I. POLICY

Investigators are responsible for conducting human subjects research following ethical standards and practices, and in accordance with Federal, State, local, and institutional rules and regulations.

Principal investigators (PIs) at Children’s National Medical Center (CNMC) are expected to understand and apply their obligation to protect the rights and welfare of research subjects.

Definitions

A Clinical trial/Investigation, as defined by the National Institutes of Health (NIH), is a prospective biomedical or behavioral research study of human subjects that is designed to answer specific questions about biomedical or behavioral interventions (such as drugs, treatments, devices, or new ways of using known drugs, treatments, or devices).

An Investigator is a person who conducts a clinical investigation of a drug, biological product, or medical device (21 CFR 312.3(b) and 21 CFR 812.3(i)), or of a behavioral treatment.

II. ACCOUNTABLE EXECUTIVE AND REVIEWER(S)

A. Accountable Executive: Chief Academic Officer/Institutional Official for the Federalwide Assurance
B. Department Responsible for Review: Office for the Protection of Human Subjects
C. Committee Responsible for Review: Institutional Review Board Executive Committee
   Research Policy/Procedure Working Group

III. APPROVAL

Approved by:
IV. **APPLICABILITY**

Areas where the policy and procedure applies: Children’s Research Institute, Children’s National Medical Center

Persons to whom the policy and procedure applies: Investigators engaged in human subjects research

V. **REVIEW OR REVISION DATE**

Original:

VI. **REFERENCES**

AAHRPP Element(s):


Policies and Procedures: RA:HRPP:01.02 and 01.02P, *Statement of Ethical Principles for the Human Research Protection Program*

RA:HRPP:01.03 and 01.03P, *Statement of Regulatory Requirements for Human Subjects Research*
I. PROCEDURE

A. The principal investigator (PI) is responsible for personally conducting or supervising the conduct of human-subjects research and for protecting the rights, safety, and welfare of the subjects enrolled in the research. The PI must ensure that all human-subjects research is conducted in an ethical manner and in accordance with all Federal, State, and local laws and regulations, institutional policies, and requirements or determinations of the Institutional Review Board (IRB).

B. Ethical Standards

1. Investigators have a responsibility to be knowledgeable regarding ethical standards and practices in human subjects research. (RA:HRPP:01.02 and 01.02P, *Statement of Ethical Principles for the Human Research Protection Program*; RA:HRPP:10.3 and 10.3P, *Education and Training: Investigators and Research Staff*)

2. Investigators are to acknowledge and accept their responsibility for protecting the rights and welfare of human subjects, and for complying with all applicable provisions of the Children’s National Medical Center (CNMC) assurance of compliance with the U.S. Department of Health and Human Services (DHHS) Office for Human Research Protections (OHRP), with Federal, State and local regulations, and with all CNMC policies. (RA:HRPP:01.03 and 01.03P, *Statement of Regulatory Requirements for Human Subjects Research*)

3. When required, investigators who intend to use human subjects are responsible for obtaining the review and approval of the Institutional Review Board (IRB) prior to initiation of the research. (RA:HRPP:03.01 and 03.01P, *Institutional Review Board Jurisdiction*)

4. Investigators are responsible for ensuring that the research is conducted in accordance with IRB-approved protocols and any conditions that are set in order to receive final approval.

5. For any study with human subjects actively receiving treatment, the Principal Investigator or a co-investigator must be available 24 hours a day, 7 days a week.
6. Investigators are responsible for conducting research with sufficient and appropriate resources to ensure appropriate care, oversight, and safety of the research subjects throughout the course of the research. (RA:HRPP:10.08 and 10.08P, Investigator Resource Requirements for Protecting Human Subjects)

7. Investigators and research staff are responsible for using recruitment processes that are fair and equitable. (RA:HRPP:10.07 and 10.07P, Investigator Responsibilities for Fair and Equitable Subject Recruitment)

