

*AAU Association of American Universities*  
*COGR Council on Governmental Relations*

---

May 19, 2010

Division of Docket Management (HFA-305)  
Food and Drug Administration  
5630 Fisher Lane, Room 1061  
Rockville, MD 20852

Subject: Reporting Information Regarding Falsification of Data  
Docket No. FDA-2008-N-0115

The Council on Governmental Relations (COGR) is an association of 182 research universities and their affiliated academic medical centers and research institutes. COGR concerns itself with the impact of federal regulations, policies, and practices on the performance of research conducted at its member institutions. The Association of American Universities (AAU) is an association of 61 preeminent public and private U.S. research universities. AAU focuses on national and institutional issues important to research-intensive universities, including funding for research, research and education policy, and graduate and undergraduate education. The institutions represented by COGR and AAU conduct a significant number of clinical trials under the sponsorship of external companies and organizations that eventually support applications to the Food and Drug Administration (FDA). Research organizations, themselves, provide support for investigator-initiated clinical research and trials that build the foundation for future FDA applications. As research performers, we are particularly concerned with the FDA's proposal concerning the reporting of information regarding the falsification of data.

**Federal Policy on Research Misconduct**

We urge the FDA to follow the Research Misconduct policy established by the Department of Health and Human Services (HHS) through the Public Health Service (PHS, 42CFR93). The HHS/PHS policy conforms to the Federal Policy on Research Misconduct of December 2000 (here forward referred to as the "Federal Policy") – a policy implemented with minor agency-specific modifications by twelve other federal agencies.

We find the FDA's rationale for abandoning the HHS/PHS policy insufficient and the consequences for the research community significant enough to urge the FDA to forego the proposed amendment to its regulations. FDA argues that the HHS/PHS policy – the most expansive of all the federal agency policies – is not adequate in scope to meet the research subject to evaluation by the FDA. We would disagree and believe that the HHS/PHS policy can be modified, if appropriate, and implemented to focus on those areas – such as data falsification – that meet the FDA's specific needs.

The FDA should implement regulations that meet the Federal Policy on Research Misconduct (December 2000) as its alternative. This approach would bring the FDA into compliance with the Federal Policy like all other agencies addressing research misconduct. The Federal Policy outlines the responsibilities of the agency and the investigator's home institution or organization, which is the prescribed and appropriate mechanism for the initial inquiry and investigation of allegations of research misconduct including fabrication of data. The FDA regulations focus on the sponsor of various studies as the applicant or petitioner under the FDA's various regulations. We understand that focus but, in the case of misconduct, the role of the investigator's home institution or organization, if applicable, cannot be dismissed or ignored by the FDA.

Research universities and their affiliated academic medical centers and research institutes conduct a significant proportion of the clinical trials that lead to applications or petitions to the FDA. These institutions are required by HHS/PHS policy and consistent with the Federal Policy to maintain policies and procedures to manage allegations of research misconduct. The Federal Policy provides standards for performance and compliance that help ensure rigorous investigations while protecting investigators from frivolous allegations. The standard definitions and processes allow for timely review and mechanisms for response by the investigator, the institution and the federal agency.

Without these federal-wide standards, institutions will find it difficult to meet their compliance obligations. We urge the FDA to implement the Federal Policy for those individuals who are identified as having engaged in the falsification of data.

If the FDA does not use the Federal Policy, institutions may be placed in the vulnerable position of violating their own and other federal agency policies. The proposed FDA regulations call into question: a) the meaning or definition of falsification; b) the timetable for the inquiries and investigations; and c) the relationship between the FDA, other federal and private industry sponsors, and the investigator's home institution. Many FDA-regulated studies are supported by the National Institutes of Health (NIH). In such instances, complying with the proposed FDA regulations will bring an institution into direct conflict and non-compliance with the HHS/PHS regulations governing the NIH-supported study. This could lead to the untenable situation in which two reviews of an allegation would be conducted simultaneously – one by the FDA and one by the home institution.

### **Definition**

The definition for falsification of data proposed by the FDA is clearly covered by the Federal Policy and should be used by the FDA. The FDA argues that the breadth of the definition of research misconduct included in the Federal Policy and the HHS/PHS policy on research misconduct does not include the kinds of falsification of data encountered by the FDA.

