



CASE CONFLICT OF INTEREST COMMITTEE

**Case Western Reserve University
Faculty and Sponsored Research
Conflict of Interest Procedures Manual
September, 2007**

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I. INTRODUCTION

A. Case Policy on Conflict of Interest

The Case Policy on Conflict of Interest, which can be found at:

http://ora.ra.cwru.edu/research/orc/Attachments/COI/COI_GeneralPolicy.pdf

describes the overall University policy regarding conflict of interest (COI) and the general framework for review and management of reported potential conflicts of interest. However, the specific details regarding the process by which potential conflicts of interest are reported, reviewed, and managed are not elaborated upon in the policy.

B. Purpose of the COI Procedures Manual

The purpose of the present document is to provide additional information regarding procedures related to faculty and sponsored research conflicts of interest at Case: to define more specifically who is required to report significant financial interests that could lead to a potential COI, what constitutes a significant financial interest, how COI reporting is reviewed, and how COIs can be managed. The intent of these procedures is to protect the integrity and credibility of Case and its faculty and staff and to maintain compliance with federal regulations. These procedures may be amended from time to time by the University as the need arises.

II. THE CASE CONFLICT OF INTEREST COMMITTEE

A. COIC Membership

The Case Conflict of Interest Committee (COIC) is composed of members appointed on an annual basis by the President of Case who are 1) University officials and who represent or have access to the following Offices: Research Administration, Technology Transfer, Finance and Administration, and General Counsel and Internal Audit (the latter two in an advisory, non-voting capacity), 2) Faculty, and 3) Compliance representatives from University Hospitals of Cleveland, the MetroHealth System, Louis Stokes Cleveland Department of Veterans Affairs Medical Center, and the Cleveland Clinic Foundation, to include representatives who have direct administrative responsibility for their IRBs or research compliance officers charged by their respective institutions with serving as liaison to the pertinent IRBs.

B. Duties of the COIC

The primary duties of this Committee are as follows:

1. The ongoing development of conflict of interest policy and procedures. (Where appropriate, these policies and procedures will be reviewed and approved by the Faculty Senate Research Committee, the Faculty Senate in its entirety, and/or the Board of Trustees).
2. Coordination of these policies and procedures with the affiliate/partner hospitals.
3. The review of conflict of interest reporting submitted by Faculty and investigators on sponsored research.
4. The development of conflict of interest management plans, in consultation with Deans and Department chairs, as necessary.

III. THE COI ADMINISTRATOR

The role of the COI Administrator is to administer the Case Conflict of Interest policies and procedures.

A. Duties of the COI Administrator:

The responsibilities of the COI Administrator will include:

1. Tracking COI reporting information, and providing data on compliance to the COIC and the Assistant Vice President for Research Compliance.
2. Consulting with investigators and with members of the COIC, as needed, and drafting COI management plans.
3. Documenting COIC review of management plans and communicating with investigators regarding same.
4. Monitoring COI management plans periodically to review compliance with and the need for alteration to the management plan.
5. Providing staffing support to the COIC.
6. Developing and implementing mechanisms for communicating to Faculty and Staff policy and procedure changes as they relate to conflict of interest.
7. Providing education and training programs for Faculty and Staff in the area of Conflict of Interest.

8. Maintaining the COI web page.
9. Maintaining COI reporting information and COI management documents in a secure and confidential manner.

B. The COI Web Page.

The Case COI Policy, as well as this Case COI Procedures Manual can both be accessed from the Case Office of Research Compliance web page. For further information regarding Case Faculty and Sponsored Research COI policy and procedures, Case COI reporting, and links to many of the guidance references cited below, please see:

<http://ora.ra.cwru.edu/research/orc/coi/index.cfm>

C. COI Record-Keeping

It will be the responsibility of the COI Administrator to ensure, on behalf of the Case COIC, that paper records of financial reporting (and action taken to manage conflicts) will be maintained in a secure and confidential manner for at least three years after the termination or completion of the project to which they pertain or resolution of any civil, government or University actions involving the records, whichever is later.

It will also be the responsibility of the COI Administrator to work with the IT Manager to ensure that electronic records are maintained in a secure and confidential manner.

IV. CASE COI REPORTING POLICY AND FEDERAL REGULATIONS

A. Faculty COI Reporting

Per the Case Policy on Conflict of Interest, all Faculty members are required to annually report:

“situations involving conflicts of interest, such as (but not limited to): financial dealings that are contrary to the University's best interests, membership or employment relationships that may be in conflict, acceptance of favors, money or other considerations, which might obligate the recipient to take actions adverse to the University's interest.”

