October 11, 2011

Jerry Menikoff, M. D., J. D.
Office for Human Research Protections
Department of Health and Human Services
1101 Wooton Parkway, Suite 200
Rockville, MD 20852

Re: Comments on the advance notice for proposed rulemaking on human participants research protections (HHS-OPHS-2011-0005)

Dear Dr. Menikoff:

The American Psychological Association (APA) applauds the Department of Health and Human Services Office for Human Research Protections (OHRP) for undertaking the process of revising the federal regulations for the protection of human research participants with the purpose of ensuring that the regulations remain relevant to current research. The proposed revisions to the Common Rule outlined in the advance notice of proposed rulemaking (ANPRM) that was published on July 26, 2011, in the *Federal Register* will have a significant impact on research in the behavioral and psychological sciences, and as such APA is especially grateful for the opportunity to comment.

However, APA would like to note that this rare opportunity to revise the regulatory system for oversight of research with human participants would ideally have entailed a more systematic review of all current regulations, instead of focusing exclusively on the Common Rule. A more in-depth examination of the interplay and overlap between the various regulations, with the involvement of all stakeholders, including the regulatory agencies, the research community, and the public, would have been a more effective mechanism to ensure that burden, delay, and ambiguity for researchers is reduced, while enhancing protections for research participants.

With a membership of over 155,000 researchers, educators, clinicians, consultants, and students, APA is the largest scientific and professional organization representing psychology in the United States and is the world's largest association of psychologists. Through its divisions in 54 sub-fields of psychology and affiliations with 60 state, territorial, and Canadian provincial associations, APA works to advance psychology as a science, as a profession, and as a means of promoting human

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welfare. For decades behavioral and psychological scientists as well as social scientists have been advocating for revisions to the federal regulations for the protection of human research participants. The changes they sought would substantially reduce the regulatory and administrative burden associated with the oversight of much behavioral and social science research, without compromising research participant protections. For many, the revisions envisioned were minor adjustments to certain requirements of the Common Rule, which would greatly facilitate the conduct of research that involves no more than minimal risk of harm to participants. The changes proposed in the ANPRM, however, are substantive, and likely will have some positive effects but may also have many unintended negative consequences for the conduct of behavioral and psychological research with human participants. Instead of addressing each of the 74 questions raised in the ANPRM, APA is providing general comments, though we do note when our comments address one or more of the questions.

I) General concerns regarding biomedical focus of the proposed changes

APA recognizes and appreciates the need to reduce unnecessary regulatory burden – that is, regulatory requirements that have little, if any, impact on the protections afforded human research participants. To that extent, the proposal to focus scarce institutional resources on the oversight of high risk research, rather than research that is of no more than minimal risk is warranted. Although APA is supportive of the proposal to undertake a re-evaluation of both the types of research that may be exempt from IRB oversight and the categories of research that qualify for expedited review, we consider the proposed new standards for data security and information protection (and in some cases informed consent) as germane to research in a very specific area (i.e., genetic/genomics research), but as inappropriate for research in many of the disciplines and sub-disciplines covered by these regulations.

A major strength of the Common Rule is its inherent flexibility that makes it applicable to all types of research, ranging from high risk biomedical studies and clinical trials to minimal risk behavioral research to low or no risk social research. One of our major concerns regarding the proposed new regulations is that they appear to be based largely on a biomedical research model and apply almost exclusively to health data. This seemingly singular focus ignores the existence and value of other research models that generate different types of data. To illustrate our point: throughout the ANPRM the terms biospecimens and “other existing data” are often used interchangeably. Given the breadth of data types that exist, it seems imprudent to base regulations on one specific type of data (i.e., biospecimens) and diminish the significance of all other data types by relegating them to a generic “other existing data” category.

