Policy / Procedure:

Conflicts of Interest in Research

KEY TERMS: Awardee, COI, Conflict, Conflict of Interest, FCOI, FDA, Funding, Grant, Interest, IRB, National Institutes of Health, NIH, PHS, Principal Investigator, Research, Subrecipient

I. PURPOSE:

This policy outlines the standards and procedures to ensure that the design, conduct, and reporting of Research activities will not be compromised by any conflicting interest on the part of the Principal Investigator(s) or other Key Research Personnel through implementing a system for the identification, disclosure, evaluation, management, reduction, and/or elimination of potential Conflicts of Interest in accordance with applicable local, state, and federal laws and regulations as well as relevant Carilion Clinic policy.

II. SCOPE:

This Policy applies to all members of the Carilion Clinic Workforce, or those of its subsidiaries, who conduct Research on behalf of Carilion. Such personnel include, but are not limited to contracted faculty and staff, volunteers, and fellows. When Carilion conducts research with external Investigators from other institutions, the disclosure requirements of this Policy will only apply in instances in which the non-Carilion institution does not possess a Public Health Service (PHS)-compliant Financial Conflict of Interest (FCOI) Policy or Carilion and the collaborating institution contractually agree to follow Carilion's *Conflicts of Interest in Research Policy*.

III. DEFINITIONS:

Conflict of Interest (COI): A situation in which an Investigator's, and/or their Family Member's, financial, professional, or other personal considerations may directly or indirectly affect, or reasonably appear to affect, the Investigator's professional judgement in performing their Institutional Responsibilities. A Conflict of Interest may be actual, apparent, or potential.

***de minimis* Threshold:** The minimum threshold for which an Investigator must disclose Financial Interests.

Equity Interest: The ownership share of an individual in a public or private business.

Executive Position: Any position that is responsible for a material part of the operation or management of an organization, which includes but is not limited to: Chief Executive Officer, Chief Operations Officer, Chief Scientific Officer, Chief Medical Officer, Chief Information Officer, Chief Technology Officer, Scientific Director, or Medical Director.

Family Member: For purposes of this Policy, the Investigator's spouse/domestic partner and/or any individual who is related by blood or adoption (e.g., dependent children) to the Investigator.

FCOI Report: Carilion's report of a Financial Conflict of Interest to a PHS Awarding Component, to a lead institution if required under the terms of the sub-recipient agreement, or to a sponsor if required under the contract.

Financial Conflict of Interest (FCOI): A Significant Financial Interest that could directly and significantly affect, or appear to affect, the design, conduct, or reporting of Research.

Financial Interest: Any monetary interest in a sponsor of Research or other key party, held by the Investigator or the Investigator's Family Member within twelve (12) months of the proposal or awarding of Research funding. Under 42 C.F.R. 50.603, a Financial Interest is defined as *anything of monetary value, whether or not the value is readily ascertainable*.

Institutional Official: The individual authorized to act for Carilion in Human Subjects Research protections and who assumes the obligations of the Federalwide Assurance (FWA) for the protection of human subjects with the Office for Human Research Protection (OHRP).

Institutional Responsibilities: An Investigator's professional responsibilities on behalf of the institution, and as defined by the institution in its Policy on Financial Conflicts of Interest, which may include activities such as Research, research consultation, teaching, professional practice, institutional committee memberships, and service on panels such as Institutional Review Boards or Data Safety Monitoring Boards.

Institutional Review Board (IRB): An appropriately constituted group that has been formally designated to review and monitor biomedical Research involving human subjects and is charged with the responsibility for compliance with Federal regulations for the protections of human subjects in Research. An Institutional Review Board (or Boards) has jurisdiction over the research as specified in the Federalwide Assurance (FWA) that the organization has provided to the U.S. Department of Health and Human Services (DHHS), or as otherwise established under DHHS or Food and Drug Administration (FDA) regulation or policy.

Intellectual Property (IP): Patents, copyrights, trademarks, trade secrets, technology, databases, software, and any other tangible or intangible intellectual property.

Investigator: The project director or Principal Investigator, and any other person, regardless of title or position, who is responsible for the design, conduct, or reporting of actual or proposed Research, or proposed funding for Research (e.g., co-Investigators, collaborators, consultants, medical staff members, fellows, students, administrators, or other Key Research Personnel).

Key Research Personnel: Any person, other than the Principal Investigator, who is independently responsible for the design, conduct, or reporting of sponsored Research or educational activities conducted in whole or in part at a Carilion facility.

Management Plan: A strategy developed by the Carilion Research Conflicts of Interest Committee (RCOIC) to mitigate, minimize and/or eliminate COI that could or could reasonably appear to affect a Research project.

Organizational Integrity and Compliance (OIC): The Carilion department responsible for advising on and auditing for institutional compliance with all relevant federal, state, local, and institutional regulations and Policies. The COI administrative staff is located in this department, and OIC's leader, the Chief Compliance Officer, serves as the COI Official and sits on the RCOIC.

PHS: The Public Health Service of the U.S. Department of Health and Human Services, and any components of the PHS to which the authority involved may be delegated, including the National Institutes of Health (NIH).

PHS Awarding Component: The organizational unit of the PHS that funds the Research that is subject to 42 C.F.R. Part 50, Subpart F, 50.601-50.607 and 45 C.F.R. Part 94, 94.1-94.6.

Principal Investigator: The project director or Investigator who meets the qualifications and requirements outlined in the Carilion Clinic Policy: " Principal Investigator (PI) Eligibility", regardless of funding source, and who has the full and final responsibility for the conduct of the activities as described in the protocol as well as protecting the rights and welfare of participants involved in the Research.

Research: A systematic investigation, study, or experiment designed to develop or contribute to generalizable knowledge relating broadly to public health, including behavioral and social-sciences Research. The term encompasses basic and applied Research and product development when such Research or product development is funded by the Public Health Service (PHS). It includes any such activity for which Research funding is available from a PHS Awarding Component through a grant or cooperative agreement, whether authorized under the PHS Act or other statutory authority, such as a Research grant, career development award, center grant, individual fellowship award, infrastructure award, institutional training grant, program project, or Research resources award. It also includes all Research meeting the definition of "Research" performed with "human subjects" as these terms are defined in the Federal Common Rule (45 C.F.R. 46 and 21 C.F.R. 56), regardless of the source of Research funding or whether the Research is otherwise subject to federal regulation.

Research Conflicts of Interest Committee (RCOIC): The body at Carilion responsible for reviewing disclosed COIs/FCOIs related to research activities and for creating management plans to mitigate or eliminate any identified conflicts. For more information, see the Carilion Clinic Policy: *Research Conflict of Interest Committee Policy*, (OIC).

Significant Financial Interest (SFI): For the purposes of this Policy, a Significant Financial Interest (SFI) includes an external Financial Interest consisting of one or more of the following interests of an Investigator (and those of the Investigator's Family Member[s]) reasonably related to their Institutional Responsibilities, when combined for the twelve (12) months preceding the disclosure date, or reasonably known to occur in the twelve (12) months following the disclosure date, when combined from a single entity:

i. Renumeration, compensation, and/or other payments for services (e.g., consulting, speaking), which exceed $5,000.

ii. Equity interests in a single publicly traded entity, which exceeds $5,000 or 5% ownership.

iii. Equity Interests, including stock options, in a non-publicly traded entity (e.g., a start-up company) of any amount.

iv. Intellectual property rights and interests (e.g., patents, copyrights), upon receipt of income related to such rights and interests.

v. Sponsored or reimbursed travel for Investigators, which is paid on behalf of the Investigator and not reimbursed to the Investigator, related to their Institutional Responsibilities. This definition does not include travel that is reimbursed or sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), a research institute that is affiliated with an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, or a medical center.

vi. This definition does not include income from seminars, lectures, or teaching engagements sponsored by a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), a research institute that is affiliated with an institution of higher education as defined at 20 U.S.C. 1001(a), or an academic teaching hospital.

vii. This definition does not include income from service on advisory committees or review panels for a Federal, state, or local government agency, an Institution of higher education as defined at 20 U.S.C. 1001(a), a research institute that is affiliated with an institution of higher education as defined at 20 U.S.C. 1001(a), an academic teaching hospital, or a medical center.

viii. This definition does not include income from investment vehicles, such as mutual funds and retirement accounts, as long as the Investigator does not directly control the investment decisions made in these financial vehicles.

Subrecipient: A third-party organization that receives funding from a primary recipient or another subrecipient to collaborate in carrying out externally funded research or a program. This may include subcontractors, subawardees, and cooperative/consortium members.

Trainee: An individual working as a mentee of a Principal Investigator. This can include, residents, fellows, postdoctoral associates, and students.

Workforce: Carilion Clinic employees and contractors, suppliers, volunteers, researchers, clinical and non-clinical students, residents and non-employed members of a Carilion Clinic hospital medical staff only when their conduct, in the performance of work for Carilion Clinic, is under the direct control of Carilion Clinic.