Such conflicts might include preferential procurement of supplies from a Company in which the Faculty member has a financial interest, or preferential

contractual agreement with a Company for which the Faculty member's spouse is employed.

B. Sponsored Research COI Reporting

1. Regulations and Guidance

The University has designed its conflict of interest procedures to be in compliance with federal regulations concerning objectivity in research and according to guidelines from the Association of American Universities, the American Association of Medical Colleges, and other professional associations (see Appendix). As a result, all researchers who propose or conduct sponsored research, **regardless of the source of funds**, must report certain financial interests to the University. The University must decide whether there could be the appearance that the financial interests reported could bias the design, conduct, or reporting of research projects, thus constituting a conflict of interest. If so, the University must manage, reduce, or eliminate the conflict of interest prior to the expenditure of any funds under an award.

Per the federal regulations, which can be found at:

<http://grants.nih.gov/grants/guide/notice-files/not95-179.html>

all **investigators** must report to the University any significant financial interests that could reasonably affect or be affected by their federally sponsored research. An "investigator" is defined as, "the principal investigator, a co-investigator or any other person responsible for the design, conduct, or reporting of sponsored research funded or proposed for funding."

Please see:

<http://grants.nih.gov/grants/policy/coifaq.htm>

These individuals must report to the University all significant financial interests that could reasonably affect or be affected by their federally sponsored research by the time a grant application is submitted to a federal sponsor or before a federal contract is executed.

Conflict of interest and its potential effect on objectivity and the conduct of research is not only an issue for federally sponsored research. The potential for conscious or unconscious bias, additional risk for human subjects, creating the perception of possible bias/risks, and the potential erosion of public trust extends to all sponsored research. Many institutions and professional societies have adopted or recommended policies for full disclosure by investigators involved in all sponsored research. Websites that contain descriptions of these policies or recommendations include the following:

<http://www.aamc.org/research/coi/start.htm>

<http://www.upenn.edu/almanac/v47/n21/ORdisclosure.html>

http://grants.nih.gov/grants/policy/nihgps_2001/part_ia_1.htm#_Toc504811782

To this end, Case's COI procedures require that all investigators who are seeking or engaged in sponsored research report to the University all significant financial interests that could reasonably affect or be affected by their sponsored research by the time a grant application is submitted to any sponsor or before a contract is executed. Please see the Appendix for examples of situations that need to be reported and those that do not.

2. Definition of a Sponsored Research Conflict of Interest

A sponsored research **conflict of interest** exists when the University determines that a **significant financial interest** could directly and significantly affect or be affected by the design, conduct, or reporting of sponsored research or activities.

A significant financial interest generally involves anything of monetary value above certain thresholds set by the federal government, but not including salary and compensation from Case and certain types of other income. More specifically, a significant financial interest is defined as:

1) Salary or other payments for services, e.g., consulting fees or honoraria expected to exceed \$10,000 from a single entity in the next twelve months (when aggregated to the investigator, investigator's spouse and dependent children);

2) An equity interest e.g., stock, stock options, or other ownership interests, etc., with a fair market value over \$10,000 or which represents more than a 5% ownership in any single publicly held entity (when aggregated for the investigator, investigator's spouse, and dependent children);

3) Any equity interest in a privately held company (by the investigator, the investigator's spouse or dependent children)

4) Holding the position of officer (e.g., CEO, Chief Scientific Officer, VP for Research) or board member (Board of Directors, Scientific Advisory Board) of a company (by the investigator, the investigator's spouse or dependent children).

5) Intellectual property rights (e.g., licensed patents, copyrights and royalties from the rights)

6) Note: While NIH does not require that notification of financial interests that are related to Small Business Innovation Research (SBIR) or Small Business Technology Transfer (STTR) grants, Case does require that information regarding such financial interests be reported to the University.

It is important to note that these thresholds are applied in the aggregate to the investigator and his/her immediate family (i.e., spouse and dependent children).

c. Financial Interests, the reporting of which is not required

Investigators are not required to report the following:

- 1) Salary, royalties, or other compensation from Case;
- 2) Income from seminars, lectures, or teaching sponsored by public or nonprofit entities;
- 3) Income from service on advisory committees or review panels for public or nonprofit entities;
- 4) Income from mutual funds;

V. THE CASE COI REPORTING PROCESS

A. The Annual Faculty and Sponsored Research COI Form

At Case, the reporting of significant financial interests for faculty members and investigators on sponsored research is conducted annually and is updated, as necessary, at the time of a grant submission and during the period of an award, as new reportable significant financial interests are obtained. It should be noted that no sponsored project account will be established by the university unless current COI reporting has been done by all investigators associated with the project.

