

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

1. POLICY

Steering Committee approved 1/31/11

Organizational and/or individual financial and/or non-financial interests may present real or perceived risks to research integrity and to the welfare and rights of human research participants. Therefore, research conflicts of interest (COI) are subject to reporting and review and appropriate management by Aurora’s Research Integrity Committee.

Specific Policies

The following are definitions of key terms used in this policy. Terms used in this policy but not defined herein shall have the meanings set forth in the Glossary.

1.1. Definitions

1.1.1. **“Compensation affected by the outcome of the study”** means compensation that could be higher for a favorable outcome than for an unfavorable outcome such as compensation that is explicitly greater for a favorable study result or compensation to the investigator in the form of an equity interest in the study sponsor or in the form of compensation tied to the sales of a study product such as a royalty interest.

1.1.2 For purposes of this policy, **“Covered Party”** is an investigator, research staff that are designated by the investigator to conduct research activities, RSPP staff member, IRB member or administrator or Aurora Official who is compensated or otherwise supported by Aurora for his/her services or who appears to act as an agent of Aurora in using, controlling or assigning to others the use of Aurora facilities and resources in the conduct of research.

1.1.3. A **“conflict of interest related to human subject research”**(“COI”) refers to:

(i) a situation in which the financial or non-financial interests of Aurora, or of an- Aurora Official or other Covered Party acting within his or her authority on behalf of Aurora Health Care, might affect, or reasonably appear to affect, institutional processes for the conduct, review or oversight of human subjects research; or

(ii) a situation in which financial or non-financial considerations may compromise, or have the appearance of compromising, an investigator’s professional judgment in conducting or reporting research.

1.1.4 **“Required Disclosure”** means the release of relevant information about a conflict of interest in human subjects research to parties outside of the IRB and Aurora’s Research Integrity Committee and management process (e.g., to research subjects or journal editors).

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

1.1.5 “Immediate Family” means spouse, dependent children, and/or other persons living in the household.

1.1.6 “Financial Interest Related to the Research” means financial interest in the sponsor, product or service being tested, or competitor of the sponsor.

1.1.7. “Significant financial interests” include the following:

(i) Ownership interest, stock options, or other financial interest related to the research unless it meets each of these four tests:

- (1) Less than \$10,000 when aggregated for the immediate family.
- (2) Publicly traded on a stock exchange.
- (3) Value will not be affected by the outcome of the research.
- (4) Less than 5% interest in any one single entity.

(ii) Compensation related to the research unless it meets two tests:

- (1) Less than \$10,000 in the past year when aggregated for the immediate family.
- (2) Amount will not be affected by the outcome of the research.

(iii) Proprietary interest related to the research including, but not limited to, a patent, trademark, copyright or licensing agreement.

1.1.8. “Significant Non-Financial interests” include the following:

(i) Serving as an officer, director, or fiduciary for the study sponsor or its affiliates;

(ii) Having -a non-financial interest that may compromise, or have the appearance of compromising, professional judgment in the conduct of the study or in the reporting of study results.

(iii) In the case of IRB members, RSPP staff, consultants, and administrators, “Non-Financial Interest” includes involvement in the design, conduct, or reporting of the research.

1.1.9. “Finder’s Fee” means money or other non-monetary reward given by a study sponsor (or by a physician or other entity) to a physician or physician group in payment for identifying or recruiting a potential research subject into a research study.

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

Finder’s Fees include bonus or milestone payments for successfully enrolling a particular number of subjects or for successfully meeting a deadline in recruiting subjects.

1.1.10. “Completion Fees” means money or other non-monetary reward given by a study sponsor (or by a physician or other entity) to a physician or physician group in payment for each subject’s successful completion of a research study or protocol. Completion fees include bonus or milestone payments for a particular number of patients successfully completing the research study or for successfully completing it within a specified time frame.

1.1.11. “Vendor” means a company, including any employee, agent or representative of a company, that currently supplies or has the potential to supply products or services to Aurora Health Care or is otherwise in a position to do business with Aurora Health Care.

1.1.12. “Aurora Official”, for purposes of this policy, means Aurora Health Care board members, executive leaders, and other employees in a position of manager of above.

1.2. Composition of the Research Integrity Committee

The Aurora Research Integrity Committee (“RIC”) shall be comprised of the following members: (1) Institutional Official; (2) non-research affiliated Corporate Director; and (3) a Bioethicist. The RIC may consult with any third party who, in the opinion of the members of the RIC, would provide additional useful information to the RIC for resolution of a reported conflict of interest. Such third-party consultants may include, without limitation, health care providers, unaffiliated individuals in the community, and prior research subjects or their family members.

