*). Do not return the completed form to this address.

NCI PEDIATRIC CENTRAL IRB (CIRB) APPLICATION FOR TREATMENT STUDIES

For CIRB Use Only:
Receipt Date:

SECTION A : GENERAL INFORMATION

FORM COMPLETION DATE (Initial submission): _____

DATE OF CURRENT REVISIONS TO FORM INFORMATION: _____

COOPERATIVE GROUP: _____ PHASE OF STUDY _____

GROUP STUDY NUMBER: _____ CTSU PROTOCOL: ☐ Yes ☐ No

PROTOCOL VERSION AND DATE: _____

STUDY TITLE:

STUDY CHAIR	
Name	
Title	
Specialty	
Site	
Address	
Phone #	
E-mail	
FAX #	

STUDY CO-CHAIR (If applicable)	
Name	
Title	
Specialty	
Site	
Address	
Phone #	
E-mail	
FAX #	

COOPERATIVE GROUP CONTACT PERSON	
Name	
Title	
Specialty	
Site	
Address	
Phone #	
E-mail	
FAX #	

PLEASE NOTE: ***CIRB membership includes individuals who are not part of the oncology and/or the scientific community. Therefore, you must use lay language (non medical, non legal terms) and define all terms unique to science when completing this application.***

SECTION B

SUMMARY OF STUDY

1. **State the question that this study will answer (i.e. hypothesis or study objectives):**

2. **Briefly describe the background research that has led to your hypothesis/study objectives Note: The background section of the COG protocol must contain enough additional information for review by the CIRB.**

STUDY DESIGN

1. **Briefly describe the study design, and include a schema.**

2. **Describe sequentially all procedures, interventions and evaluations to be applied to subjects, and identify any that are experimental or performed exclusively for research purposes.** *Note: A biomedical research protocol may involve interventions that are strictly experimental or may involve some aspect of research (e.g., randomization among standard treatments for collection and analysis of routine clinical data for research purposes). It is important for this section to distinguish between interventions that are experimental and/or carried out for research purposes versus those procedures that are considered standard therapy. In addition, routine procedures performed solely for research purposes (e.g., additional diagnostic or follow-up tests) should be identified.*

3. **Describe the follow-up of subjects and identify any procedures that are performed exclusively for research purposes, or performed more frequently than would normally be clinically indicated (e.g. additional or more frequent radiologic evaluations)**

4. **Will the participant be withdrawn from or denied standard of care for any condition in order to participate in the study?**

   ☐ **Yes** ☐ **No** **If yes, please provide justification.**

5. **How would this participant be treated in a non-investigational setting? Please describe the treatment that is considered standard of care, as well as any alternative procedures or drugs or other courses of therapy that might be used, if such alternatives exist.**

6. **Describe the interim safety monitoring plan for this study, including the specific stopping rules for the research? If there is no interim safety plan, please provide justification.**

SECTION C

PARTICIPANTS

1. **Number of participants to be enrolled in the study: _____**

2. **Participant profile**
   a) Are there any enrollment restrictions based on gender? If so, provide justification.

   b) b. Are there any enrollment restrictions based on child-bearing potential? If so, provide justification.

   c) c. Are pregnant or breast feeding women excluded from participation? If so, provide justification.

   d) d. Are there any subject enrollment restrictions based upon race or ethnic origin? If so, explain the nature of the restrictions and provide justification.

3. **What is the age range of the subjects, and what is the rationale for selecting this age range?**

4. **Which of the following vulnerable populations are eligible to be participants (Check each item yes or no. A "no" indicates that all persons in that category are excluded.):**

   Incompetent persons (excluding minors): ☐ Yes ☐ No

   Note: Incompetent persons include those who have a legal guardian or those whose mental status prevents them from giving truly informed consent and making decisions. Inclusion of such subjects may require additional protections, such as appointment of a legal guardian.

   Handicapped ☐ Yes ☐ No

   Note: Handicapped persons include those with a physical or mental impairment which substantially limits one or more major life activities [e.g. speaking, breathing, learning, working, caring for oneself, performing manual tasks, walking, seeing, hearing, etc.], has a record of such an impairment, or is regarded as having such an impairment.

   Note: Exclusion of handicapped persons requires specific justification.

Prisoners: ☐ Yes ☐ No

***Note: Research involving prisoners must comply with HHS regulations at 45CFR46 Subpart C. Subpart C provides additional protection for prisoners enrolled in research because they are considered to be a vulnerable subject population. ***

5. **Recruitment**

   a) Provide any recruitment materials (if applicable) that participants will see.

   b) Will the participants be paid or receive any other inducements (e.g., free medication, free medical care) for participating?