The annual COI reporting process for faculty and investigators on sponsored research is conducted by the Conflict of Interest Administrator in the Office of Research Compliance, under the direction of the Case Conflict of Interest Committee and the Assistant Vice President for Research Compliance. The information reported on these forms is maintained in confidence by the Case COIC, and used only for assessing and managing conflicts of interest and not for any other purpose.

Any reporting of a significant financial interest should provide sufficient detail to permit an accurate and objective review by the Case Conflict of Interest Committee assisted by the COI Administrator. Additional information may be requested.

1. COI Reporting by All Faculty Members

With respect to faculty, each year a request to complete the Faculty and Sponsored Research Conflict of Interest Form ("COI form") is sent by the Deans' offices to their respective faculty members as part of the reappointment process. Faculty members are defined as Board of Trustees-appointed full professors, associate professors and assistant professors, as well as senior instructors and instructors. COI reporting must be submitted, even if there are no significant financial interests to report.

2. COI Reporting by Faculty Investigators

All faculty members should complete the Faculty section of the COI form. Faculty members who are also investigators or key personnel on sponsored research should complete the Sponsored Research section of the COI form, as well.

Federal conflict of interest regulations define the "investigator" as the "principal investigator and any other person who is responsible for the design, conduct, or reporting of funded research," including the investigator's spouse and dependent children (42 CFR § 50.603). According to the NIH COI site review report, "(NIH) Targeted Site Reviews on Financial Conflict of Interest Observations of February 14, 2007," this definition should be interpreted broadly (please see:)

http://grants.nih.gov/grants/policy/coi/TSR_Observations_2-14-2007.doc

3. COI Reporting by Non-Faculty Investigators

Each year non-faculty investigators receive a request from the Conflict of Interest Administrator to complete the Faculty and Sponsored Research COI form. Investigators who are not faculty should complete only the Sponsored Research section of the form.

If the investigator does not comply with the request for the annual COI form (even if there are no significant financial interests to report), the principal investigator of the sponsored project is contacted for assistance in collecting the form.

4. Updating the Case Faculty and Sponsored Research COI Form

Faculty and investigators must update their Case conflict of interest reporting information during the period of any award whenever a new reportable significant financial interest arises, or in the case of investigators, if the relationship changes between the significant financial interest(s) and the sponsored research.

5. Instructions for submitting the Case Faculty and Sponsored Research COI Form

For a link to the Case Faculty and Sponsored Research Conflict of Interest form, links to the Case COI policy and procedures documents, as well as information regarding the Case Conflict of Interest Committee, please see the Case Office of Research Compliance Conflict of Interest web page

<http://ora.ra.cwru.edu/research/orc/coi/index.cfm>

B. COI Reporting on the University Review Form

In addition to annual COI reporting, the University Review Form, which is submitted with each sponsored project grant application or contract, requires basic conflict of interest reporting information for all investigators. This includes whether any of the investigators has a conflict of interest with the proposed sponsored research. Based on the information provided on the University Review Form, a revised Conflict of Interest form may be required.

Enforcement/Sanctions: The Grants and Contracts Office will not submit a proposal to a sponsor or execute a research agreement on behalf of an investigator who has not submitted the required annual Case COI form. The University will not accept or administer grants or contracts whose investigators have not complied with these directives.

C. COI Reporting by Collaborators/Subcontractors

In accordance with DHHS rule entitled, "Responsibility of Applicants for Promoting Objectivity in Research for which PHS Funding is Sought" (42 CFR Part 50, Subpart F), SUBCONTRACTOR certifies that it has established Conflict of Interest Policy that complies with all requirements, rules, procedures, and principles of 42 CFR Part 50, Subpart F, incorporated herein by reference. Per this DHHS rule, should SUBCONTRACTOR identify an investigator(s) who has a conflict of interest with the Statement of Work, the SUBCONTRACTOR will notify CASE of said conflict of interest and whether it is being eliminated, reduced or managed within 30 days of it being identified by the SUBCONTRACTOR.

If Subcontractor does not have a Conflict of Interest Policy, it agrees to abide by and comply with all rules, regulations, and procedures of CASE's Conflict of Interest Policy (http://ora.ra.Case.edu/main_research_compliance_page.htm). Upon written request by CASE, Subcontractor also agrees to furnish a copy of its Conflict of Interest Policy to CASE within 30 days of receipt of request.

D. COI Reporting to the IACUC and IRBs

Finally, the Institutional Animal Care and Use Committee (IACUC) and the Institutional Review Boards (IRBs) of Case, University Hospitals of Cleveland,

The MetroHealth System, the Louis Stokes Cleveland Department of Veterans Affairs Medical Center, and the Cleveland Clinic Foundation require that basic conflict of interest information for all investigators be reported with each application to the IACUC or the IRB.

