



October 26, 2011

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Department of Health and Human Services
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Re: HHS– OPHS–2011–0005 (Comments on 45 CFR Parts 46, 160, and 164 and 21 CFR Parts 50 and 56, “Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators”)

AcademyHealth, as the nonpartisan, professional home for more than 4,500 health services researchers, policy analysts, and practitioners, welcomes the opportunity to respond to the Advance Notice of Public Rulemaking (ANPRM) published July 26, 2011, “Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators.”

Human subjects research protections are a moral compass critical to the public good. Health services researchers—from an array of disciplines ranging from outcomes research to health economics—are subject to the Common Rule, which ensures that the individuals who participate in health services research are protected, and that the data with which we work are collected, used, and stored ethically and appropriately. In revisiting the Common Rule, the U.S. Department of Health and Human Services (HHS) has the unique and difficult challenge of balancing the need for rigorous protection of human subjects without inadvertently creating administrative burdens that unnecessarily hinder scientific innovation and progress.

We support HHS’s efforts to modernize regulations for protecting human research subjects while reducing the burden, delay, and ambiguity for investigators to produce valuable research. We are therefore pleased to offer the following suggestions for your consideration as you draft the proposed rule. We first summarize those areas where we offer general support, and follow by raising specific issues for your further consideration before issuing the proposed rule.

General Support for Common Rule Enhancements

Human subjects research protections apply to more than each primary study and data acquisition; data have many generations of utility for researchers. The rapid growth, landscape, and expansion of human subjects research in the advent of health informatics and technology necessitates a revision of the Common Rule. AcademyHealth endorses revisions that set ethically and morally rigorous standards for conducting research and that protect human subjects from physical, psychological, and informational risks. In this regard,

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AcademyHealth applauds the Office of the Secretary and the U.S. Food and Drug Administration for issuing this ANPRM. We agree that it is time to revise current regulations for protecting human subjects who participate in research and that it is possible to better protect human subjects while facilitating research and reducing burden, delay, and ambiguity for investigators and research institutions. AcademyHealth supports, in concept and intent, many of the proposed changes as described in the following seven sections of the current regulatory framework.

- Section II: Ensuring Risk-Based Protections. The ANPRM’s proposed refinements to the current review framework are a positive step toward ensuring that protections more appropriately reflect the level of risk of the research study. Currently, too many minimal-risk research projects are delayed by prolonged human subjects review, with the effect of reducing the number of studies conducted, delaying the time until we can inform the public and policymakers of results, and increasing the costs of research.

AcademyHealth also supports building in mandatory data security and information protection standards, and revising, clarifying, and continually updating review categories and processes. Reforming and expanding the current “exempt” category into an “excused” or “registered” category with default permission to proceed would encourage both responsible oversight of a broader swath of research as well as reduce the fixed burdens of minimal-risk research. However, these important benefits to the research enterprise need to be weighed against the potential risks created by shifting responsibility of the determination of exempt status to investigators, as noted later in this document. If these changes are adopted, explicit guidance to IRBs and the field will be essential to ensure consistency of implementation. Monitoring and early evaluation of the use of the new risk-based categories, in particular the new “registered” category, will be particularly critical to ensuring their appropriate use. Thus periodic monitoring of IRBs is warranted.

- Section III: Streamlining IRB Review of Multi-Site Studies. Utilization of a single IRB review of record for domestic sites of multi-site studies would be a significant improvement to the current process, whereby the review processes and variations in determination associated with multi-site reviews can often delay for months even low-risk projects. We recognize that this significant change will require substantial work with sites and clear guidance to minimize the likely resistance to relinquishing control that some institutions may exhibit.
- Section IV: Improving Informed Consent. Efforts should be made to streamline and simplify consent forms to achieve truly informed consent from human subjects. AcademyHealth supports those revisions to the Common Rule that eliminate confusion by defining appropriate content, restricting content that is inappropriate, enhancing readability, limiting the length of forms, reducing institutional boilerplates, and making

available consent form templates, while minimizing administrative burden and unnecessary hurdles to conducting research.

- Section V: Strengthening Data Protections to Minimize Information Risks. There is a great deal to learn from the Health Insurance Portability and Accountability Act (HIPAA) standards for identifiable and de-identified information and limited data sets, and AcademyHealth supports efforts to enhance data security and information protection under the Common Rule. AcademyHealth also supports continuing the practice whereby HIPAA-covered entities obtain data use agreements before disclosing limited data sets to investigators for research purposes.
- Section VI: Data Collection to Enhance System Oversight. AcademyHealth supports changes to the Common Rule that will simplify and consolidate safety data reporting already required of investigators. Streamlining data elements, implementing a Web-based, interagency data reporting tool, and harmonizing safety reporting guidance across federal research agencies would eliminate much of the current confusion and duplication associated with adverse event reporting. Such enhancements would also yield better data for more powerful and meaningful analyses of patient safety.
- Section VII: Extension of Federal Regulations. AcademyHealth believes that all entities conducting research—regardless of research funder—should abide by the Common Rule. As stated in the ANPRM, most institutions already voluntarily extend the applicability of their Federalwide Assurance (FWA) or other assurance of compliance to all research conducted at their institution, as the Common Rule sets the standard for liability. In the interest of simplicity and efficiency, AcademyHealth believes that the Common Rule protections should be extended to all research with human subjects conducted in the United States, regardless of the funding source, as recommended by the Institutes of Medicine, among others.
- Section VIII: Clarifying and Harmonizing Regulatory Requirements and Agency Guidance. AcademyHealth supports efforts to address variations in guidance and enhance consistency across the federal government, where appropriate. Such efforts will reduce uncertainty among researchers and human subjects, and reduce regulatory burden.

Items for Consideration in Proposed Rule

In order to achieve a learning health care system and improve quality, we need continuous evaluation, generation of evidence, learning, and application of that knowledge. We applaud HHS for initiating this national dialogue, particularly as it concerns the integration of research and quality improvement goals and methods. We think this dialogue is critical both to the success and safety of current national efforts to increase value in health care and to the continued development of the health services research tools and methods needed to support these efforts.

Despite AcademyHealth's overarching support of HHS's efforts to modernize the Common Rule, the ANPRM proposes many changes that—if promulgated as currently proposed—could inadvertently stymie data access and the production of health services research used to improve health and health care. AcademyHealth thus urges HHS to carefully consider the following issues when drafting the proposed rule.

- Section II: Ensuring Risk-Based Protections. Building risk-based protections into the Common Rule and thereby relieving IRBs of the task of evaluating informational risks is conscientious. Nevertheless, there may be studies where some IRB involvement is beneficial. The change proposed in the ANPRM exempts a large swath of research from IRB review based solely on its methodology, not its topic. While this proposal may be appropriate for the vast majority of survey, focus group, and interview studies, HHS should consider including a modification that such studies that involve sensitive topics be subject to some level of IRB review.

Determinations of minimal risk should align with review categories, whether full, expedited, or exempt/registered. As discussed in Question 13 of the ANPRM, a reporting requirement and/or registration may be burdensome, but it is nonetheless valuable to engage IRBs in ongoing research and provide some transparency for the research enterprise. AcademyHealth recommends that HHS consider incorporating evaluation into any new procedure to ensure it is having the intended effect and not unduly obstructing research or oversight.

Additionally, Question 24 raises the issue of application of the Common Rule to quality improvement (QI), public health activities, and program evaluation. Recent years have seen substantial growth in the number and types of quality improvement activities to improve the safety and quality of care. The majority of those activities are integral to the process of providing care and need not necessarily be subject to IRB oversight. However, exemption from IRB oversight does not relieve organizations from their responsibility to have a mechanism to review their quality improvement projects and studies to ensure that they are designed well—well enough certainly to produce the desired learning—and that unintended consequences have been considered and, if necessary, will be monitored. In addition, mechanisms for assessing and managing privacy and data security concerns related to QI projects will require continued development.

Formal research methods have increasingly been applied to quality improvement activities, and this emerging body of work—at times labeled quality improvement research, implementation science, or yet other terms—exhibits wide variation in how it is treated by institutions and investigators. Some actively seek, or are required to seek, IRB review while others do not. Further clarification will be required in the proposed rule; HHS must carefully consider how to address the intersection between the quality

improvement and research worlds without hindering the ability of health care and other organizations to improve their performance and monitor the effects of such improvements. HHS might consider developing a reasonable risk framework to guide IRB oversight of these activities. Reducing the complexity of proceeding with a simplified IRB submission under the newly proposed “registered” category could encourage faculty in “registering” more QI projects.

Similarly, legal distinctions permit governmental public health agencies to exercise public health authority to undertake activities involving interventions and to measure the value of those activities. Likewise, a designated IRB review track for program evaluation would be beneficial, though clarification is important for when activities would or would not fall under IRB oversight. A registered category would be appropriate to document and track important research, as well as ensure consistent processes across all research sites involved and develop cross-site knowledge.

- Section III: Streamlining IRB Review of Multi-Site Studies. Single IRB review would undoubtedly reduce administrative burden and enhance the timeliness of research, but in drafting the proposed rule HHS must address the political, administrative, and legal complexities. For instance, what criteria should be used to identify the single IRB in a multi-site study, e.g., principal investigator location, IRB specialty, reputation, or existing relationships with an IRB? Many protocols currently direct subjects to contact the institution’s IRB with issues or questions. How do you address institutional accountability when there is a single IRB for a multi-site study? HHS must also address secondary consequences, such as how to allocate liability, and whether an appeals process is necessary.