We believe the Federal Policy definition addresses the FDA's concerns. Defined as manipulating materials, equipment, or processes or changing or omitting data or results "such that the research is not accurately reflected in the research record," the Federal Policy definition – repeated in the HHS/PHS policy – by any measures covers "creating, altering, recording or omitting data in such a way that the data do not represent what actually occurred."

The FDA's decision to abandon the Federal Policy and/or HHS/PHS policy because the research misconduct policy covers other elements of misconduct including fabrication and plagiarism ignores the manner in which these other elements can contribute to the notion of falsification. In its implementation, the FDA can decline to investigate reports of fabrication and plagiarism without abandoning the HHS/PHS policy.

### **Reporting Timetable**

The proposed 45-day reporting window violates the standard set by the Federal Policy for a fair and timely process of inquiry, investigation, adjudication and appeal at the home institution. Institutions are required by the federal agencies to conduct these phases in a timely manner. HHS/PHS directs the institution to complete the inquiry in 60 days and report to HHS's Office of Research Integrity (ORI) within 30 days of a finding that

warrants an investigation. The investigation must be complete within 120 days with appeals following the report to ORI.

This timetable is structured to ensure a thorough and careful review that provides the respondent to the complaint the opportunity to provide information and respond to the allegation. Throughout this process, the institution is required to report to the appropriate federal agency in a number of situations including if it determines that: the public health or safety is at risk; agency resources are threatened; the research should be suspended; and/or there is an indication of violations of civil or criminal law.

The requirement that a sponsor report within 45 days would not allow them time to work with the institution to conduct an appropriate inquiry into the allegations. Without the time necessary to conduct a structured and fair review, sponsors are likely to report allegations that an investigator may have engaged in falsification whether or not the sponsor can determine the intent of the alleged activity. This would do more harm than good and create a significant burden for all parties involved, including the FDA.

### **Investigation and Evidentiary Standard**

The FDA fails to describe what it will do or how it will proceed when it receives a sponsor's report. The FDA states in the Supplemental Information that it will examine "patterns, potential signals or other indications of misconduct" in order to conduct an investigation. If the FDA determines falsification has occurred, then the range of responses available to the FDA include excluding the affected clinical trial data from consideration in its deliberations to criminal proceedings.

How the FDA will conduct these investigations is a critical component to a fair response. The FDA asks what evidentiary standard or threshold should be used for the required reporting. The standard used by other federal agencies is defined in the Federal Policy as a preponderance of the evidence demonstrating a significant departure from accepted practices committed intentionally, knowingly, or recklessly. Honest errors or differences of opinion do not constitute misconduct. Again, we urge the FDA to use the Federal Policy as a model.

### **Exempt Research Institutions**

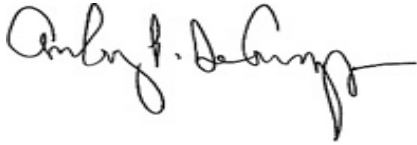
The FDA should exempt sponsors working with investigators from research institutions that fall under the HHS/PHS policy from the reporting requirement. Sponsors should be directed to report to the investigator's home institution and that institution would then report to the FDA in compliance with the HHS/PHS policy. The burden of the inquiry, investigation, adjudication, and appeals process would fall to the institution. The institution would use the same standards to report that it uses for other HHS departments and agencies including NIH.

We urge the FDA to: 1) bring its Falsification of Data proposal into conformity with the Federal Policy on Research Misconduct, and 2) define a role for research institutions as delineated in the Federal Policy. Having a policy at the FDA that is significantly different from all other federal agency policies will wreak havoc on the ability of institutions to meet their compliance obligations.

Institutions take seriously their responsibility to fully comply with federal policies regarding research misconduct. However, to force institutions to use increasingly scarce resources to address different policies,

conduct different types of reviews, and train staff to ensure compliance with different regulatory requirements without an obvious improvement in achieving the goal introduces unnecessary complexity into the process and imposes unreasonable burdens on our institutions.

Sincerely,



Tony DeCrappeo  
Council on Governmental Relations



Robert M. Berdahl  
Association of American Universities