VI. COIC REVIEW OF COIs REPORTED

A. Review of Faculty COI Reporting

Faculty conflicts of interest reported on the annual form and collected by the Conflict of Interest Administrator will be reviewed by the Conflict of Interest Committee. Unless these Faculty COIs involve sponsored research, they will be referred to the appropriate University official, e.g., Department Chairs, Deans or the Provost. Please see the General Conflict of Interest policy for further information.

http://ora.ra.cwru.edu/research/orc/Attachments/COI/COI_GeneralPolicy.pdf

Or please refer to the Faculty Handbook

B. Review of Sponsored Research COI Reporting

Possible sponsored research conflicts of interest may be reported to the COIC by the investigator / key personnel on the annual form; by the IACUC or IRBs; by the Office of Technology Transfer; or by members of the research community. When a possible conflict of interest is identified, the COI Administrator and/or other members of the Case COIC will consult, as necessary, with the investigator(s) to assess the possible conflict of interest.

The COI Administrator will draft, with the assistance of the investigator, appropriate documentation of the financial interest, the sponsored research, and the relationship between financial interest and sponsored research, if any, and such documentation will be then brought before the COIC.

1. COIC Actions in Response to a Conflict of Interest.

Federal regulations require that conflicts of interest be reduced, managed or eliminated. Options for managing the conflict of interest in sponsored research include:

- a. Accept the sponsored project without any restrictions;
- b. 2. Accept the sponsored project with certain conditions or restrictions, which could include any of the following:

1) Eliminate the conflict.

- Divestiture of the financial interest that results in the perceived conflict / severance of relationships that create the perceived conflict of interest

OR-

- Recusal of the conflicted investigator from participation in the sponsored research.

2) Develop a COI management plan to include any of the following:

- Appropriate public disclosure of significant financial interests (e.g., on publications and presentations, to research staff and advisees, to relevant IRB and IACUC officials, on informed consent documents);
- Adoption of specially created review procedures to ensure that conflicting interests do not compromise the integrity of the design, conduct or reporting of the funded research project;
- Monitoring of the research by independent reviewers;
- Modification of the research plan;
- Withdrawal of conflicted investigators from all or a part of the funded research project that would be affected by the significant financial interests (e.g., from subject selection, from data analysis, as principal investigator);

(Please see Section IX for additional detail on COI management plan options).

- c. Refuse the sponsored project

2. The COI Management Plan

Possible sponsored research conflicts of interest reported in the annual Faculty and Sponsored Research COI form will be compiled for and presented to the Case COI Committee by the Case COI Administrator. Further information will be collected by the COI Administrator on specific possible conflicts of interest deemed a priority by the COI Committee. Where the Committee determines that a conflict of interest exists for a particular investigator, the Committee will decide upon the appropriate action.

Once a conflict of interest has been identified, a plan of conditions or restrictions to manage, reduce or eliminate any such conflict will be designed in consultation with the conflicted investigator, and possibly in conjunction with the appropriate department chair and/or dean. The Case Conflict of Interest Committee will review the draft conflict of interest management plan.

a. Review of Management Plans by the COIC

Review and approval of management plans may occur via a quorum of the convened Case Conflict of Interest Committee or via email vote.

The COIC may approve a management plan by email vote as long as quorum is met, the vote is unanimous, and there is no call by any COIC member for discussion and vote at the convened Committee meeting.

b. Concurrent COIC and IRB review

If an investigator is working with the Case COIC to develop a COI management plan at the same time as she or he is submitting a protocol to a Case or affiliate IRB for IRB review, then COIC review may occur concurrently with the Case or affiliate IRB protocol review, if there is no objection by the COIC or by the pertinent IRB. A draft COI management plan can be provided by the COI Administrator to the appropriate Case or affiliate IRB representative on the COIC. As required for IRB review, excerpts of the draft COI management plan pertaining to conduct of human subjects research may be made available to the IRB members in the form of a letter to the Board from the COIC.

The Case or affiliate IRB may conditionally approve a protocol pending COIC final approval of the COI management plan, with the understanding that a change by the COIC to the final approved COI management plan could result in amendments to the IRB protocol.

The IRBs have the option of imposing additional COI requirements that may be more, but not less stringent than those recommended in the final COIC-approved COI management plan.

c. Investigator Notification of the COIC-approved Management Plan

As the COI draft management plan is being developed, the investigator will have the opportunity to suggest edits and provide comments to drafts of the document, which will be addressed administratively or communicated to the COIC, as appropriate. Once a conflict of interest management plan is approved by the COIC, the Committee's decision concerning the management of the conflict of interest shall be communicated in writing to the investigator.

