AAMC ***Association of American Medical Colleges***
AAU ***Association of American Universities***
ACE ***American Council on Education***
APLU ***Association of Public and Land-grant Universities***

August 17, 2010

Jerry Moore
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Reference: Regulatory information number 0925-AA53 and docket number NIH-2010-0001, Notice of Proposed Rulemaking concerning *Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors*, published in the May 21, 2010 *Federal Register* (75 FR 28687), and a request for additional comments published in the July 21, 2010 *Federal Register* (75 FR 42362)

Dear Mr. Moore:

The Association of American Universities, the Association of American Medical Colleges, the American Council on Education, and the Association of Public and Land-grant Universities appreciate the opportunity to submit comments in response to the Notice of Proposed Rulemaking concerning *Responsibility of Applicants for Promoting Objectivity in Research for Which Public Health Service Funding Is Sought and Responsible Prospective Contractors*.

The Association of American Medical Colleges (AAMC) is a not-for-profit association representing all 133 accredited U.S. and 17 accredited Canadian medical schools; nearly 400 major teaching hospitals and health systems, and 89 academic and scientific societies. Through these institutions and organizations, the AAMC represents 125,000 faculty members, 75,000 medical students, and 106,000 resident physicians.

The Association of American Universities (AAU) represents 61 leading U.S. research universities who together perform nearly 60 percent of all federally funded university-based research and annually award more than half of all Ph.D. degrees earned in our country.

Founded in 1918, the American Council on Education (ACE) is the nation's unifying voice for higher education. Its more than 1,800 members include a substantial majority of colleges and universities in the United States and represent all sectors of American higher education—public and private, large and small, denominational and nondenominational.

The Association of Public and Land-grant Universities (A·P·L·U) is an association of over 215 public research universities, land-grant institutions, and many state public university systems. A·P·L·U member campuses enroll more than 3.5 million undergraduate and 1.1 million graduate students, employ more than 645,000 faculty members, and conduct nearly two-thirds of all academic research, totaling more than $34 billion annually.

AAMC, AAU, ACE and APLU have a long history of collaboration and policy development on issues of interest to the research enterprise and higher education. Most recently, AAMC and AAU issued the joint report, *Protecting Patients, Preserving Integrity, Advancing Health: Accelerating the Implementation of COI Policies in Human Subjects Research*, issued February 2008, calling on all medical schools and major research universities to develop and implement institutional conflict of interest (COI) policies within the next two years, and to refine standards for addressing individual financial COI.

Trust is the essential currency of the biomedical research enterprise. The vitality of the research enterprise relies on the public's trust in the institutions and individuals conducting research and in the federal agencies and employees responsible for managing the review, allocation, and disbursement of limited financial resources on critical research activities. Maintaining the public's trust is a shared responsibility of all those involved in the enterprise. Minimizing, and when necessary, managing financial conflicts of interest is an important obligation of institutions receiving federal funds and contributes to ensuring that research and the research record remain objective and unbiased.

Federal agencies trust institutions to scrupulously adhere to financial conflict of interest regulations; institutions trust that faculty will faithfully comply with reporting mandates and abide, when necessary, with requirements to follow management plans prescribed by the institution; and institutions and researchers trust that federal agencies will abide by the reasonable judgments of institutions and researchers in ascertaining and managing potential conflicts. While this trust needs to be continually verified, reasonable standards and processes are essential to maintain compliance and promote our shared values throughout the research enterprise. If this trust is willfully breached

by researchers and institutions, appropriate institutional and federal sanctions should be imposed so as to reinforce compliance and assure the public that the enterprise can monitor adherence, correct behaviors, and enforce and advance our shared commitment to trust and accountability.

The public has every right to expect objectivity in research, and accountability regarding the management of potential financial conflicts of interest in research. Advancing the interests of the public and providing them the information they need to make informed judgments in assessing the research record and the scientific basis of clinical decisions should be at the core of federal regulations on financial conflicts of interest.

There is a paucity of evidence that the disclosure and management of financial conflicts of interest affect objectivity and integrity. In the absence of such evidence, onerous regulations are not only unwarranted, but could create a glut of policies that increase activity without adding protections and at the same time erode the trust between the regulators and those being regulated.

