

**The Children's Memorial
Research Integrity and Compliance Program
Manual**

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**Children's Memorial
Research Integrity and Compliance Program Manual**

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Introduction

As a leading pediatric research hospital and academic medical center, The Children's Memorial Medical Center¹ (collectively "Children's Memorial") conducts itself in accordance with the highest level of research ethics and in compliance with applicable laws, rules, and regulations. The Children's Memorial Research Integrity and Compliance Program Manual focuses on compliance around the research activities of Children's Memorial Research Center ("CMRC"). The CMRC Office of Research Integrity and Compliance Program (the "ORIC Compliance Program") was developed by the CMRC Office of Research Integrity and Compliance ("ORIC") in accordance with applicable laws, rules and regulations, and with guidance from appropriate federal and State of Illinois sources, including the Office of Research Integrity ("ORI") of the Department of Health and Human Services ("DHHS"), the Office for Human Research Protections ("OHRP"), the Food and Drug Administration ("FDA"), National Institutes of Health ("NIH"), United States Department of Agriculture ("USDA"), Office of Laboratory Animal Welfare ("OLAW"), and the DHHS Office of Inspector General ("OIG").

The purpose of this manual is to provide instruction and to serve as a resource for individuals governed by this manual, which includes any person employed by Children's Memorial and its officers, directors, volunteers, researchers, trainees and medical and dental staff (collectively "staff members" or "staff") who are involved in research activities. The ORIC Compliance Program is also intended to cover any other person or organization engaged by Children's Memorial to provide products or services.

This manual explains the infrastructure of the ORIC Compliance Program, identifies roles and functions, provides an overview of compliance processes at Children's Memorial, and offers direction about where to find additional, detailed information. The content is intended to complement, not replace, other policies.

With the ORIC Compliance Program, Children's Memorial will continue to: (a) promote the responsible conduct of research that is fully compliant with the governing regulations, (b) foster an environment that promotes ethical conduct by principal investigators, research staff members and compliance oversight committees, and (c) provide guidance to staff members for their individual and collective conduct. The Manual is intended to generally define the scope of conduct which the ORIC Compliance Program is intended to cover but is not intended to be all-inclusive.

The ORIC Compliance Program aligns with and abides by the Children's Memorial Corporate Compliance Program as it sets forth overarching compliance standards across the organization. The content of the ORIC Compliance Program is guided by the OHRP Compliance Oversight Procedures for Evaluation Institutions, published in October 2005.

¹ The Children's Memorial Medical Center includes current and future subsidiaries and affiliates, which currently includes The Children's Memorial Hospital, The Children's Memorial Research Center, The Children's Memorial Foundation, Pediatric Faculty Foundation, Inc., Park West Realty Corporation and Children's Memorial Medical Group, LLC.

The ORIC Compliance Program's Policy on Integrity in Research is based upon guidance established by ORI in compliance with the Public Health Service Policies on Research Misconduct (42 CFR Part 93), that became final in June 2005. The elements provide the basis for organizing and focusing written standards, policies, and procedures.

The ORIC Compliance Program is a "living" document and the ORIC will update it periodically to keep staff members informed of and in compliance with a large number of current laws, rules and regulations.

Section 1: Research and Integrity Compliance Program Oversight

The ORIC Compliance Program Oversight provides a focal point for all research compliance activities.

A. Director, Office of Research Integrity and Compliance

The Director, ORIC, reports to the Senior Vice-President and Chief Operating Officer, CMRC. The Senior Vice-President and Chief Operating Officer, CMRC will retain ultimate responsibility for the supervision and oversight of the ORIC. The Director oversees research integrity related matters and provides guidance and oversight to the compliance committees, including but not limited to: the Institutional Review Board (“IRB”), the Institutional Animal Care and Use Committee (“IACUC”), the Institutional Biosafety Committee (“IBC”), and the Radiation Safety Committee. The Director works closely with the Legal Department and the Corporate Compliance Office. The Director is responsible for guiding and monitoring compliance activities, maintaining a current knowledge of laws and regulatory requirements, and developing a system whereby related information and updates are disseminated throughout the organization to ensure that Children’s Memorial is addressing research integrity and compliance issues. The Director has authority to review all documents and other information that are relevant to research compliance activities. For a description of the primary responsibilities of the Director, ORIC, please see Exhibit A.

B. Institutional Review Board

The IRB is the group designated by the institution to review, approve and conduct periodic reviews of clinical research studies involving human subjects. The IRB, its membership and operations are established in conformance with the governing federal regulations and, as required, has a Federalwide Assurance Number. The IRB is subject to audit by the OHRP, ORI, FDA and others on a routine basis, or ‘for cause’ basis.

The primary purpose of the IRB is to assure, both in advance and by periodic review, that appropriate steps are taken to protect the rights and welfare of humans participating in research. It carefully balances the risks and benefits to ensure the principles of autonomy, beneficence, justice and equity of selection of research subjects are observed. This is done by reviewing the research plan, informed consent/assent forms, recruitment materials and other related research documents. The IRB has 14 scheduled meetings per year and may as needed conduct business by conference call of the convened IRB.

As the patient population at Children's Memorial is pediatric, the IRB is required to follow an additional layer of regulations specific to the protection of children (45 CFR Part 46, Subpart D).

The Director, under the guidance of the Senior Vice-President and Chief Operating Officer, CMRC, duly informs the authorities concerning instances of misconduct and/or

non-compliance that meet the reporting criteria as set forth by the OHRP, ORI and FDA. In addition, ORIC is required to provide an annual report to the ORI.

C. Institutional Animal Care and Use Committee

The goal of the IACUC is to ensure the humane care and use of animals used in research, and that such research is done in accordance with the applicable guidelines and regulations. Each institution is required to have an Animal Welfare Assurance that is renewed every five years. On an annual basis, the IACUC submits reports to the USDA and OLAW.

The IACUC reviews, initially and periodically, all animal research conducted at CMRC to ensure compliance with governing regulations. The review evaluates all aspects of the protocols such as, but not limited to, animal care procedures, animal numbers and justification of animal numbers, husbandry, adequate training of research personnel, research outcomes and endpoints. The IACUC meets monthly or more often as deemed necessary. There are two additional Administrative meetings scheduled per year that focus on education and training of IACUC committee members and discussion of administrative policies and procedures.

CMRC IACUC membership conforms to OLAW requirements and reports to the Institutional Official for CMRC. In keeping with the regulations, the IACUC performs semi-annual inspections of the research facility and program review. These reports, as federally mandated, are submitted to the Institutional Official for CMRC.

D. Institutional Biosafety Committee

Each institution conducting research using recombinant DNA is required to follow the *NIH Guidelines for Research Involving Recombinant DNA Molecules* (“*NIH Guidelines*”). The Office of Biotechnological Activities (“OBA”) of the NIH holds each institution’s IBC responsible for ensuring that the research and research personnel involving recombinant DNA employ procedures and practices that are in compliance with the *NIH Guidelines*.

The IBC review of recombinant DNA research conducted at CMRC is done when a project is initiated and then annually, or more frequently if necessary. The review includes areas such as containment levels, training and expertise of research personnel, assessment of facilities and laboratory safety. The IBC submits an annual report to OBA of the NIH. The IBC meets monthly or more often as deemed necessary.

The membership of the CMRC IBC is in accordance with the *NIH Guidelines*.

At least once per year, and more often as deemed appropriate, the IBC conducts laboratory inspections to ensure regulatory and institutional compliance.

E. Compliance Advisory Committee

The Director, ORIC serves on the Compliance Advisory Committee, a multi-disciplinary team that meets regularly and is responsible for implementing the compliance process and ensuring that the appropriate level of compliance activity exists. The Chief Compliance Officer appoints the members of the committee with advice and counsel from the Corporate Compliance Director.

F. Public Data Reporting Committee

The Director, ORIC serves on the Public Data Reporting Committee. The aim of this committee is to be the coordinator for all public data reporting for the purpose of ensuring the most accurate data submission respective to Children's Memorial performance. The scope of data reporting includes all external venues whereby Children's Memorial performance data is to be submitted, e.g. national and state performance reporting statutory requirements, employer-based initiative (Leapfrog), regulatory initiatives (Joint Commission, Centers for Medicare and Medicaid Services), and outcome data required for managed care contracting.