This narrow biomedical focus also undergirds the proposed data security and information protection standards modeled after the Health Insurance Portability and Accountability Act’s (HIPAA) Privacy Rule requirements, which are cumbersome at best and are in many ways also

inappropriate for non-health-related data/information. In many circumstances, the application of HIPAA Privacy Rule requirements to behavioral and psychological research data will be unnecessarily burdensome as much of the data generated in such research do not require the same level of protection as confidential, individually-identifiable health information. Thus, we cannot overemphasize the need to be cognizant of the fact that, like the current Common Rule, these proposed new regulations would apply to *all* research with human participants, not only biomedical studies. For this reason, we kept non-biomedical research foremost in mind as we reviewed the proposed changes.

II) Ensuring risk-based protections

APA has long been an advocate for ensuring the highest level of human research participant protections with the lowest level of regulatory burden. Thus, we welcome the proposal to ensure that the human research participant protections are commensurate with the risks of harm associated with participation in the research.

(a) New data security and information protection standards to minimize informational risks

The ANPRM asserts that risks associated with all non-biomedical research (which includes behavioral, cognitive, educational, psychological, and social research) stem primarily from inappropriate use or disclosure of information (i.e., informational risks). The ANPRM further asserts that IRB members may not have the expertise to evaluate such risks. Thus, the ANPRM proposes to relieve the IRB of the responsibility to assess informational risks by adopting new data security and information protection standards modeled after the Privacy Rule promulgated under HIPAA. The Privacy Rule applies specifically to individually identifiable health information (IIHI) or protected health information (PHI). Applying the same data security and information protection standards to *all* identifiable data, regardless of whether it is health-related and regardless of the risk associated with disclosure of that information is of great concern to APA. Such a blanket application of these standards might well render much secondary analyses of data in the behavioral and social sciences extremely difficult, if not impossible. APA opposes the blanket application of standards modeled after the Privacy Rule as described in HIPAA across all types of research data.

In lieu of making these onerous data security and information protection standards mandatory for all research, APA strongly recommends that OHRP explore mechanisms for effectively incorporating this responsibility within the IRB. One model is to require that all IRBs include an individual trained to assess informational risks, similar to the requirement for a prisoner representative when a study involving incarcerated individuals is being reviewed by an IRB. In fact, IRBs at the Department of Veterans Affairs (VA) facilities already include an individual whose responsibility it is to evaluate the informational risks engendered by a research protocol. Another, perhaps more effective model that would make best use of individual IRB members' expertise and contributions, is to require

mandatory training in informational risk assessment for all IRB members. By not having the decision rely on the expert judgment of one individual ensures that the IRB will not defer to the opinion or views of only one IRB member when one or more of the other members might also have valuable insights.

(b) Eliminating continuing reviews

APA agrees that studies initially approved using the expedited review mechanism should not require continuing review. APA also supports the caveat that the reviewer would have the authority to require continuing review of specific studies, with justification. APA therefore recommends that the regulations include a requirement for institutions to report to OHRP on an annual or semi-annual basis on all such deviations from the default "no continuing review" requirement to ensure that justifications are valid. Without this reporting requirement, there is a risk of institutions/IRBs continuing the current practice of insisting on going above and beyond the regulations. This insistence, often more for the protection of the institution than the research participants, could well defeat the spirit of these newly proposed changes to reduce burden and delay in the approval and conduct of safe and ethical research with human participants. (Questions 2 and 13)

Although eliminating the requirement for continuing review of those studies which have been approved through a convened review but which no longer involve direct interaction with participants will greatly reduce both IRB and investigator burden, APA recommends that OHRP provide clear and explicit guidance about circumstances under which an IRB might mandate continuing review when the study is in the data analysis phase. Clear and explicit guidance in this regard would preclude risk-averse IRBs from routinely mandating continuing review of such studies. In addition, requiring IRBs to provide written justification to OHRP as to why the default "no continuing review" was not followed would enable the requirements to be fine-tuned. This reporting requirement would involve no penalty, other than over-ruling of the IRB decision, if deemed appropriate by OHRP. Such a reporting mechanism would serve a dual purpose of easing IRB fears of non-compliance and deterring unnecessary over-regulation by IRBs in response to institutional pressures. (Question 3)