The Notice in many cases appropriately establishes the balance between disclosure and reporting that advances the public's interest, and a cumulative regulatory burden that diverts needed resources away from research. However, beyond acknowledging the increased compliance burdens, we urge HHS to consider mechanisms to help mitigate the burdens on the institutions and the investigators. (Please see section: Cumulative Effect of Regulatory Burdens). Below we identify specific areas of the proposed Notice that we believe can be improved, clarified, or made more effective:

The Definition Of Significant Financial Interests

The Notice continues the exclusion from reportable Significant Financial Interests remuneration from seminars, lectures or teaching engagements, as well as service on advisory committees or review panels of institutions of higher education as defined at 20 U.S.C. 1001(a), as well as federal, state, or local governments. The Notice omits academic teaching hospitals and other independent non-profit research centers. We urge the exclusion of similar remuneration from academic teaching hospitals, medical centers, research institutes affiliated with an institute of higher education, and other non-profit research centers.

The Notice does not exclude remuneration from non-profit organizations from the definition of Significant Financial Interests. We recognize the importance of including remuneration from non-profit entities that receive the preponderance of their revenues from a few for-profit entities and/or when a commercial entity directly or indirectly controls the organization. However, we urge HHS to exclude remuneration received from non-profit organizations that provide competitive research grants. This would exempt from disclosure and reporting remuneration from *bona fide* voluntary health organizations, such as the American Cancer Society, the American Heart Association, the Juvenile Diabetes Foundation, as well as independent research institutes, such as the Howard

Hughes Medical Institute. We see no public benefit from their inclusion, and the administrative and researcher compliance burden will be significant.

Further we urge the exclusion of remuneration from non-profit organizations for presentations in continuing medical education courses that meet the standards of the Accreditation Council for Continuing Medical Education (ACCME).

In a change from current regulations, the Notice does not exclude travel reimbursements from the definition of Significant Financial Interests. We urge that the proposed rule be amended to exclude the reporting of reasonable and customary travel reimbursements. In many cases, investigators are unaware of the value of such travel reimbursement. For example, faculty participating in many member-based scientific society and academic association activities are required to make their travel arrangements through the non-profit's travel office and are usually not informed of the cost. To require reporting of such reimbursements does not advance the federal or public interest.

The Notice fails to exclude unlicensed intellectual property from the definition of Significant Financial Interest. We believe that such an exclusion is both warranted and in the public interest. Studies have shown that the majority of university-owned patents are unlicensed. Intellectual property may be patented to keep it in the public domain or to defend against possible other claims. Trying to assess the potential value of unlicensed patents and other intellectual property wastes resources, creates administrative burdens, and does not serve the public interest.

In addition, in order to promote consistency we suggest that the definition of intellectual property rights be changed to make it subject to the annual $5,000 threshold level and that royalties shared with an investigator from rights assigned to the investigator's employing institution be exempt.

We also urge that mutual funds and retirement accounts expressly be made exempt from the definition of Significant Financial Interests since investigators do not control the choices made on their behalf by fund managers.

In some cases, the Notice mandates that Significant Financial Interests include the interests of an investigator's spouse and dependent children. We urge that domestic partners be covered by the Notice, to the same extent that spouses may be so covered.

Institutional Responsibility, Investigatory Responsibility and the Proposed Relatedness Standard

The relatedness standard contained in the Notice raises questions concerning how institutions can responsibly and accurately judge whether a Significant Financial Interest is related to an investigator's PHS research. We believe that in many cases, it will be necessary for the institution to involve the investigator in making such a determination, though our Associations agree that the

ultimate responsibility belongs to the institution. This is a process consistent with the inherent relationship of trust between the investigator and the institution. To clarify the responsibilities and expectations of the Institution and the Investigator, we urge a slight modification of the PHS proposal:

1. The investigator must disclose all Significant Financial Interests which s/he, in good faith, believes are related, directly or indirectly, to his or her institutional RESEARCH responsibilities, using the examples currently provided in the Notice.
2. The institution's responsibility is to review the Significant Financial Interests and determine whether any relate to the investigator's PHS-funded research.
3. If the institution determines that any of the Significant Financial Interests relate to the investigator's PHS-funded research, the institution then would determine if a financial conflict of interest exists and how it should be managed.