G. Legal Counsel

Children's Memorial Legal Department will assist the Director, ORIC, and other appropriate Children's Memorial person in identifying and addressing applicable laws, rules, and regulations relevant to the ORIC Compliance Program. The Legal Department will serve as an advisor to Children's Memorial in relation to such laws, rules, and regulations, and will assist the ORIC in maintaining the ORIC Compliance Program in compliance with current laws, rules, and regulations. The Legal Department will review policies and procedures related to the ORIC Compliance Program on a regular basis to ensure that they adhere to federal, state and other applicable laws, rules and regulations.

Activities related to the ORIC Compliance Program will be conducted as advised by Legal Department. ORIC will notify the Corporate Compliance Office and legal counsel of all reports of material non-compliance, at which time the Director, in conjunction and under guidance provided by the Legal Department, will coordinate an investigation of the reported incident. Children's Memorial will make every effort to preserve and maintain the attorney-client privilege in connection with such investigations, as well as comply with existing and applicable whistleblower protection laws.

H. Corporate Compliance Office

The Corporate Compliance Office includes both the Chief Compliance Officer and the Corporate Compliance Director. Primary responsibilities of this Office include oversight of the Children's Memorial Corporate Compliance Program.

Section 2: Policies and Procedures and Code of Conduct

Children's Memorial policies and procedures and Code of Conduct, are intended to articulate the commitment to comply with federal, state and other applicable laws, rules and regulations, with an emphasis on preventing fraud and abuse. Children's Memorial is committed to having written policies and procedures in place throughout the organization and providing staff with access to these while performing their duties. Many of these policies are reviewed regularly by the ORIC. ORIC, in conjunction with the appropriate compliance committees, will advise affected individuals of any changes and necessary training that will occur as set forth herein.

A. Communication Regarding Research Integrity and Compliance Program

The ORIC Compliance Program is communicated to Principal Investigators and staff members via the CMRC employee orientation. Current research ethics and compliance guidance documents are available on the CMRC website. Existing staff may receive additional training through their respective departments or the ORIC. Annual revisions to the ORIC Compliance Program and regulatory updates are available to all individuals through the Office of Sponsored Programs ("OSP")/ORIC Outreach Program (See Section 3 – Education and Training).

B. Communication Regarding Code of Conduct Guidelines

Children's Memorial has developed the Code of Conduct (the "Code") as a guideline to explain its ethical and legal obligations, and professional conduct standards. The Code is intended to serve as a resource for principal investigators and staff members and is reinforced through ongoing communication training and monitoring activities. The Code is available online through CMRC Research Ethics and Compliance website, The Point, and the Corporate Compliance Office. Please refer to [Exhibit H](#) to review the Code of Conduct.

C. Conflict of Interest Policies

Issues surrounding conflict of interest or perceived conflict of interest are taken very seriously by the ORIC. There are two separate processes addressing conflict of interest. The Policy on Conflict of Interest for Sponsored Programs addresses the issue of conflict of interest for the principal/research investigators and staff when conducting research activities. The Children's Memorial Hospital Institutional Review Board Member Policy on Disclosing Conflicts of Interest addresses conflict of interest affecting those individuals who sit on the compliance review committees (IRB, IACUC, and IBC).

Both policies document how to manage conflict of interests in order to avoid any conflict of interest or the appearance of conflict of interest on the part of the interested parties. Each compliance committee includes these policies as part of their policy and procedure manuals.

Please see [Exhibit F](#) and [Exhibit G](#) for the policies discussed above.

C. Other Policies and Procedures

Children's Memorial also has numerous other policies, including Administrative Policies, Human Resources Policies, Health Insurance Portability and Accountability Act ("HIPAA") Policies, Occupational Health Policies, and Emergency Policies and Procedures available online through The Point.

Section 3: Education and Training

Ongoing education and training is a significant element of the ORIC Compliance Program. The training program includes, but is not limited to, sessions highlighting the ORIC Compliance Program and the individual committees, regulatory guidelines governing the conduct of research activities, issues surrounding scientific integrity and misconduct, HIPAA, and any new regulations or guidance issued by the governing bodies. Documentation of formal training undertaken as part of the ORIC Compliance Program is retained by the ORIC. Each person is held accountable for compliance with all applicable regulations that affect his or her job.

In collaboration with the OSP, all research staff receives specific training on the regulations and organizational policies and procedures applicable to their job function.

A. Office of Sponsored Program and Office of Research Integrity and Compliance Outreach Programs

On an ongoing basis research personnel receive information and training updates on the ORIC Compliance Program and emerging issues applicable to them. This information is disseminated through the OSP and ORIC departments, through methods including, but not limited to flyers, fraud alerts, booklets, global (institution-wide) email announcements, and dedicated training sessions.

The staff members of the ORIC and the OSP, under the supervision of their respective Directors, conduct several outreach sessions through out the year focusing on CMRC policies and procedures, current and proposed regulations and how CMRC ensures compliance.

B. Institutional Review Board

The IRB has specific education requirements for researchers set forth by the federal government. Certification and documentation of completion of the education requirements is a prerequisite for IRB approval of any project. Please see the IRB Policy and Procedure Manual, located on the CMRC website, regarding specific information related to education and training of research personnel. IRB members also have specific education requirements and attend an annual IRB meeting dedicated to the discussion of research ethics and human subjects protection to fulfill this requirement.

C. Institutional Animal Care and Use Committee

The IACUC requires that all individuals involved in animal research undergo animal training with the Director of the Research Support Facility. The IACUC Policy and Procedure Manual includes specific information related to education and training of research personnel. In addition, as federally mandated, those individuals who as part of their responsibilities have contact with animals are required to enroll in the Occupational Health and Safety Program.

ORIC, in conjunction with the IACUC office, Director, RSF, Facilities Management and Safety Officers, has developed the CMRC Disaster Plan that addresses the needs of both staff and the animals housed in the facility.

D. Institutional Biosafety Committee

All Principal Investigators must provide assurance to the IBC that all lab personnel involved in the projects are trained and familiar with relevant biosafety practices, protective equipment and techniques and emergency procedures.

E. Office of Research Integrity and Compliance

Members of the compliance committees and ORIC staff attend, on a regular basis, meetings sponsored by federal agencies and national organizations to ensure that current practices at CMRC are in compliance with regulatory guidelines. As individuals progress through their career to enter management positions, further education is received as part of new managers training.

Section 4: Channels of Communication

CMRC believes in an environment of open and candid communications. Staff members at all levels are encouraged to report in good faith suspected or actual misconduct and any potential violation of law or the ORIC Compliance Program, so that it can be investigated and properly addressed.

A. Open Door

Children's Memorial has an "open door" policy that permits staff to present to management any suspected violation of research ethics or regulatory compliance, the ORIC Compliance Program, the Conflict of Interest Policy, the Code, or related policies. When reporting a concern about a legal or ethical issue, staff may choose to first report the concern to their supervisor or to go directly to the ORIC or available senior management. In addition, reports can be made to the Corporate Compliance Office. The Corporate Compliance Office will work in collaboration with the ORIC on research related compliance matters. The ORIC will protect, to the fullest extent permitted by law, the identity of staff who desire to remain anonymous. Staff members who report concerns or suspected problems in good faith can do so without fear of retaliation..

Children's Memorial has also established internal and external helplines to encourage staff to report knowledge or suspicion of illegal or unethical acts. Children's Memorial will protect to the fullest extent permitted by law the identity of callers who desire to remain anonymous and will not tolerate retaliation against individuals who report concerns or suspected problems in good faith.

Internal Helpline

When calling the internal Helpline, staff members may leave a message reporting their concern. The internal Helpline is active twenty-four (24) hours a day and is always answered by voice mail. This number is checked daily by the Corporate Compliance Office.

- **To leave a message reporting a concern, dial 1-773-880-6302.**

External Helpline

When calling the external Helpline, staff members are greeted by an outside service that will ask for detailed information about their concern. The report will be reviewed with the caller to assure the information is documented accurately and is then forwarded to the Corporate Compliance Office within twenty-four (24) hours of receipt. Callers wanting to remain anonymous will receive an ID number to be used so they can call back to report more details or receive a follow-up response. This Helpline is available twenty-four (24) hours a day, seven (7) days a week.

To call the external Helpline, dial 1-800-273-8452.