(c) Expanding categories of research either eligible for expedited review or exempt from the regulations

APA also welcomes the proposed review and revision of the list of types of research considered eligible for expedited review. This revision has the potential to facilitate the bulk of the research conducted in the behavioral and psychological sciences. The proposal to streamline documents to be submitted for review is also appreciated. However, APA is concerned that the proposal in the ANPRM lacks specificity about the review process as well as details about the information that would be required to be submitted for review. The new rule needs to clearly specify the process,

including time-line and nature of documents that need to be submitted for review to ensure that the administrative advantages of these changes are realized. In the absence of such clear rules, IRBs might react by capitulating to institutional pressures to over-regulate, thereby maintaining the status quo.

Although simplifying the regulations regarding exempt (or "excused") studies is a commendable goal, the proposed data security and information protection standards (about which we have already stated our concerns) actually complicate review and conduct of these studies substantially and may lead to expenditure of considerable resources and energy by institutions. Thus, APA is strongly opposed to the proposal to move away from the concept of exempt, to the new category of "excused" research, which would be required to meet complex data security and information protection standards. APA urges OHRP to use this opportunity to further clarify and simplify mechanisms for determining when a study is exempt.

With regard to single-form registration of exempt studies, any new regulations must specify exactly what information is required in the registration form, as lack of pertinent information will render retrospective audits meaningless. In addition, APA is uncertain how institutions are expected to deal with studies that were wrongly classified as exempt by the investigator and which a later audit finds required either expedited or convened review. One option would be to continue current practice and mandate that someone other than the investigator needs to make the determination of exempt status. In the interest of allowing institutions to effectively oversee research that is being conducted on their campuses, perhaps the person making exempt determinations could be a dedicated IRB staff administrator, with necessary expertise. It can be expected that expanding the list of categories of research that would be exempt from the regulations, along with expanding the list of expedited review categories of research, will significantly reduce IRB burden; that in turn will allow for a designated staff person to review and certify research as exempt, thereby ensuring that there are no unnecessary delays in getting such research started. (Questions 12 and 22)

(d) Definition of "minimal risk" research

APA has concerns about the proposed definition of "competent adult" as one who is capable of giving legally valid consent. The regulations are unclear about the methods used to make that determination and about the qualifications of the person making the determination, especially when participants are being recruited from the general population and there is no obvious or overt evidence of lack of ability to consent (e.g., an obvious cognitive impairment). APA recommends that the regulations clearly state who is capable of making such a determination, and how the determination will be made.

Although adding a new category with specific types of research that might qualify for exemption seems reasonable, focusing *solely* on methodology to determine if a study involves only minimal

risk of harm is misguided. Risk of harm in research stems from an interaction of various factors including topic of study, population being studied, methodology used, and the training and qualifications of the person conducting the interaction or intervention with the participants (for example, principal investigator vs. graduate student vs. undergraduate research assistant with limited experience). Ultimately, a given study might well involve only minimal risk, but that might be by virtue of the protections in place, and not based solely on the methodology. Therefore, APA recommends that the regulations not base risk of harm solely on methodology, but take into consideration the various factors associated with conducting research with human participants.

The proposed new rule does not provide additional information, guidance, or definition of "psychological risks" or how they should be assessed appropriately, making it likely that some IRBs will continue to evaluate such risks erroneously and hinder valuable research. To avoid this problem, the regulations should clearly specify that when assessing risks of harm, whether physical or psychological, IRBs should consider both probability and magnitude. Furthermore, IRBs should focus on reasonably *foreseeable risks* of harm, recognizing that not all conceivable or possible harms are equally probable or equal in magnitude. (Question 4)

