Section 1: Overview of the Research Compliance Program

The Children's Hospital of Chicago Medical Center and its affiliates including the Ann & Robert H. Lurie Children's Hospital of Chicago and the Stanley Manne Children's Research Institute (hereafter collectively referred to as the "Institution") are dedicated to upholding the highest ethical standards in the conduct of research. The Research Compliance Program is intended to promote the responsible conduct of research fully compliant with all applicable regulations (federal, state and local), serve as a resource for any person engaged in research activities at the Institution, and align with the Institution's Corporate Compliance Program.

The Research Compliance Program and policies apply to all persons engaged in research who are affiliated with the Institution, including researchers, fellows, residents, students, and other research staff, regardless of the funding source of the research. They apply to all activities related to the design, conduct or reporting of basic, translational, biomedical, and behavioral research, research training programs, the process of applying for funds, compliance with the sponsor's terms of grants, contracts, or other forms of support, and the expenditure or fiscal reporting on the use of such funds.

1.1 Key Components of the Research Compliance Program

The following are the key components to the Research Compliance Program:

*Standards and Procedures: I*mplement written policies and procedures and standards of conduct that further the Institution's mission and commitment to compliance and address areas of risk.

Oversight: The Chief Operating Officer (COO) of the Stanley Manne Children's Research Institute serves as the Research Integrity Officer who, with the support of the Director of ORIC, directs the Research Compliance Program. They engage others with key functions within the Institution that advise and support the Research Compliance Program (i.e., Office of Integrity and Compliance, Legal Counsel, Privacy Office, Sponsored Programs, etc.).

Training & Education: Provide regular, relevant and effective training and education for researchers, staff, and trainees.

Reporting: Develop avenues of communication that encourage employees to report concerns, complaints, and incidents that protect anonymity and prevent retaliation. All reports are taken seriously, examined, and addressed.

Enforcement & Discipline: Enforce compliance with the Institution's Code of Conduct and other relevant policies and regulations through corrective and disciplinary actions.

Auditing & Monitoring: Conduct internal auditing and monitoring as a means of ongoing evaluation and assessment to encourage compliance and ensure effective education and corrective actions as indicated.

Investigation & Remediation: Respond promptly to reported or detected offenses and develop and undertake corrective actions.

1.2 Key Definitions and Roles

Allegation: An assertion of possible research misconduct or noncompliance that has yet to be proved or supported by evidence.

Chief Research Officer (CRO): The CRO is the most senior executive at the Stanley Manne Children's Research Institute and is responsible for the research that supports the Institution's mission and vision. The CRO reports to the Chief Executive Officer of the Children's Hospital of Chicago Medical Center.

Complainant: A person who makes an allegation of scientific misconduct or serious/continuing noncompliance.

Compliance: Knowing the rules and regulations and following them.

Continuing Noncompliance: A pattern of non-compliance that persists after the researcher has knowledge of the problem or a failure to respond to a request from a regulatory authority to resolve an issue. Continuing noncompliance suggests lack of understanding or disregard of Institutional policies or applicable regulations that protect the rights and welfare of participants, the Institution, and others.

Ethics: Understanding the difference between right and wrong. Choosing to do the right thing.

Fabrication: Making up data or results and recording or reporting them.

Falsification: Manipulating research materials, equipment, or processes, or changing or omitting data or results.

Institutional Official (IO): The IO is the individual who is legally authorized to act for the

institution and, on behalf of the Institution. The IO is responsible for ensuring that the Human Research Protection Program (HRPP) functions effectively and that the institution provides the resources and support necessary to comply with all requirements applicable to research involving human subjects. The IO represents the institution named in the Federalwide Assurance (FWA) and obligates the Institution to the Terms of the Assurance.

Integrity: Consistently doing the right thing, even when no one is looking.

Noncompliance: Any violation or failure to comply with any federal regulations, state laws, or Institutional policies, including but not limited to, failure to follow the investigational plan (protocol) and/or the determinations or requirements of the Institutional Review Board (IRB), Institutional Animal Care and Use Committee (IACUC), or Institutional Biosafety Committee (IBC).

