PURPOSE:

The purpose of this policy is to promote the highest ethical standards in situations where conflicts of interest (COI) may occur in the design, conduct or reporting of Research. This Policy sets forth the process for identifying and disclosing potential COI and the methods by which COI in Research Committee (COIRC) manages such COI.

Children's Hospital Los Angeles ("CHLA") encourages its Investigators to participate in meaningful professional relationships with industry and other partners outside of CHLA. These partnerships are established for mutually beneficial reasons and many times produce knowledge and technology that will help to meet societal needs.

In certain circumstances, relationships with outside entities or involving outside interests can create or appear to create COI. Having a COI does not, in itself, equate to wrongdoing or inappropriate activity; however, COI require review and management to ensure that they do not appear to improperly influence how CHLA Research is designed, conducted, or reported. All potential COI covered by this Policy must be disclosed promptly and completely so that they may be properly managed.

This policy represents one aspect of CHLA's commitment to address and manage COI. Other CHLA policies that address COI include:

i) CHLA's COMP – 022.0 Conflict of Interest in Research policy addresses COI that arise when the financial interests of CHLA have the potential to cause bias in the conduct of Research.

ii) CHLA's COMP – 020.0 Conflicts of Interest policy addresses individual COI with respect to employment and business practices, conflicts of commitment, and personal COI.

iii) CHLA's COMP – 028.0 Physician Conflict of Interest policy addresses physician COI with respect to professional relationships with outside interests.

iv) For CHLA Team Members engaged in international collaborations, please review the following and contact the OCP for disclosure guidance:

   a. COMP - 039.0 Export Control Policy

   b. USC Office of Culture, Ethics and Compliance guidance on International Collaborations and Disclosure Requirements

SCOPE:

This policy applies to all CHLA faculty members (including part-time and visiting faculty), staff and other employees, and students (including postdoctoral and clinical fellows) or any other persons who propose, conduct or report research on behalf of CHLA, regardless of funding source. This policy applies to all sponsored projects, including government and non-government funded projects (such as industry or foundation sponsors), CHLA funded projects, clinical trials and unfunded research projects. Disclosure and evaluation criteria for Conflict of Interest and Commitment in Research do not vary by funding or regulatory oversight. Reporting of Financial Conflicts of Interest to government agencies may differ depending on funding source.

DEFINITIONS:

A. COI in Research Committee. ("COIRC") consists of members appointed by the Director of The Saban Research Institute or the Director's designee, and may be chosen from CHLA faculty members, administrative and research operational staff, and other CHLA employees displaying familiarity with issues relevant to research including scientific methods, medical treatments, financial management, intellectual property, and/or public affairs. The COIRC is charged with reviewing COI disclosures and formulating recommendations to manage, reduce, or eliminate COI. The Director of The Saban Research Institute or the Director's designee shall also select the Committee Chair(s).

B. Research. "Research" is a systematic investigation designed to develop or contribute to generalizable knowledge, including biomedical, behavioral and social-sciences research or other scholarly activity.

C. Investigator. "Investigator" is any person, regardless of title or position who is responsible for the design, conduct, or reporting of CHLA Research, and which may include for example, collaborators or consultants. Includes investigators who plan to participate in or who participate in CHLA Research.

D. Close Relation. "Close Relation" means the spouse, domestic partner, or dependent child of an Investigator.

E. CHLA Responsibilities. "CHLA Responsibilities" means an Investigator's professional responsibilities on behalf of CHLA, including but not limited to activities such as research, teaching, professional practice, patient care and administration including service on CHLA committees including the Institutional Review Board or Data and Safety Monitoring Boards.

F. Compliance. "Compliance" means CHLA's Office of Compliance and Privacy.

G. Significant Financial Interest. ("SFI") is a financial interest consisting of one or more interests of the Investigator (and those of the Investigator's and Close Relation) that reasonably appear to be related to the Investigator CHLA Responsibilities. All SFIs must be disclosed in accordance with this policy.