Federal Compliance Requirements vs. Institutional Standards

Under the Notice, institutions that maintain policies on financial conflicts of interest with standards more stringent (e.g., that require a more extensive disclosure of financial interests) than federal standards will be required to report based on their institutional policies and thresholds and not on a uniform federal standard. A varying standard for reporting is not in the federal interest, nor does it advance consistency in transparency. We urge HHS to use a uniform federal standard across recipient institutions that will allow for greater consistency in enforcement.

The justification for the varying standard is not explained in the Notice. In addition, we believe the requirement will have the perverse effect of reducing reporting as institutions are likely to alter their internal standards and gravitate to the HHS threshold to reduce compliance risk.

Publicly Accessible Website

The Notice requires that an institution make available, through a publicly accessible Web site, information concerning any Significant Financial Interest disclosed to the institution that meets stated criteria. The information is to remain available via the institution's publicly accessible Web site for at least five years from the date that the information was last updated and updates are to be made annually. We support the concept of public disclosure and transparency. However, there are serious and reasonable concerns among our members that the Web posting will be of little practical value to the public and, without context for the information, could lead to confusion rather than clarity regarding financial conflicts of interest and how they are managed. To advance our shared goal of enhancing the public's trust in the research enterprise, we urge HHS to ensure that any required Web postings provide patients and the public with appropriate and accurate information, education and context. It should also help inform members of the public about how such interests can be successfully managed.

If the goal is to improve transparency through a publicly accessible website regarding the management of financial conflicts of interest, we urge HHS to engage the potential stakeholders (patients, public representatives, institutional officials, and researchers) to design a data-driven public-reporting website that is easily accessible and navigable and that includes explanatory information about how conflicts of interest are effectively managed. Further, since all of the mandated data elements are to be provided to the relevant PHS agencies, we suggest that HHS consider maintaining the public reporting system, rather than to require each individual institution to maintain a unique Web reporting resource. Recipients of PHS grants and contracts could then be required to provide appropriate links to the HHS centralized reporting system on appropriate research and clinical trial Web sites.

We note that under the provisions of the Physician Payment Sunshine Act enacted as part of the Patient Protection and Affordable Care Act [P.L. 111-148], the Secretary is charged with creating an Internet resource based on company submissions by September 30, 2013. Developing a similar system for conflict of interest reports would be a complementary initiative that would help maximize the utility of such reports to patients and the public.

Should HHS retain the proposed reporting paradigm, we urge HHS to clarify that a robust searchable data base is not being mandated, although some institutions are likely to make such a resource available on their Web sites. Other institutions with limited resources may decide to post alternative formats on the Web, such as PDF files.

We urge that the HHS alter the Web site posting availability dates to maintain consistency with agency record retention requirements. We also urge HHS to more explicitly state the personnel whose disclosures are subject to the Web posting requirement. For example, we understand that it is not the Department's intent to require the posting of information concerning holdings of spouses or children of investigators. This should be clearly stated in the regulations.

Significant Financial Interest Threshold Harmonization

The Notice mandates the disclosure by investigators to their institution of any Significant Financial Interest that reasonably appears to be related to the investigator's institutional responsibilities with an annual aggregate value of $5,000 or more in the case of remuneration and publicly traded securities, and the value of all non-publicly traded securities. Whatever threshold is included in the final regulations, we urge that the Food and Drug Administration's reporting levels be harmonized with that of other PHS agencies. The July 27, 2010 comments of the Secretary's Advisory Committee on Human Research Protections on the harmonization issue are compelling.

Mitigation Plans

The Notice establishes a new mandate involving the creation of a mitigation plan when a Significant Financial Interest was either not disclosed in a timely manner or was not reviewed earlier "for

whatever reason." The Notice also requires that in these cases an institution must determine whether any PHS-funded research, or portion thereof, conducted prior to the identification and management of the financial conflict of interest was biased in the design, conduct, or reporting of such research. We believe this requirement is unnecessary, excessive and geared toward a small number of cases which will require the expenditure of significant institutional resources that could better be allocated to research activities of higher risk. This provision presumes bad faith on the part of the investigator or other key personnel and is unwarranted without further evidence. We believe that the normal process for assessing Significant Financial Interests, and if necessary, preparing a management plan, should be sufficient. We urge that this requirement be withdrawn. Should either the PHS agency or the institution believe that an unreported financial conflict of interest was willful, sanctions exist to manage such compliance challenges. If PHS or the institution believes that non-disclosure is related to research misconduct, the existing PHS policies and regulations on research misconduct are available to address such situations.

