December 31, 2015

(submitted electronically at www.regulations.gov)

Jerry Menikoff, MD, JD
Director
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-2015-0008
Notice of Proposed Rule Making, "Federal Policy for the Protection of Human Subjects"

Dear Dr. Menikoff,

The American College of Physicians (ACP) appreciates the opportunity to offer comments on the notice of the United States. ACP members include 143,000 internal medicine physicians (internists), related subspecialists, and medical students. Internal medicine physicians are specialists who apply scientific knowledge and clinical expertise to the diagnosis, treatment, and compassionate care of adults across the spectrum from health to complex illness. Many internists contribute to medical research.

General Comments:
ACP shares the goals of the NPRM to modernize and make more effective the regulations for the protection of human subjects. Despite the goal of the NPRM to enhance the protections of human subjects, however, and in answer to Question 1 for public comment, the proposed changes to the regulations do not consistently prioritize enhancing protections for subjects over reducing burdens for investigators. They also do not help to build trust and confidence in how research is conducted. Question 1 gets the priorities backwards when it says: "Public comment is sought on whether the proposed changes will achieve the objectives of (i) decreasing administrative burden, delay and ambiguity for investigators, institutions, and IRBs, and (ii) strengthening, modernizing, and making the regulations more effective in protecting research subjects."

We agree with the characterization of many 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 multisite 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.

We note that the Secretary's Advisory Committee on Human Research Protections (SACHRP) has called for a comprehensive rewrite of the NPRM to simplify and focus the proposed changes. SACHRP commented that, "Despite extensive study of the NPRM in collaboration with numerous colleagues, the universal assessment is that the proposals are virtually impenetrable due to opaque language, unclear concepts, the overlapping nature of various elements, and the intricate relationships of elements to one another. A common refrain is, "If we cannot understand this, where will that leave the average IRB, administrator, and investigator?"" We agree.

ACP also agrees with SACHRP, Public Responsibility in Medicine and Research (PRIM&R) and others who have recommended formal and comprehensive research ethics education programs along with clear delineation of investigator responsibilities, a lost opportunity not addressed in the NPRM.

Further, the NPRM discussion of ethical principles in research and its treatment of "beneficence" emphasize beneficence for society, which leads to conclusions that are not appropriately protective of human subjects (see ACP's specific comments below). The Belmont Report notes the concept of societal beneficence but

Additionally, the NPRM frequently speaks of the principle of autonomy when the principle at stake is actually respect for persons, which is broader and includes respect for autonomy.

The NPRM's fundamental misinterpretation of the Belmont Report and research ethics principles has resulted in proposals that are not sufficiently protective of human subjects.

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informed consent for broad consent to the storage, maintenance, and secondary research use of biospecimens or identifiable private information should include: (i) A general description of the types of research that may be conducted with information and biospecimens and the information that is expected to be generated from the research, the types of information or biospecimens that might be used in research, and the types of institutions that might conduct research with the biospecimens or information…"

Many potential subjects, however, would only consent to use of their biospecimens or information for research on a particular disease— say, cancer research— or even more specifically, breast cancer research (and many might strongly object to uses other than those specifically enumerated, as did the Havasupai tribe). In the provision above, "A general description" should be changed to something along the lines of: *A description of the types or categories of research such as a disease category (ie, cancer) or specific disease (ie, breast cancer) that may be conducted…* This would allow for more meaningful consent when implemented along with the other provisions of this section.

Single IRB and Streamlining IRB Review of Multi-Site Studies

ACP supports the proposal that all domestic sites in a multi-site study use a single IRB as the IRB of record, chosen by the funder to help safeguard against IRB-shopping. If workable, this might help lessen delays in research. However, criteria for how the IRB is to be chosen need to be established and there needs to be a robust mechanism for engagement and input by local IRBs based on local perspectives, laws, training requirements and community consultation. Guidelines on how to accomplish this are needed.

Improving Informed Consent

ACP supports more emphasis on the process, not just documentation, of informed consent. We support the proposed simplifications and refocusing of informed consent documents with guidance for clearly defined information. However, ACP has concerns about the proposed consent process for biospecimens and identifiable information in research as noted above.

Data Collection to Enhance System Oversight

ACP supports establishment of an electronic reporting system for adverse events and is disappointed this has been removed from the NPRM.

Extension of Federal Regulations

ACP supports extending the Common Rule to all clinical trials conducted at US institutions that are federally funded for human subjects research.

Final Comments:

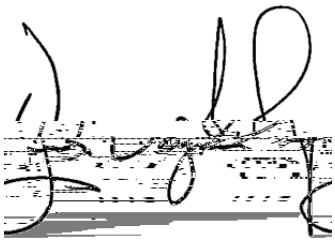
Throughout the NPRM the terms "subjects" and "participants" are both used, while the Common Rule uses subjects to refer to those who volunteer for research. We urge that any changes to the Common rule also use the term "subjects." This is a deliberate choice of laws, tissue specimens a Collection institutions

necessarily benefit from the research. They should not be identified with a passive term such as participants. "Subjects" recognizes the power and knowledge imbalance between investigators conducting the research and individuals on whom the research is conducted, and makes clearer the need for regulations and processes to help ensure respect, and protection, for those who volunteer.

We were also concerned to learn that most of the 1051 comments on the ANPRM were received from investigators and urge that HHS make a concerted effort to solicit more input from subjects, research ethicists and the research protections community for a more balanced approach. Also, as ethics is not a matter of majority opinion, we would hope that the many summaries of the "majority of comments" throughout the NPRM do not necessarily represent the direction of the final rule. We hope that attention to ethical concerns will be heightened above concerns about efficiencies in research.

Thank you for the opportunity to comment on the 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 Sulmasy, JD, Director of ACP's Center for Ethics and Professionalism at 215/351-2835 or lsnyder@acponline.org.

Sincerely,



Wayne J. Riley, MD, MPH, MBA, MACP
President, American College of Physicians

cc: Lois Snyder Sulmasy, JD