(i) With regard to a publicly traded company or other entity, an SFI exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure; and the value of any equity interest in the entity as of the date of disclosure, when aggregated, exceeds $5,000. Such remuneration includes salary and any payment for services including consulting fees, honoraria, paid authorship; equity interest (includes stock, stock options, or other ownership interest, as determined through reference to public prices or other reasonable measures of fair market value).

(ii) With regard to a non-publicly traded company or other entity, an SFI exists if the value of any remuneration received from the entity in the twelve months preceding the disclosure, when aggregated, exceeds $5,000, or when the Investigator (or Investigator's Close Relation) holds any equity interest (e.g., stock, stock options, or other ownership interest) in the entity; or

(iii) Personal receipt of intellectual property rights (e.g., patents, copyrights, or royalties) directly from a research sponsor or a company having an economic interest in the research (e.g., licensee).

(iv) Sponsored travel or reimbursement of expenses associated with travel and provision of services that totals $5,000 or more when aggregated per sponsor over a 12-month period is also considered an SFI to the extent the sponsorship/reimbursement is not reasonable. Unreasonable sponsored/reimbursed travel may include, for example, travel paid for or reimbursed for the Investigator's family.

(v) Payments and travel reimbursement from seminars, lectures, teaching arrangements, or service on advisory committees or review panels are excluded1 if they are from (i) a United States federal, state, or local government agency; (ii) a United States university or research institute affiliated with a university; or (iii) a United States academic medical center or teaching hospital.

H. Conflict of Interest. ("COI") occurs when financial or other personal considerations may compromise, or have the appearance of compromising, an individual's professional judgment in proposing,

[1] This exclusion does not apply to financial interests received from a foreign university or institution of higher education, academic medical center or teaching hospital, or the government of another country (which includes local, provincial, or equivalent governments of another country).

conducting, supervising, or reporting research. COI include non-financial as well as Financial Conflicts of Interest (as defined below). Non-financial interests can also come into conflict with an Investigator's primary commitment to maintain scientific objectivity. Investigators must disclose all potential COI as described herein. Whether a relationship or situation constitutes a COI requiring a management plan is determined by the COIRC and any other applicable COI Committees per COMP 020.0.

COI includes the following types of interests maintained by an Investigator or his or her Close Relations. The following must be disclosed in accordance with this policy:

(i) Management Roles. Any position that has significant decision-making authority (e.g., a director, officer, or other) for a of CHLA Research sponsor or a company that holds an economic interest in the outcome of CHLA Research (e.g., licensee).

(ii) Prohibited Conflict. COI that is not acceptable because there is not a feasible way to manage the conflict. These conflicts call into question the integrity of the research and create significant reputational risk for both the Investigator and CHLA. Prohibited Conflicts include, but are not limited to:

i) Participating in a paid "speakers bureau" (i.e., contractual relationships to give talks in which the topic(s) and/or content are provided by the company) for any company that has sponsored the Investigator's research, or that of their Close Relations.

ii) Any personal incentive payments, bonus payments, finder fees, or any type of payment or incentive based on outcome that are made directly to the Investigator relating to the proposal, conduct, supervision, or reporting of research (e.g., additional personal payments by research sponsors to Investigators who enroll a certain number of participants in a project within a certain period of time), or with respect to the evaluation of a product or service intended for a commercial market (e.g., a clinical trial for a pharmaceutical company), regardless of the amount of compensation or payments received.

iii) Any sponsored agreement in which publication rights are restricted, except for reasonable delays in order to protect proprietary rights (i.e. patent rights), in combination with the Investigator's or Close Relation's COI.

iv) Accepting personal gifts, gratuities or special favors from an actual or prospective sponsor of an Investigator's research, other than occasional gifts of nominal or modest value (less than $25

in value or isolated invitations to meals).2

(iii) Significant Conflict. "Significant Conflict" is any COI with the potential for actual or perceived bias great enough that the Investigator must present compelling circumstances as to why the research should proceed despite the presence of the conflict. A Significant Conflict includes situations when an Investigator and/or his or her Close Relation maintains any of the following interests:

i) Equity in a privately held entity (e.g., stocks, stock options, or other ownership interests) that is a research sponsor, unless the Investigator provides verification that the equity interest is less than 10% of the outstanding stock of the research sponsor.