   ☐ Yes (**If yes, please explain)** ☐ No

6. **Will the participants bear any costs which are not a part of standard of care?**

   ☐ Yes ☐ No

   If yes,

   a. List the relevant tests, procedures, hospitalizations, etc., for which the participants would be financially responsible.

   b. Are there available means of subsidizing these extra costs for participants who cannot afford them?

   ☐ Yes (**If yes, please explain)** ☐ No

SECTION D

DRUGS

1. **Please provide the following information for all drugs to be used in this study. This includes the study drugs *and* other medications specified in the protocol that the participant will receive while on this study (attach additional page if necessary):**

   a) Are the drugs/study drugs being conducted under an IND? ☐ Yes ☐ No
   (If no, skip to (b) below)

   b) If yes, include each IND #, the name of the organization that holds each IND, the manufacturer of the drug, and the supplier of the drug. Submit one copy of any applicable Investigator's Brochure(s) with this application.

IND#_____ **Holder of the IND**: _____

Manufacturer: _____

Supplier: _____

IND#_____ **Holder of the IND**: _____

Manufacturer: _____

Supplier: _____

c) Does this study include an off-label use of an FDA-approved drug?

☐ Yes ☐ No

d) If yes, is an IND required for this drug?

☐ Yes, already applied for (provide documentation) ☐ Exempt

Note: In general, an IND is not required for an approved drug unless the results of this study be used by the manufacturer to support (a) a new indication for the drug, (b) a significant change in the labeling for the drug, or (c) a significant change in the advertising for the drug.

SECTION E

RADIATION

1. **Does this study involve radiation?** ☐ **Yes** ☐ **No (If no, skip to Section F.)**

2. **Briefly describe the radiation therapy to be administered (type, dose, field).**

3. **Will the participant receive a radiation dose that is substantially different from that normally received in the course of standard of care for this disease or condition?**

   ☐ Yes ☐ No

   If yes, please describe and provide justification.

   Note: if the justification is already described in the background section of this application, please refer to that section.

4. **Will the participant receive radiation therapy that is delivered in a manner that is substantially different from standard of care for this disease or condition? Note: this includes dose rate, fractionation, field, or source?**

   ☐ Yes ☐ No

   If yes, please describe and provide justification.

   Note: if the justification is already described in the background section of this application, please refer to that section.

SECTION F

RISKS, BENEFITS AND ALTERNATIVES

Describe only the risks of interventions that are part of the experimental portion of the study (that is, those interventions which contribute to answering one or more of the research questions designed in the aims of the study). Risks associated with standard supportive care, with non-experimental surgical procedures or radiotherapy need not be included here.

1. **Risks of Study Interventions**

   a) Describe any risks associated with study drugs that is part of the experimental portion of this protocol. For each study drug, provide the following information:

      i. The name of the study drug:_____

ii. Common/bothersome effects that are study drug/drug class/regimen specific:

iii. Known serious or life-threatening effects that are study drug/drug class/regimen specific:

Note: If data are available, estimate the probability that a given harm may occur and its potential reversibility.

b) Describe risks associated with any radiation therapy that is part of the experimental portion of this protocol. Note: If data are available, estimate the probability that a given harm may occur and its potential reversibility

c) Describe risks associated with any surgical procedures that are part of the experimental portion of this protocol. Note: If data are available, estimate the probability that a given harm may occur and its potential reversibility

2. Other Risks

a) List any known or foreseeable risks or discomforts to the participant from procedures or treatment unrelated to study interventions like drugs, radiation or surgery (such as randomization, placebo, withdrawal or withholding standard treatment). If known, list the frequency and severity of each risk.

3. What is the risk classification of this research? Note: A research protocol may include multiple research interventions, which may fall into different categories. Please provide the highest risk level, or classify each of the interventions separately.

☐ Minimal Risk (Minimal risk means risks that are not greater in and of themselves than those ordinarily encountered in the daily life of normal children or during the performance of routine physical or psychological examinations or tests).

☐ Minor Increase over Minimal Risk - (A minor increase in risk which, while it goes beyond the boundaries of minimal risk, poses no significant threat to the child's health or well being)

☐ Greater than Minimal Risk (All other risks)

4. What specific procedures will be utilized to prevent or minimize potential risks or discomforts associated with study interventions and procedures?