IV. PROCEDURE:

A. Procedural Background:

The mission of Carilion Clinic is to improve the health of the communities we serve by providing patient-centered care, supporting excellence in medical education, and accelerating clinical and translational Research. Consistent with this mission, Carilion, and its designees, will collaborate with partners in industry, government, academia, and other organizations to accomplish those goals. By their nature, these relationships are often complex and require careful navigation to preserve the integrity of the Research conducted at Carilion as well as to ensure the safety of those participating in Research. It is important to avoid instances where the interests of an individual can (or can reasonably appear to) affect the design, conduct, or reporting of Research.

Carilion Clinic has adopted the Conflict of Interest standards of the Public Health Service (PHS) for all its Research activities, committing to the highest ethical standards with respect to Conflict of Interest in Research. Any interests or relationships shall be disclosed *at the time* any Research is submitted to Carilion's Office for Research and Development for review and initial approval, or *before* Research funding is applied for or expended.
It is important to note, that the mere disclosure of an interest or relationship does not necessarily mean that a conflict exists, or that if it a conflict exists that it is averse to applicable regulatory requirements, Research-related activities or the interest of Carilion Clinic.

B. Situations or Relationships in Which a Conflict Impacting Research May Arise:

1. Under this Policy, potential Conflicts of Interest in Research include, but are not limited to, the following as it relates to a specific Research study, sponsor, or other related organization, company, or individual:
    a. An arrangement between Carilion, the Investigator, or a company in which the Investigator has an interest that involves compensation, business courtesies/gifts, a transfer of property, or a right to use property. This includes, but is not limited to:
        i. Employment;
        ii. Holding Executive Positions or serving on advisory boards;
        iii. Receiving honorarium(-ia) for consulting, advising, or participating on speaker's bureaus;
        iv. Having Intellectual Property rights (e.g., patents, copyrights, royalties);
        v. Having an Equity Interest, such as stocks, stock options, or ownership interests; or

vi. Receiving any gifts, courtesies, or travel expenses paid on their behalf;

b. An Investigator's Financial Interest in agencies, organizations, and associations, which have the potential to influence or affect the applicable research study;
c. A loan between the Investigator and a sponsor of a research study;
d. A grant scholarship or other financial assistance between the Investigator and a sponsor of a research study; or
e. An Investigator's Family Member or business relationship interest in any of the above.

The items described above are only examples of situations or relationships in which a conflict may arise. Conflicts may arise in other situations or through other relationships. The Chief Compliance Officer (as COI Official), Chief Legal Counsel, Institutional Official and their respective teams are available to discuss particular scenarios with Investigators when questions arise.

C. Disclosure:

1. PHS-funded Institutions are required by federal regulation to appoint a COI Official whose responsibilities are to solicit and review Financial Interests in PHS-sponsored Research. The Carilion Chief Compliance Officer serves in that capacity, and the COI staff in Organization Integrity and Compliance (OIC) reviews relevant Financial Interests via the administration of an annual COI disclosure process.
2. Disclosure or reaffirmation of previous disclosure to Carilion must be performed:
    a. Within fourteen (14) days of starting work at Carilion via the annual COI disclosure instrument.
    b. At the time of joining a Research study as Key Research Personnel if an annual COI disclosure was not already required.
    c. At the time of application for Research funding.
    d. At the time of an IRB application, continuing review, or amendment.
    e. Within thirty (30) days of a change, addition, or elimination of a previously disclosed SFI.
    f. Within thirty (30) days of the occurrence of any trip for which there is reimbursement or sponsored travel that constitutes an SFI.

Previously submitted COI disclosures are reaffirmed and/or updated on an annual basis by personnel regardless of participation in Research at Carilion.

D. Review of COI Disclosures:

1. All individuals subject to Carilion's COI disclosure process due to the classification of their position must submit an annual COI disclosure to Carilion within fourteen (14) days of starting work.
2. Carilion OIC is responsible for the collection and initial screening review of all annual COI disclosures.
3. OIC COI staff will send an email acknowledgement in response to COI disclosures that contain either no Financial Interest or are less than the *de minimis* Threshold.
4. OIC COI staff will refer COI disclosures that identify a potential COI, to the Carilion Research Conflicts of Interest Committee (RCOIC) for further evaluation and when applicable, the RCOIC will appropriately manage the COI.

5. The review, determination whether or not a COI exists, and development of a management plan, when applicable, will be completed as soon as possible to avoid delays in the conduct of Research.
6. Information provided in COI disclosures will remain confidential to the extent allowable by applicable laws and regulations.

E. Management of Actual and Potential COI or FCOI:

1. When the RCOIC finds that an Investigator's disclosure is a COI, a Management Plan will be developed and implemented to specify the actions that will be taken to manage the specific COI. Examples of conditions or restrictions to manage a COI include, but are not limited to:
    a. Public disclosure of the COI (e.g. when presenting or publishing the research or addendum to previously published presentations);
    b. For Research projects involving human subjects Research, disclosure of the COI directly to the participants;
    c. Appointment of an independent monitor capable of taking measures to protect the design, conduct, and reporting of the Research;
    d. Modification of the Research study;
    e. Change of personnel or personnel responsibilities, or disqualification of personnel from participation in all or a portion of the research;
    f. Reduction or elimination of the Financial Interests (e.g. sale of an Equity Interest);
    g. Severance of relationships that create financial conflicts; or
    h. No administrative approval for a specific Research study.

2. **Most COI situations involve common disclosures for which the RCOIC can develop standard Management Plans.** However, some cases of COI can be more complex, and customized Management Plans may need to be developed at the discretion of the RCOIC.

F. Reporting Requirements to the National Institutes of Health (NIH):

1. Prior to the expenditure of any funds under a PHS-funded Research project, the COI Official (or designee) shall either:
    a. Notify the Carilion Clinic Office of Research and Development that no FCOI exists; or
    b. If a FCOI exists, provide a FCOI report for the Investigator's and Subrecipient's Investigator's FCOIs to include the applicable Management Plan to the PHS Awarding Component.
    c. If the identified FCOI has been eliminated prior to the expenditure of PHS-awarded funds, no report will be provided to the PHS Awarding Component.
2. The COI Official (or designee) will provide a FCOI report to the PHS Awarding Component for any newly identified FCOI during an ongoing PHS-funded research project including the applicable management plan within sixty (60) days of disclosure.

3. If a FCOI is not disclosed, identified or managed in a compliant and timely manner, Carilion shall complete a retrospective review and file a report to the PHS Awarding Component within 120 days of the discovery of noncompliance. This review will be completed as indicated in Section IV. J. of this Policy.
4. For ongoing PHS-funded Research, including extensions with or without funding, the COI Official (or designee) shall provide an annual FCOI report to the PHS Awarding Component that addresses the status of the FCOI and any changes to the management plan for the duration of the PHS-funded Research project. The submission of the annual FCOI report shall be completed at the same time as the annual progress report or multi-year progress report submitted by Carilion or other Carilion entity to PHS.
5. In any case in which the HHS 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 has been designed, conducted, or reported by an Investigator with a FCOI that was not managed or reported by the Carilion as required, Carilion shall require the Investigator to disclose the FCOI in each public presentation of the results of the Research and to request an addendum to previously published presentations.

G. Training Requirements:

1. Each Investigator who is new to Carilion is required to initially complete COI training prior to submitting a Research study for approval by the Office of Research and Development or applying for Research funding for the first time.
2. At a minimum, Investigator(s) will complete the COI training every four (4) years, and as requested, if Carilion significantly revises this Policy or if an Investigator is not in compliance with the policy or applicable Management Plan.
3. The COI training module will be made available electronically, and Investigators will receive a notification when they are due to complete COI training. Alternative methods of training will be made available when deemed necessary.

H. Public Accessibility Requirements:

1. Members of the public may request access to this Policy by sending a request to Carilion OIC at researchcompliance@carilionclinic.org. Within five (5) business days of the request being made to OIC, Carilion shall make available a copy of this Policy to the requestor.
2. Members of the public may also contact Carilion OIC at researchcompliance@carilionclinic.org to request information concerning any related FCOIs that have been identified and are still held by PHS-funded Investigators. Such requests will be fulfilled within five (5) business days of the request being made to OIC. The provided information will include current information pertaining to any identified FCOI as follows:
    a. Investigator's name, title with respect to the involved Research project;
    b. Name of the entity in which the FCOI is held;
    c. Nature of the FCOI (e.g. honorarium, travel reimbursement, etc.); and
    d. Approximate dollar value or range of the FCOI or a statement that the interest is one whose value cannot be readily determined through reference to public prices or other reasonable measures of fair market value.

I. Subrecipients:

1. Subrecipients to Carilion Clinic
    a. When Carilion is a primary/Subrecipient and engages another Subrecipient to assist in the funded Research/program, the written agreement between Carilion and the Subrecipient shall include terms that establish whether Carilion's COI Policy or that of the Subrecipient will apply to the Subrecipient's Investigators. This determination will be made on a case by case basis.
        i. If a determination is made that the COI Policy of the Subrecipient will be followed: The Subrecipient shall certify as part of the agreement that its policy complies with 42 C.F.R. 50, Subpart F, 50.604, and
        ii. The agreement shall specify time period(s) for the Subrecipient to report all identified COIs to Carilion in a timely manner.
    b. If the agreement establishes that the Subrecipient Investigators will comply with the Carilion COI Policy or the Subrecipient is unable to provide certification of compliance with 42 C.F.R. 50, Subpart F, 50.604, the Subrecipient Investigators shall report disclosures of Financial Interests relating to the Investigator's work as defined in the agreement to Carilion within a timely manner.
        i. The timing of the Subrecipient's reporting shall allow Carilion sufficient time to comply with reporting obligations as stated above in Section F.
        ii. The COI Official (or designee) will be responsible for providing FCOI reports to any applicable external agencies or primary recipients regarding all Subrecipient Investigator's FCOI in accordance with this Policy and other applicable standards.
2. Carilion Clinic as a Subrecipient
    a. When Carilion Clinic is acting as a Subrecipient, the written agreement between Carilion Clinic and the prime/Subrecipient should include terms that establish whether Carilion's COI Policy or that of the other party will apply to Carilion Investigators.
    b. If a determination is made that the COI Policy of the other party will be followed, Carilion shall abide to the policy and contract requirements.
    c. If a determination is made that the Carilion's COI Policy will be followed, the COI Official (or designee) will be responsible for providing FCOI reports to the prime/Subrecipient.

J. Consequences of Noncompliance:

1. If a COI is not disclosed, identified or managed in a compliant and timely manner, the RCOIC will be notified, and Carilion will complete a retrospective review within one hundred twenty (120) days of the discovery of noncompliance. The COI Official (or designee) will conduct and document the retrospective review to include the following elements:
    a. Reasons for the retrospective review;
    b. Research project title, number, and Principal Investigator;
    c. Name of Investigator with the COI;
    d. Method for completing the review;

e. Nature and value of the COI;
f. Findings and conclusion of the review (including an analysis of whether the Research study is salvageable); and
g. Description of the key elements of the Management Plan including:
   i. The role and principal duties of the conflicted Investigator in the Research project;
   ii. Conditions of the Management Plan;
   iii. How the Management Plan is designed to safeguard objectivity in the Research;
   iv. Confirmation of the Investigator's agreement to the Management Plan;
   v. How the Management Plan will be monitored to ensure Investigator compliance; and
   vi. Other information as needed.

2. Carilion may determine that interim measures will be necessary with regard to the Investigator's participation in the study between the date that the COI or the Investigator's noncompliance is determined and the completion of the retrospective review. Such a determination will be based on the recommendation of the RCOIC in consultation with Carilion leadership.
3. The COI Official (or designee) will present the findings of the retrospective review to the RCOIC to determine what additional measures, if any, are necessary.
4. Carilion will update any previously submitted FCOI reports made to external agencies or funding sources (e.g. primary award recipients), specifically addressing the identified non-compliance, actions to be taken to manage the FCOI going forward and if any bias was identified. (Refer to Section IV. F. for reporting requirements).
5. The COI Official (or designee) in collaboration with the RCOIC and Carilion leadership will monitor Management Plans for Investigator compliance on an ongoing basis until the completion of the Research project

V. OTHER ISSUES / CONCERNS:

References:

- 21 C.F.R. Part 54 Financial Disclosure by Clinical Investigators

- 42 C.F.R. Part 50, Subpart F, 50.601-50.607 and 45 C.F.R. Part 94, 94.1-94.6, as amended by the Finale Rule on Financial Conflict of Interest Regulations, revised regulations, Responsibility of Applicants for Promoting Objectivity in Research for which Public Health Service Funding is Sought and Responsible Prospective Contractors (76 FR 53288), dated August 25, 2011 and effective August 24, 2012.

- 45 C.F.R. Parts 160 and 164, as amended by the Privacy and Security Provisions set forth in Section 13400 of the Health Information Technology for Economic and Clinical Health Act, Public Law 111-5 ("HITECH Act") and the rules promulgated thereunder (collectively referred to herein as the "HIPAA Rules").

- Carilion Clinic Policy: *Principal Investigator (PI) Eligibility*, (Research and Development)
- Carilion Clinic Policy: *Research Conflict of Interest Committee Policy*, (OIC)

Approvals

Name	Title	Dept./Committee	Date
Jeanne Armentrout	CAO and EVP	Administration	06-12-2020
Patrice Weiss	CMO and EVP	Administration	06-12-2020
Ralph E. Whatley	Research Liaison	Education and Research	06-02-2020