

COI Guidance: Research Rebuttable Presumption

Research involving human participants is critical in developing knowledge and discoveries that will benefit society. Protecting the rights and welfare of human research participants is of the utmost importance and a requirement of all research personnel and Weill Cornell Medicine (WCM). Of particular concern, therefore, are external commitments and financial interests that compromise or appear to compromise the rights and well-being of human research participants. WCM scrutinizes the roles in such research of personnel who have external commitments or financial interests with a sponsor or with an external entity that is related to, or can be affected by, the research.

WCM has instituted a rebuttable presumption that: **research personnel who are involved in the design, participant selection, informed consent process, or the clinical management of a trial cannot have a significant ongoing financial interest or executive position (e.g., equity stake, officer or director title, intellectual property rights, start-up ownership) in an entity whose interest could be affected by the research.** In other words, the default position is that participation in human participant research by conflicted research personnel is not allowed. However, there may be compelling circumstances in which conflicted research personnel would be permitted to participate in the research. In these cases, the management strategies for the involvement of conflicted researchers must be carefully adjusted to the level of anticipated risk. All financial interests and external relationships related to human participant research that are not eliminated must be disclosed to all participants in the related research.

Note: the rebuttable presumption only needs to be met if the conflicted researcher seeks to serve as an investigator. Conflicted researchers are generally permitted to serve as consultants on such studies.

Meeting the Rebuttable Presumption

To meet the rebuttable presumption, the conflicted researcher must draft a letter to WCM's Conflicts Advisory Panel (CAP) explaining the following:

1. Information about the individual's expertise/research
2. Information about the entity in which the conflicted researcher has a financial relationship with (e.g., company purpose, capitalization, relevant products/services)
3. The individual's role with the entity
4. Details (including the IRB protocol #(s)) about the proposed study at issue involving the company or technology.
5. Most importantly, state why it is necessary for you, rather than a non-conflicted researcher, to serve as the PI (or perhaps a co-investigator) on the study (provide compelling circumstances). You should mention why serving as a consultant on the study would not suffice.
6. Proposed conflict mitigation strategies for the study.

The letter should be provided to the Conflict of Interest (COI) Office via conflicts@med.cornell.edu, for an initial review. Next, the CAP will review the letter and provide a recommendation to WCM's Institutional Review Board (IRB). The IRB makes the final determination as to whether the rebuttable presumption has been met. Please be prepared to meet with the CAP to present your rebuttable presumption proposal, if needed.

For more directed guidance, please contact the COI Office at conflicts@med.cornell.edu. WCM-Q faculty and staff, please contact Dr. Amal Robay, Director of Research Compliance, at amr2018@qatar-med.cornell.edu. Additional information can be found on [WCM's COI Office Website](#).

Examples of Successful Rebuttable Presumption Proposals

Case 1: Researcher with multiple clinical trials receives equity from financially-interested company

- Background
 - Dr. X, PI for three separate studies that involved a WCM product, licensed to a WCM start-up company.
 - Recently, Dr. X joined the scientific advisory board for the company and received equity compensation.
 - Although the company has no role in Dr. X's research, it may still financially benefit from the results of Dr. X's research.
 - The company plans to provide future funding to these studies.
 - Dr. X would like to remain an investigator on these studies.
 - Dr. X would like to mentor trainees to eventually be able to lead such studies.
- Compelling Circumstances
 - They are already PI and designed, implemented, and obtained funding for the studies.
 - They hold the IND for the study drugs.
 - They have the expertise to conduct the studies and directly negotiate with the FDA.
 - No one else at WCM would be able to perform this phase of the studies, especially with the level of expertise required.
 - The studies are Phase 1.
 - The studies have an independent medical monitor, external from the team.
 - The studies report to an external Data Safety Monitoring Committee (DSMC).
- CAP Determination
 - Dr. X was placed on a comprehensive conflicts management plan (cCMP) for oversight.
 - Dr. X is allowed to serve as a co-investigator for Phase 1 of these studies.
 - The Informed Consent Form (ICF) will include necessary disclosures, both personal and institutional.
 - Disclosures must be provided in all relevant publications and presentations.
 - Although the company has not yet provided funding to the studies, Dr. X must step down as PI immediately.
 - Dr. X is allowed to mentor the trainees, with oversight by an "ombudsman."

Case 2: Researchers developed IP and seeks to perform Phase 1 clinical trial to test safety

- Background
 - Dr. X and Dr. Y, from different departments, jointly developed intellectual property (IP) that is not yet commercialized.
 - Both faculty members want to serve as co-investigators for a Phase 1 clinical trial involving the IP.
- Compelling Circumstances
 - The combined technical expertise of Dr. X and Dr. Y is required for the execution of the study.
 - The uncommercialized IP requires their oversight to ensure it is developed properly.
 - This is a Phase 1 study.
- CAP Determination
 - Both researchers were placed on a cCMP for oversight.
 - Dr. X was permitted to review identifiable data.

