



November 3, 2005

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By electronic mail to ReducingRegulatoryBurden@hhs.gov

Subject: Recommendations for Regulatory Reform

Dear Mr. O'Grady:

The Association of American Medical Colleges (AAMC) welcomes the opportunity you have provided to identify federal health care regulations that could be coordinated and simplified to reduce costs and burdens and improve the translation of biomedical research into medical practice (70 Federal Register 57877). The AAMC is a nonprofit association representing all 126 accredited U.S. medical schools, nearly 400 major teaching hospitals and health systems, and 94 academic and scientific societies. Through these institutions and organizations, the AAMC represents 109,000 faculty members, 67,000 medical students, and 104,000 resident physicians.

HIPAA and National Provider Identification (NPI) Implementation

The administrative simplification provisions of the Health Insurance Portability and Accountability Act (HIPAA) included requirements for a standard, unique health identifier for health care providers and other health care systems. On January 24, 2004, the Secretary published the final rule that established a unique health identifier for health care providers, the National Provider Identifier (NPI). Subsequently, on May 6, 2005, HHS published a communication outlining the 2005 NPI-related activities of CMS and crucial to the provider community. Providers (other than small health plans) must use NPIs in all standard electronic transactions by May 23, 2007, eliminating the use of other identifiers in use currently.

The communication also identified that NPIs could be applied for in one of three ways:

1. Through a web-based application process, initiated on May 23, 2005
2. Through a paper application process, available as of July 1, 2005 or

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Through an electronic file, when a provider granted permission to an employer, professional organization or other such entity, "available in the fall of 2005".

The faculty practice medical groups of the nation's medical schools employ, on average, 500 faculty physicians as well as additional health professionals who submit claims for services rendered to patients to CMS and other entities included in HIPAA requirements. Several faculty practice groups employ over one thousand clinical faculty.

Thus, many academic centers chose to wait for the availability of the electronic NPI enrollment process, stated to be available in fall 2005. As of the writing of this letter, the electronic process is not yet available and there have been some indications that the process will not be in place before January 2006, if then.

Delay of the availability of the electronic application process is creating burden in several ways. First, some entities, such as some of the more than 100 Department of Veterans Affairs medical centers affiliated with the nation's medical schools, have begun to initiate paper enrollment processes with physicians. Many of these faculty are employed by academic medical centers. This is causing confusion in the community, and faculty are turning to administrative staff to clarify their responsibilities and obligations. If this continues to happen during the prolonged delay of the electronic enrollment process, it will consume resources within the medical groups. Administrative staff will need to communicate with faculty about enrollment requests that were not initiated by the employing academic medical center, but which are likely to create continued confusion and unnecessary dual enrollments. Further, this problem may be exacerbated by the fact that specialty societies have also been informed that they can submit enrollments on behalf members and many faculty also belong to specialty societies.

Still further, if CMS continues to delay the implementation of the electronic enrollment process, it will cause other administrative burdens on academic medical centers. First, some institutions are already questioning whether or not they can afford to wait for the electronic systems, especially in light of the above-mentioned activity by other partnering entities, and instead need to implement enrollment processes for their faculty through the web-based program. If this option is pursued, institutions will likely need to hire temporary staff or pay overtime to staff to ensure that ongoing staff functions are fulfilled.

Finally, the absence of electronic transfer specifications at this time is leaving academic medical centers without an option of conducting a cost-benefit analysis of the programming requirements and thus the programming costs, compared to paying for the above-mentioned temporary or overtime staff.

HIPAA Privacy Rule and Research

AAMC has repeatedly pointed out the necessity for considering the significant and costly regulatory burdens that the Privacy Rule imposes on human subjects research.

On September 1, 2004, the Secretary's Advisory Committee on Human Research Protections (SACHRP) submitted to Secretary Thompson nine recommendations concerning needed clarification and modification of the Privacy Rule's impact on human subject research. That letter described SACHRP's motivation as follows:

“SACHRP fully and strongly supports the Department's commitment to enhancing privacy protections for human research subjects, and notes that consideration of privacy issues has long been a required part of the research application and approval process.... However, commentary from representatives of the Association of American Medical Colleges, the National Committee on Health and Vital Statistics, and a number of academic health science centers indicates that there have, and continue to be, significant problems associated with the implementation of HIPAA in the context of research involving human subjects.”

Previously, the AAMC, in collaboration with several highly respected scientific and professional societies, had conducted a survey in 2003 on the impacts of the Privacy Rule on research. The results showed alarmingly negative effects and formed the basis of a series of recommendations that we first presented to the National Committee on Health and Vital Statistics and then to SACHRP.