B. Integrity in Research

It is the policy of Children's Memorial, specifically CMRC, to require high ethical standards in research and to this end, the ORIC takes very seriously any and all allegations of misconduct and/or non-compliance. ORIC will inquire into, and if necessary, investigate in a timely manner all instances of alleged misconduct.

The ORIC submits an annual report to the ORI of the DHHS regarding any issues of misconduct at Children's Memorial related to human subjects. The ORIC and IRB comply with FDA and OHRP reporting requirements related to research activities. The IRB federal assurance is updated as required every three years.

The ORIC, in conjunction with the IACUC, submits annual reports to OLAW and the USDA regarding animal research activities. The Animal Welfare Assurance is updated as required every five years.

The ORIC, in conjunction with the IBC, and in compliance with *NIH Guidelines*, submits an annual registration and assurance report to the DHHS.

Section 5: Monitoring and Auditing Systems

The ORIC performs regular auditing and monitoring in order to demonstrate compliance with the ORIC Compliance Program. Proactive monitoring and auditing functions are designed to verify compliance with legal requirements and with the internal written compliance standards, and federal, state and local laws, regulations and rules. These functions also may assist CMRC in identifying possible misconduct or non-compliance.

A. Internal Reviews

Periodic audits shall be performed to manage high risk areas as identified through communication and/or reports, and as recommended by the ORI. Potential areas of audits include, but are not limited to:

1. HIPAA and research requirements
2. Obtaining and documenting informed consent.
3. Issues surrounding conflicts of interest for researcher and compliance committee board members.
 - a. Researcher COI is evaluated by the IRB at the time of protocol submission, and annually by the OSP office.
 - b. Committee members are required to complete an annual disclosure form
4. Instances of recurrent non-compliance by a specific investigator or department.
5. Issues related to fraudulent research billing charges or misuse of research funds.

B. Self-disclosure to Government Authorities

Any detected violations of regulations or reportable non-compliance will be reported to the appropriate governing agencies as per the guidelines specified by OHRP, USDA, FDA, NIH, OLAW and ORI. As necessary, ORIC will consult with legal counsel and the Corporate Compliance Office to ensure appropriate compliance with governing reporting regulations and legal obligations.

Section 6: Enforcement and Discipline

The effectiveness of an organization's compliance effort is generally tied directly to its ability to affect the conduct of each individual in or associated with the organization. In many instances the ORIC Compliance Program's success will be achieved one individual at a time. Building and maintaining meaningful structures of accountability is critical to this effort. When compliance failures occur, there must be a process for enforcing compliance standards and for disciplining responsible individuals when discipline is appropriate. Enforcing standards and disciplining those individuals who violate them emphasizes CMRC's commitment to compliance.

In many instances of research misconduct or serious non-compliance, disciplinary action by the federal government may apply. These actions are public and disseminated in the Federal Register as well as on the ORI website.

Disciplinary action will vary depending on the severity of the offense and such determinations will require the input of legal counsel, Human Resources, ORIC, senior management and leadership.

A. Failure to Report or Detect an Offense

Staff members have a duty to report conduct to Children's Memorial that is unlawful or unethical.

Management discusses with employees the compliance policies and legal requirements applicable to their function and explains that strict compliance with these policies and requirements is a condition of employment. Members of management have a duty to report any suspected violations. Failure to adequately instruct employees or to detect non-compliance, where reasonable diligence on the part of the supervisor should have led to discovery of non-compliance problems, may result in disciplinary procedures for the supervisor and will be reflected in his or her performance evaluation.

B. Reporting False Information

It is a violation of the ORIC Compliance Program to knowingly report false information to Children's Memorial or a government agency and there may be consequences for reporting false information (See Section 4 for additional information).

C. Employee Violations

Children's Memorial documents the reasons for disciplinary actions taken against its employees for violations of the ORIC Compliance Program and related policies. The determination of the appropriate discipline is made in accordance with the Human Resources Disciplinary Action Policy. Disciplinary actions are in proportion to an employee's conduct. Administered discipline is documented in the employee's personnel file. The following factors, among others, may be taken into account by Children's

Memorial in determining the appropriate disciplinary action to be imposed for a violation of the ORIC Compliance Program or related policies:

1. Nature of the violation and the ramifications of the violation for Children's Memorial;
2. Disciplinary action imposed for similar violations;
3. History of past violations;
4. Whether the violation was willful or unintentional;
5. Whether the individual was directly or indirectly involved in the violation;
6. Whether the violation represented an isolated occurrence or a pattern of conduct;
7. If the violation consisted of the failure to supervise another individual who violated the ORIC Compliance Program or related policies, the extent to which the circumstances reflect lack of diligence;
8. If the violation consisted of retaliation against another individual for reporting a violation or cooperating with an investigation, the nature of such retaliation;
9. Whether the individual in question reported the violation; and
10. Degree to which the individual cooperated with the investigation.

Section 7: Issues Related to Non-Compliance

The ORIC will manage the range of issues related to non-compliance with regulations in order to ensure the protection of human subjects and animals in research. Non-compliance can be the result of actions by the Principal Investigator, the research staff or the compliance committee (e.g. IRB, IACUC and IBC).

The regulations that govern issues related to non-compliance for federally funded research are 45 CFR Part 46 and for FDA regulated research, 21 CFR Parts 50, 56, 312 and 812.

Exhibit B defines the process for reporting, investigating, evaluating and taking action relative to an allegation of non-compliance. CMRC requires the reporting of all types of non-compliance. All reports will be reviewed and evaluated by persons other than the Principal Investigator and research staff.

Non-Compliance

Any of the following actions can be considered non-compliance: (1) the failure to follow the required determinations of the IRB, the IACUC or the IBC; (2) failure to follow their respective policies and procedures; (3) failure to follow institutional policies related to the participation of human subjects or animals in research, (4) or failure to follow the applicable regulations.

Range of Non-compliance

The following should be considered when evaluating non-compliance.

- Unintentional to willful
- One time to several times
- Degree of harm to human subjects or animals
- Degree of harm to the integrity of the data

Serious Non-compliance is defined as an action or omission in the conduct or oversight of research that affects the rights and welfare of the subjects, increases the risks to the subjects, decreases the potential benefits or compromises the integrity or validity of the data or research.

Continuing Non-compliance is defined as those incidents of non-compliance that occur more than once representing a pattern of non-compliance.

Principal Investigators, research personnel or any one else at Children's Memorial (e.g. pharmacy, nursing) are responsible for reporting any allegations of non-compliance promptly. Reporting can be made to department heads, the appropriate compliance committee (e.g. IRB, IACUC or IBC), research administration, or Corporate Compliance Office. Patients, sponsors, research subjects, family members or study staff may also report allegations of non-compliance (See Section 4, Part A for additional information).

The ORIC, under the direction of senior management and in consultation with legal counsel as deemed necessary, may temporarily suspend the research pending the outcome of the inquiry or investigation; may permit research to continue during the inquiry or investigation; may require modification to the research as a condition for the research; and may require additional education and training for research staff and the investigator. As necessary, the Corporate Compliance Office will be made aware of final decisions around non-compliance.

Non-compliance of the Institutional Review Board, the Institutional Animal Care and Use Committee or the Institutional Biosafety Committee

Non-compliance by one of the committee includes, but is not limited to, meetings held without a quorum, research reviewed without the appropriate expertise, block voting on proposals or voting by members with a conflict of interest.

The committee chair may be found to be in non-compliance should the chair not manage the meeting to allow for adequate discussion and deliberation of proposals, if the members do not follow the applicable regulations in reviewing the research, and if minutes do not appropriately reflect the decisions and determinations of the committee.

Institutional Review Board

For policies specific to the managing and reporting of non-compliance in the conduct of research of human subjects, please see the CMRC IRB Policies and Procedures Manual.

Section 8: Investigation, Response and Prevention

The term “investigation” is often used to describe the various responses CMRC might take to address known or suspected misconduct. Depending on the circumstances involved in the incidence, an investigation may be merely an informal inquiry, or it may involve more formal steps such as a detailed audit of research records. In addition to other preventative measures, an effective response to identified non-compliance will include appropriate monitoring of ongoing activities to assure that preventative measures are effective in eliminating recurrences of the non-compliance.