8. When drugs, biological products, and devices are being investigated or used, they are managed and controlled as required by institutional policy and, when applicable, FDA regulations 21 CRF 312 and 21 CFR 812. (RA:HRPP:09.02 and 09.02P, Drugs, Biologics, and Dietary Supplements in Research; CNMC Investigational Drug Services policies and procedures)

9. Investigators are responsible for reporting to the Institutional Review Board all actions or processes that deviate from the protocol procedures approved by the IRB. (RA:HRPP:05.07 and 05.07P, Protocol Deviations)

10. Investigators are responsible for ensuring appropriate qualifications and knowledge of study personnel and research staff under their supervision. (RA:HRPP:10.02 and 10.02P, Investigator and Research Staff Qualifications)

11. Should IRB approval lapse, research procedures such as recruitment and enrollment of subjects, study procedures on currently enrolled subjects, review of health/medical records, collection of tissue or other samples, or analysis of data, are not conducted until the IRB re-approves the research or until special permission is obtained from the IRB to continue previously enrolled subjects because it is in their best interests to do so. (RA:HRPP:05.08 and 05.08P, Continuing Review and Study Closure)

12. When the research has been completed or is being closed out prior to completion, investigators are responsible for submitting a final continuing review report to the IRB. (RA:HRPP:05.08, 05.08P)

C. Informed Consent

1. Investigators are responsible for obtaining and documenting informed consent in accordance with the regulatory requirements unless otherwise authorized by the Institutional Review Board. Investigators are permitted to delegate to appropriate individuals the authority to obtain consent on their behalf; however, they are ultimately responsible. Individuals designated to obtain informed consent from subjects and families must have the necessary qualifications as described in RA:HRPP:07.02 and 07.02P, Informed Consent/Parental Permission and Assent Process, section I.F.2.
2. Investigators have an ethical responsibility to ensure that subjects and families understand, through the informed consent process, the nature of the research, the requirements of participation, the associated risks and benefits, and any alternatives. Research investigators must take whatever steps are necessary to ensure this understanding and to facilitate implementation of a bona fide informed consent process. (RA:HRPP:07.02, 07.02P; RA:HRPP:07.03 and 07.03P, Documentation of Informed Consent/Parental Permission and Assent)

3. Investigators and their research staff are not to use exculpatory language when communicating with a prospective subject or the legally authorized representative.

4. Investigators are responsible for providing a signed copy of the IRB-approved informed consent to each subject at the time of consent unless the IRB has specifically waived this requirement (RA:HRPP:07.03, 07.03P). All informed consent documents are to be maintained in a manner approved by the IRB (RA:HRPP:10.14 and 10.14P, Storage and Retention of Research Data and Informed Consent Documents).

D. Protocol Documentation

1. Investigators are responsible for maintaining for each study a current protocol file or binder that contains, at a minimum, the following documents:
   a) Approved IRB protocol;
   b) Approved informed consent/parental permission and assent forms;
   c) Approved recruitment materials;
   d) Approved study materials (e.g., surveys, questionnaires);
   e) Pertinent correspondence with the IRB (and the sponsor, if applicable);
   f) Investigational brochure for drug and device studies, and Forms 1571 and 1572, if applicable.

2. Investigators are encouraged to document and file all Institutional Review Board (and sponsor, if applicable) submissions, responses, and pertinent correspondence.

3. Investigators are responsible for promptly reporting to the IRB any proposed changes to previously approved human subject protocols. These changes are not to be initiated without IRB review and approval except when required to avoid apparent immediate harm to the subjects. (RA:HRPP:05.06 and 05.06P, Protocol Modifications and Revisions)

4. Investigators are responsible for reporting the progress of the approved research to the IRB, in the manner and frequency prescribed by the IRB (based on the risk to subjects), but not less than once per year. (RA:HRPP:05.08, 05.08P)
5. Investigators are to promptly report to the IRB unanticipated, serious events or other unanticipated problems that involve risks to subjects or others. (RA:HRPP:06.02 and 06.02P, Unanticipated Problems Involving Risks to Subjects or Others, Including Adverse Events)