ii) Equity in a publicly traded entity in excess of $50,000, where that entity is a research sponsor (except when the interest is maintained in an investment vehicle, such as mutual funds and retirement accounts, where the Investigator does not directly control the investment decisions made).

iii) Receipt of personal funding and compensation that totals $25,000 or more when aggregated in any twelve-month period, from a sponsor or a company that holds an economic interest (e.g., licensee) in the outcome of a human subject trial.

iv) Receipt of payment for services related to promoting, marketing, or selling products (e.g., paid public appearances, endorsements or speaking engagements aimed to encourage purchase or use of products) on behalf of a company for whom the Investigator has also conducted (or intends to conduct) CHLA research as an independent evaluator of the company's products (note that participation in a paid speaker's bureau for a research sponsor is a Prohibited Conflict).

v) Management Roles in a research sponsor.

(iv) Financial Conflict of Interest. ("FCOI") means an SFI that could directly and significantly affect the design, conduct or reporting of Public Health Service (PHS)-funded research. Whether an SFI constitutes a FCOI is a determination made by the COIRC in accordance with this Policy.

[2] Investigators who are healthcare providers are subject to additional requirements under CHLA COMP - 017.0 Gifts and Interactions with Industry

(v) Student or Trainee COI. "Student or Trainee COI" exists when a company in which an Investigator or Close Relation has an ownership interest or Management Role retains a student to provide services (paid or unpaid) and:

i) The Investigator or Close Relation currently supervises the student in an academic capacity;

ii) The Investigator or Close Relation could influence the academic progress of the student; or

iii) The Investigator or Close Relation otherwise supervises the student as a research assistant or student employee.

I. Conflict of Commitment. ("COC") arises when an Investigator undertakes a role (paid or unpaid) outside of CHLA that interferes, appears to interfere, or has the potential to interfere with the Investigator's ability to perform core responsibilities and commitments to CHLA.

POLICY:

Investigators are responsible for identifying and disclosing all potential COI covered by this Policy at least annually. Investigators must evaluate potential COI not only at the outset of their research, but also when a change occurs in their relationship with an outside entity. This may occur at the time a new proposal is submitted, when a new relationship is established with an outside entity, or when a prior relationship with an outside entity changes.

All Investigator's, as defined by this policy, disclosures are to be reported via the University of Southern California's (USC) on-line disclosure system (diSClose) which is used by USC and CHLA for the administration of COI in research, personal conflicts, COC, and business conflicts.

PROCEDURE:

DISCLOSURE OF POTENTIAL COI:

Investigators must disclose potential COI:

i) Prior to, but in no event later than at the time of, funding proposal submission

ii) In connection with human subjects research, at the time of submission of the initial and continuing review application to the Institutional Review Board (IRB) and/or in connection with animal research, at the time of submission of the initial and continuing review application

to the Institutional Animal Care and Use Committee (IACUC).

iii) Within 30 days of discovering or acquiring a new or previously undisclosed outside relationship, or change an existing relationship, which creates a potential COI under this policy.

iv) At least annually.

v) In accordance with other sponsor- or publisher-specific disclosure requirements.

vi) Note, additional disclosures may be needed under other CHLA and USC policies:

The COIRC will make an initial determination regarding whether a disclosure constitutes a COI. If a COI is found to be manageable, the COIRC will require the implementation of a management plan designed to mitigate or eliminate the conflict. Investigators must comply with all elements of a COIRC Management Plan.

Given the complexity of financial and non-financial relationships, disclosures will be evaluated on a case-by-case basis by the COIRC. The disclosure, along with other materials required to evaluate the potential COI will be forwarded to the COIRC, as appropriate. The COIRC shall meet on a regular basis, as reflected in the COIRC Charter.

COIRC determinations will depend in all cases upon the nature of the science, the nature of the interest, how closely the interest is related to the research, the degree to which the interest may be affected by the research, and the degree to which the interest may be affected by the research. When a disclosure reveals a Significant Conflict, the COIRC will assess whether compelling circumstances exist that justify allowing the research to proceed despite the presence of the Significant Conflict.