A. Investigation of Reported Violations

The ORIC initiates investigations of reported violations, implements corrective action, and, if appropriate, will take the necessary steps to secure or prevent the destruction of documents or other evidence relevant to the investigation.

The ORIC may consult with legal counsel and/or the Corporate Compliance Office regarding the manner in which to respond to a report (e.g., internally or externally directed investigations required disclosures or actions to be taken in response to a report of a violation of the ORIC Compliance Program or related policies). To the extent permitted by law, and in order to protect the reputation of those involved, the confidentiality and identity of the parties will be respected.

Upon receipt of reports of reasonable indications of suspected non-compliance, the ORIC will promptly assess the conduct in question to determine whether a material violation of applicable law or ORIC Compliance Program has occurred. Instances of non-compliance are evaluated on a case-by-case basis. The internal investigation may include interviews and a review of relevant documents. As appropriate, records of the investigation should contain documentation of the alleged violation, a description of the investigative process (including objectivity of investigators and methodologies utilized), key documents, a log of witnesses interviewed and the corrective action taken. Retention of records related to the investigation will be in accordance with applicable regulations.

ORIC, under the direction of senior management, reserves the right to remove the person(s) under investigation, or the person(s) allegedly involved in the misconduct from his/her/their current work activity until the investigation is completed.

B. Corrective Action

CMRC responds quickly and appropriately to all reported violations. ORIC policies and procedures may be modified to guard against further violations. All violations of law, regulations or policies are processed through established disciplinary procedures.

Should the investigation reveal that there is systemic non-compliance, ORIC may consult with legal counsel, and others as deemed appropriate, to determine: (a) what form of corrective action Children’s Memorial should take, if any, and (b) whether the ORIC

Compliance Program and related policies should be modified to address such non-compliance.

C. Government Audits and Investigations

Government agencies such as the OHRP, the FDA, or the USDA may at anytime conduct audits of the compliance committees. These audits may be “for cause”, where there is reasonable belief on the part of the agency that there is non-compliance, or they may be routine in nature (scheduled visits at regular intervals), to assess current practices. If any government entity institutes an investigation, ORIC will inform the President and Director, CMRC; Institutional Officials; relevant Compliance Committee Chairs and ORIC staff members that the government is conducting an investigation of certain matters and that government investigators may contact them in connection with the investigation. If such an investigation occurs, legal counsel will be notified and may inform staff members of their rights and obligations with respect to requests for interviews from governmental investigators.

If any Principal Investigator is contacted by a research sponsor or regulatory agency regarding an audit or investigation, ORIC should be notified so as to be available to provide support and any necessary regulatory documentation related to the research activities.

Staff members should refer any contact from a government official regarding an investigation or inquiry to the Director, ORIC. The Corporate Compliance Office will also be made aware of any investigations.

For the complete, in depth, ORIC Policy or Research Integrity and Procedures, see Exhibits B through E.

Section 9: Updates & Modifications

The Director, ORIC, under the guidance of the Chief Administrative Officer and Deputy Director of CMRC and advice of the Corporate Compliance Office, will review at least annually the ORIC Compliance Program to determine if revisions and/or updates are necessary to address new issues encountered in their administration, the enactment of new laws and/or the promulgation of new regulations, or other relevant changes.

The President and Scientific Director of CMRC will approve all amendments and modifications to the ORIC Compliance Program.

DISCLAIMER

This ORIC Compliance Program is not intended to and does not create contract rights in any person. It is informational in nature and is used by Children's Memorial to guide it in the exercise of its discretion. It is subject to change or revocation without prior notice.

Exhibit A
Director, Office of Research Integrity and Compliance

The Director will act in an advisory capacity to all who carry compliance responsibilities on a wide range of compliance issues, including:

- Institutional and governmental policies and regulations involving the use of human and animal subjects;
- Institutional and governmental policies and regulations related to Recombinant DNA research and biosafety;
- Protection of personal research information;
- Grant submission, management, and contracting, including financial oversight; licensing, commercializing, and/or exporting developed technology;
- Institutional and governmental policies and regulations involving occupational health and safety and environmental compliance;
- Research integrity, including conflict of interest and scholarly misconduct;
- Financial compliance issues associated with research administration, from the pre-award functions of proposal preparation, negotiation, award, and budget establishment to the post-award functions of expenditure control and management, financial reporting, and audit support; and
- Development, implementation and oversight of the ORIC Compliance Program.

Principal Duties and Responsibilities:

1. Provides leadership and overall guidance to the staff of the Office of Research Integrity and Compliance.
2. Supervises and oversees the various institutional compliance committees including the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), Institutional Biosafety Committee (IBC), Radiation Safety and other committees.
3. Advises physicians and scientists concerning their responsibilities in the area of research integrity and compliance.
4. In conjunction with the Chief Administrative Officer and President and Scientific Director, develops and implements policies and procedures for ensuring integrity and compliance.
5. Develops, coordinates, and participates in educational and training programs that focus on the elements of the ORIC Compliance Program, to ensure that all appropriate staff members are knowledgeable of, and comply with, pertinent federal and state standards.
6. Monitors the performance of administrative duties of the Chairs and staff members of the compliance committees.
7. Serves as the senior CMMC administrative representative to the CMH Radiation Safety Committee, Institutional Animal Care and Use Committee (IACUC) and Institutional Biosafety Committee (IBC).
8. Serves as liaison between Children's Memorial and external regulatory agencies and professional research organizations.

9. Assists other departments, such as Office of Sponsored Projects and Finance in coordinating internal compliance and monitoring activities related to research related budgets and charges.

Exhibit B
Office of Research Integrity and Compliance
Policy on Research Integrity and Procedures for Reviewing Allegations of
Misconduct (Revised June 2005)

A. Statement of Principles

This Policy provides a statement on integrity in Research; describes the responsibilities of Research personnel, administrators, and others in the medical center community; and sets forth the procedures to timely, effectively and fairly respond to Allegations of Research Misconduct.

Maintaining high ethical standards in the conduct of scientific Research is an important responsibility imposed by public trust and is essential to the discovery of new knowledge and the reputation of Research, Researchers and Research institutions. Misconduct or apparent misconduct in scientific Research challenges the integrity of the scientific enterprise at large and threatens to undermine public trust in Research.

It is the policy of The Children's Memorial Medical Center ("CMMC"), The Children's Memorial Hospital ("CMH"), and The Children's Memorial Research Center ("CMRC") to require high ethical standards in Research; to inquire into and, if necessary, to investigate and resolve promptly and fairly all instances of alleged misconduct; to comply in a timely manner with agency requirements for reporting on cases of possible misconduct when sponsored project funds are involved; and to provide full and continuing cooperation with granting agencies during their oversight review under this Policy and applicable Federal regulations. This Policy offers explicit and official policies necessary to assure that Allegations of Research Misconduct are properly addressed and to promote ethical standards in scientific Research and dealing with alleged misconduct.

Because a charge of misconduct, even if unjustified, may damage an individual's career, any such issue must be handled in a prudent and confidential manner. To help protect the confidentiality of Respondents, Complainants and Witnesses, all disclosures identifying these persons should be limited to those who have a need to know the information consistent with a thorough, competent, objective and fair Research Misconduct proceeding. Also, an Inquiry or Investigation must be handled promptly and expeditiously with full attention given to the rights of all individuals involved.

The review process for determining whether Research Misconduct has occurred and for providing corrective actions consists of three phases: **Inquiry**, **Investigation**, and **Adjudication**. The goal of these procedures is to ensure fair treatment for each person alleged to have committed an act of Research Misconduct. Therefore, every Inquiry and subsequent Investigation will be based on a presumption of innocence until proven otherwise. It is not intended that the proceedings be adversarial. Rather, all phases of the procedure should be conducted in the spirit of peer review.

B. Applicability

This Policy applies to all persons affiliated with CMMC, CMH, and CMRC, whether the Research is funded or not, and is applicable to physicians, fellows, residents, students, and all other members of the Research staff. Cases of Research Misconduct involving residents and students are subject to the normal disciplinary rules governing residents and students, but may be reviewed, as appropriate, under this Policy.

This Policy applies to:

the conduct of extramural and intramural biomedical or behavioral Research or activities related to that Research the conduct of biomedical or behavioral Research training programs or activities related to that Research training, contracts and other forms of support, regardless of source, grants, procurement contracts and cooperative agreements, presentation or publication of results, the process of applying for funds, and the expenditure or fiscal reporting on the use of project funds.

