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INTERNAL MEDICINE | *Doctors for Adults*

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(submitted electronically at www.regulations.gov)

Jerry Menikoff, MD, JD
Office for Human Research Protections
U.S. Department of Health and Human Services
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Re: Docket HHS-OPHS-2011-0005
Advance Notice of Proposed Rule Making, *"Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators"*

Dear Dr. Menikoff,

The American College of Physicians (ACP) appreciates the opportunity to offer comments on the advance notice of proposed rulemaking (ANPRM) on human subjects research protections, better known as the Common Rule. ACP is the largest physician specialty society and second-largest physician membership organization in the United States. ACP represents 132,000 internal medicine physicians and medical student members. Internists specialize in primary and comprehensive care of adolescents and adults.

General comments:
ACP shares the goals of the ANPRM to modernize and make more effective the regulations for the protection of human subjects. Despite the name of the ANPRM, however, it is not always clear that the proposed changes to the regulations consistently prioritize enhancing protections for subjects over reducing burdens for investigators. Also, opportunities have been missed to try to address issues regarding education about the regulations; to clarify and provide guidance on research versus quality improvement activities; and to explore issues regarding commercial institutional review boards.

Specific comments:

I. Background

We agree with the characterization of the ANPRM of the problems regarding the current Common Rule: that the system does not adequately calibrate the review process to research risk; there are inefficiencies in review of multi-site studies by multiple institutional review boards (IRBs); and there are concerns about the informed consent process; risks associated with use of genetic information, biospecimens and other data; monitoring and evaluation of the current system; adequate protection of all research subjects; and multiple regulatory requirements and variability across IRBs regarding interpretation and implementation. While we largely agree with the diagnosis, the suggested "cures" do not always seem to put subjects first.

II. Ensuring Risk-Based Protections

1. Full Convened IRB Review

   ACP agrees with maintaining the requirement that research involving greater than minimal risk be reviewed by a convened IRB. We also agree with the proposal that continuing review not be required (as long as the IRB has the option to override this default) where the remaining study activities are limited to data analysis or accessing follow-up clinical data from procedures subjects would undergo as part of standard care. We would, however, require continuing review if a study involved cognitively impaired subjects.

2. Revise Approach to Expedited Review

   ACP supports the updating of the list of research activities that qualify a study for expedited review along with a standing panel that would periodically update the list based on a systematic, empirical assessment of levels of risk. We also support establishing a default presumption that a study including only activities on the list is a minimal risk study subject to expedited review. Eliminating continuing review for these studies would be acceptable (with the default that a reviewer could determine that continuing review for a particular study enhances protections).

3. Moving Away From the Concept of Exempt

   ACP disagrees with the revisions to the category of exempt research and the conclusion that these revisions increase protections. We find the use of the concept "Excused" studies unclear and inadequate to protect subjects. We disagree with the assertion that the new data security and information protection standards make it possible to enlarge the coverage of the "Excused" category, especially regarding use of biospecimens, which are not truly de-identifiable. As the ANPRM itself recognizes, "…what constitutes "identifiable" and "de-identified" data is fluid; rapidly evolving advances in technology coupled with increasing volume of data readily available may soon allow identification of an individual from data that is currently considered de-identified. In this sense, much of what is currently considered de-identified is also potentially identifiable data."

ACP policy asserts that research with human biological materials has implications for the privacy of research subjects and individuals with a genetic relationship to research subjects. Fully informed and transparent consent requires the disclosure of all potential uses of patient data. The consent process needs to include the desired preferences of research subjects regarding future contact for notification about results and/or consent for additional research participation. Research should be limited to the use specified by the protocol during the informed consent process. Communication of the risks and benefits of research involving biological material allows research subjects to make a well-informed decision. Further study is needed to resolve informed consent issues related to future research use, including biologic materials. The 2009 Institute of Medicine (IOM) report, *Beyond the HIPAA Privacy Rule: Enhancing Privacy, Improving Health Through Research*, recommends allowing future use of existing materials for research if the following conditions are met: "(1) the individual's authorization describes the types or categories of research that may be conducted with the PHI stored in the database or biobank; and (2) an IRB determines that the proposed new research is not incompatible with the initial consent and authorization, and poses no more than a minimal risk." These issues require far more consideration than is given in the ANPRM.

The proposed rule does not give sufficient weight to the importance of informational risks and puts too much reliance on determinations that would be made by investigators, not IRB reviewers, eliminating necessary checks and balances. Instead of an expanded and largely unregulated "Excused category," proposed changes to the rule should instead provide guidance on the development of tools for more standardized review.

III. Streamlining IRB Review of Multi-Site Studies

The desirability of a mandate that all domestic sites in a multi-site study use a single IRB as their IRB of record for that study is unclear. On the one hand, this could lessen delay and burden on investigators. However, it could also lead to IRB-shopping (as noted in the ANPRM in question 34) and it eliminates local IRB review based on local needs and interests. And where does this leave community consultation? A potential compromise position seems to be stated in the ANPRM when it says, "For research where local perspectives might be distinctly important (e.g., in relation to certain kinds of vulnerable populations targeted for recruitment) local IRB review could be limited to such considerations…" Also, as the ANPRM notes, "While the Common Rule does require each institution engaged in a multi-site study obtain IRB approval of the study, *it does not require that a separate local IRB at each institution conduct such review* [emphasis added]." Education on

these points and perhaps guidelines spelling out limited circumstances for which local review would be appropriate would be helpful.

IV. Improving Informed Consent

ACP supports more emphasis on the process, not just documentation, of informed consent. This would include simplifications in informed consent documents with guidance for clearly defined information, but only after the standards for such consent are established. For example, ACP does not support a brief form to obtain consent if it is for future open-ended use of biospecimens in research.

V. Strengthening Data Protections To Minimize Information Risks

ACP supports common definitions for identifiable and de-identified information under both HIPAA and the Common Rule.

VI. Data Collection to Enhance System Oversight

ACP supports establishment of an electronic reporting system for adverse events.

VII. Extension of Federal Regulations

ACP supports requiring domestic institutions that receive some federal funding from a Common Rule agency for research with human subjects to extend the Common Rule protections to all research studies at their institution.

Thank you for the opportunity to comment on the advance notice of proposed rulemaking on human subjects research protections. We hope these comments are of assistance. If you have any questions, please feel free to contact Lois Snyder, JD, Director of ACP's Center for Ethics and Professionalism at 215/351-2835 or lsnyder@acponline.org.

Sincerely,

Virginia L. Hood, MBBS, MPH, FACP
President, American College of Physicians

cc: Lois Snyder, JD