In drafting this provision, AcademyHealth encourages HHS to consider the experiences of IRB systems that have already implemented more centralized IRB review processes, such as the Veterans Health Administration’s VA Central Institutional Review Board. After a four-year, deliberative phase-in process, the VA system is functioning effectively and integrating a local review level to respond to concerns that sites would be mandated by default to carry out activities to which they did not agree.

- Section IV: Improving Informed Consent. Technology has advanced to the point where researchers can conduct probabilistic linkages that they could not years ago. Informed consent standards and restrictions should accordingly take into account the multi-generational benefits of collected data. Nevertheless, HHS’s proposal regarding consent for future uses of data previously collected for research purposes is intensely controversial, and there is substantial variation in the health services research community regarding whether or not informed consent should be required on the reuse of data beyond the initial collection.

On the one hand, there are good reasons to require new consent—or at a minimum, a blanket consent for future data uses—even if the data are not personally identifiable. For example, receiving consent for one research purpose and using the research for another purpose without consent may be offensive or harmful to the research subject(s). Considering the interests and preferences of research subjects is always beneficial to science, and has the potential to enhance subjects’ willingness to participate in future research.

On the other hand, requiring consent for data reuse is clearly impracticable in many cases, especially in terms of use of the types of established multi-use data sets that meet current data use and privacy protection standards. In this regard, requiring consent could unduly hinder the generation of evidence used to answer critical health care quality, delivery, financing, and policy questions.

Given the lack of clear consensus, and the significant implications for health services research, AcademyHealth encourages HHS to carefully consider the impact of informed consent provisions on the reuse of data beyond the initial collection and determine how best to leverage existing, de-identified data sets to generate knowledge in a way that is consistent with the protection of rights. In so doing, HHS might consider an approach that establishes a presumption that new consent is required, allowing a waiver of that requirement in certain circumstances depending on the practicability of obtaining consent and the risk concerns for patient safety and privacy. HHS might also consider “blanket” reuse consents as a standard that IRBs would accept under most circumstances for certain types of data (e.g., claims data).

- Section V: Strengthening Data Protections to Minimize Information Risks. Further deliberation and clarification is needed on what would qualify as sensitive information under the proposed rule. For example, if a higher level of security, consent, or review is required for mental health data, as suggested in the proposed rule, important progress on critical parity gains may be lost. Screening and treatment for depression is recommended in many clinical situations (perinatal care, chronic disease care), and labeling such information as ‘sensitive’ would require that many low risk studies undergo full review. In addition, such a label might discourage investigators from collecting such important information, an unintended consequence that would decrease research validity. This issue is of course separate from federal rules that appropriately apply to substance abuse and other circumstances. Similarly, legal implications also should apply as appropriate (e.g., subpoenas).

Further consideration is also needed on Question 62 and whether HIPAA-covered entities should be able to obtain limited data sets for research without establishing a data use agreement (DUA). Although DUAs introduce administrative costs and burden into the research process, they are also a crucial cornerstone to prevent inappropriate uses of data,

to clarify the expectations between the parties, and to underscore key security controls that must be in place and the actions necessary in the event of security breach.

The proposed prohibition to re-identify de-identified data raised in Question 63 is one of particular concern for the field of health services research. Such an absolute prohibition could inhibit the ability to link data sets via re-introduced data fields. For example, an autism research registry could use re-identified data to link statewide patient and parent-reported data with Medicaid claims data in order to study treatment practices, and many other critical research and policy questions. Researchers have typically addressed this challenge by engaging a trusted third-party to re-identify the data as an honest broker that facilitates data linkage while preserving researchers' distance from possible identification. HHS may wish to consider issuing broad guidance to inform IRB decisions as to the reasonableness of trusted-third parties.

Finally, AcademyHealth encourages HHS to incorporate a regular review of the Common Rule regulatory framework into the proposed rule to ensure that human subjects research protections are responsive and flexible to evolving research needs and practice. We hope that the current effort to revise the Common Rule is the start of a nationally sponsored dialogue that succeeds in further protecting human subjects rights and incentivizing innovative health care research.

Thank you for the opportunity to submit these comments. We look forward to working with you to finalize and implement the proposed rule, and address our concerns and suggestions.

Sincerely,

A handwritten signature in black ink, appearing to read "Lisa Simpson". The signature is fluid and cursive, with the first name "Lisa" and last name "Simpson" clearly distinguishable.

Lisa Simpson, M.B., B.Ch., M.P.H., F.A.A.P.

President and CEO, AcademyHealth