Conflict of Interest Guidance Document

What is a Conflict of Interest ("COI")?
• **COI** is defined in the Research Subject Protection Program (RSPP) glossary as “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 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.”

What are the different types of COI?
• COI can arise where Significant Financial Interests or Significant Non-Financial Interests exist.
• These COIs could arise because of Significant Financial or Significant Non-Financial Interests of investigators, research staff, RSPP staff, IRB members, or Aurora Officials, or their immediate family, or both.

What’s the difference between the types of COI?
• **Significant Financial** Interests relate to any money, ownership interest, stock options, and other financial or proprietary interests related to the research. For example:
  o If money is paid to an investigator if the research has favorable outcomes.
  o If the coordinator or investigator has stock in the company.
  o If the investigator has a patent on the investigational product.
• **Significant Non-Financial** Interests commonly relate to involvement in the design of the research, or having a board or executive position with the sponsor of the research.
  o For example, if the investigator or his immediate family member served on the Board of Directors of the company that manufactured the investigational product being studied in the research, there may be a COI.

What interests must be reported and why may these interests be considered COI?
• **Significant Financial** Interests are often more easily understood as possibly creating COI than their significant non-financial counterpart. If an investigator has a significant financial **stake** in the outcome of the research (s/he/family owns stock, is a paid consultant to the sponsor, has a patent on the investigational product, is paid for favorable study outcomes), there is a potential for bias to occur when s/he is reviewing, gathering or analyzing study data or results.

Any interests that may actually bias or have the perception of potentially biasing the data or results not only jeopardize the study's integrity, but may put subjects at risk for harm. For example, following the death of research subject Jesse Gelsinger it
was learned that there was potential for significant financial benefit to the principal investigator if the study succeeded. Some believe that this led to deviations from the study protocol and failure by the investigator to properly disclose potential risks and benefits of the study during the informed consent process.

- **Significant Non-Financial** Interests are often less well understood. The most common significant non-financial interest is a study where the PI (or his immediate family) is involved in the study design. These studies are seen as situations where the PI may have *more* interest in the study’s success, for both personal and professional reasons, than an investigator who was not involved in the study design. As with Significant Financial Interests, bias could be introduced and reported outcomes could be misleading (intentionally or unintentionally), which could negatively impact the research integrity, as well as potentially affect subject safety.

*Why is it important for the IRB/RSPP/Research Integrity Committee ("RIC") to be notified of these interests?*

- No one intends to let financial or non-financial interests impact a study, but it is important for the IRB/RSPP/RIC to know about such interests because of the potential for or appearance of compromising the conduct, review or oversight of the research. The investigator can then work with the IRB/RSPP/RIC to minimize, eliminate, or manage any COI and thereby assure that subjects are adequately protected.
- The IRB/RSPP/RIC considers it a good thing to disclose financial and non-financial interests related to research! Just because a COI exists doesn’t mean that the investigator or his/her research is unethical. Rather, by recognizing the importance of disclosing this information, the investigator or other Covered Party is protecting the integrity of the study and the research subjects’ welfare and rights. Transparency is an important element of public trust.

*What should be included on the COI Statement?*

- The "Protocol for Research Involving Human Subjects Study-Specific Conflict of Interest Statement" form is available on the RSPP website. (http://www.aurorahealthcare.org/misc/irb/conflict-of-interest.asp)
- The top section should be completely filled out regarding the name of the Investigator/Key Personnel completing the form and protocol title.
- Any/all Significant Financial or Significant Non-Financial Interests of the Investigator/Key Personnel or his/her immediate family must be identified.
  - Note: If any box is checked, the submitter must complete a statement on a separate sheet of paper with details of the interest. If the first box is checked, the planned steps to prevent the reported interest from interfering with subject protection or from compromising his/her judgment in conducting the study or reporting the research results must be addressed. This statement can be submitted with the form or submitted confidentially as directed.
- The form should then be signed and dated.
• **IMPORTANT NOTES:**
  - An original signature is required. If the form is altered, or if there are any omissions, a new form will need to be completed with the new original signature.
  - For electronic submissions (received via Cyber), COI forms do not need to be originals. They can be scanned and included within the electronic submission. (The signed original should be kept in the research record and made available upon request.)
  - Investigators/Key Personnel must complete this form themselves; that is, no Investigator/Key Personnel may complete the form for another individual.
  - Every Investigator/Key Personnel on a study must complete and sign the form to provide disclosures specific to that study. (Since individual interests vary, there currently is no “blanket” form or process to capture disclosures annually. The Investigator/Key Personnel must complete a separate form for each study s/he is involved in.)
  - The study coordinator is responsible for ensuring that the COI form is correctly completed, and that any appropriate documentation is attached.

_How can the potential risk of harm to subjects due to a COI be minimized?_
• Disclosing financial and non-financial interests is an important first step. It demonstrates that the investigator is committed to ethical and honest research guided by transparency.
• Taking actions to minimize subject’s risk of harm also depends on the level of the risk of the research. Appropriate consideration of these risks is especially important for Significant Non-Financial Interests, since this type of potential COI is less well understood.
  - Non-financial interests associated with low/minimal risk research, such as a retrospective chart review, may not pose a high risk of harm to the subjects. However, there are steps that may be indicated to lessen the risk of bias in assessing the outcome of the research (e.g., with respect to an investigator-designed study, having data analysis performed by a statistician, not the PI).
  - For studies that inherently pose higher risks to subjects (such as randomized clinical trials (RCTs), drug and device studies, etc.), if the investigator had a role in designing the study, it may again be important to have someone other than the PI doing the data analysis, in order to protect against investigator bias. Other aspects of the study must also be considered (such as determining enrollment and eligibility, and obtaining informed consent). In some cases, it may be advisable that the investigator not enroll subjects nor obtain informed consent, nor determine eligibility.

_Are there going to be changes to COI reporting requirements in the future?_
• The U.S. Department of Health and Human Services (HHS) has issued a final rule in the [Federal Register](https://www.federalregister.gov/) that amends the Public Health Service (PHS) regulations on Responsibility of Applicants for Promoting Objectivity in Research for which PHS
Funding is Sought (42 C.F.R. Part 50, Subpart F) and Responsible Prospective Contractors (45 C.F.R. Part 94). An Institution applying for or receiving NIH funding from a grant or cooperative agreement must be in compliance with all of the revised regulatory requirements no later than 365 days after publication of the regulation in the Federal Register, i.e., August 24, 2012, and immediately upon making the Institution’s Financial Conflict of Interest policy publicly accessible as described in 42 CFR part 50.604(a). Institutions must comply with the 1995 financial conflict of interest regulation until the Institution fully implements all of the regulatory requirements of the 2011 revised regulation.

- The RSPP/RIC are currently evaluating the revised regulations and will be implementing appropriate changes to ensure compliance by August 24, 2012.

*Any questions about COI and how they can be minimized?*
- Contact the RSPP office for additional guidance and clarification.