"Compelling circumstances" should address the following, at a minimum and where applicable:

i) Unique qualifications of CHLA and/or its Investigators (e.g., facilities and equipment, eligible patient population, unique expertise);

ii) The degree of risk to human subjects posed by the research study;

iii) Any steps taken by Investigators or others that serve to manage the risk of bias the conflict poses for research at CHLA;

iv) Additional items as requested by the COIRC or the Office of Compliance & Privacy.

The COIRC will make the final determination as to whether the potential COI is in fact a COI. The COIRC will then determine whether the research may proceed:

i) Permitted as is (e.g., no COI exists);

ii) Permitted contingent upon implementation of a Management Plan; or

iii) Unacceptable, and thus constitutes a Prohibited Conflict.

If the COIRC determines that the conflict cannot be effectively mitigated or eliminated through the implementation of a Management Plan, the research will not be allowed to proceed unless the Investigator eliminates the outside interest or activity giving rise to the conflict.

A Management Plan is a written document defining the actions the COIRC has determined necessary to manage a relationship or interest it has determined is a COI. Examples of potential Management Plan elements include, but are not limited to:

i) All relevant publications, proposals and presentations must contain a statement disclosing support received from, or financial interests in, any source of the COI.

ii) All informed consent documents in the context of human subjects research must disclose support received from, or financial interests in, any source outside of CHLA.

iii) Disclosure to co-investigators, collaborators, or study sponsors;

iv) Disclosure to the Office of Procurement when purchasing products or services;

v) Restrictions on an investigator's ability to recruit or obtain informed consent from prospective subjects;

vi) The Investigator and their Close Relations will not represent CHLA in any intellectual property negotiations, or other contractual negotiations, between CHLA and the outside entity;

vii) Investigators must notify students of the presence of a COI if the student is to perform as a research assistant on the Research, along with a notification to the student and his or her advisor of the student's rights.

viii) Monitoring and oversight by the COIRC or by an individual delegated to monitor by the COIRC or Chief Scientific Officer (or designee), or close monitoring of the research project by independent reviewers;

ix) Referral to a COIRC or Chief Scientific Officer (or designee) appointed subcommittee for oversight.

x) Reformulation of the research workplan;

xi) Restrictions on the analysis of data;

xii) Termination or reduction of involvement in the relevant research project(s);

xiii) Termination of inappropriate student involvement in projects;

xiv) Creation of an escrow account and/or blind trust to hold equity interests or intellectual property interests that constitute a COI;

xv) Divestiture of relevant financial interests or severance of outside relationships that pose a COI.

xvi) Restrictions on the ability to conduct the study at CHLA

Regarding SFIs which are disclosed in connection with PHS-funded research, the COIRC will make the determination as to whether the SFI is related to PHS-funded research. If so, the COIRC will then determine whether the SFI constitutes an FCOI. In making this determination, the COIRC may meet with the Investigator and others, as appropriate, and may request and/or examine data, reports, laboratory notebooks and other records.

(i) An Investigator's SFI is related to PHS-funded Research when the COIRC reasonably determines that the SFI could be affected by the PHS-funded Research or is in an entity whose financial interest could be affected by the PHS-funded research.

(ii) A FCOI exists when the COIRC reasonably determines that the SFI could directly and significantly affect the design, conduct, or reporting of the PHS-funded Research.

(iii) When required in relation to PHS-funded research, CHLA will develop and implement a Management Plan:

a. Before CHLA's expenditure of funds, for new PHS-funded projects;

b. Within sixty (60) days whenever CHLA identifies an SFI that was not disclosed timely by an Investigator or not previously reviewed by CHLA during an ongoing PHS-funded project;

c. Within sixty (60) days whenever an Investigator who is new to an ongoing PHS-funded project discloses an SFI, or whenever an existing Investigator discloses a new SFI.

(iv) It is the responsibility of the Investigator to comply with each element of a required Management Plan. The Investigator must also provide all required follow-up disclosures updating the COIRC on the status of the COI and Investigator's compliance with the measures put in place to manage it.