One of the purported goals of the revisions to the Common Rule is to reduce the burden on IRBs by absolving them of the responsibility to review and approve minimal risk research, thus allowing the boards to focus their energies and limited resources on oversight of more than minimal risk research. However, the proposal to require even minimal risk research to comply with the new data security and information protection standards contradicts the central premise of the revision to the Common Rule. Requiring even minimal risk research to meet new data security and information protection standards and informed consent requirements would require someone with adequate knowledge and expertise to make the determination that the proposed minimal risk research does indeed meet these new standards. In addition, the ANPRM reference to use of existing data with oral consent under the current regulations is not accurate – currently, secondary use of de-identified data is exempt from the regulations because use of de-identified data does not constitute "research with human participants." Furthermore, under the current regulations, in some instances consent may be waived for secondary use of identifiable data, but under the proposed rule it appears that a waiver would not be permissible. (Questions 5 and 23)

III) Streamlining IRB review of multi-site studies

APA agrees that inefficiencies in having multiple reviews are considerable and can slow the conduct of research. We welcome steps to streamline the review process for such research. Requiring single review of multi-site studies provides an opportunity to eliminate a large volume of duplicative review efforts. However, we want to stress the importance of having clear regulations about how such an IRB of record would function and about the role and responsibilities of the IRBs at the affiliated sites. Below are some of the issues on which detailed regulations are needed to ensure

that the proposed change is feasible and accomplishes the intended goal of reducing inefficiencies in review, while retaining the important contributions of knowledge of the local context.

Identifying the IRB of record – The regulations need to clearly specify a variety of mechanisms for determining which IRB would function as the IRB of record for any particular multi-site study. Options include the IRB of the study's lead investigator's institution, contracted research institutions, and federally-convened IRBs that are topic specific. (Question 34)

Issues of accountability and legal responsibility – There is a concern that local IRBs may not want to take on the additional burdens associated with being the IRB of record unless mandated to do so. Providing a financial incentive (e.g., through grant funds) may be one way to counteract this problem. It will be critical to have clear rules about the roles, responsibilities, and obligations of all the institutions involved in the multi-site study and clear rules about who will be held accountable for non-compliance with human research protection regulations at individual sites. Issues that the regulations will need to address include: Who is responsible when there is a regulatory violation that relates to responsibilities of IRB: would it be the local institution or IRB of record? Who is responsible for ensuring and maintaining administrative records documenting compliance with regulations: would this happen locally (as currently the case, even when a central IRB is used) or would it be the IRB of record? In APA's view the local IRB might be better suited to oversee and enforce regulatory compliance in multi-site studies.

Concerns about central IRB's ability to understand the local context of the research – We agree that it is important that there be a way to assess issues pertinent to local sites (e.g., institutional commitment; participant accessibility; feasibility; PI competence; local community attitudes, state and local laws and ordinances). Feasibility is an important factor in considering whether a study should be conducted. An external IRB may not know how many studies are ongoing with a limited participant pool, or that a study might interfere with ongoing studies. A suggested approach to dealing with this issue is currently used by the VA for studies reviewed by a central IRB. The central IRB provides local IRBs a limited time period to provide input on relevant local issues prior to review by the central IRB. Although this additional step adds some time burden, it is much less burdensome and more efficient than multiple independent reviews. Alternatively, a local IRB representative could be given the opportunity to participate by phone/electronically in the discussion by the IRB of record of a protocol in which the institution participates. (Question 31)

Communications – The regulations need to clearly articulate mechanisms for communications between the IRB of record, local IRBs, and investigators. This is particularly important with regard to reporting of compliance incidents, adverse events, and unanticipated problems.

Mechanisms for preventing "IRB shopping" might include requiring that the IRB of record be identified in the grant proposal. (Question 34)

Including the option for individual sites to conduct their own internal review defeats the very purpose of this proposed new regulation (i.e., to reduce burden and delay). Internal reviews would be just as time-consuming and result in the same kinds of conflicts and delays as is the case with the current practice of multiple reviews. Furthermore, if the local institution no longer has any regulatory status, this review would not provide additional protections for research participants, and would only be a waste of the IRB's valuable time and limited resources.