1.3. Policies and Procedures on Organizational COIs Relating to Aurora Health Care Financial and Business Relationships

1.3.1 Aurora Health Care separates the functions and administrative responsibilities related to research from those related to investments and purchasing.

a. Decisions with respect to investment of funds are delegated to- and are overseen by the Aurora Treasury Department. Individual investment decisions are delegated to and made by outside investment advisors or managers.

c. Purchasing decisions are delegated to System Logistics and overseen by the Chief Financial Officer.

d. The criteria that govern decisions related to investments and purchasing specifically preclude consideration of information related to Aurora Health Care research activities.

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

1.3.2 Aurora Health Care implements a policy that generally prohibits solicitation or acceptance of gifts from Vendors and patients by Aurora caregivers – including officers, directors, employees and agents of Aurora Health Care who act as agents of Aurora in using, controlling or assigning to others the use of Aurora facilities and resources in the conduct of research. (See Policy No. 130, AHC System Administrative Manual and Aurora Health Care “Code of Ethical Conduct”.) This policy helps to assure that organizational financial conflicts of interest will not influence the conduct of research or the integrity of the Human Research Protection Program.

1.3.3 Aurora Health Care adheres to a “Code of Ethical Conduct” and implements a Conflict of Interest Policy (Policy No. 80) that prohibit Conflicts of Interest where personal interests of an employee, board member or physician may affect the ability of that individual to act in the best interests of Aurora Health Care and its patients. Pursuant to the Conflict of Interest Policy, all board members and all employees in a position of manager or above submit a signed Conflict of Interest Statement on an annual basis; in addition, Material Conflicts of Interest must be immediately disclosed. Annual Conflict of Interest statements and disclosures of Material Conflicts of Interest will be forwarded to and reviewed by the RIC if the information bears on the conduct, review or oversight of research.

1.3.4 Any proposed gift to Aurora Health Care from a research sponsor will be referred to and reviewed by the RIC.

1.3.5. If any person affiliated with Aurora Health Care believes that Aurora Health Care, as an organization, may have a conflict of interest that is not being addressed, with respect to the conduct, review or oversight of research, (s)he should immediately inform the Chief Compliance Officer, who will refer the matter to the RIC.

1.3.6 If the RIC receives a referral regarding a potential organizational conflict of interest relating to research, it will investigate the matter and determine if a real or apparent conflict exists. If the RIC determines that a real or apparent organizational conflict of interest directly related to research exists, and that the conduct or results of such research or the safety of research subjects may be affected thereby, the RIC shall make a recommendation for management or elimination of the conflict.

1.3.7 The RIC shall prepare a written COI report that summarizes the nature of the conflict and includes any recommendations or conditions imposed. A copy of such report must be sent to the RSPP Manager, who will forward to the IRB Chair and/or any other person(s) deemed appropriate by the RSPP Manager, RIC or IRB Chair.

1.3.8 The IRB will review the RIC determinations forwarded to it and has the final authority to decide whether the COI and its management allow the research to be approved.

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

1.3.9 The IRB will maintain the RIC written report in a confidential file in the RSPP Manager’s office and will document the action taken by the RIC and the IRB in the relevant meeting minutes.

1.4 Individual Conflicts of Interest

1.4.1 Reporting a Covered Party’s COI to the IRB and RIC

Covered Parties shall report all Significant Financial and Significant Non-Financial Interests of the Covered Party and his/her Immediate Family, and any other conflicts of interests related to human subject research to the IRB and RIC in accordance with the table set forth below. The IRB is responsible for collecting the conflicts of interest reports and submitting them to the RIC for consideration in accordance with Section 1.4.2 below. The forms upon which such reports shall be made and the frequency upon which such reports are required varies depending on the type of Covered Party making such report.