(v) This policy does not preclude the Department Chair or CEO from requiring faculty or staff to provide additional COI information or to do so on a more regular basis than prescribed by this policy.

Once the COIRC makes its final determination, the COIRC may notify the following individuals and/or entities in writing, as appropriate:

(i) The individual(s) who has disclosed the potential COI. If this individual(s) is someone other than the Investigator, the Investigator will be notified;

(ii) The relevant Department Chair;

(iii) The Research Compliance Committee; and

(iv) Other individuals at CHLA who have a "need to know" (e.g., principal investigator).

In cases where the COIRC's review of a disclosure raises a potential COC, the COIRC will notify the Investigator's supervisor, Division Chief, Chair or CEO, as appropriate. The Investigator's supervisor, Division Chief, or Department Chair should provide a copy of all documentation reflecting his or her determinations with respect to the COC to the Investigator.

When an Investigator discloses a COC, the Investigator must provide a copy of all documentation reflecting any determinations regarding COC management made by the Investigators supervisor, Department Head, or any other oversight bodies identified in applicable CHLA or USC policies or the USC Faculty Handbook. Any subsequent disclosures with respect to a COC, as well as any

documentation reflecting subsequent management decisions must also be provided to the COIRC, when requested.

AUDIT:

The Office of Compliance and Privacy may conduct routine or for-cause audits to evaluate compliance with CHLA policies. Concerns regarding compliance with this policy may be directed to the General Compliance Line at (323)361-2302 or at compliance@chla.usc.edu. You may also report anonymously through CHLA's Compliance Hotline by calling 1-877-992-6675, faxing information to (323) 361-5269, or by submitting a report online at www.mycompliancereport.com (company ID: LAC).

VIOLATIONS AND SANCTIONS:

Failure to report a potential COI or to submit an annual or updated disclosure, or refusal to cooperate in the management of a COI, may be cause for disciplinary action. Possible violations of this policy include, but are not limited to, failure to file the disclosure form or furnishing false, misleading, or incomplete information on the disclosure form, or failure to follow a Management Plan.

Sanctions for violations of this policy for staff or other non-faculty may include termination. Human Resources will notify both the department and the non-faculty employee of the prescribed action. Departments are required to implement the remedial or disciplinary action prescribed by Human Resources. A non-faculty employee may file a written appeal to Human Resources and/or the Office of Compliance and Privacy within ten business days of his or her receipt of notice of the disciplinary action. Sanctions for violations of this policy for students will require that students observe all provisions of their institutions policies.

The COIRC must respond to the employee's appeal within 30 business days.

Violations that appear to involve a misrepresentation of research results will be handled according to the CHLA's Research Misconduct Policy COMP – 025.0, and other misconduct will be handled under the procedures specified in the Faculty Handbook, and for non-faculty employees as described above. Violations of federal or state statutes and guidelines must be handled according to federal and state laws and requirements.

If the Department of Health and Human Services determines that a PHS-funded project of clinical research, whose purpose is to evaluate the safety or effectiveness of a drug, medical device, or treatment, was designed, conducted, or reported by an Investigator with an FCOI that was not properly disclosed or

managed, then CHLA will require the Investigator(s) to: (i) disclose the FCOI in each public presentation of the results of the research, and (ii) request an addendum to previously published presentations.

GOVERNMENT REPORTING AND APPEALS:

A faculty member seeking review of the decision by the COIRC may do so by filing a grievance under the provisions of the Faculty Handbook on any of the grounds on which a tenure decision may be grieved. The decision of the COIRC will remain in full force and effect throughout the review process.

When a FCOI has been identified in connection with PHS funded awards, the Director of The Saban Research Institute, or his or her designee, will report to the federal awarding agency the existence of the FCOI and assure that the conflict has been managed, reduced, or eliminated prior to the expenditure of any funds under the award as described herein (the "FCOI Report").