The investigator is asked to maintain a conflict of interest file containing the approved, signed management plan, as well as other documents, as required by the management plan. These documents may be requested upon conflict of interest monitoring (see below).

d. Distribution of the Final Management Plan to the IACUC and/or IRB(s)

A final approved management plan is provided by the COI Administrator to the members of the COIC who represent all affected regulatory committees, (e.g., IRBs, IACUC). These COIC members may report to the pertinent IRB membership on the content of the management plan as it pertains to human subjects research, or the COIC may provide to the pertinent IRB membership excerpts of the management plan that pertain to human subjects research, as needed. The IRB or IACUC cannot approve a protocol that contains a management plan that is less strict than the one approved by the COIC. However, the IRB or IACUC can require elements that are more stringent than those required by the COIC. The IRBs and IACUC will be asked keep the COIC informed of any such additional mandates related to conflict of interest.

If the COIC-approved management plan is sent to the respective IRB or IACUC representatives after a protocol has already been approved, the IRB or IACUC will require the investigator to submit an amendment that incorporates those elements of the COIC-approved management plan that are not already contained in the protocol approved by the IRB or IACUC.

e. Appeal of the COIC Decision

If the investigator is dissatisfied with the determination of the Committee, the investigator may submit a written appeal to the Provost within ten (10) days of receipt of the decision. The decision of the Provost is final.

f. Disciplinary Action Resulting from Failure to Comply with COI Requirements

Failure to report significant financial interests in a timely manner or refusal to cooperate in the management, reduction, or elimination of conflicts of interest will be grounds for disciplinary action consistent with the Case Human Resources Policies and Procedures or the Faculty Handbook. Other actions could include suspending the research project or prohibiting the establishment of a sponsored project account.

3. Monitoring of COI Management Plans

The Case Conflict of Interest Committee, pursuant to Federal regulation 42 CFR part 15, requires monitoring of documented conflicts of interest involving any individual covered by the Case COI policy for whom a conflict of interest management plan has been instituted. Monitoring of the management plan will be scheduled to document compliance with the most recent management plan, to determine whether the relationship between significant financial interests and sponsored research has changed or is expected to change, and to update the

management plan based on new information from the investigator and new standards established by the Conflict of Interest Committee.

a. Frequency of COI Monitoring

Monitoring will be conducted by the Conflict of Interest Administrator, in conjunction with a member or members of the Conflict of Interest Committee, as needed (e.g., IRB Officials or Compliance Officers of the affiliate/partner hospitals). Monitoring of previously drafted management plans will be performed at least every three years. The COIC may determine that a management plan requires more frequent monitoring (e.g., involves human subject research). More frequent monitoring may also be initiated if problems are identified by either the COI Administrator or members of the COIC.

b. The Monitoring Process

Monitoring will include review of the individual's current COI file. The investigator will be notified in writing that his or her file has been selected for monitoring and given the reason for such selection, e.g., routine monitoring, and further information will be requested of the investigator via interview, written response or site visit.

A monitoring report will be generated by the monitors, brought before the COIC for review and approval, and kept in the investigator's conflict of interest file in the Office of Research Compliance. A monitoring report must be brought to the COIC for a vote (with one exception, as below), and if the COI management plan is revised, then the revised COI plan also requires a vote.

The exception to the rule that monitoring reports require a vote would be if upon monitoring, it is determined administratively that there is currently no conflict of interest. This monitoring report would be accompanied by an Administrative Review (a document that does not require review or vote--see below for further details). In this event, the COIC would be informed of this administrative determination. However, any member could request that the monitoring report and administrative review document be reviewed and, as required by the Committee, voted upon by the COIC

c. Revised management plan

If changes in the management plan are recommended by the monitors, then a revised management plan will be drafted, forwarded to the investigator for comments, and brought to the COIC for review and approval. (For a description of review, notification, distribution, appeal and disciplinary procedures applicable to revised management plans, please see #VII.B.1-5 above).

4. Amended COI Management Plans

If the COIC is notified, either by the investigator or from another source—IRB, research administrative office, etc—that there has been a change in the investigator's significant financial interest, in the investigator's sponsored research, or in the relationship between financial interest and sponsored research, then it may be necessary to amend the management plan.

The amended management plan will be drafted, forwarded to the investigator for comments, and brought to the COIC for review and approval. An example would be, an NIH grant has been awarded that was not previously described in the COI plan, and this research is related to the investigator's financial interest, such that NIH notification is now required. (For a description of review, notification, distribution, appeal and disciplinary procedures applicable to amended management plans, please see #VII.B.1-5 above).

