Association of
American Medical Colleges
655 K Street, N.W., Suite 100, Washington, D.C. 20001-2399
T 202 828 0400 F 202 828 1125
www.aamc.org

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Division of Dockets Management (HFA-305)
Food and Drug Administration
5630 Fishers Lane, Rm. 1061
Rockville, MD 20852
Submitted electronically at www.regulations.gov

Re: Docket No. FDA-2017-N-5093, "Review of Existing General Regulatory and Information Collection Requirements of the Food and Drug Administration"

The Association of American Medical Colleges (AAMC) appreciates the opportunity to respond to the Food and Drug Administration's (FDA) request for comments and information on ways to "identify existing regulations and related paperwork requirements that could be modified, repealed, or replaced … to achieve meaningful burden reduction" and assist with implementation of Executive Orders (EO) 13771 ("Reducing Regulation and Controlling Regulatory Costs") and 13777 ("Enforcing the Regulatory Reform Agenda").

The AAMC is a not-for-profit association representing all 149 accredited U.S. and 17 accredited Canadian medical schools; nearly 400 major teaching hospitals and health systems, and more than 80 academic and scientific societies. Through these institutions and organizations, the AAMC represents nearly 167,000 full-time faculty members, 88,000 medical students, 124,000 resident physicians, and thousands of graduate students and postdoctoral trainees in the biomedical sciences.

I. General Comments on the Regulatory Reform Agenda

In addition to the FDA's request for information and supporting data about specific regulations that should be modified or repealed, the FDA has solicited general comments on its regulatory reform agenda in support of its public health mission and obligations under EOs 13771 and 13777.

Recent reports from the AAMC,[1] the National Academies of Sciences, Engineering, and Medicine ("the Academies")[2], the Government Accountability Office[3], and the Commission on Evidence-Based Policymaking,[4] identify a need for federal agencies to harmonize regulations, reduce workload and costs, and consider evidence-based regulatory approaches. Through its review of existing regulations governing federally funded research, the Academies' report found "little rigorous analysis or supporting data precisely quantifying the total burden and cost to investigators and research institutions of complying with federal regulations specific to the conduct of federally funded research."[5] Notably, the report also

[1] AAMC Analysis in Brief, "Implementing the Regulations on Financial Conflicts of Interest, Results from the AAMC Conflict of Interest Metrics Project," (Vol.15, 2015) https://www.aamc.org/download/429214/data/april2015implementingtheregulationsonfinancialconflictsofintere.pdf.
[2] "Optimizing the Nations Investment in Academic Research, A New Regulatory Framework for the 21st Century," (2016)https://www.nap.edu/catalog/21824/optimizing-the-nations-investment-in-academic-research-a-new-regulatory.
[3] "Federal Research Grants: Opportunities Remain for Agencies to Streamline Administrative Requirements," (2016) http://www.gao.gov/assets/680/677949.pdf.
[4] "The Promise of Evidence-Based Policymaking, Report of the Commission on Evidence-Based Policymaking" (September, 2017) https://www.cep.gov/content/dam/cep/report/cep-final-report.pdf.
[5] Supra, Note 2.

highlights the difficulties associated with finding this data and cites the AAMC's Conflict of Interest (COI) Metrics Project as an example of how data can be used to quantify the impact and burden of research regulations on academic institutions.[6]

The AAMC supports the implementation of the Academies' recommendations and the FDA's thoughtful assessment of whether existing regulations are effective and efficient, but notes that the appropriate regulation of science and research serves to ensure the safety, confidentiality and integrity of the research process. Federal agencies and departments should use or collect credible evidence about a regulation's impact, burden, and outcome as a framework for the review of its regulations, policies, and programs, an approach that would help to "deliver[] a smarter, more innovative, and more accountable government for citizens."[7] The AAMC further recommends that the FDA take steps to improve its policymaking and program performance by incorporating robust *prospective* and *retrospective* evaluation into its rulemaking and program development process to further ensure that its regulations, policies, and programs meet the agency's intended goals.[8]

The AAMC recommends that the FDA, on an ongoing basis, solicit public and stakeholder feedback on the methods and strategies used for evaluating regulations that should be modified, repealed, or replaced. Opportunities for routine public feedback not only builds accountability in the collection and use of data to inform government decision-making, it increases the public's trust and transparency in government decision-making.