The Policy also applies to any Research proposed, performed, reviewed, or reported, or any Research Record generated from that Research, regardless of whether the user or reviewer receives Federal support or whether an application or proposal for Federal funds resulted in a grant, contract, cooperative agreement, or other form of Federal support. Research Misconduct proceedings involving Federally-supported Research shall be conducted in accordance with all applicable Federal policies and regulations. Research Misconduct proceedings not involving Federally-supported Research shall be guided by those same principles.

2. DEFINITIONS

Abuse of Confidentiality means the use of ideas and preliminary data gained from (i) access to information not otherwise available through the opportunity for editorial review of manuscripts submitted to journals, and (ii) the opportunity for peer review of proposals being considered for funding by agency panels or by internal committees such as the Institutional Review Board, the Institutional Animal Care and Use Committee, or the Radiation Safety Committee.

Allegation is a disclosure of possible Research Misconduct through any means of communication. The disclosure may be by written or oral statement or other communication to an institutional or HHS official.

Complainant is the person(s) who in *Good Faith* makes an *Allegation of Research Misconduct*.

Deciding Officer is the President and Scientific Director who serve as the Deciding Officer for the purposes of this policy.

Evidence means any document, tangible item, or testimony offered or obtained during a Research Misconduct proceeding that tends to prove or disprove the existence of an alleged fact.

Fabrication is making up data or results and recording or reporting them.

Falsification is manipulating Research materials, equipment, or processes, or changing or omitting data or results such that the Research is not accurately represented in the Research Record.

Good Faith means having a belief in the truth of one's Allegation or testimony that a reasonable person in the Complainant's or witness's position could have based on the information known to the Complainant or witness at the time. An Allegation or cooperation with a Research Misconduct proceeding is not in Good Faith if made with knowing or reckless disregard for information that would negate the Allegation or testimony.

Inquiry is the preliminary information-gathering and preliminary fact-finding to determine whether an Allegation or apparent instance of Research Misconduct has substance and if an Investigation is warranted.

Investigation is the formal development of a factual Record and the examination of that record leading to a decision not to make a finding of Research Misconduct or to a recommendation for a finding of Research Misconduct or other appropriate remedies, including administrative actions.

Preponderance of the Evidence means the proof by information that, compared with that opposing it, leads to the conclusion that the fact at issue is more probably true than not.

Plagiarism is the appropriation of another person's ideas, processes, results, or words without giving appropriate credit.

Research means a systematic experiment, study, evaluation, demonstration or survey designed to develop or contribute to general knowledge (basic Research) or specific knowledge (applied Research) relating broadly to public health by establishing, discovering, developing, elucidating or confirming information about, or the underlying mechanism relating to, biological causes, functions or effects, disease treatments, or related matters to be studied.

Research Integrity Officer is the Deputy Director for Administration, CMRC or another person with sufficient knowledge and experience to handle the procedural and regulatory requirements person who is appointed by the CMRC President and Scientific Director to serve as the Research Integrity Officer.

Research Misconduct is *Fabrication, Falsification, or Plagiarism* in proposing, performing, or reviewing Research, or in reporting research results. It also includes *Abuse of Confidentiality*. Research Misconduct does not include honest error or honest differences of opinion.

Research Record is the record of data or results that embody the facts resulting from scientific Inquiry, including but not limited to, Research proposals, laboratory records, both physical and electronic, progress reports, abstracts, theses, oral presentations, internal reports, journal articles, and any documents and materials provided to HHS or an institutional official by a Respondent in the course of the Research Misconduct proceeding.

Respondent is the person(s) against whom an *Allegation of Research Misconduct* is directed or who is the subject of a Research Misconduct proceeding.

Retaliation means an adverse action taken against a Complainant, witness, or committee member by an institution or one of its members in response to (a) a Good Faith Allegation of Research Misconduct; or (b) Good Faith cooperation with a Research Misconduct proceeding.

3. **RESPONSIBILITIES**

- A. Research Personnel.** Researchers are responsible for maintaining the highest ethical standards in their Research. Principal investigators are responsible for:
- (1) assuring that these standards are communicated to and maintained by all who work under their supervision, directly or indirectly,
 - (2) assuring the validity of all information communicated by their Research groups, and
 - (3) Assuring adequate citation of contributions from those within and without each Research group. Co-authorship should reflect scientific involvement and responsibility for work reported. Although collaborative relationships between investigators are based on trust, some joint evaluation of data should be an integral part of the review process, even when unique laboratory procedures necessitate long-distance collaboration.
- B. Administrators.** The President of CMMC and the CMRC President and Scientific Director are responsible for ensuring the implementation of this Policy for integrity in Research and for updating of the Policy. They will provide widespread dissemination of the Policy and will assure that appropriate review procedures are promptly implemented when Allegations of Research Misconduct are reported. The CMRC President and Scientific Director will maintain accurate records and, where required,

will ensure that proper and timely reporting to relevant agencies is made for any Investigation of Research Misconduct which CMRC must report. The CMRC President and Scientific Director also represents CMRC and CMH when it is determined that present or former Research personnel are the subject of complaints or Investigations that involve outside institutions. In the event of a determination of Research Misconduct, the President may invoke sanctions according to established CMMC, CMH or CMRC procedures.

- C. **Members of the Medical Center Community.** Members of the medical center community are responsible for reporting what they believe to be Research Misconduct on the part of Research personnel. To the extent consistent with the needs of an Inquiry or Investigation, the identity of confidential sources will be protected. Those who provide information in Good Faith about questionable conduct are to be protected against Retaliation.

4. **PROCEDURES FOR REVIEWING RESEARCH MISCONDUCT**

A. **REPORTING ALLEGATIONS**

- (1) Reports of alleged Research Misconduct on the part of employees or persons within the control of CMRC, CMMC, or CMH are to be made by written or oral statement or other communication directly to the appropriate department head, who will immediately inform the Senior Vice President and Chief Operating Officer, CMRC, of the substance of the Allegations. Complaints that relate to CMRC Research programs, involve more than one department, or by their nature require special consideration (e.g., cases brought by or against a department head) may be addressed directly to the Senior Vice President and Chief Operating Officer, CMRC, who will then notify the CMMC President and the CMRC President and Scientific Director of the Allegation and thereafter of its disposition. Generally, the alleged Research Misconduct must have occurred within six (6) years of the date the Allegation is reported to an institution or HHS.
- (2) The institution must, either before or when the institution notifies the Respondent of the Allegation, Inquiry or Investigation, promptly take all reasonable and practical efforts to obtain custody of all the Research Records and evidence needed to conduct the Research Misconduct proceeding and sequester them in a secure manner. Reasonable accommodations for access to data or copies of sequestered records will be made when necessary and appropriate.

- (3) A preliminary and informational evaluation of the complaint will be made by Senior Vice President and Chief Operating Officer, CMRC, who may consult in confidence with others as appropriate before passing on the matter.
- (4) If the Senior Vice President and Chief Operating Officer, CMRC finds there is no sufficiently credible and specific evidence supporting the Research Misconduct Allegation, and the CMRC President and Scientific Director concurs, the complaint will be dismissed without giving any notice to the Respondent. A written report stating the reasons for the dismissal shall be maintained, but will not be made a part of the records of the Respondent. The Complainant, who shall be notified of the dismissal, may appeal a decision for dismissal directly to the CMRC President and Scientific Director or to the President. If the complaint is not dismissed, then an Inquiry will be made.
- (5) If, after evaluation, the Senior Vice President and Chief Operating Officer, CMRC, believes an Allegation describes an instance of Research Misconduct and is sufficiently credible and specific so that potential evidence of Research Misconduct may be identified, the Senior Vice President and Chief Operating Officer, CMRC, shall refer the case directly to the CMRC President and Scientific Director for Inquiry. In either event, the Respondent shall be notified in writing of the Allegation and shall be given a copy of the procedures for review of Research Misconduct. Individuals with supervisory responsibility for the Respondent will also be notified as appropriate.