For minor changes that do not materially change the provisions in the management plan, e.g., anticipated research was not funded, a revised COI management plan may not be necessary, and it may be possible to document the change via an administrative review, documentation that does not require a vote. (see below for more detail regarding the administrative review).

However, a substantial change to a COI management plan that significantly alters the summary of the financial interest and/or the stipulations of the management plan will be documented in an amended management plan that must be reviewed and voted upon by the COIC.

5. Administrative Reviews

An Administrative Review document can be drafted where there is a need for documentation, but where discussion and vote by the COIC may not be required. The Administrative Reviewer must be a voting member of the COIC. Although the Administrative Reviewer by means of the administrative review document is recommending that the Committee be informed of the content without discussion and vote by the members, all Committee members are provided with Administrative Review documents and have the opportunity to request COI further COI follow-up, discussion and vote.

Administrative review can occur under the following conditions:

- On further investigation it has been determined that no conflict of interest exists.
- Updates/minor revisions that do not require a change in the provisions of an approved COI management plan will be completed by editing the approved plan before it is signed by the investigator, or by attaching the administrative

review to the most recent approved signed management plan, so that, if still applicable, the content of the administrative review can be incorporated into the full COI management plan when it is next revised or amended.

- The COIC has voted to approve administrative review.
- There is an individual COI but there is no human subjects research and no institutional COI.¹

NOTE: An Administrative Review will be brought to the COIC for discussion and, if necessary, vote if there are controverted issues that require discussion, or if the Administrative Review is accompanied by a COI monitoring report.

6. Institutional Conflict of Interest Management Plans

Where Case and/or UHCMC have an institutional financial interest that is related to sponsored research, it may be necessary to develop an institutional COI plan that would stipulate, for example, disclose of the institutional conflict of interest on publications arising from the research.

Most often an institutional COI accompanies individual conflicts of interest on the part of investigators. However, it is possible that there could be an institutional conflict of interest in the absence of an individual conflict of interest, for example, if a company sponsors research at Case and/or UHCMC, where Case has a financial interest in the company, but none of the investigators from Case have a conflict of interest.

In this instance, then an institutional COI management plan must be developed for the institution, to be signed by the Provost and by those individual investigators who will be implementing the institutional COI management plan provisions.

Administrative Review documents for individual investigators to document that they do not have an individual conflict of interest will be attached to the institutional COI management plan.

7. COIC Reports to Deans and Department Chairs

Deans and Department Chairs may be consulted while COI management plans are being developed by the COIC. In addition, a list of all investigators with active COI management plans within a given School or College will be distributed annually to the respective Deans by the COIC. The Deans may choose to share

¹ NOTE: The working definitions of the terms, "individual conflict of interest" and "institutional conflict of interest" provided in Appendix II will be updated to be consistent with the draft COI policy for the University, now undergoing revision. The definitions of the terms, "human subject" and "research" are taken from the Case University Policy on Research Protection:
<http://ora.ra.cwru.edu/research/orc/Attachments/Case%20HRPP/HumanResearchProtectionPolicy1-2006.pdf>

this information with Department Chairs, and the Deans and/or Department Chairs may request copies of individual management plans.

VII. Reporting to Federal Agencies:

The University will comply with any reporting obligations imposed by federal agencies. Currently, the Public Health Service (PHS) requires reporting of the existence of any identified conflict of interest and assurance that the interest has been managed, reduced, or eliminated before the expenditure of funds under the award or within 60 days of determination that a conflict of interest has been identified during the period of an award. PHS does not require reporting of the nature of the interest or other details. The National Science Foundation (NSF) currently requires reporting of any conflict which the University has been unable to manage, reduce or eliminate.

Where the COIC has identified a conflict of interest in relation to PHS-funded research administered through Case, then PHS disclosure will be stipulated in the investigator's Case COI conflict of interest management plan. In that event, the Case COIC will request of the designated Case Grants and Contracts officer that a letter be sent to the appropriate PHS program officer stating that the University investigator has a conflict of interest in relation to research conducted under this grant, and that the conflict of interest is being managed, reduced or eliminated.²

Case will follow PHS and American Association of Medical Colleges (AAMC) guidelines when identifying conflicts of interest that require PHS notification. On June 28, 1994 the Department of Health and Human Services (HHS) published proposed regulations (59 FR 33242). These guidelines were clarified in the 1995 NIH guidance, "Objectivity in Research" where a "significant financial interest" is defined as:

"anything of monetary value, including but not limited to, salary or other payments for services (e.g., consulting fees or honoraria); equity interests (e.g., stocks, stock options or other ownership interests); and intellectual property rights (e.g., patents, copyrights and royalties from such rights)" excluding... "an equity interest that when aggregated for the Investigator and the Investigator's spouse and dependent children, meets both of the following tests: does not exceed \$10,000 in value as determined through reference to public prices or other reasonable measures of fair market value, and does not represent more than a five percent ownership interest in any single entity; or (6) salary, royalties or other payments that when aggregated for the investigator and the

² Note: The NIH does not require notification of COIs related to SBIR or STTR grants. However, Case does require that investigators report this information to the University.

investigator's spouse and dependent children over the next twelve months, are not reasonably expected to exceed \$10,000."

<http://grants.nih.gov/grants/guide/notice-files/not95-179.html>

In a 2001 guidance, the AAMC recommended that the following be added to the definition of a significant financial interest:

"Equity interests, including stock options, of *any amount* in a non-publicly-traded financially interested company (or entitlement to the same).

Service as an officer, director, or in any other fiduciary role for a financially interested company, whether or not remuneration is received for such service."

<http://www.aamc.org/research/coi/firstreport.pdf>

It will be Case's procedure that, if the affiliated hospitals and respective IRBs choose to impose more stringent reporting requirements than these upon investigators, it is their prerogative to do so. However, in the interest of uniformity across institutions, Case will report to the NIH only "Significant Financial Interests" as defined in the Case COI Procedures manual, following the above guidelines.

VIII. FINANCIAL COIs AND HUMAN SUBJECTS RESEARCH

Research involving humans creates risks that non-human research does not. Recent, highly publicized episodes at other institutions underscore these risks when human subjects experience adverse events on research projects where the principal investigator and, in some cases, the institution have a financial stake in the outcome of the research.

A. Guidance References for Human Subjects Research

As a result, the Office for Human Research Protection (OHRP), the American Association of Medical Colleges (AAMC), the Council on Governmental Relations (COGR), and the American Association of Universities (AAU) have all developed guidelines that emphasize the increased scrutiny required when there is a financial conflict of interest associated with human subject research.

The 2004 OHRP COI guidance emphasizes the enhanced importance of attention to human subject protection where conflict of interest exists

<http://www.hhs.gov/ohrp/humansubjects/finreltn/fguid.pdf>

“to the extent financial interests may affect the rights and welfare of human subjects in research, IRBs, institutions, and investigators need to consider what actions regarding financial interests may be necessary to protect those subjects.” The 2001 AAMC policy and guidelines characterize financial interest where human subject research is involved as “potentially problematic”

<http://www.aamc.org/research/coi/firstreport.pdf>

“With the welfare of research subjects always of foremost concern, an institution should regard all significant financial interests in human subjects research as potentially problematic and, therefore, as requiring close scrutiny. Institutional policies should establish the rebuttable presumption that an individual who holds a significant financial interest in research involving human subjects may not conduct such research.”

In a 2002 guidance

<http://www.cogr.edu/docs/COIFinal.pdf>

the COGR recommends a “conservative” approach:

“If real financial conflicts of interest exist, they must be addressed in the most conservative manner to ensure human research participants that the studies are adhering to the highest ethical standards. Ambiguities or appearances of questionable judgment by individuals or institutions are unlikely to be tolerated by the public when the research places at risk the life or health of a participant. “

Finally, the 2001 AAU Guidelines on Financial Conflict of Interest

<http://www.aau.edu/research/COI.01.pdf>

take the position that such research should only be allowable under strict conditions:

“...any related financial interest in research involving humans should generally not be allowable. If compelling circumstances justify an exception to this general rule, the research should be subject to more stringent management measures (including disclosure to research participants and students) to ensure integrity of the research and the safety of the human participants.”

These guidelines and others generally agree on the following practices for dealing with financial conflict of interest involving human subject research:

1. Individuals (and the institution, if applicable) divest themselves of the financial interest ^a;

2. If divestiture is not possible then:
 - a) Identify another individual or individuals who will be responsible for the actual conduct of the human subject protocol including its direction, study design, eligibility decisions, informed consent process, data collection, analysis, and reporting; **-and/or-**
 - b) Disclose financial conflict of interest to research subjects through the informed consent process; **-and-**
 - c) Have an independent panel review data, results and reporting on a regular basis; **-and-**
 - d) Disclose financial conflict of interest on all publications and presentations

B. COI Management Options for Sponsored Research, Including Human Subjects Research

Case will adopt these “Best Practices” when reviewing and managing financial conflict of interest involving human subject research. Conflict of Interest management plans are developed according to the nature of the significant financial interest and of the sponsored research--e.g., whether there is an institutional, in addition to an individual conflict of interest; whether the investigator is conducting bench, animal or human subjects research, etc. These best practices of the Case COIC are adapted to individual circumstances and to evolving standards, and will periodically be updated. Suggested management plan stipulations could be:

- 1). Suggested COI management options for all research:
 - Disclosure on publications / presentations
 - Disclosure to study staff and advisees
 - Management of "mentoring conflicts of interest" in relation to advisees
- 2) Suggested COI management options for sponsored service agreements:
 - Designation of a non-conflicted Project Director to oversee processing of invoices.
 - Documentation that utilization of University resources is compensated at fair market value.
- 3). Suggested COI management options for animal research
 - All the points listed in #1 above and...
 - Disclosure to the Case Institutional Animal Care and Use Committee

- 4). Suggested COI management options for human subjects research
 - All the points listed in #1 above and/or:
 - Disclosure to the appropriate IRB(s)
 - Disclosure, if applicable, to prospective research participants on the informed consent documents.
 - Firewall between conflicted investigators and aspects of the human subjects research conducted under the IRB protocol (e.g., from subject selection, obtaining informed consent, primary data analysis);
 - Possible recusal as principal investigator or co-investigator on the IRB protocol.
 - Designation of a non-conflicted independent Reviewer to periodically review data and issue reports.
 - Designation of a non-conflicted Data and Safety Monitoring Board to periodically review data, including those pertaining to research subjects safety issues, and to issue reports.

- 5). Suggested COI management options for institutional conflicts of interest
 - Disclosure of the institutional conflicts of interest wherever disclosure of the individual COI is required by the management plan.
 - Designation of a DSMB or independent reviewer not affiliated with the conflicted institution(s)
 - In the case of a conflicted institutional official, designation of a senior faculty member to whom advisees can report.
 - Referral to an outside IRB.

^a Required when the individual is considered a government employee (e.g., with a VA appointment - with or without compensation).

APPENDIX I - Examples of Significant Financial Interests

Examples of Significant Financial Interests that **must be** reported:

1. An investigator has stock in a publicly-held company that has licensed a product from the university where the value of the stock exceeds \$10,000 and the product is the focus of a NIH grant on which the investigator participates.
2. An investigator has stock (regardless of value) in a privately-held company, which, per a technology transfer agreement with the university, has an exclusive option to license any intellectual property of the investigator in a certain area of research and NIH has funded a grant in that area.
3. An investigator has consulting income from a company that exceeds \$10,000 and that company also sponsors research conducted by the investigator.
4. The spouse of an investigator is employed by a company (and receives annual income greater than \$10,000), the company has an exclusive option to license intellectual property of the investigator in a certain area of research, and NIH has funded a project of the investigator in that area.
5. An investigator has intellectual property rights (i.e., a patent) for a technology that is the focus of a research project funded by a company that may be interested in licensing the technology.
6. An investigator receives income of more than \$10,000 per year from a company (for providing lectures and seminars) and that company's product is also the focus of a research project conducted by the investigator with NIH funds.

Examples of Significant Financial Interests that **do not** need to be reported:

1. An investigator has stock in a publicly-held company that is also sponsoring research that he/she is conducting, but the value of the stock is less than \$10,000 and does not represent more than 5% of the ownership interest.
2. An investigator has stock (regardless of value) in a privately-held company, but he/she is not involved in any research sponsored by that company or any research of that company's products or services sponsored by another entity (e.g., NIH).
3. More than \$10,000 of an investigator's salary from the university is covered by funds from a company that has sponsored research at the university.
4. An investigator receives more than \$10,000 per year from a mutual fund that has purchased stock in a variety of companies whose identities are unknown to investigator.
5. An investigator receives income of more than \$10,000 per year from a local government agency for providing lectures and seminars and the local

government agency also sponsors projects of the investigator at the university.

APPENDIX II - Working definitions

- **Individual Conflict of Interest**, occurs in situations where an Individual's own Financial Interests or those of the Individual's spouse, domestic partner or children, could directly or indirectly unduly influence – or appear to influence – the Individual's professional obligations or judgment in carrying out his/her responsibilities as a member of the University community. These responsibilities include but are not limited to: teaching; mentoring; purchasing of equipment or supplies; research; patient care; and administration.
- **Institutional Conflict of Interest**, occurs in situations where the Institution's Financial Interests or the Financial Interests of Institutional Officials could directly or indirectly unduly influence the decisions relating to investment, purchasing, research, and patient care.
- **Research**: "Research" is defined in Code of Federal Regulations 45 CFR 46 as "systematic investigation designed to develop or contribute to generalizable knowledge."
- **Human subject**: "Human subject" is defined in 45 CFR 46 as a "living individual about whom an investigator (whether professional or student) conducting research obtains data through intervention or interaction with the individual or identifiable private information."