II. Harmonization of the FDA Regulations for the Protection of Human Subjects

On January 19, 2017, the *Federal Policy for the Protection of Human Subjects* (the Common Rule) was issued by HHS and 15 other federal departments and agencies, with a general compliance date of January 19, 2018. The FDA is not a signatory to the Final Rule, and the Common Rule's preamble discusses HHS's intentions to work with the FDA to align the differences between the two regulations in compliance with Sec. 3023 of the 21st Century Cures Act (P.L. 114-255, "Cures Act."). **The AAMC urges the FDA to begin the rulemaking process to revise 21 CFR Parts 50 and 56 to align those regulations with the Common Rule. We encourage the FDA to further align with HHS's interpretation of the human subject protections regulations by simultaneously adopting joint guidance issued by the Common Rule agencies and departments.[9]**

The Cures Act requires that the HHS Secretary "to the extent practical and consistent with other statutory provisions, […] harmonize the differences between the HHS Human Subject Regulations (45 CFR part 46, Subpart A) and the FDA Human Subject Regulations" (21 CFR Parts 50 and 56) within three years from the Cures Act's enactment date (by December 13, 2019). Recognizing that the Food Drug and Cosmetic Act has erected obstacles to greater harmonization, the Cures Act also modified some of the provisions that proved barriers to harmonization, such as removing the requirement that clinical investigations using devices must be approved by a local Institutional Review Board (IRB), which had prohibited implementation of the cooperative review requirement of the Common Rule (Sec. 3056), and permitting a waiver of informed consent for certain minimal risk research (Sec. 3024). The FDA has

[6] See, AAMC COI Metrics Project webpage, https://www.aamc.org/initiatives/research/coi/metricsproject/.
[7] "Next Steps in the Evidence and Innovation Agenda," Memorandum to the Heads of Departments and Agencies" (July 26, 2013) https://www.whitehouse.gov/sites/default/files/omb/memoranda/2013/m-13-17.pdf.
[8] AAMC Comment Letter to the Commission on Evidence-Based Policymaking (November 14, 2016) available at: https://www.aamc.org/download/473104/data/aamccommentlettertocommissiononevidencebasedpolicy.pdf.
[9] AAMC Comment Letter "Notice of Proposed Rulemaking: Federal Policy for the Protection of Human Subjects" (January 4, 2016).

recently taken steps toward implementing this latter change by issuing guidance for immediate implementation.[10]

Through an interim final rule, the effective date of the Common Rule has been delayed for six months, to July 2018. Part of the justification for the delay in this rule is the lack of existing implementing guidance and harmonization. Institutions have grown increasingly concerned that when the Common Rule goes into effect the FDA's human subject protection regulations will remain consistent with the current Common Rule's pre-2018 requirements, while the other 16 federal agencies and departments including HHS, will be under a substantially revised set of regulations. Thus, federally funded research also regulated by the FDA will be subject to two different sets of regulations with differing review and oversight requirements. Harmonized regulations and guidance would have a profound effect on regulatory burden, especially with respect to informed consent requirements and templates, definitions, requirements for continuing review, and the future treatment of and identifiability standards for biospecimens.

The AAMC strongly recommends that the FDA use the Common Rule implementation delay as an opportunity to initiate and finalize rulemaking that would harmonize the FDA regulations with the Common Rule. Although the statutory deadline for harmonization (through the Cures Act) is not for two years, there are no barriers preventing the FDA from moving forward with this process immediately.