Based on its independent review, SACHRP developed its own recommendations for modification and clarification of the Privacy Rule's research provisions, many of which incorporate the AAMC's recommendations and all of which AAMC strongly endorses. Evidence and documentation continue to mount of the Privacy Rule's deleterious effects on human subjects research (see most recently Armstrong, D. et al., *Potential Impact of the HIPAA Privacy Rule on Data Collection in a Registry of Patients with Acute Coronary Syndrome*, Arch Intern Med. 2005; 165:1125-1129).

To date, there has been no action on or even response to the SACHRP recommendations of September 30, 2004 from the office of the Secretary of Health and Human Services. The Privacy Rule's negative impact on the ability to carry out vital aspects of translating innovation to the benefit of the public through medical practice – human subject research – is a matter of continuing and grave concern to the AAMC on behalf of the academic biomedical research community. The accruing costs on the research enterprise and on the ability to conduct research studies critical to human health are well documented. These burdens do not add measurably to patient privacy, and they significantly encumber critical types of research, including clinical trials, registry research, epidemiological and health services research, genetic research, and many other types. Adoption of SACHRP's recommendations of September 30, 2004 would substantially relieve these regulatory burdens and would not negatively affect patient safety or privacy.

Protection of Human Subjects (45 C.F.R. Part 46 and 21 C.F.R. Parts 50 and 56)

One of the most frustrating and costly areas of duplication, inefficiency, confusion, and disarticulation of federal regulations affecting health care can be found in the discordant regulations governing human research subjects as administered, respectively, by OHRP and the FDA.

In 1981, the Food and Drug Administration (FDA) and the Department of Health and Human Services (DHHS) reissued separate regulations for the protection of human subjects. The FDA regulations can be found at 21 C.F.R. Parts 50 and 56 and those for DHHS at 45 C.F.R. Part 46. The issuance was in response to a cry for harmonization between the FDA and DHHS. Any organization that receives federal funds and conducts a clinical investigation involving a test article must follow both sets of regulations.

Whereas the FDA and DHHS achieved harmonization in many ways, there remain significant discordances between the regulations that impose a vexing and unnecessary burden on universities and academic medical centers. Making the problem worse, there is no guidance from either FDA or DHHS as to how to manage these discrepancies when they arise in a particular research study.

The National Bioethics Advisory Commission conducted a thorough review of the two sets of regulations as part of its background work on the oversight system. In part, the discordances led the Commission to recommend the creation of one set of regulations. The Institute of Medicine made the same recommendation following its deliberations on ways to improve the human research protections oversight system. Further, bills introduced in both the House and the Senate over the past four years called with some urgency for the harmonization of the FDA and DHHS regulations.

General discrepancies that affect institutions include the following.

1. DHHS regulations require an institution to have an assurance of compliance. There is no such requirement in the FDA regulations.
2. FDA regulations require that only one IRB must review a research study whereas the DHHS regulations require that every institution engaged in the research is responsible for protecting human subjects and for complying with the regulations. This normally translates into each organization's conducting its own IRB review even though the regulations allow for the institution to make arrangements with another institution or entity for joint review. This regulation is the root cause of the IRB burden in multi-site research.

General discrepancies that affect IRBs include the following.

1. FDA and DHHS have different definitions of research. FDA defines a clinical investigation involving a test article as research, whereas DHHS defines research in terms of activities that are designed to generate or contribute to generalizable knowledge. Activities become subject to FDA regulations on the basis of their methods (use of drugs or medical devices) or if the research data will be submitted to or held for inspection by FDA. Activities become subject to DHHS regulation based on a DHHS funding source.
2. DHHS permits exemption of certain types of research studies from the federal regulations. The FDA permits the use of exemption for only two types of research, viz., for taste and food studies, and for emergency use of a test article. FDA and DHHS share only the exemption for taste and food studies. Under DHHS regulations, emergency use of a test article is not research.
3. DHHS has additional protections specified for pregnant women and fetuses in Subpart B and for prisoners in Subpart C; FDA does not have additional protections for these two populations.
4. FDA provides that sponsors and sponsor-investigators may request a waiver of IRB review (but not informed consent requirements); DHHS does not provide a comparable waiver.
5. FDA and DHHS allow the IRB to waive the requirement to document informed consent when the research involves no more than minimal risk; however, the criteria for waiver of documentation differ. FDA allows a waiver in only one circumstance, viz., when the research involves no more than minimal risk and involves no procedures for which written consent is normally required outside the research context. DHHS permits a waiver of documentation under either of two circumstances. The first is the same circumstance as the FDA. The second is when the only record linking the subjects and the research would be the consent document, and the principal risk would be potential harm from a breach of confidentiality.
6. DHHS regulations allow for waiving or altering the elements of informed consent (and parental permission) under certain conditions where the research is minimal risk. FDA has no such provision. FDA has a provision for a presidential waiver; DHHS does not.
7. FDA regulations provide for an exception from the informed consent requirements in emergency situations; DHHS regulations have no such exception.
8. FDA regulations require that subjects be informed that FDA may inspect the records of the study. DHHS regulations have no comparable requirement.

9. FDA regulations require that consent forms be dated as well as signed by the subject or the subject's legally authorized representative. DHHS regulations do not require that consent forms be dated.
10. FDA regulations require IRBs to follow written procedures for ensuring prompt reporting to the IRB of changes in research activity. DHHS regulations require IRBs to follow written procedures for ensuring prompt reporting to the IRB of proposed changes in research activities. Generally the FDA allows investigators to make minor changes to the research and report the change to the IRB. DHHS requires all changes to be IRB approved before implementation.
11. FDA regulations define a human subject to include the use of a specimen in research involving investigational devices, including use in a control group. This means that in FDA-regulated research involving the use of specimens and investigational devices, the investigator must obtain informed consent from the subject. This may be feasible when the specimens are identifiable. However, there is another requirement in the FDA regulations stating that when studies involve investigational devices and the use of *unidentified* tissues specimens, these studies involve human subjects and the investigator also must obtain informed consent.

In the DHHS regulations, studies that involve existing specimens that are identifiable may be exempt from the regulations, or if not, the provision to waive the requirement of informed consent may be exercised. For studies involving the use of unidentifiable specimens, the studies do not involve human subjects.

When the FDA and DHHS regulations directly conflict, the institution is at a loss as to how to comply. Further, important research might not go forward because it cannot be conducted in a fashion that meets the requirements of both the FDA and DHHS. This is an especially serious matter for academic research institutions.

Additional issues relating to human subject protections include the issue of informed consent. Informed consent documents have routinely become so lengthy (often 20 or 30 pages or more) that it raises doubt as to whether they are really read and comprehended, especially if the research subject is under stress from illness or without reading or language skills that match the complexity of the forms. Unnecessarily daunting consent forms can deter potential subjects and add to delays in human subject research. This hinders the process of true informed consent. However, because of the litigious nature of our culture, institutions are reluctant to remedy this situation without a clear mandate to do so from the Federal government. Guidance should be generated for the creation of short, readable, effective, and informative informed consents that contain all the required elements.

Finally, many enforcement actions taken by OHRP have exhibited a minute focus on process and an appearance of elevating mechanics over the substance of human subject protections. Regardless of the accuracy of this perception, it is vitally important, given the huge unfunded

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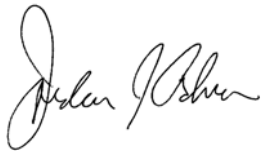
regulatory load that IRBs carry, that OHRP conduct studies to demonstrate which of the protections imbedded in 45 CFR Part 46 and in OHRP interpretations thereof actually contribute measurably to the protection of human subjects and which do not, and then to regulate and enforce accordingly.

Additional Regulatory Burdens relating to Research

Biomedical and health research faces a broad and complex array of regulations in addition to those noted above. Ranging from hazardous materials to radioactive isotopes to select agents to conflicts of interest, every research proposal submitted by an academic institution for federal funding must be accompanied by numerous certifications, assurances, and other compliance verifications. Such regulations often serve compelling social interests or provide important protections, and many serve as indispensable vehicles for scientific accountability. Frequently, however, it is the accumulation of regulations, each mandating distinct or duplicative requirements that has greatly increased the burden and costs of compliance. See The Council on Governmental Relations, Report of the Working Group on the Cost of Doing Business, June 2, 2003, <http://206.151.87.67/docs/CODB%20FINAL%206-02-03.doc>. The Department should look for opportunities to harmonize reporting requirements and other procedures where appropriate.

If you have any questions about these comments, please contact Denise Dodero at ddodero@aamc.org or Susan Ehringhaus at sehringhaus@aamc.org. Thank you for your consideration of the comments of AAMC.

Sincerely,

A handwritten signature in black ink, appearing to read "Jordan J. Cohen". The signature is fluid and cursive, with the first name "Jordan" being the most prominent part.

Jordan J. Cohen, M.D.