6. Investigators are responsible for submitting to the IRB copies of all external monitoring reports, Data Safety and Monitoring Board reports and updates, and FDA annual reviews, if applicable. (RA:HRPP:05.08, 05.08P)

7. Investigators are responsible for reporting to the IRB any noncompliance with regulations or CNMC policies and procedures. (RA:HRPP:06.03 and 06.03P, Investigator Noncompliance: Investigations and Determinations)

8. Investigators are responsible for the safe and secure storage of research data and protecting the confidentiality of the data. (RA:HRPP:10.14, 10.14P)

E. Clinical Trials/Investigations

In addition to the responsibilities outlined elsewhere in this and other policies and procedures, investigators who conduct biomedical or behavioral clinical trials are obligated to observe the following Good Clinical Practice (GCP) guidelines.

1. Investigator qualifications and agreements.
   a) The investigator is familiar with the appropriate use of the investigational product(s) or treatment(s) as described in the protocol and, when applicable, in the current investigator's brochure, product information, and other information sources provided by the sponsor.
   b) The investigator is aware of and complies with GCP and the applicable regulatory requirements.
   c) The investigator permits monitoring and auditing by the sponsor, and inspection by the appropriate regulatory authorities.
   d) The investigator maintains a list of appropriately qualified persons to whom the investigator has delegated significant trial-related duties.

2. Medical care of trial subjects.
   a) A qualified physician (or qualified dentist, when appropriate) provides the medical care given to, and medical decisions made on behalf of, subjects.
   b) The investigator is responsible for providing reasonable access to needed medical care, either by the investigator or by another identified, qualified individual (e.g., when the investigator is unavailable; when specialized care is needed).
   c) The investigator is responsible for providing reasonable medical care for study subjects for medical problems arising during participation in the trial that are, or could be, related to the study intervention.
d) When appropriate, the investigator informs the subject’s primary physician about the subject’s participation in the clinical trial if the subject has a primary physician and if the subject agrees to the primary physician being informed.

e) Although a subject is not obliged to give his or her reasons for withdrawing prematurely from the clinical trial, the investigator should make a reasonable effort to ascertain the reason, while fully respecting the subject’s rights.

3. **Compliance with the protocol.**
   a) The investigator should adhere to the protocol so that study subjects are not exposed to unreasonable risks.
   b) The investigator should follow the trial's randomization procedures, if any, and should ensure that the code is broken only in accordance with the protocol. If the trial is blinded, the investigator should promptly document and explain to the sponsor any premature unblinding.
   c) The investigator ensures that the investigational product is used only in accordance with the approved protocol.
   d) Responsibility for accountability of the investigational product at the clinical trial site rests with the investigator.

4. **Records and reports.**
   a) The investigator ensures the accuracy, completeness, legibility, and timeliness of the data reports to the sponsor.
   b) The investigator maintains the clinical trial documents as specified under FDA regulation 21 CFR 312.62.
   c) The investigator shall retain records required to be maintained for a period of 2 years following the date a marketing application is approved for the drug for the indication for which it is being investigated; or, if no application is to be filed or if the application is not approved for such indication, until 2 years after the investigation is discontinued and FDA is notified.

5. **Reporting requirements.**
   a) Investigators provide written reports to the sponsor and the Institutional Review Board on any changes significantly affecting the conduct of the clinical trial or increasing the risk to subjects.
   b) Investigators report all serious adverse events (SAEs) to the sponsor except for those SAEs that the protocol or other document (e.g., investigator's brochure) identifies as not needing immediate reporting. The investigator follows regulatory requirements and institutional policy related to the reporting of unexpected serious adverse drug reactions to the regulatory authority and the IRB. (RA:HRPP:06.02 and 06.02P, Unanticipated Problems Involving Risks to Subjects or Others, Including Adverse Events)
c) Investigators report adverse events or laboratory abnormalities identified in the protocol as critical to safety evaluations to the sponsor according to the reporting requirements and within the time periods specified by the sponsor in the protocol.