Implementation Schedule of the New Rule

The Notice is silent on the implementation period for the various new requirements that are being proposed. A staggered and extended implementation period should be designated by HHS in consultation with the community, which would not require full implementation until October 1, 2013.

While new and/or revised deliverables are being proposed (management plans, enhanced reports, mitigation plans, Web postings, etc.), the design of new work and responsibility processes, internal reporting changes such as transactional to annual reporting, new faculty and staff training requirements, and the development of new data bases and Web sites will take considerable time and effort. NIH and other PHS agencies should provide adequate time for internal systems to be developed and for institutions to engage in full collaborative consultation with agencies before new mandates are implemented. We believe these new requirements could be effectively implemented by our institutions by October 1, 2013 which is consistent with the time frames provided for similar disclosures to be made by pharmaceutical companies and other industrial firms under the new "Sunshine" provisions included as a part of the Patient Protection and Affordable Care Act (P.L. 111-148).

During the implementation period, we urge HHS and PHS-agencies to consider explicitly exempting specific mechanisms and grant types from the new regulations in an effort to facilitate compliance. For example, retroactive application of the new regulations during the transition phase to non-competing continuations, existing awards, and training grants offers little benefit. In addition, we urge that the Web posting requirements be significantly delayed to allow internal systems to be established and data base architecture to be standardized. Again, we suggest that full implementation of the final Web posting requirement not be required before October 1, 2013 and that adequate testing and training time be provided before such resources are operational.

Reporting Period

In the Notice, disclosures are based on the preceding 12-month period as a baseline. While we support the requirement for an annual report, we urge that institutions be empowered to establish their own specific reporting periods. Institutions seek to mange potential conflicts of interest across various institutional missions. A rigid reporting period based on PHS grant agency award dates is unnecessary and fails to recognize institutional variations (such as calendar, academic, and fiscal year reporting).

Training Requirements

The Notice mandates that covered investigators complete training in financial conflicts of interest management prior to engaging in PHS-funded research and, thereafter, at least once every two years. The intent of training is to keep investigators abreast of development in financial conflict of interest. We support initial training, but believe that institutions are in the best position to determine when additional training is warranted. NIH has also stated this position in the Frequently Asked Questions (FAQ) on NIH Requirement for Education on the Protection of Human Subjects: Question: "How often do investigators involved in the design and conduct of human subjects research need to complete the education? Answer: The NIH policy is silent on the frequency of education. The intent of the education requirement is for investigators to keep abreast of developments in human subjects protection. We believe that institutions and investigators are in the best position to determine when additional education is warranted." The human subjects training requirement seems appropriate for conflicts of interest training as well.

Subrecipients

The Notice states that if an institution carries out the PHS-funded research through a subrecipient (e.g., subgrantee, contractor, or collaborator) it must incorporate as part of a written agreement with the subrecipient legally enforceable terms that establish whether the financial conflicts of interest policy of the awardee institution or that of the subrecipient applies to the subrecipient's investigators.

We believe that it is operationally impossible for a grantee to evaluate the COI program of its subrecipients. As we advocated in our response to the ANPR, if a subrecipient certifies to the grantee that its FCOI program conforms to applicable federal regulations, that should be sufficient insofar as the grantee is concerned (absent clear and substantial evidence that the certification is false). Subrecipients that also serve as prime grantees to PHS agencies should be exempt from this certification process.

We are particularly troubled by the potential impact the Notice's restrictive language may have on non-traditional and under-resourced potential subrecipients (for example, various health and research centers in the developing world). It is exactly these types of organizations that the research enterprise must involve more directly in the research continuum if patients are to fully benefit from research. For example, in many cases, establishing "legally enforceable terms" with foreign subrecipients may not be possible. This provision may lead to many valuable research programs and projects grinding to a halt.