When required, CHLA shall submit a FCOI Report:

i) Before CHLA's expenditure of funds, for new PHS-funded projects;

ii) Within sixty (60) days whenever the COIRC determines an Investigator who is new to an ongoing PHS-funded project has a FCOI, or whenever the COIRC determines an existing Investigator has a new, or newly identified, FCOI;

iii) At least annually until the completion of the project, to provide the status of a FCOI and any changes to any relevant Management Plan; and

iv) Following a Retrospective Review, as described at 42 CFR 50.605.

If the COIRC determines that an Investigator has failed to comply with this policy or a Management Plan as required by the COIRC, resulting in potential bias in the design, conduct or reporting of PHS-funded research, CHLA will notify the PHS awarding component and promptly take corrective action, as required by 42 CFR 50.605 and 50.606.

If the COIRC determines that bias has occurred within the research design, conduct, or reporting of PHS-funded research following a Retrospective Review, CHLA will submit a Mitigation Report as required by 42 CFR 50.605.

All FCOI Reports will include sufficient information to enable the PHS awarding component to understand the FCOI and to assess the Management Plan implemented by the COIRC. At a minimum,

FCOI Reports will include the required elements at 42 CFR 50.605(b)(3).

With respect to research funded by the NSF, if for any reason the COI cannot be managed satisfactorily, then the Director of The Saban Research Institute, or his or her designee, will promptly inform the NSF of this fact.

TRAINING, RECORDS, AND SUBRECIPIENTS

All Investigators must complete training relating to COI in research as prescribed by this policy.

Each Investigator is required to complete COI training: (i) prior to engaging in PHS-funded research; (ii) at least every four (4) years thereafter; and (iii) immediately if: (a) CHLA revises this policy in a way that affects Investigators' obligations, (b) upon hiring, or (c) the COIRC determines that an Investigator is not in compliance with this policy or a Management Plan.

Records relating to disclosures of potential COI and the determinations of the COIRC will be kept by the Compliance Office for three years after the termination or completion of the project, whichever is later, and/or for PHS Research, as described under HHS regulation 42 CFR Part 50 Subpart F

CHLA may carry out PHS-funded Research through a subrecipient entity (e.g., subcontractors or consortium members). CHLA shall take reasonable steps to ensure that any subrecipient investigator complies with federal FCOI regulations by establishing such compliance via a written agreement.

PUBLIC ACCESSIBILITY:

CHLA shall make this policy, as may be updated from time to time, publicly accessible on CHLA's website.

For PHS-funded research, CHLA shall make publicly accessible certain information concerning Financial COI held by senior/key personnel, defined as the principal investigator and any other person identified as senior/key personnel by CHLA in the grant application, progress report, or any other report submitted to the PHS funding agency. Such information shall be provided within five (5) business days of CHLA's receipt of a written request. Requests should be directed to the Compliance Office.

Such responses will only be made in response to a written request related to a Significant Financial Interest of a senior/key personnel about which the COIRC has determined:

i) The SFI was disclosed and is still held by the senior/key personnel,

ii) COIRC has determined that the SFI is related to the PHS-funded research, and

iii) COIRC has determined that the SFI constitutes a FCOI.

Information concerning the Significant Financial Interests of senior/key personnel that is provided upon written request will be available for responses to written requests for at least three (3) years from the date that the information was most recently updated.

CHLA will prepare and approve a timely response that will be communicated to the requestor through a CHLA-appointed designee. Such response will include all required elements set forth at 42 CFR 50.605(a)(5)(ii).

RESOURCES:

1. 42 CFR Part 50 and 45 CFR Part 94.
2. Conflict of Interest Policies — NSF Grant Policy Manual
3. Food and Drugs: FDA Guidance on Financial Disclosure by Clinical Investigators
4. FIN – 010.0 Procurement
5. COMP – 017.0 Gifts and Interactions with Industry
6. EGEN – 013.0 Intellectual Property Policy
7. COMP – 020.0 Conflicts of Interest Policy
8. COMP – 025.0 Research Misconduct Policy
9. NOT-OD-18-160, Financial Conflict of Interest: Investigator Disclosures of Foreign Financial Interests

POLICY OWNER:
Office of Compliance & Privacy