- Both researchers are permitted to serve as co-investigators, given their technical expertise required for the execution of the study. Establishing Drs. X and Y as co-investigators mitigates conflicts risk, because they will each be required to monitor all study operations and procedures and ensure the integrity of the clinical protocol data acquisition and reporting.
- The ICF will include the necessary disclosure of all individual and institutional financial interests.
- For this study, both Dr. X and Dr. Y cannot be involved in the consenting of patients, performing surgery on patients, or data analysis.
- Both researchers are allowed to train physicians participating in the study to use the technology and troubleshoot any related issues.
- Both researchers can be authors on publications resulting from this study, and must provide the necessary financial disclosures to the journal.

Case 3: Researcher developed software and seeks to perform Phase 1 trial to test functionality

- Background
 - Dr. X co-founded a company for the purpose of developing a healthcare app.
 - Dr. X is CEO of the company, due to a lack of funding to recruit externally.
 - The proposed study to validate the technology will involve human subjects.
- Compelling Circumstances
 - Dr. X, as co-founder, has unique knowledge of the technology.
 - Dr. X's participation in the analysis of the recorded data will be critical to determine the proper functionality of the app.
 - Serving as a consultant instead of an investigator was not an option in this case, because they would be unable to make technology decisions without reviewing data developed from the protocol.
- CAP Determination
 - Dr. X was placed on a cCMP for oversight.
 - Dr. X may be a co-investigator on Phase 1 of the study.
 - A non-conflicted PI must oversee all study operations and procedures, and ensure the integrity of the clinical protocol data acquisition and reporting.
 - An external reviewer, independent of the study and the company, will perform an independent review of the clinical trial protocol and review all data that emerges from this study prior to publication or presentation at conferences.
 - Dr. X must step down as co-investigator once the study goes to Phase 2.

Case 4: Researcher with departmental leadership role seeks to have WCM as a Phase 1 trial site for study utilizing their IP

- Background
 - A Phase 1 study involves technology that forms the basis for the trial.
 - Dr. X, the PI, has equity in the company that owns the technology.
 - Dr. Y, a co-investigator, is an equity stock owner of the company.
- Compelling Circumstances
 - Dr. X's participation is required to complete the study because their clinical volume represents the main study population.
 - The disease being studied is rare.
 - Major challenge to get another institution to prioritize this in-house developed technology.
- CAP Determination
 - The ICF must include a disclosure of all individual and institutional financial interests with the company.
 - Dr. X should not be involved in this study.
 - Dr. X's patients can be enrolled, but Dr. X cannot enroll or consent patients.

- A new non-conflicted study PI, Dr. Z, was selected. Since Dr. Z reports to Dr. X, for purposes of this study Dr. Z should report to the chair of the department.
- An additional non-conflicted WCM faculty member has been designated as a co-investigator external to the division, and will also serve as study liaison to the Data Safety Monitoring Board (DSMB).
- Dr. X and Dr. Y should not be involved in the grading and assessment of adverse events.
- Dr. Y should not consent any patients for this study. Alternative personnel have been selected to approach and consent patients. Dr. Z or other co-investigators should answer any additional study-related questions.
- The alternative personnel selected should not report to Dr. Y regarding the interim outcomes of the study patients.
- If the researchers decide to use WCM's DSMB, it must include external individuals.
- A Research Subject Advocate should be involved in this study to aid in the consenting process.

Case 5: Researcher seeks to have WCM as a Phase 1 trial site to investigate a rare disease

- Background
 - Dr. X proposed a Phase I clinical trial take place at WCM, with Dr. X as PI.
 - Dr. X has equity in the company that is sponsoring the clinical trial.
 - Dr. X's company relationship is managed by a cCMP, limiting their involvement to consultant in any company sponsored research.
- Compelling Circumstances
 - Current management of this patient population predicts less than a 1-year overall survival, with no viable options.
 - Due to the rarity of the disease, only an anticipated 2,000 patients in the US would meet the enrollment criteria.
 - WCM is one of the elite institutions with the expertise and experience to treat patients with this rare disease, using advanced therapeutics.
 - Novel aspects of the science involved, including real time patient imaging, have been developed at WCM.
 - Assembling such a cross-disciplinary team elsewhere, spanning the expertise and specialties across multiple departments as done here, would require exhaustive and time-consuming effort.
 - The trial sponsor may not be able to remain in operation without the timely financing of this Phase I study.
 - All prior work conducted in preparation for this study has been NIH funded. This research advancement will be an important contribution to the field that builds directly on prior studies conducted here at WCM. A recent RO1 grant proposal has been submitted, but the award will not be able to be accepted if this study is not approved.
- CAP Determination
 - The rebuttable presumption was met for the company sponsored clinical trial to be conducted under PIs other than Dr. X at WCM.
 - Dr. X is not permitted to serve as an investigator, as that component of the rebuttable presumption was not satisfied.
 - An external third-party PI is required to join the clinical trial.
 - Dr. X's participation in this study is limited to consultant.