d) For reported deaths, the investigator supplies the sponsor and the IRB with any additional requested information (e.g. autopsy reports and final medical reports).

e) If the investigator terminates or suspends a clinical trial without prior agreement of the sponsor, the investigator informs the IRB and the sponsor.

f) If the sponsor terminates or suspends a clinical trial, the investigator informs the IRB.

g) If the IRB terminates or suspends its approval of the clinical trial, the investigator should promptly notify the sponsor.

h) Upon completion of the trial, the investigator provides the IRB with a summary of the trial’s outcome and submits to the regulatory authority (e.g. FDA) any required reports.

i) If all or part of the trial is conducted in the Clinical Research Center (CRC), any information the investigator reports to the IRB as per a) through h) above is also reported by the investigator to the CRC nurse manager and Research Participant and Family Advocate (RPFA).

F. Subject and Research Team Member Concerns

1. Investigators are responsible for immediately addressing any concern or question raised by a research subject before, during, or after his or her (child’s) participation in the research study.

   a) All concerns and complaints are to be addressed in a timely and thorough manner.

   b) Any PI, member of the research team, or health care provider who receives a research subject/family member complaint must notify the Director of Research Regulatory Affairs by telephone (301-565-8488) or email (abrigatt@childrensnational.org), or by completing an adverse event/complaint form, which asks for details regarding the complaint or concern raised. The Director should also be informed when and how the issue is resolved.

2. Investigators are responsible for addressing any concerns raised by any member of their research team. This responsibility includes the following:

   a) Investigators are to meet frequently with their research teams for the purpose of reviewing the progress of the research, and to encourage discussion of any concerns about the research in general or about a specific research subject.

   b) Investigators are to inform each member of the research team individually of his or her responsibility to voice any concerns he or she may have, without fear of repercussions.
c) Investigators must take seriously any concern raised. They are to fully investigate each expressed concern, and report back to the individual who raised it. No concern is to be dismissed.

d) Investigators may not censure or take retribution on an individual who brings a concern to their attention.

e) Investigators are responsible for reporting to the IRB any expressed concerns that result in findings regarding subject safety, compliance with the research protocol, informed consent violations, or the integrity of the research data.

II. REVIEW OR REVISION DATE

Original:

III. REFERENCES

AAHRPP Element(s):
Federal Regulations: U. S. Department of Health and Human Services (DHHS) 45 CFR 46
Food and Drug Administration (FDA) 21 CRF 312; 21 CRF 812


Policies and Procedures: RA:HRPP:01.02 and 01.02P, Statement of Ethical Principles for the Human Research Protection Program
RA:HRPP:01.03 and 01.03P, Statement of Regulatory Requirements for Human Subjects Research
RA:HRPP:03.01 and 03.01P, Institutional Review Board Jurisdiction
RA:HRPP:05.06 and 05.06P, Protocol Modifications and Revisions
RA:HRPP:05.07 and 05.07P, Protocol Deviations
RA:HRPP:05.08 and 05.08P, Continuing Review and Study Closure
RA:HRPP:06.02 and 06.02P, Unanticipated Problems Involving Risks to Subjects or Others, Including Adverse Events
RA:HRPP:06.03 and 06.03P, Investigator Noncompliance: Investigations and Determinations
RA:HRPP:07.02 and 07.02P, Informed Consent/Parental Permission and Assent Process
RA:HRPP:07.03 and 07.03P, Documentation of Informed Consent/Parental Permission and Assent
RA:HRPP:09.02 and 09.02P, Drugs, Biologics, and Dietary Supplements in Research
RA:HRPP:10.03 and 10.03P, *Education and Training: Investigators and Research Staff*
RA:HRPP:10.02 and 10.02P, *Investigator and Research Staff Qualifications*
RA:HRPP:10.07 and 10.07P, *Investigator Responsibilities for Fair and Equitable Subject Recruitment*
RA:HRPP:10.08 and 10.08P, *Investigator Resource Requirements for Protecting Human Subjects*

CNMC Investigational Drug Services Policies and Procedures