5. **What are the specific subject withdrawal criteria?**

6. **What are the potential benefits to the subject associated with the research? Note: A research protocol may include multiple research interventions, which may have different types or levels of benefit. Please classify each of the interventions separately.**

7. **How will the new information gathered from the study impact the treatment of this disease or disorder?**

SECTION G

GENETIC RESEARCH

1. **Does this study include genetic research on samples or tissues?**

   ☐ **Yes** ☐ **No (If no, go to Part H)**

   It may be useful to think of genetic research as being carried out on a continuum comprising of four stages: (1) pedigree studies (to discover the pattern of inheritance of a disease and to catalog the range of symptoms involved); (2) positional cloning studies (to localize and identify specific genes); (3) DNA diagnostic studies (to develop techniques for determining the presence of specific DNA mutations); and (4) gene therapy research (to develop treatments for genetic disease at the DNA level).*

   If yes:

   a) Why is this patient population appropriate for genetic research?

   b) Will results be disclosed to the participants?

      ☐ Yes (**If yes, describe in what way)** ☐ No

   c) Will participants be given the option of not receiving information about themselves?

   d) Will the possible psychological and social risks of genetic research be adequately considered in the consent process? Will appropriate counseling be provided, both as part of the consent process and also when communicating test or other research results to participants? Please explain.

e) Will participants be informed about the possibility that incidental findings may be made?

f) Will the data be protected from disclosure to third parties, such as employers and insurance companies? Describe confidentiality measures.

g) Will research findings be disclosed to participants' physicians for clinical use?

h) Will this plan be discussed with the participants and their consent obtained?

i) Will vulnerable populations be adequately protected? (See Part C, Question # 4.)

☐ Yes (**If yes, how?)** ☐ No

j) What provisions have been made for protecting against misuse of tissue samples?

k) What provisions have been made for the treatment of data and tissue samples in the event of participant withdrawal from study?

l) Describe ways that participants' privacy and confidentiality will be protected when publications are planned.

SECTION H

STORAGE OF SPECIMENS FOR UNSPECIFIED FUTURE RESEARCH STUDIES

1. **Does this study involve collection of specimens for unspecified future research studies?**

☐ Yes ☐ No **(If no, skip to SECTION I.)**

If yes:

a) What are the types and amounts of specimens to be collected? Justify the types and amounts.

b) How will the specimens be linked to the participants?

c) For what types of research do you anticipate using the samples in the future?

d) How will access to the specimens be governed?

e) What procedure will be used if the participant withdraws consent after the specimen has been collected and stored?

f) Will research findings be disclosed to participants or to participant's physicians?

SECTION I

ANCILLARY STUDIES

2. **Will participants enrolled in this protocol be asked to register in any ancillary/companion protocols?**

☐ Yes ☐ No

If yes, are these protocols:

☐ Mandatory

☐ Optional

☐ Both

NOTE: If a protocol requires that its participants also enroll in an ancillary/companion protocol, the CIRB must review the ancillary/companion protocol. A separate, Ancillary Protocol Application, the ancillary/companion protocol, and associated informed consent document(s) must be submitted to the CIRB for review and approval. Once an ancillary/companion protocol has been approved, it will not need to be resubmitted with each treatment protocol that it accompanies.

The CIRB will review all ancillary/companion protocols whose participation is mandatory for participants enrolled in an associated main treatment protocol, regardless of when the ancillary/companion protocol was activated and open to enrollment.

The CIRB will not review an ancillary/companion protocol if participation is optional and the protocol was activated and open to enrollment prior to the associated main treatment protocol's submission for CIRB review.*

SECTION J

CONFLICTS OF INTEREST

1. **Does the Study Chair or any principal involved in the development or coordination of this study have any significant financial conflicts of interest as defined in the Conflict of Interest Policy for Cooperative Group Phase 3 Clinical Trials?**

   ☐ Yes ☐ No If yes, please answer question #2.

2. **Does the Cooperative Group have a management plan in place to address the conflicts disclosed in question #1**

   ☐ Yes ☐ No If yes, please provide a copy of the management plan

SECTION K

INFORMED CONSENT

1. **Please submit a copy of the informed consent document(s) for this protocol along with this application.**

   Important Note: A Word® file containing the informed consent document(s) must also be emailed to the CIRB Project Office in order for this application to be considered complete. Kindly send the completed CIRB application and the informed consent document(s) to pediatriccirb@emmes.com.*