Covered Party	Reporting Requirements	Reporting Period	Further Action Required if COI Exists
Investigators (Principal Investigators, Co-investigators, Sub-investigators, and Research Staff)	Must report whether a COI exists each time a research study is submitted to the IRB on the Investigator COI Statement (Form 104-A).	With each new IRB submission and periodically thereafter if a COI arises or there is a material change in an existing COI during the research study.	Divestment or imposed conditions as recommended by the RIC.
IRB Members	Must review and sign an IRB Member Recusal Agreement (Form GA 104-B) upon appointment.	Upon appointment and then periodically thereafter if a COI arises or there is a material change in an existing COI during the reporting period.	May not participate in the review of research (by either the convened IRB or the expedited procedure) in which the member has a Significant Financial Interest or Significant Non-Financial Interest except to provide information requested by the IRB.(See SOP 304, section 1.4.2)

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

Aurora Officials	Must submit signed Conflict of Interest statement pursuant to Aurora Policy No. 80	Annual basis and periodically thereafter if COI arises or there is a material change in an existing COI during the reporting period.	Referral to RIC, by Corporate Compliance, or responsible department president or vice-president, or Aurora Conflict of Interest Committee, as indicated; imposed conditions as recommended by RIC.
RSPP Staff Member	Must report any COI on the Administrator / RIC /RSPP Staff COI Report (Form GA 104-C).	Annual basis and periodically thereafter if a COI arises or there is a material change in an existing COI during the reporting period.	Divestment or imposed conditions as recommended by the RIC. May not participate in the review (by either the convened IRB or the expedited procedure) in which the RSPP Staff Member has a Significant Financial Interest or Significant Non-Financial Interest.
Consultants	Must report any COI on the Consultant COI Statement (Form GA 104-D).	As required by protocol review.	May not participate in the review (by either the convened IRB or the expedited procedure) in which the Consultant has a Significant Financial Interest or Significant Non-Financial Interest.

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

1.4.2 RIC Review, Recommendations, and Documentation Relating to Covered Parties' COIs

1.4.2.1 Review and Recommendations Concerning Covered Parties' Significant Financial Interests and Significant Non-Financial Interests.

When reviewing a reported Significant Financial Interest or Significant Non-Financial Interest, the RIC shall first determine if a Significant Financial Interest or Significant Non-Financial Interest exists. In making such a determination the RIC shall request additional information as needed directly from the individual submitting such a report or from others, as appropriate.

a. Significant Financial Interest or Significant Non-Financial Interest. If the RIC determines that a Significant Financial Interest or Significant Non-Financial Interest exists, the RIC shall take one of the following alternative actions:

(1) require divestment of such interest by the Covered Party (e.g., an investigator would be prohibited from conducting or participating in the human subject research in which he/she has a Significant Financial Interest or Significant Non-Financial Interest until he/she divests such interest; or

(2) determine that “compelling circumstances” exist that justify such Covered Party’s participation in or oversight of the human subject research, and impose conditions that effectively eliminate any significant risk to the safety of human subjects and preserve the integrity of research data. The RIC shall NOT make such a determination if the imposed conditions cannot adequately protect against risks to human subjects or preserve the research integrity. In making such a determination, the RIC shall consider:

- the nature of the science;
- the nature of the interest;
- how closely the investigator’s interest is related to the human subjects research study at issue; and
- the degree to which the interest may be affected by the human subjects research, or the results thereof; or

(3) in the case of a Consultant, determine that the individual may not provide information to the IRB on that particular study; or

(4) in the case of an IRB member, RSPP staff member, or Aurora Official, determine that the individual must absent themselves from the meeting room during the convened review of research, and not be involved in the review of research using the

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

expedited procedure in which the individual has a Significant Financial Interest or Significant Non-Financial Interest, except to provide information requested by the IRB.

1.4.2.2. Review and Recommendations by the RIC Concerning Other COIs

With respect to COIs that are not determined to be a Significant Financial Interest or Significant Non-Financial Interest, if the RIC finds that the reported COI is directly related to any research study and that the results of such research or the safety of research subjects enrolled in the research study may be affected by such COI, the RIC shall, at its discretion, impose any of the following applicable conditions, or any other requirement deemed appropriate:

(i) That the involved Covered Party be required to eliminate the relevant financial or non-financial interest before participating in the research;

(ii) That the involved Covered Party not be allowed to perform certain research activities, e.g. serve as principal investigator, determine subject eligibility, solicit subject consent, or serve as voting IRB member with respect to review of a specific protocol;

(iii) That the involved Covered Party provide full oral and/or written disclosure (during the consent process and on the consent form) of the COI to the potential research subject;

(iv) That an independent monitoring board oversee the research study;

(v) That the IRB assign a Research Intermediary when subjects are recruited and informed consent is obtained;

(vi) That an escrow account be established and contain the financial interest until the investigational article has been on the market and approved for a specified time.

1.4.2.3. Written Reports

The RIC shall prepare a written COI report that summarizes the nature of the conflict, and any recommendations or conditions imposed. A copy of such report must be sent to the RSPP Manager who will forward to the appropriate IRB Chair(s), and any other person(s) deemed appropriate by the RSPP Manager, RIC, or IRB Chair.