III. Financial Conflicts of Interest

The AAMC appreciates the FDA's intended efforts to strengthen and modernize its regulatory framework to keep pace with scientific advancement.[11] Consistent with these efforts, Section 2034 of the Cures Act requires the Secretary of HHS to review regulations and policies related to the disclosure and reporting of financial conflicts of interest (FCOI) to reduce administrative burden for federally funded researchers. **In furtherance of the Cures Act's requirements, we recommend that the FDA work with HHS, other federal agencies, and key stakeholders to identify common elements for the disclosure and evaluation of COI (e.g., standardization of definitions, disclosure forms, and monetary thresholds).**

Several federal departments and agencies such as the FDA, National Institutes of Health (NIH), Centers for Medicare and Medicaid Services (CMS), and National Science Foundation (NSF), in addition to academic medical centers, require the disclosure of financial interests and management of those interests when a conflict of interest is identified. The variation in COI requirements across federal agencies "imposes significant financial and administrative burden on institutions and researchers, diminishing the productivity and return of federal investment in research."[12]

In addition, the AAMC recommends that the FDA better align its requirements for determining COI and eligibility for participation on FDA advisory committees under 18 USC 208(b) and its process for evaluating "appearance issues" under the government-wide regulation of ethical conduct for government employees (5 CFR 2635.50, "Section 502").

In 2008, the FDA published guidance on the process for determining a COI under 18 USC 208(b) and last year, the FDA released draft guidance on when to grant an authorization for a committee member with an

[10] "IRB Waiver or Alteration of Informed Consent for Clinical Investigations Involving No More Than Minimal Risk to Human Subjects, Guidance for Sponsors, Investigators, and Institutional Review Boards" (July 2017) https://www.fda.gov/downloads/RegulatoryInformation/Guidances/UCM566948.pdf.
[11] "FDA's plan to engage the public in the agency's new effort to strengthen and modernize FDA's regulatory framework" (September 2016) https://blogs.fda.gov/fdavoice/index.php/2017/09/fdas-plan-to-engage-the-public-in-the-agencys-new-effort-to-strengthen-and-modernize-fdas-regulatory-framework/.
[12] Supra Note 2.

"appearance issue," the first time the FDA has addressed appearance issues in guidance. In the draft guidance, the interaction between these two legal requirements highlights several inconsistencies and potential complications when the FDA applies two distinct legal standards to make a determination as to whether an individual is eligible to participate in the activities of an FDA advisory committee. In its response to the FDA's 2016 draft guidance,[13] the AAMC raised several concerns about the application of these two standards, pointing to several instances where redundancies and inconsistencies between the sets of legal requirements complicate the understanding of what needs to be disclosed to the FDA and how the FDA makes final determinations about advisory committee participation. The AAMC recommends that the FDA clarify the distinction between a *conflict of interest* and an *appearance issue,* as the two are treated distinctly for the purposes of determining eligibility for advisory committee participation. As stated in our letter:

> "This is not a distinction that is regularly made in other conflict of interest regulations, policies, and discussions. Certain relationships create actual or apparent conflicts of interest that need to be reviewed or managed, and are typically addressed without being labeled as one or the other. Thus, special government employees from academic communities will not be as familiar with this distinction. Clarifying this position […] would improve understanding both of what needs to be disclosed to the FDA and why financial determinations or authorizations were made."

We appreciate the FDA's commitment to ensuring objectivity and transparency in its COI screening process and hope that the FDA clarifies and streamlines its procedures for determining advisory committee participation. This would reduce ambiguity in the decision-making process for both FDA officials and prospective members of an FDA advisory committee.

The AAMC appreciates the opportunity to provide the FDA with comments on the important issues of regulatory burden and regulatory reform. To the extent we can continue to help the FDA identify ways to advance its regulatory reform efforts or provide additional information on specific regulations or regulatory burden issues affecting the academic research community, please contact me or Heather Pierce, Senior Director for Science Policy and Regulatory Counsel at hpierce@aamc.org or (202) 478-9926.

Sincerely,

Ross McKinney, MD
Chief Scientific Officer

cc: Heather Pierce, JD, MPH

[13] AAMC Comment Letter, "Procedures for Evaluating Appearance Issues and Granting Authorization for Participation in Food and Drug Administration Advisory Committees," Available at: https://www.aamc.org/download/485082/data/fdaappearancecommentletter.pdf.