B. INQUIRY

- (1) The purpose of an Inquiry is to determine whether an Allegation or apparent instance of Research Misconduct warrants a full Investigation or requires that special action be taken pending resolution of the Allegation or apparent misconduct. The Inquiry will determine whether the Allegation of Research Misconduct appears to be well-founded, the seriousness of the alleged misconduct, the scope of the alleged incident, and the relevance of any other information that is available. Because an Inquiry is an initial review, it does not require a full review of all of the evidence related to the Allegation. An Inquiry should be completed within sixty (60) calendar days after an Allegation is made.
- (2) To the extent possible, Inquiries (and resultant Investigations) will be conducted in a confidential manner so as to protect the affected parties. Although a person participating directly in the conduct of

an Inquiry or Investigation must be qualified to evaluate the situation, no such person may have unresolved, personal, professional, or financial conflicts of interest with the Complainant, Respondent or witnesses.

- (3) If an Inquiry is made, the CMRC President and Scientific Director will appoint an ad hoc committee of at least three (3) full-time staff members, and the same procedures for Inquiry will be followed. Additionally, the Senior Vice President and Chief Operating Officer, CMRC, shall serve as a non-voting staff member of the Inquiry committee.
- (4) The CMRC President and Scientific Director shall abide by any applicable protocols for appropriate custody and maintenance of all the Research Records and evidence needed to conduct the Research Misconduct proceeding.
- (5) The Inquiry Committee will review the merits of the Allegations and recommend a course of action to the CMRC President and Scientific Director, as appropriate, including whether a full Investigation should be conducted. The committee may have access to documents relating to the alleged misconduct and may interview the Complainant, Respondent and any relevant witnesses. It shall not, however, attempt to reach a decision on the merits of the complaint. The committee shall prepare a written Inquiry report that states what evidence was reviewed, summarizes relevant interviews, and includes the conclusions of the Inquiry.
- (6) After receiving the written report of the Inquiry committee, the committee will forward a copy of its report, along with its recommendations, to the CMRC President and Scientific Director, the department head, and to the Respondent. The Respondent may make written comments to the CMRC President and Scientific Director. The CMRC President and Scientific Director will determine whether to dismiss the case or to proceed with an Investigation. The Respondent and the division chair, if applicable, and department chair will be notified in writing of the decision of the CMRC President and Scientific Director.
- (7) If the Complainant disagrees with a decision of the CMRC President and Scientific Director to dismiss the case, the Complainant may appeal to the President. A notice of appeal should also be provided to the Respondent. The President then will review the case and make a final determination as to appropriate action.

- (8) If a decision not to investigate is rendered, all the information assembled in the course of the Inquiry will be maintained in confidence for at least seven (7) years to permit a later assessment of the reason for determining that an Investigation was not warranted. See also Section D.2 of this Policy for certain notification requirements that may be applicable.
- (9) If the Inquiry concludes that there appears to be grounds for a charge of Research Misconduct, the CMRC President and Scientific Director will initiate a formal Investigation into the matter in accordance with Policy Section C. The President and the Respondent must be notified of the decision to commence a formal Investigation. If the matter involves federally supported Research or an application for federal support, the Office for Research Integrity will also be notified in the time and manner required by federal regulations.

C. INVESTIGATION

- (1) The purpose of an Investigation is to examine thoroughly in an unbiased, impartial manner, an Allegation of Research Misconduct and to determine whether such misconduct has taken place. A finding of Research Misconduct requires that there be a significant departure from accepted practices of the relevant Research community, that the misconduct be committed intentionally, knowingly, or recklessly and that evidentiary standards are satisfied.

Evidentiary Standards:

Burden of Proof: The institution has the burden of proof for making a finding of Research Misconduct. The Respondent has the burden of proof as to any affirmative defenses and mitigating factors. However, destruction of Research Records or Respondent's failure to furnish Research Records adequately documenting the questioned Research, establishes a rebuttable presumption of Research Misconduct that may be relied upon by the institution.

Standard of Proof: A determination that Research Misconduct has occurred must be established by a Preponderance of the Evidence.

- (2) If the CMRC President and Scientific Director determines to proceed with an Investigation, he will appoint a committee of full-time staff members without any unresolved, personal, professional, or financial conflicts of interest with the Complainant, Respondent

or witnesses to investigate the complaint and will notify the Respondent within a reasonable time but before the Investigation begins. If not already performed, the institution must take custody of the records before or concurrently with the notification of the Respondent. The Complainant is not a party to the misconduct proceeding, but rather acts as a witness after the Allegation is made. When appropriate, the CMRC President and Scientific Director may appoint experts who are not full-time clinical staff members of the CMMC to serve on the committee. Granting agencies supporting the Research work under Investigation will be notified by the CMRC President and Scientific Director that an Investigation is taking place, as may be required by the agency. Specific agency requirements, such as the time within which certain steps are to be taken will be observed and will be communicated by the CMRC President and Scientific Director to the investigating committee and to the Respondent. For example, PHS guidelines require that an Investigation start within thirty (30) days of completion of an Inquiry and that the Investigation concludes within one hundred twenty (120) days, unless permission for extension is granted by the relevant funding agency.

- (3) The Investigation will include, but not be limited to, review of grant or contract files, reports, scholarly publications, manuscripts, and other documents; inspection of laboratory or clinical facilities and/or materials; interviewing of parties with an involvement in or knowledge about the case; and submission of a formal report of committee findings, including response of the Respondent.
- (4) The Respondent will be kept informed by the investigatory committee chairperson of the general progress of the Investigation, and will be given the opportunity to respond to the Complainant orally and in writing and to provide information for consideration by the committee.
- (5) The investigatory committee will focus on matters limited to the charge given to it by the CMRC President and Scientific Director, but may review previous Research efforts of the affected personnel, or records of previous complaints of Research Misconduct, if germane to the Investigation.
- (6) Neither CMMC (including CMH and CMRC) nor the Respondent may have legal counsel present at the meetings, except at the express invitation of the committee. Should legal counsel be invited, the invitation will be extended to both parties. When invited, legal counsel may observe but shall not participate in the proceedings. With the prior approval of the investigatory

committee, the Respondent may be accompanied by a non-attorney colleague.

- (7) The investigatory committee will prepare a draft final report and provide a copy of such report to the Respondent, who may review and comment, offer corrections, accept its conclusions, or deny the Allegations within thirty (30) days of receipt. The investigatory committee will then compile the final report and will transmit it to the CMRC President and Scientific Director along with any minority reports and responses by the Respondent. The committee's report will respond to the charge given by the CMRC President and Scientific Director, will assess the validity of the Allegations of misconduct and will recommend sanctions or other action.
- (8) The report of the committee and its attachments along with the recommendations of the CMRC President and Scientific Director will be forwarded by the CMRC President and Scientific Director to the President for review and disposition. If the President finds that the Respondent has not engaged in Research Misconduct, the President will dismiss the complaint. If the President finds that the Respondent has engaged in Research Misconduct, the President may order appropriate sanctions and may initiate medical center procedures leading to possible additional sanctions. The President will inform the Respondent, the CMRC President and Scientific Director, the department head, and the division chair of their decision.

D. ADJUDICATION

- (1) At the conclusion of the Investigation, or at any other time required by an involved granting agency, the CMRC President and Scientific Director will notify the granting agency of the facts of the case, the conclusions rendered, and the disposition of the matter by the CMMC. The CMRC President and Scientific Director will notify other outside parties as may be appropriate, including publishers or institutions with whom the party found to have committed Research Misconduct is now or has been professionally affiliated. The President will consider release of information about the incidence to the public.
- (2) For PHS-supported, CMRC President and Scientific Director must carry Inquiries and Investigations through to completion and pursue diligently all significant issues. CMRC President and Scientific Director must notify ORI in advance if the institution plans to close a case at the Inquiry, Investigation, or appeal stage on the basis that the Respondent has admitted guilt, a settlement

with the Respondent has been reached, or for any other reason. CMRC President and Scientific Director need not report to ORI the closing of a case at the Inquiry stage on the basis that an Investigation is not warranted. CMRC President and Scientific Director must report a finding of no misconduct at the Investigation stage, but this need not occur in advance of the decision.