1.4.3 IRB Review of RIC Report

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

The IRB final determination letter for a research proposal will be withheld pending completion of RIC review and establishment of management plan. The IRB shall review the RIC determinations and has final authority to decide whether the COI and its management is appropriate. The IRB may impose additional requirements as deemed appropriate. The IRB shall maintain the RIC written report in a confidential file in the RSPP Manager’s office and shall document the action taken by RIC and the IRB in the relevant meeting minutes. 1.4.4 Required Disclosure of Significant Financial Interest

Investigators. Investigators are required to report their Significant Financial Interests to: (1) state/federal officials in accordance with applicable law; (2) sponsors funding the research in accordance with pertinent contractual or grant obligations and/or regulations; (3) publication editors to which the investigator submits a transcript concerning human subjects research; and (4) the public in any oral or written communication that sets forth the results of such human subjects research study.

The Organization. If the funding or regulatory agency has a reporting requirement, the RSPP Manager will ensure the reporting requirements are met.

1.4.5 Consent Forms

The IRB requires that any consent form approved by IRB should fully disclose the existence of any Significant Financial Interest or any Significant Non-Financial Interest, as recommended by the RIC. If an investigator or an Aurora Facility receives payment by the sponsor or granting agency to conduct research or provide support services to allow the conduct of such research, such payment must be disclosed to the research subject in the Consent Form. Precise wording of the disclosure is left to the sole discretion of the reviewing IRB.

1.4.6 Other Related Issues

The position of the IRB is that Finder’s Fees, Completion Fees (defined above in Sections 1.1.6 and 1.1.7, respectively), and enrollment milestone ‘bonus’ payments (payments to the site/investigator based solely upon reaching enrollment targets) essentially constitute an improper inducement. A physician, investigator, or research staff receiving such fees for patient recruitment or subject completion is an impermissible conflict of interest since there is a divergence between the physician’s/investigator’s/research staff’s private interests and his or her obligations to the research subjects. The IRB expressly prohibits the offer or acceptance of finder’s fees, completion fees or enrollment milestone bonus payments.

1.4.7 Disciplinary Action

In the event that the IRB receives information that any Covered Party has failed to disclose a COI-in accordance with this SOP, the Chair of such IRB shall report such failure

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

to the RIC. The RIC shall evaluate the noncompliance and shall make disciplinary recommendations and report them to the appropriate body in Aurora for implementation of such recommendation.

1.4.8 Education and Training in COI

Investigators, research staff, IRB members, RSPP staff and certain administrators and Aurora Officials identified by the RIC are required to participate in education and training activities related to COI issues.

1.4.9 Protection of Covered Parties' Financial Information

Any Financial Interest reported to the IRB on the Forms set forth in section 1.4.1 above shall not divulge the specific information relative to a Covered Party's financial interest in a sponsor, other company or product. Upon receiving any reported COI, the RIC shall make a direct inquiry to the reporting Covered Party to obtain adequate information to make a conflict of interest determination. The RIC shall maintain the confidentiality of any financial information and shall disclose such information to the IRB only as necessary to ensure adequate protection of human subjects and maintain the integrity of the research data.

2. SCOPE

These policies and procedures apply to all IRB members, RSPP staff, Aurora Officials, and unaffiliated investigators/research staff for whom an IRB is reviewing one or more research studies.

3. APPLICABLE REGULATIONS, GUIDELINES AND STANDARDS

45 C.F.R. 46.103, 46.107

21 C.F.R. 56.107, 312.64(d)

21 C.F.R. 54 (as reference)

ICH Guidelines 4.9.6

FDA Information Sheets, FAQs, Section II, question 12

OHRP Final Guidance on Financial Relationships and Interests in Research Involving Human Subjects: Guidance for Human Subject Protection, 05/05/04

AAHRPP Standard I-6, Elements I.6.A. and I.6.B.

SOP: GA 104 Version No.: 7 Effective Date: 2/11/11	CONFLICTS OF INTEREST IN HUMAN SUBJECT RESEARCH	Supersedes Document Dated: 12/7/10
---	--	---

AAMC Task Force on Financial Conflict of Interest in Clinical Research: Protecting Subjects, Preserving Trust, Promoting Progress-Policy and Guidelines for the Oversight of Individual Financial Interests in Human Subjects Research, December 2001

NHRPAC Recommendations on HHS's Draft Guidance on Financial Relationships in Clinical Research, October 2001

4. REFERENCES TO OTHER APPLICABLE SOPS

This SOP affects all other SOPs.