We support the inclusion of the following language, which we believe serves the federal interest and will be operationally effective: "When the institute participates in PHS sponsored research with a subrecipient, the institution will take reasonable steps to ensure that subrecipient is adequately informed of its obligation to comply with all applicable conflict of interest reporting, review, and disclosure requirements as required by HHS regulations governing objectivity in research. This requirement is satisfied if the institution's contract or other binding agreement with the subrecipient includes provisions setting forth these obligations. The institution's contract with the subrecipient must explicitly state whether the institution's conflicts of interest policy or that of the subrecipient applies to the subrecipient's investigators and key personnel."

Cumulative Effect of Regulatory Burdens

The Notice offers no evidence that the proposed increased compliance burden will actually improve accountability or meet federal interests in any appreciable way. In light of the absence of such evidence, the cumulative administrative burden on institutions and researchers should be carefully weighed.

Further, we urge HHS to carefully review how the requirements under this Notice could be adjusted to allow institutions and PHS agencies to better focus review and reporting resources on managing conflicts that the institution judges to be of higher risk to human subjects, students, staff and the integrity of research. Simply mandating more intense reviews and reporting of all relationships absent recognizing the institution's ability to stratify the level of risk has the potential to divert scarce resources from managing areas of potential conflict that should be a priority. To this end, HHS should consider excluding some low-risk grant mechanism, such as equipment, construction, and training grants, from the COI rules entirely.

As proposed, institutions will need to add personnel and expand their infrastructure to meet the unfunded federal mandates included in the Notice. Although many institutions currently have systems in place to manage financial conflicts, reporting required under these new rules will significantly increase and internal systems will need to be more robust to manage the volume and extent of the new requirements.

The reporting burden on individual faculty also will increase significantly as a result of the changes proposed in the Notice. According to a 2005 survey conducted by the Federal Demonstration Project Faculty Standing Committee, investigators reported devoting 42 percent of their activities to management and administrative requirements, up from 18 percent just two decades ago. Further increasing the administrative burden on faculty will reduce research productivity, which is counter to the interests of both patients and the government. We urge the HHS to fund clerical and administrative assistance for investigators so that these increased compliance burdens do not further restrict their research productivity.

Recovering Compliance Costs

Institutions will not be able to recover these added costs due to the administrative cap of 26 percent currently imposed on institutions subject to OMB Circular A-21. This cap has remained unchanged since 1991. We again urge HHS to work with the OMB to lift the administrative cap so that the federal government can more readily fund the true cost of federally-sponsored research and help restore vitality to the federal-academic research partnership.

We also urge HHS and PHS-agencies to provide institutional grants to assist in the implementation of these new compliance burdens. A similar grants program was implemented when PHS agencies imposed new regulatory burdens regarding human subjects research. Such assistance proved invaluable in helping institutions manage the compliance transition and in moving more rapidly toward full implementation.

Issues Related to the Transfer of an Investigator or Research Project

A July 19, 2010 notice in the Federal Register (75 FR 42362) sought additional comments on the authorities that exist under the current regulations and the proposed revisions to enable the PHS to enforce compliance by institutions and investigators with the regulations when an investigator or a PHS-funded research project transfers from one institution to another. We believe the current and proposed regulations are clear concerning PHS's enforcement authorities and that the range of remedies available to HHS and the PHS awarding component are sufficient.

Establishing a formal process to notify an investigator's destination institution of previously determined financial conflicts of interest and existing management plans is unnecessary. If the NPRM is implemented as proposed the information concerning an identified FCOI related to PHS-funded research will be posted to a publicly accessible website and should meet any need for notification. We do not support a requirement that the destination institution "must consider" a determination made by another institution. Compliance with the regulations is an institutional responsibility met jointly by the institution and the investigator. Each institution will have specific policies and procedures for disclosures, determinations and management and should have the freedom to utilize whatever information it considers appropriate and germane in making its determinations.

Thank you for the opportunity to present our views. We would be happy to work with the Department on any of the issues discussed above or other topics that involve the academic research community. If you have questions regarding our comments, please feel free to contact Ann Bonham, Ph.D., AAMC Chief Science Officer, at 202-828-0400 or at abonham@aamc.org, or Tobin Smith, AAU Vice President for Policy, at 202-408-7500 or at toby_smith@aau.edu.

Sincerely,

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