- (3) If the alleged misconduct is not substantiated by the Investigation, diligent efforts will be made to restore fully the reputation of the Respondent. In addition, all reasonable and practical efforts will be made to protect or restore the position and reputation of any Complainant, witness or committee member and to counter potential or actual Retaliation against them. However, if it is further demonstrated that the charges were brought under malicious or dishonest circumstances, then the President may bring appropriate action against the Complainant or others involved.
- (4) A permanent record of committee reports, exhibits, minutes of meetings, and other materials will be kept by the CMRC President and Scientific Director for 7 years after the completion of any PHS proceeding involving the Research Misconduct Allegations. These records will be protected from release if release would compromise the conduct of an Investigation, constitute unwarranted invasion of privacy, or reveal the content of communications or recommendations of action to be taken. In the case of sponsored projects, the CMRC President and Scientific Director is responsible for determining and complying with reporting requirements; representing the CMMC in all negotiations with the sponsor; and implementing any administrative actions that may be directed by the sponsor.
- (5) Consistent with procedures described above, those responsible for the conduct of inquiries and Investigations shall have at any time the authority to supplement and clarify applicable procedures, provided that adequate notice is given to persons affected by such actions.
- (6) The CMRC President and Scientific Director or the President may take action, and notify the Federal Office of Research Integrity, without prior hearing or review should either of them conclude that any of the following conditions exist:
 - (a) The health or safety of the public is at risk, including an immediate need to protect human or animal subjects;
 - (b) HHS resources or interests are threatened

- (c) Research activities should be suspended
- (d) There is a reasonable indication of possible violation of civil or criminal law;
- (e) Federal action is required to protect the interest of those involved in the Research Misconduct proceeding;
- (f) The CMRC President and Scientific Director or the President believe the Research Misconduct proceeding may be made public prematurely so that HHS may take appropriate steps to safeguard evidence and protect the rights of those involved; or
- (g) The Research community or public should be informed

SOURCE: 70 Federal Register 28369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit C
Protocol for Custody of Records – June 2005
Retention and Custody of the Research Misconduct Proceeding Record

Once CMRC undertakes any actions related to alleged Research Misconduct including Allegation assessment, Inquiries, Investigations, or ORI oversight reviews, the CMRC must promptly take all reasonable and practical steps to obtain custody of all the research records and evidence needed to conduct the Research Misconduct proceeding, inventory the records and evidence, and sequester them in a secure manner.

Records of the Research Misconduct proceeding that must be taken into custody include:

- The records that CMRC secures for the proceeding, except to the extent CMRC subsequently determines and documents that those records are not relevant to the proceeding or that the records duplicate other records that are being retained;
- The documentation of the determination of irrelevant or duplicate records;
- The Inquiry Report and final documents (not drafts) produced in the course of preparing that report, including the documentation of any decision not to investigate;
- The Investigation Report and all records (other than drafts of the report) in support of that report, including the recordings or transcriptions of each interview (version after interviewee is given opportunity to correct); and
- The complete record of any institutional appeal, if provided.

Maintenance of Records

Unless custody has been transferred to HHS, or ORI has advised CMRC in writing that it no longer needs to retain the records, CMRC will maintain all records of the Research Misconduct proceeding identified above in a secure manner for seven (7) years after completion of the proceeding or the completion of any PHS proceeding involving the research misconduct allegation, whichever is later.

Provision for HHS custody

On request, CMRC must transfer custody of or provide copies to HHS, of any Institutional record relevant to a Research Misconduct Allegation, including the research records and evidence, to perform forensic or other analyses or as otherwise needed to conduct an HHS inquiry or investigation, or for ORI to conduct its review or to present evidence in any proceeding.

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit D
Protocol for Inquiry Report
June 2005
Drafting the Inquiry Report

Within 30 days of finding that an Investigation is warranted, the CMRC must provide ORI with the written finding by the CMRC President and Scientific Director and a copy of the Inquiry Report. The Inquiry Report must be in writing and include:

- The name and position of the Respondent;
- A description of the allegations of research misconduct;
- The PHS support, including, for example, grant numbers, grant applications, contracts, and publications listing PHS support;
- The basis for recommending that the alleged actions warrant an investigation; and
- Any comments on the report by the Respondent or the Complainant.

CMRC must have the following information and documentations ready and available to provide to ORI upon request:

- The institutional policies and procedures under which the inquiry was conducted;
- The research records and evidence reviewed, transcripts or recordings of any interviews, and copies of all relevant documents; and
- The charges for the investigation to consider.

If CMRC makes a finding that an Investigation is not warranted, then CMRC must keep sufficiently detailed documentation of the Inquiry to permit a later assessment by ORI of the reasons why CMRC decided not to conduct an Investigation.

Consistent with the Custody of Records Protocol, the Institution must keep these records in a secure manner for at least seven (7) years after the termination of the inquiry, and upon request, provide them to ORI or other authorized HHS personnel.

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit E
Protocol for Investigation Report
Drafting the Investigation Report

Within 120 days of initiating the Investigation, CMRC must provide ORI with the Final Institutional Investigation Report by the CMRC President and Scientific Director. The Investigation Report must be in writing and include:

- A description of the nature of the allegations of Research Misconduct;
- A description of the PHS support, including, for example, any grant numbers, grant applications, contracts, and publications listing PHS support;
- A description of the specific allegations of Research Misconduct for consideration in the Investigation;
- A copy of the institutional policies and procedures under which the Investigation was conducted, (if not already provided to ORI with the Inquiry Report);
- Identification and summary of the Research Records and evidence reviewed, and identification of any evidence taken into custody but not reviewed;
- For each separate allegation of Research Misconduct identified during the investigation, provision of a finding as to whether Research Misconduct did or did not occur, and if so -
 - Identification of whether the Research Misconduct was falsification, fabrication, or plagiarism, and if it was intentional, knowing, or in reckless disregard;
 - Summary the facts and the analysis which support the conclusion and consider the merits of any reasonable explanation by the Respondent;
 - Identification of the specific PHS support;
 - Identification of whether any publications need correction or retraction;
 - Identification of the person(s) responsible for the Research Misconduct; and
 - Listing of any current support or known applications or proposals for support that the respondent has pending with non-PHS Federal agencies

SOURCE: 70 Federal Register 28,369 (May 17, 2005) (Public Health Service Policies on Research Misconduct Final Rule).

Exhibit F
Conflict of Interest for Compliance Board Members

The following policy on conflict of interest although initially written for the Institutional Review Board, is applicable to all compliance committees: Institutional Review Board, Institutional Animal Care and Use Committee and the Institutional Biosafety Committee.

Children's Memorial Hospital ("CMH") Institutional Review
Board Member
Policy on Disclosing Conflicts of Interest

I. ETHICAL CONTEXT AND PRINCIPLES

CMH and the Children's Memorial Research Center (CMRC) are committed to IRBs composed of impartial members who are not subject to undue influence by pressures to approve research in which the IRB member (or an immediate family member) has a conflict of interest. Conflicts of interest may be either financial or professional/personal in nature. Identifying and disclosing potential conflicts of interest are essential to preserving the integrity and ethical propriety of the informed consent process and to maintaining public trust in and support for Children's Memorial's research endeavors. Children's Memorial's commitment to the integrity and ethical conduct of research may be compromised if the self-interest of an IRB member interferes with, or is perceived to interfere with, professional judgments.

II. POLICY STATEMENT

For these reasons, all CMH IRB members must identify potential conflicts of interest and disclose such interests as set forth in accordance with this policy. Where a conflict of interest exists, the IRB member may not participate in the review of any project that is the basis for the IRB member's conflict of interest, except to provide information to the IRB at the IRB's request.

III. DEFINITIONS

1. **Conflict of Interest** exist when, as determined by the IRB Chair (or Vice Chair where appropriate), an IRB member's (or an **immediate family member's**) financial interest(s) or personal/professional interest(s) or relationship(s) could directly and significantly affect, or give the appearance of affecting, the IRB member's ability to be objective and to exercise independent judgment in protecting the

rights and welfare of human research participants. What types of arrangements and/or relationships constitute a potential conflict of interest is discussed below in Section V.

2. **Immediate family members** are a spouse, dependant children, and other persons living in the same household.
3. **Research** is any systematic investigation involving human subjects which is designed (in whole or in part) to develop or contribute to generalizable knowledge.
4. **Review** means not only the review of a new protocol but also review of continuing review reports and adverse event reports, and the like.