IV) Improving informed consent

The proposed changes on improving informed consent are focused entirely on the consent form and not the process. Criticisms about the length and complexity of consent forms are legitimate, especially in the case of biomedical studies, but it is also often true in behavioral and social science research. This problem stems not from the regulations per se but from the real or perceived fears of litigation and negative publicity on the part of institutional administrations. Thus, APA strongly urges that any proposed new regulations for the protection of human participants focus on the consent process, highlighting the fact that the singular purpose of the exercise is to provide prospective research participants with information allowing them to make a voluntary and informed decision about participation in a study, and not to protect the institution from liability. (Question 35)

With reference to consent forms, APA believes that the proposal to include prescriptive language as indicated in Sections IVA (1) and (4) of the ANPRM reduces the flexibility inherent in current regulations and prevents the application of PIs' professional judgment in specific instances. APA recognizes that, in general, the eight required elements of informed consent are necessary for ensuring that prospective participants are truly making an informed decision, especially in clinical research. However, we note that all eight elements are not always relevant to all research studies, particularly in much behavioral and psychological research, which often offer no direct benefits to participants. There is a degree of flexibility in the current regulations that is not mirrored in the proposed new rule. It is important to note that the problem with the current regulations is primarily the administrative burden of documentation (e.g., IRBs need to document an alteration or waiver of one or more of the eight required elements for consent, regardless of whether it is oral or written, even when one or more of the elements are irrelevant in a specific study). Prescriptive language in the proposed new rules would result in the same kinds of administrative burdens that exist under the current regulations' mandatory eight elements of informed consent, without improving the process itself. (Question 37)

APA recognizes the value in making full use of existing data for the benefit of society. However, as we have alluded to earlier in our comments, we object to the conflating of biospecimens and all other existing data. Furthermore, we disagree that a broad and open-ended consent for all yet-to-be-determined future research use can actually strengthen protections for research participants. If

participants do not have any sense of what the future research might be, how can they meaningfully consent to it? We believe that furthering our understanding of human health and behavior to benefit society should not come at the expense of undermining the very cornerstone of research with human participants (i.e., truly *informed* consent). Any regulation regarding the use of a general consent for all future use of pre-existing data requires more deliberation by the regulatory agencies, research community, bioethicists, and the public at large. Thus, the implementation of such a policy at this time is premature. We recommend that OHRP work with the research community and other stakeholders to further investigate this important issue and develop an ethically sound and more widely accepted policy for making best use of biospecimens and other existing data. (Question 49)

V) Strengthening data protections to minimize information risks

An argument could be made that strengthening data protections would reduce the possibility of informational risks. However, as we have indicated earlier, we strongly oppose the proposal mandating that all research adhere to the HIPAA Privacy Rule. HIPAA was created and designed for privacy protection with respect to health information, not for use as a data security and information protection standard. Investigators in various research disciplines should not be forced to comply with HIPAA rules merely because the HIPAA rules appear to be adaptable (though inappropriately so) for research settings. (Questions 54 and 59)

Beyond the use of HIPAA for data protection, there are several additional concerns that need to be addressed. The rationale for the new data security and information protection standards in the proposed rule is that IRBs are not qualified to assess informational risks. But the rule does not specify who will be responsible for evaluating and monitoring adherence to these standards. APA is concerned that this new requirement only serves to add another layer of bureaucracy that will impede the conduct of research. As mentioned above, in lieu of new data security and information protection standards modeled on the HIPAA Privacy Rule for *all* research, APA recommends that the HIPAA model be restricted to health-related data in non-research settings, and that the rule enforce a new requirement in the composition of the IRB – namely an informational risk analyst. In addition, OHRP should issue detailed guidance on assessing and ameliorating informational risks in different research settings. (Questions 54 and 59)

VI) Data collection to enhance system oversight

APA strongly supports an empirical, evidence-based approach to human research participant protections. To that end, creating a central database of *all* federally-funded research, which will include information about the nature of the study, number of participants enrolled, and unanticipated problems and adverse events, if any, will be a valuable resource for assessing real risks posed by participation in various types of research. This information will also be useful for the

periodic review and updating of categories of research that might be exempt from the regulations and of the list of research eligible for expedited review. However, the ANPRM does not provide information about whether this central repository will be publicly available, or accessible to institutions with a federal-wide assurance (FWA). One advantage of making the repository accessible to FWA-institutions is that both IRBs and PIs can use the information for making more informed and accurate determinations about risks of harm posed by participation in different types of research studies. (Questions 68 and 69)

APA recognizes that reporting information in such a database could have the potential to substantially increase the burden on researchers and institutions. Thus, APA recommends that OHRP, in collaboration with the various federal funding agencies, (i) examine all current reporting requirements with the goal of developing a single synchronized or coordinated system that would convey relevant information to appropriate entities across all the agencies and thereby reduce the burden on researchers and their institutions; and (ii) identify key pieces of information that would be have to be input into the database so that research studies and outcomes can be tracked accurately and to ensure that the database does indeed achieve the goals for which it is designed.

VII) Extension of Federal regulations

APA is unclear about the statutory basis for "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 conducted at their institution" (regardless of the source of funding for a particular study). Currently, institutions can opt to "not check the box" yet require that all research conducted on their campuses meet high ethical standards, without the regulatory and paperwork burden associated with compliance with the Common Rule. In other words, institutions can have all research, regardless of funding, be overseen by the IRB (or comparable parallel entities), but need to go through the exercise of documenting alterations, waivers, etc. only for federally funded studies. Allowing institutions to avail of this option greatly reduces administrative burden on IRBs. (Question 71)

VIII) Clarifying and harmonizing regulatory requirements and agency guidance

APA supports the idea of all Common Rule agencies adopting and promulgating a single set of guidance for human research participant protections across the different disciplines and research settings. Given that the FWA mechanism is implemented by OHRP, institutions tend to rely on OHRP's guidance and interpretation of regulatory requirements, regardless of the agency funding a particular study (with the exception of perhaps FDA). This supremacy of OHRP guidance over other agencies' interpretation of the regulations is often a source of conflict between PIs and IRBs, and also between IRBs and funding agencies, other than HHS. Thus, issuing a single set of guidance

across all Common Rule agencies would not only protect human research participants but would also facilitate the conduct of research. (Questions 73 and 74)

In conclusion, APA strongly supports the proposals to (i) calibrate the level of review to the level of risk of harm; (ii) expand exempt research categories but urges OHRP to retain the current practice for exempt studies rather than adopt the proposed "excused research" model; (iii) periodically review and revise the list of research categories eligible for expedited review; (iv) eliminate continuing review of studies initially approved using the expedited review mechanism and of studies approved by convened review but which no longer involve interaction with human participants; (v) mandate a single IRB of record for multi-site studies; (vi) create a central database that allows researchers to upload specific information about their study as well as any adverse events or unanticipated problems that occurred; and, (vii) clarify and harmonize regulatory requirements and guidance across all Common Rule agencies. We are, however, strongly opposed to (i) new requirements for data security and information protection based on the HIPAA Privacy Rule; (ii) inclusion of prescriptive language for the format and content of consent forms, as such prescriptive language will be inappropriate for many types of research and thus increase administrative burden; and, (iii) a broad, general, open-ended consent for unspecified future use of data as we believe this threatens the fundamental ethical principle of respect for persons.

APA thanks OHRP and OSTP for this opportunity to share our comments on proposed changes to the Common Rule. We recognize the importance of the Common Rule in ensuring basic protections for participants in behavioral, biomedical and social research and we offer our concerns and suggestions in order to ensure that the Common Rule retains its current flexibility and remains equally applicable to all types of research. If you have any questions, or if we can provide any further information, please feel free to contact me at 202-336-6000, or by email at sbreckler@apa.org.

Sincerely,

Steven J. Breckler, PhD
Executive Director for Science
American Psychological Association