Office of Research Integrity & Compliance (ORIC): ORIC manages matters related to research integrity, provides guidance and oversight to the research compliance committees including the Institutional Review Board (IRB) and Institutional Biosafety Committee (IBC), and has authority to review all documents and other information that are relevant to research compliance activities.

Plagiarism: Misuse of another's ideas, processes, results, or words without giving appropriate credit.

Research Integrity Officer (RIO): The CRO has delegated the ultimate responsibility for the Research Compliance Program to the COO of the Stanley Manne Children's Research Institute who serves as the RIO. The COO serves as the RIO as well as the Institutional Official (IO).

Research Misconduct: Any fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results.

Respondent: Person against whom an allegation of noncompliance or misconduct is made.

Serious Noncompliance: Any action or omission in the conduct of research that adversely affects the rights and welfare of research subjects, significantly increases risks to participants, decreases potential benefits, or com: promises the integrity or validity of the research data.

Section 2: Standards & Procedures: Research Policies and Relevant Regulatory Authorities and Regulations

2.1: Institutional Research Policies

Handling Allegations of Research Misconduct Policy: This policy outlines the process for the handling allegations of research misconduct (i.e., suspected fabrication, falsification, or plagiarism in proposing, performing, or reviewing research, or in reporting research results) involving an employee, an agent of, collaborator, and person affiliated by contract or agreement with the Stanley Manne Children's Research Institute.

Financial Conflicts of Interest in Research and Sponsored Programs Policy: This policy confirms the Institution's commitment to manage, reduce, or eliminate any actual or potential conflict of interest that may be presented by a financial interest of any person responsible for the design, conduct, or reporting of research.

Research Confidential Information: Ownership, Stewardship, Retention, and Access Policy: This policy outlines the procedures related to the appropriate access, use, and sharing of data used in research.

Safe Handling, Administration, and Disposal of Study Biological Agents: This policy outlines baseline safety practices and containment procedures for clinical research involving recombinant or synthetic nucleic acid molecules. To ensure study biological agents used in research (i.e., gene therapy and/or live vaccine trials) are handled and administered appropriately to prevent occupational hazards and environmental contamination.

IRB Policy & Procedure Manual: All policies related to research involving human participants and/or their identifiable data are outlined in the Policy & Procedure Manual of the Institutional Review Board (IRB).

Other Manne Research Institute Policies: Can be located in the Policy Directory in the Researcher Toolkit.

Other Organizational Policies: This policy outlines the procedures related to the appropriate access, use and sharing of data used in research.

2.2 Regulatory Authorities and Regulations

DISCLAIMER: This policy was developed solely for the use of Stanley Manne Children's Research Institute. The information contained herein shall not be relied upon by individuals or entities outside the Research Institute for accuracy, timeliness, or any other purpose.

Note: This list identifies the regulatory authorities commonly applicable to research conducted at the Institution; it is not intended to be an exhaustive list.

Department of Health and Human Services (DHHS): Regulations related to the protection of research participants based on the basic ethical principles outlined in the Belmont Report: Beneficence, Justice, and Respect for Persons. 45 CFR 46 and subparts A (Common Rule), B (additional protections for pregnant women, human fetuses, and neonates), C (additional protection for prisoners), and D (additional protection for children).

Office of Human Research Protection (OHRP): OHRP provides leadership and a variety of policy and regulatory guidance materials to assist the research community in conducting ethical research that is compliant with the DHHS regulations.

Food and Drug Administration (FDA): Regulations related to research involving the use of investigational drugs and devices.

Good Clinical Practice (GCP): The international standards for the design, conduct, performance, monitoring, auditing, recording, analyses, and reporting of clinical trials that provide assurance that the data and reported results are credible and accurate, and that the rights, integrity, and confidentiality of trial subjects are protected.

Office of Research Integrity (ORI): Oversees and directs Public Health Service (PHS) research integrity activities on behalf of the Secretary of Health and Human Services with the exception of the regulatory research integrity activities of the Food and Drug Administration.

Office of Science Policy (OSP): OSP's various offices and programs work on a wide range of issues including biosafety, biosecurity, genetic testing, genomic data sharing, human subjects protections, the organization and management of the NIH, and the outputs and value of NIH-funded research.