IV. DISCLOSURE TO THE IRB OF A POTENTIAL CONFLICT OF INTEREST

All CMH IRB members must notify the IRB Chair (or Vice-Chair where appropriate) of a potential conflict of interest in advance of the meeting, when possible; and upon contact for assignment as a primary or secondary reviewer, or an expedited reviewer.¹ Prior to the beginning of each meeting, IRB members will be asked to declare any potential conflict of interest related to the protocols under review. The IRB member need not explain in detail the nature of the potential conflict, but must provide sufficient detail for the IRB Chair to determine whether the disclosed potential conflict of interest requires the IRB member to leave the room during voting and to take the other actions set forth below in Section VI. If the IRB member chooses not to describe the potential conflict in such detail, the potential conflict may be deemed an actual conflict of interest and the steps discussed below in Section VI shall be followed.

V. FINANCIAL, PERSONAL AND PROFESSIONAL RELATIONSHIPS THAT MAY CREATE CONFLICTS OF INTEREST

An IRB member may be found to have a conflict of interest (and must disclose that interest) when s/he has a financial interest or other professional or personal relationship as set forth below:

Financial conflict of interest:

1. The IRB member (or an immediate family member or the IRB member and immediate family member in the aggregate) have received payments over the past 12 months, or anticipate receiving payments over the next 12 months, in excess of \$10,000, including salary and payment for services (*e.g.*, consulting fees or honoraria), royalty, or licensing payments from intellectual property and/or gifts

¹ 45 CFR 46.107(e) and 21 CFR 56.107(e)

from the commercial sponsor of the research, or their representative(s).

2. The IRB member (or an immediate family member or the IRB member and immediate family member in the aggregate) have an equity interest (e.g., stock, stock options or other ownership interests)² in the commercial sponsor of the research which is valued at more than \$10,000 or more than 5% of the business entity as determined by reference to publicly listed prices.
3. The IRB member (or an immediate family member) has any equity interest (e.g., stock, stock options or other ownership interests) in the commercial sponsor of the research and the value cannot be determined by reference to publicly listed prices (e.g., start-up companies).
4. The IRB member (or an immediate family member) has a financial relationship or interest, including but not limited to holding intellectual property rights (e.g., patent, copyrights and royalties from such rights), whereby the outcome of the study could influence the value of the financial relationship/interest, e.g., royalties under any royalty-sharing agreements involving CMH, Northwestern University Feinberg School of Medicine.

Professional/Personal conflict of interest:

5. The IRB member (or an immediate family member) serves as a principal investigator or secondary investigator and, thus, is listed on the IRB application, or has served as a scientific/medical advisor to the principal investigator.
6. The IRB member (or an immediate family member) is an advisor, or a direct supervisor, of a trainee's (e.g., medical, graduate or undergraduate student) research.³
7. The IRB member (or an immediate family member) holds a position as director, officer, partner, trustee, or any other significant/decision making position in the company sponsoring the research.
8. The IRB member (or an immediate family member) has a personal relationship, or a conflict, with any investigator(s) listed on the IRB

² Ownership interests arising solely from investment in a company by a mutual, pension or other institutional investment fund over which the IRB member does not have control shall not be considered included as a conflict of interest.

³ A department chair position alone may not be sufficient to create a "direct, supervisor" relationship to create a conflict. However, other facets of a relationship, such as closer oversight than the traditional chair/department member, may create a conflict.

application for review which would potentially cause the IRB member to be perceived as less than objective in his/her review.

An IRB member may be found not to have a conflict of interest when the IRB member (or an immediate family member) is listed on the IRB application for review as a participating physician or other study personnel if the IRB member's (or immediate family member's) only involvement in the protocol is the provision of clinical care to subjects and there is no expectation that the IRB member will be included as an author on any papers arising from the research.

If an IRB member is uncertain if a potential conflict of interest exists, they are encouraged to consult with the IRB Chair/Vice-Chair.

VI. DETERMINATION THAT A CONFLICT OF INTEREST EXISTS

After disclosure to the IRB Chair of a potential conflict of interest described above, the IRB Chair will determine whether an actual conflict of interest exists, and if so, the steps below in Section VII shall be followed. If the IRB Chair is not in attendance, or the IRB Chair is the person disclosing the potential conflict of interest, the IRB Vice-Chair will determine whether an actual conflict of interest exists, and if so, the steps below in Section VI shall be followed.

All CMH IRB members will be asked to disclose potential conflicts of interest, in writing, upon appointment and annually in September by completing the attached Conflict of Interest Questionnaire and submitting it to the IRB Administrative Office for review by the IRB Chair and Senior Vice President and Chief Operating Officer, CMRC. Additionally, the IRB member is obligated to update the questionnaire whenever circumstances change and a new conflict arises.

VII. ACTION BY IRB

When an IRB member is found by the IRB Chair to have a conflict of interest in categories 1 through 5 above, the IRB member may not vote on the protocol and s/he must leave the room during the IRB's discussion and voting phases of the protocol to which the conflict of interest relationship attaches. The absent IRB member is not counted towards determination of quorum during the vote on the protocol in question. If the quorum is lost on a protocol by the IRB member leaving the room, the protocol carried over to the next IRB meeting. The IRB meeting minutes will reflect that these requirements have been met.

When an IRB member is found by the IRB Chair to have a conflict of interest in categories 5 through 8 above which the Chair believes may result in or may be perceived to result in a less than objective review, the IRB member may not vote on the protocol and s/he must leave the room during the IRB's discussion and voting phases of the protocol to which the

conflict of interest relationship attaches. The absent IRB member is not counted towards determination of quorum during the vote on the protocol in question. If the quorum is lost on a protocol by the IRB member leaving the room, the protocol is carried over to the next IRB meeting. The IRB meeting minutes will reflect that these requirements have been met.

When an IRB member is found by the IRB Chair to have a conflict of interest in categories 5 through 8 above which the Chair reasonably believes will neither result nor may be perceived to result in a less than objective review, the IRB member will abstain from voting on the protocol but s/he may be present during and participate in the IRB's discussion and voting phases of the protocol to which the conflict of interest relationship attaches. The IRB member is counted towards determination of quorum during the vote on the protocol in question. The IRB meeting minutes will reflect that these requirements have been met.

VIII. Review and Approval Requirements

The CMH IRB adopted this policy at its regularly scheduled meeting of October 18, 2004. The IRB Chair and the Senior Vice President and Chief Operating Officer, CMRC, shall review the policy annually. Amendments to this policy may be amended, from time to time, by the CMH IRB during any of its regular or special meetings.

Exhibit G
Office of Sponsored Programs
Conflict of Interest Policy for Principal Investigators

INTRODUCTION

These guidelines define the general Children's Memorial Hospital and Children's Memorial Research Center (hereafter jointly referred to as "Hospital") policy and procedures regarding conflicts of interest in relationship to sponsored projects involving research, education and other sponsored activities. Their purpose is to protect the integrity and credibility of the Hospital and its faculty and staff and to ensure compliance with federal regulations.

A potential conflict of interest exists when an individual's personal or private interests might lead an independent observer reasonably to question whether the individual's professional actions or decisions are determined by considerations of significant personal interest, financial or otherwise.

In accordance with federal regulations,(42 CFR Part 50), the Hospital has a responsibility to manage, reduce, or eliminate any actual or potential conflicts of interest that may be presented by a financial interest of an investigator (as defined in this policy). Thus, the Hospital requires that *all investigators* disclose any *significant financial interest* (as defined in this policy) that could reasonably appear to affect or be affected by a sponsored project. The term *sponsored project* is defined as a grant, contract, agreement or subcontract for research or other scholarly activity between the Hospital and any outside entity or agency. This policy applies to all *investigators*.

I. DEFINITIONS

A. Investigator

The term *investigator* as used in this policy means the principal investigator/project director, co principal investigators and any other persons who are responsible for the design, conduct, or reporting of research, educational or service activities funded - or proposed for funding - by an external sponsor. This may include students, postdoctoral fellows, and other staff. For purposes of financial interests, 'investigator' includes the investigator's spouse, domestic partner, brothers or sisters (by blood, adoption or marriage), children, grandchildren and spouses of brothers, sisters, children and grandchildren, and all other persons living in the same household as the investigator.

B. Conflict of Interest

For purposes of federal regulations and this policy, a *conflict of interest* exists when a *significant financial interest* could directly and significantly affect the design, conduct or reporting of a sponsored project.

C. Significant Financial Interest

Significant financial interest means anything of monetary value including, but not limited to, the following:

