AAAS
ADVANCING SCIENCE, SERVING SOCIETY

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Jerry Menikoff, M.D., J.D.
Office for Human Research Protections
Department of Health and Human Services

Re: Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators
Submitted via www.regulations.gov

Dear Dr. Menikoff:

On behalf of the American Association for the Advancement of Science (AAAS), we welcome the opportunity to comment on the Advance Notice of Proposed Rulemaking entitled *Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators*. AAAS has a longstanding interest and expertise in research ethics, including issues related to the conduct of human subjects research. We support the thrust of the ANPRM, which recognizes the need for balancing the goals of protecting human subjects and allowing research to proceed without burdensome restrictions that provide little value. It is in that context that we offer the following comments:

Ensuring Risk-Based Protections (Section II)
Questions 5, 14, 15, 17, 19
Risk should be determined on the basis of research methods, the content of the research, and the characteristics of the participants. IRBs should have the flexibility needed to oversee research on vulnerable populations.

The list of research activities that can qualify for expedited review, not revised since the late 1990s, should be updated to reflect changes in research, technology, and any revisions forthcoming via this ANPRM. The ANPRM, however, does not include a process for such updating. We urge that whatever process is adopted be open and participatory, using the provisions of the federal Administrative Procedure Act (Public Law 79-404) applicable to the standard rulemaking process.

We support eliminating limitations on the current category 2 exemption (e.g., use of educational tests, survey procedures, interview procedures or observation of public behavior), "since these studies would be conducted with competent adults and because these studies would now be subject to standard data security and information protection standards." This list should also include safe interactive games and similar technologies.

We agree that researchers undertaking "excused" research should register with the IRB and think that a brief waiting period should be in place before such research commences. During

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this waiting period, IRBs could determine whether the research falls within the "excused" category. This way, the institution retains responsibility for determining whether IRB review is warranted.

Audits Related to Human Subjects Research (Section II, V)
Questions 13, 21, 22, 66
The ANPRM suggests that audits be considered to ascertain whether the new "excused" category is being appropriately applied, when IRBs override the default position on continuing review, and to ensure compliance with an institution's data security standards. We think it prudent that audits be conducted in these areas, with reports submitted to OHRP (or another appropriate oversight body), following the issuance of a final rule. This mechanism would enable OHRP to assess whether IRBs or other institutional entities are applying the new regulations in a consistent manner both within and among institutions. Further, it would provide a roadmap for OHRP to issue further guidance and to clarify the regulations. We are sensitive, however, to the goal of reducing the administrative burden on institutions and on federal oversight agencies. Therefore, we propose that audits be most prevalent in the few years immediately following the adoption of the new regulations, followed by a gradual reduction, as appropriate. We recommend that institutions be responsible for determining which entities should conduct the reviews.

Appeals to IRB Decisions (Section II)
Question 28
The new regulations should require institutions to adopt an appeals process, and the question of whether a study requires IRB approval should be one of the grounds for appeal. The institutions should determine the composition of the appeals entity, being careful to ensure that there are no significant conflicts of interest.

Additional IRB Activities (Section II)
Question 29
Transparency and accountability would be furthered by requiring IRBs to identify activities they undertake that are not required by regulations. Moreover, greater efficiencies are likely to be achieved when IRBs focus on what is most critical for implementing the regulations.

Improving the Informed Consent Process (Section IV)
Questions 35, 37
It is paramount that research subjects understand the research to which they are giving consent; thus, we strongly support the effort to encourage clearer consent forms. We encourage the rules to allow creative ways for researchers to convey the necessary information to subjects (e.g., video, slides) and to evaluate their understanding (e.g., follow-up questionnaires). This flexibility may be particularly important when conducting research with vulnerable populations.

Consent for Future Research (Section IV, V)
Questions 49, 52, 55
Although it is difficult to re-identify data and biospecimens that have been de-identified, we are aware that it is possible, if unlikely. Therefore, we support obtaining general consent for further research use of personal information. However, we also are mindful that this might place a heavy administrative burden when data or biospecimens are collected in a clinical or

other non-research setting, where personnel are not familiar with research issues and not prepared to address questions that might be raised when consent is sought for unspecified future research. We recommend that OHRP seek further advice on this complex subject, perhaps through workshops or some other mechanism where ideas can be discussed by those most closely involved with research of this type, as well as ethicists and others concerned with the protection of research subjects. We also believe the federal oversight entities should be aware of technological developments that could make it either easier or more difficult to de-identify data or biospecimens and update regulations and/or guidance as appropriate. To avoid an excessive administrative burden, we suggest that the new consent rules be applied prospectively only, grandfathering in biospecimens already collected.

Consent policies applicable to biospecimens in the biomedical research context should not be automatically applied to secondary uses of social science and behavioral data. We believe that consent should not be required from the original sources of the data if the latter are de-identifiable when used for other research. We take this position for two reasons. First, there is a risk of impeding the development and dissemination of new research methods. The use of existing data sets, and those yet to come, by the research community is often the best way to test newly proposed statistical or other methods before they become standard practice. Second, it is common for university instructors to use data sets for educational purposes, enabling students to "play" with real data as a learning tool. We are concerned that the availability of such data sets may be reduced. In both instances, the chances of re-identifying individuals is so small and the benefits to research and education so substantial, that the burden imposed on researchers is outweighed by the contributions such data make to future research and education.

Strengthening Data Protections (Section V)
Questions 54, 59, 61, 63
AAAS applauds the goal to harmonize and standardize data security. However, the idea to eliminate the need for IRBs to review research for information risks represents a major change in the current regulations, and some issues need to be more clearly addressed.

The HIPAA administrative, physical and technical safeguards for data security reflect a strong approach to protecting human subjects. However, HIPAA was designed to safeguard protected health information, and the HIPAA Security Rule as currently written only applies to electronic forms of information. Hence, its adoption as the single standard for protecting and safeguarding information would be difficult to apply uniformly across all types of research studies. Much social and behavioral research is likely to be subject to the new security protections, and the change has particular salience for those research fields. Furthermore, multidisciplinary research may rely on a combination of data forms, and the methods used to collect and store information, as well as information risks, may differ.

Hence, AAAS recommends that HHS carefully weigh the burden it would impose by applying such a uniform security standard across disparate research fields. With regard to social and behavioral sciences, alternative or complementary approaches to HIPAA may be found in the current body of literature and corresponding federal agency policies that address data security with the goal of minimizing information risks. We do support the idea of regularly evaluating the HIPAA de-identification standard to ensure it reflects evolving technologies and informational risks. The policy must grow with innovation.

In general, AAAS agrees that there should be a prohibition against re-identification without informed consent of the individual. However, we recognize that there are unusual circumstances when re-identification may be necessary in order to contact individuals in the interest of their personal health and safety, or some public health emergency.

Data Collection to Enhance Oversight (VI)
We generally support the proposed changes intended to improve "the collection and analysis of data on unanticipated problems and adverse events." It should be clear that the changes apply to the research protocol and its consequences for research subjects and others, and not to the broader application of research findings. Creating a single web site for reporting "unanticipated problems and adverse events" and harmonizing reporting requirements across all federal agencies would create a more efficient, and we believe safer, system for enhancing oversight.

Extension of Federal Regulatory Protections (Section VII)
We support extending the federal regulations to cover a broader sweep of human subjects research, as proposed in the ANPRM. However, we note that such an extension would still fall short of covering a source of research likely to grow in the near term. We refer to online health communities, such as PatientsLikeMe, which are attracting patients, and their health data, with increasing support from private investors and/or a for-profit business model. Neither federal funds nor IRB review are necessarily involved, yet such groups are committed to engaging in research, a reason that motivates their members in growing numbers to volunteer information about their health. One recent example is the community-based research on ALS appearing in *Nature Biotechnology* (29, 411–414, 2011). We recognize the statutory constraints on HHS to apply the regulatory protections in such cases, but nevertheless we use this opportunity to identify a significant gap in protecting patients from the risks associated with human research.

AAAS is the world's largest multidisciplinary science society, representing the interests of ten million scientists worldwide, and publisher of the prestigious peer-reviewed journal *Science*. We stand ready to assist you as you consider the vitally important questions and challenges that pertain to the protection of human research subjects.

Sincerely,

Alan Leshner