National Institutes of Health (NIH): The primary agency of the United States government responsible for biomedical and public health research.

NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules:

Outline regulations relating to research involving recombinant or synthetic nucleic acid molecules.

United States Department of Agriculture (USDA): Enforces the Animal Welfare Act which requires basic standards of care and treatment for certain animals bred or used in biomedical research to ensure adequate housing, handling, sanitation, nutrition, water, veterinary care, etc.

Section 3: Training and Education

Researchers and research staff receive communication and training on the Research Compliance Program, relevant policies, and updates to relevant regulations and policies through the Institution's website, global e-mails and training activities (i.e., Behavioral and Clinical Research Professionals Orientation Program, Research Education at Lurie (REAL) trainings, post-approval monitoring, etc.). Each person is held accountable for compliance with all applicable research regulations.

Section 4: Reporting Compliance Concerns

An environment of open and candid communications is fostered at the Institution. All employees have a duty to report conduct to the Institution that is unlawful or unethical. Employees are obligated to report suspected scientific misconduct, serious/continuing noncompliance or violation of regulations or research ethics. When reporting a concern about a legal or ethical issue, staff may choose to first report the concern to their supervisor, the Director, ORIC, the Corporate Compliance Office, or senior management. The Institution will protect, to the fullest extent permitted by law, the identity of staff who desires to remain anonymous. Staff who report concerns or suspected problems in good faith can do so without fear of retaliation.

To encourage staff to report knowledge or suspicion of illegal or unethical acts, they may also phone the Corporate Compliance Office or leave a message. The voicemail is checked daily by the Corporate Compliance Office. In addition, an anonymous hotline is available: **1.800.273.8452**. An outside service will ask for detailed information about reported concerns. The report will be reviewed with the caller for accuracy 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 hotline is available twenty-four (24) hours a day, seven (7) days a week. Any allegations of research misconduct or serious/continuing noncompliance in research will be taken seriously, examined, and addressed promptly to minimize potential harm. Review will be conducted in a manner to ensure confidentiality, fairness, and prompt action to protect all involved and the integrity of the research.

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4.1 Research Misconduct

Refer to the Handling Allegations of Research Misconduct Policy. This policy defines research misconduct, clarifies whom to contact with concerns, and outlines the process for evaluation (assessment, inquiry and/or inspection) and mitigation.

4.2 Investigations of Non-Compliance

Reports of non-compliance are investigated in a similar manner with the following steps: 1) initial assessment by the Research Quality Assurance Team; 2) thorough investigation and gathering of information; 3) review of findings with the Director, ORIC; 4) development of a corrective and preventive action plan; 5) determination if non-compliance meets the definition of serious and/or continuing; 6) reporting to the IRB if applicable; and 7) reporting to external agencies as indicated (i.e., OHRP, FDA, ORI, etc.).

The Research Quality Assurance Team will have the necessary expertise to carry out a formal investigation and authoritative evaluation of the relevant evidence. The appointed staff will not have any personal, professional, or financial conflicts of interest. All investigations are handled in a confidential, sensitive, and timely manner.

The facts gathered from the investigation are the examined in consultation with the RIO, Director, ORIC, and the IRB Chair and/or IBC Chair (or designee) as appropriate. Additional questions or follow-up requests for information may be made during the review of findings.

The records of the investigation maintained will include: documentation of the alleged noncompliance, a description of the investigation, key documents, and the proposed corrective and preventive action plan. Retention of records related to the investigation will be in accordance with applicable regulations.

A draft report of the investigation will be prepared by the Research Quality Assurance Team and presented to the Director, ORIC. The Director, ORIC, in consultation with the RIO, IRB Chair and/or IBC Chair (or designee) will assess the results of the investigation to determine whether serious or continuing noncompliance has occurred.

4.3. Corrective and Prevention Action(s)

Upon review, if the investigation reveals serious or continuing non-compliance, the Research Quality Assurance Team conducting the investigation may propose a corrective and preventive action plan. These will be reviewed by the RIO, Director, ORIC and IRB Chair and/or IBC Chair (or designee) and adjusted as necessary. Corrective and preventive action plans may include, but are not limited to, one or more of the following:

- Require modifications to the protocols and/or consent documents, including notification to the enrolled subjects and the requirement to re-consent subjects;
- Require implementation of specified corrective action measures as determined by the RIO, Director, ORIC, and/or IRB/IBC Chair.
- Require attendance by the PI and/or other research staff in tailored education sessions provided by ORIC or continuing education provided by vetted external entities (e.g., CITI modules, FDA provided training, etc.);
- Require audits of other active research studies conducted by the PI and/or department/division;
- Increase routine monitoring by Research Quality Assurance Team;
- Modification/shortening of the approval period;
- Require oversight or mentoring by a senior researcher;
- Monitor the informed consent process;
- Determination that data collected may not be used for further study and/or publication;
- Temporary halt of enrollment in the study pending implementation of corrective action;
- Temporary suspension of all research activity pending implementation of corrective action;
- Termination of IRB/IBC approval;
- Limitation or revocation of the PI's privilege to conduct human subjects research at the Institution;
- and/or any other action deemed appropriate by the IRB/IBC.

In addition, ORIC policies and procedures may be modified to guard against further violations. Should the investigation reveal that there is systemic non-compliance, the Director, ORIC may consult with the RIO, legal counsel, the Corporate Compliance Office, and others as deemed appropriate, during the drafting of the corrective and preventive action plan.

4.4 Rights of Researchers, Staff and Trainees

Due process is critical to the investigation and the response to allegations of noncompliance and ensures that the results of an investigation is reliable, respected, and valid. Notice of noncompliance allegations will be provided to the individual or entity that is subject of the allegation including access to evidence gathered in support of a complaint. In addition, an opportunity to be heard, the chance to respond to a complaint (include dispute of claim(s)), and to offer a justification/explanation will be afforded to appropriate individual(s). During the initial review, however, or if there is an emergent protocol suspension, these standards may not apply. Individuals that are the subject of allegations will be allowed to review and provide input in the corrective and preventive action plans. The reviewing authorities of allegations of noncompliance will incorporate principles of transparency and fairness during investigations and into the procedures for reporting.

4.6 Confidentiality

Identification of individuals reporting noncompliance concerns, and other information that is collected or created in relation to an investigation, will be kept confidential. The final report will also be kept confidential. These documents and final report will only be shared with appropriate individuals within the institution, on a "need-to-know" basis. In addition, these will not be release externally, except as required by application regulations or contracts.

4.7 Notification and Response to Determinations of Noncompliance

Affected individuals will be notified in writing of the findings of investigations of noncompliance and the required corrective and preventive action plans.

4.8 External Reporting Requirements

Events of serious and/or continuing noncompliance will be reported to the convened IRB. The report will include the draft corrective and preventive action plan (together with sufficient background to facilitate an informed discussion and decision). The convened IRB will review and discuss the findings and vote to approve or require additional corrective or preventive actions.

Events considered serious or continuing non-compliance will be reported to external entities, when applicable, within 30 days of recognition of the reportable event. External entities include:

- Office for Human Research Protections (OHRP) - if the study is subject to U.S. Department of Health and Human Services (HHS) regulations;
- Other federal agencies - when the research is subject to those agencies and the agency requires reporting separate from that to OHRP (e.g., Department of Defense components, etc.);
- Federal and Drug Administration (FDA) - when the research is FDA-regulated;
- Sponsors of the research - as appropriate; and/or
- Funding source of the research - as appropriate.

The RIO is responsible for submitting a report on behalf of the Institution in accordance with applicable federal, state, and local laws. In preparing the report, the Director, ORIC and RIO may consult legal counsel as appropriate. The final report and related documents, regardless of the ultimate determination, are maintained in the ORIC office.

Section 5: Enforcement and Discipline

Disciplinary actions may be warranted when:

- An employee fails to report knowledge of research misconduct or serious/continuing noncompliance to their supervisor, the Director, ORIC, the Corporate Compliance Office,

and/or to senior management;
- A supervisor fails to communicate reports of suspected violations received to the Director, ORIC, the Corporate Compliance Office, and/or to senior management;
- An employee knowingly reports false information to the Institution or a government agency; and/or
- There is a determination of serious/continuing noncompliance.

The determination of the appropriate discipline is made in accordance with the Human Resources Disciplinary Action Policy. The following factors, among others, may be taken into account by the Institution in determining the appropriate disciplinary action to be imposed for a violation of the Research Compliance Program or related policies:

- Nature of the violation and the ramifications of the violation for the Institution;
- Disciplinary action imposed for similar violations;
- History of past violations;
- Whether the violation was willful or unintentional;
- Whether the individual was directly or indirectly involved in the violation;
- Whether the violation represented an isolated occurrence or a pattern of conduct;
- If the violation consisted of the failure to supervise another individual who violated the Research Compliance Program or related policies, the extent to which the circumstances reflect lack of diligence;
- If the violation consisted of retaliation against another individual for reporting a violation or cooperating with an investigation, the nature of such retaliation;
- Whether the individual in question reported the violation; and
- Degree to which the individual cooperated with the investigation.

Section 6: Auditing and Monitoring

6.1 Internal Monitoring Activities

The ORIC remains committed to transparency and creating inclusive programs related to research integrity. ORIC communicates with Institutional leadership the vision of the Research Compliance Program and how its activities support the research enterprise.

Quality assessment (QA) and quality improvement (QI) activities are an integral part in the Research Compliance Program, and for the HRPP, in protecting the rights and welfare of human subjects. To assist with both QA/QI activities, ORIC is responsible for developing education and outreach initiatives for individuals and groups engaged in research.

Performance measurement and assessment of the research enterprise is ongoing and may include the following activities:

- Post-Approval Monitoring (PAM) of research activities;
- Not-for-Cause inspections and for-cause audits;
- Receipt, investigation, and response to complaints;
- Risk assessment;
- Maintaining accreditation of the HRPP; and
- Ongoing review of regulatory and ethical developments related to research conduct, funding, and/or applicable industry standards; including the review related to the applicability to Institutional policies.

In addition, ongoing improvement activities will be provided to the research community which may include:

- Education through global, targeted, or one-on-one sessions related to compliance issues;
- Collection of data and analysis to determine the cause and remediation of compliance issues and/or knowledge gaps;
- Development and implementation of corrective action plans in response to internal and external investigations and inspections;
- Assistance with study-specific or research self-assessments, consultations, study-management tools, and regulatory documentation.

6.2 External Audits or Investigations

Government agencies (i.e., OHRP, FDA, etc.) may conduct audits of the IRB, a specific researcher, and/or a specific study. These audits are considered "for cause," when there is reasonable belief on the part of the agency that there is evidence of non-compliance. Most often, they are considered "routine" in nature and may be scheduled at regular intervals or in support of a new drug application.

Any researcher or research staff member contacted by a regulatory agency regarding an audit or inspection is to notify the Director, ORIC or Research Quality Assurance Team immediately. The ORIC Research Quality Assurance Team will provide guidance and support in preparing for the audit/inspection. They will also alert key institutional officials including the RIO and the Chief Integrity and Compliance Officer.

It is the expectation of the Institution that researchers, research staff, ORIC, the IRB, and/or the IBC will cooperate with audits conducted by external agencies in compliance with federal regulations, funding agency and sponsor requirements.

Findings derived from external audits, either written or verbal, of research records are to be submitted to ORIC. The Director, ORIC, in consultation with the additional Institutional entities (e.g., RIO, IRB Chair, Legal Counsel, etc.) will assist investigators in response to regulatory agencies' report(s).

The Institution may temporarily suspend research pending the outcome of any inquiry or investigation or may require modification to the research as a condition for the research. In addition to other preventative measures, an effective response to any identified research non-compliance will include appropriate monitoring of ongoing activities to assure that corrective and preventative measures are effective in eliminating recurrences of the non-compliance**.**

Date Written: 07/30/20

Date Reviewed/Revised: 12/07/20

Date of Approvals:
Stanley Manne Children's Research Institute: 7/30/20; 12/16/20