December 29, 2015

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 Notice of Proposed Rulemaking to modernize, strengthen, and make more effective the Federal Policy for the Protection of Human Subjects (HHS-OPHS-2015-0008)

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 effort to revise the federal regulations for the protection of human research participants. We believe that an update aimed at ensuring that the regulations remain relevant to the changing nature of research and at minimizing burdens on investigators and IRBs, while affording the appropriate level of protections for human research participants, is long overdue. The proposed revisions to the Common Rule outlined in the notice of proposed rulemaking (NPRM) that was published on September 8, 2015, in the Federal Register will have a significant impact on research in the behavioral and psychological sciences, and therefore APA is grateful for the opportunity to comment.

With a membership of more than 122,500 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 welfare. These comments were developed with input from the APA Committee on Human Research and Board of Scientific Affairs as well as individual members of APA.

We recognize that the current regulations were formulated at a time when the nature of medical, behavioral, psychological, and mental health research was substantively different from the types of human research and accompanying concerns regarding participant protections that arise with contemporary methods and technologies. In addition, over the past several years, oversight of research at the local level has become increasingly conservative, with institutional review boards
(IRBs) being called upon not only to consider the protection of human participants in research but also to ensure that the institution is protected from liability. As a result, low risk research (e.g., an opinion survey) is often subjected to the same level of scrutiny as highly risky research (e.g., a phase 1 clinical trial). This tendency not only hinders research efficiency, it also reduces human participant protections, as overloaded IRBs are unable to give sufficient attention to monitoring protection of subjects in more risky protocols. Thus, APA commends the Common Rule signatory agencies’ attempts to improve the effectiveness and the efficiency of the federal oversight system, by primarily making the level of review commensurate with the level of risk of harm posed by participation in the research. APA is particularly appreciative of proposals to eliminate certain current requirements that have little, if anything, to do with human research protections.

Rather than separately address each of the 88 questions raised in the NPRM, APA is providing general comments. However, we note in parentheses at the ends of sections or paragraphs where our comments specifically address one or more of the questions.

A) General concerns

The changes proposed in the NPRM are substantive, and in principle, APA supports many of the recommended changes. However, we believe that the proposed rules merit additional consideration in order to achieve the stated dual objectives of 1) decreasing administrative burden, delay, and ambiguity for researchers, institutions, and institutional review boards (IRB), while 2) strengthening, modernizing, and making the regulations more effective in protecting research subjects. In our opinion, the changes proposed in the NPRM represent an excellent starting point for further discussion. However, we are concerned that the standard procedure of moving from the NPRM to final rules after this round of public comments would, in this case, be premature. We believe that issuance of an interim-final rule based on this round of comments is critical to ensuring that the final regulations reflect the concerns of the community. In particular, further revision for clarity and greater applicability to the wide range of research that the proposed rules are intended to cover (beyond that involving biospecimens and individually identifiable information) would be welcome. Specific issues are outlined below.

(i) Emphasis on biospecimens, health data, and other individually identifiable information

A major strength of the Common Rule is its inherent flexibility, which 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 emphasize a biomedical research model and could be (mis)read as applicable almost exclusively to biospecimens/health data. To illustrate our point: throughout the NPRM, the terms “biospecimens” and “other individually identifiable information” are used to an extent that downplays the existence and value of other research models that generate different types of data. Given the breadth of data types that exist, and the range of research to which these regulations apply, it seems prudent to first frame regulatory requirements broadly to encompass the full diversity of medical, psychological, and behavioral research, after which special requirements warranted by the unique nature of particular types of research/data (i.e., biospecimens) can be detailed.
In addition, neither “biospecimens” nor “other individually identifiable information” are defined in the NPRM, and these terms seem to be used interchangeably and inconsistently throughout the proposed new regulations. While the intent of the proposed new rules is to provide clarity and reduce burden on researchers and IRBs, we believe that the use of such an ill-defined catchall phrase as “individually identifiable information” could inadvertently result in making the review process more cumbersome and onerous for both researchers and IRBs. *(Questions 1 and 3)*

**(ii) General organization and language**

The general organization and imprecise language of the proposed new regulations also need improvement. More specifically, in any given section, terminology use is inconsistent and rules that apply to only a specific type of research are intermingled with rules that apply to all types of research. For example, a section may spell out some rules that apply specifically to “clinical trials,” while other requirements in the same section apply to "clinical trials and other research." Similarly, some rules reference "biospecimen only," while others in the same section refer to "biospecimen and other individually identifiable information." This somewhat muddled approach creates confusion for IRBs and investigators, which in turn, increases regulatory burden.

One alternative organizational framework that could provide greater clarity is to have non-biospecimen research rules in a separate section of 45CFR46, rather than addressing all types of research in each section. For instance, rules that are common to all research (e.g., definitions, IRB membership and functions) can be included in the early general sections of the regulations, followed by parallel sections for non-biospecimen and biospecimen research. *(Questions 1 and 3)*

**(iii) Unavailability of the proposed exemption tool, data protection template, and consent template for review and comment**

Many of the proposed changes, especially those relevant to behavioral and psychological science, are predicated on the efficacy of the proposed exemption tool. We agree that such a tool, if properly crafted, would indeed reduce delay and regulatory burden. However, given that the NPRM does not provide a draft tool for review, APA is unable to assess the effectiveness of the tool to make an accurate determination of how well it serves the interests of reducing burden while protecting the rights and welfare of the participants. In a similar vein, the inability to review a draft of the template that would meet the requirements of the proposed new data protection standards, and of the template to obtain broad consent, makes it impossible to comment on the adequacy of these tools to meet their stated goals. By extension, the absence of these tools for review limits the research community's ability to provide comprehensive comments on the NPRM as a whole, given the number of changes that rest on the successful implementation of the yet unseen tools. Consequently, APA again urges that OHRP issue an interim-final rule that includes the necessary tools and allows for another round of public comments.

**(iv) Psychological risks**

The implication in the NPRM seems to be that the only non-physical risks of harm that can arise from research participation are due to inappropriate disclosure of personal or sensitive
information. This implication may have been inadvertent, but it is certainly invalid. APA would like to highlight that risks of psychological harm can arise from sources other than informational risks. Although in some cases, psychological harm may be the result of inappropriate disclosure of the participant’s information, classic examples such as the Stanford Prison Experiment and the Milgram studies of deference to authority exemplify the potential for serious psychological harms that may be associated with participation in non-biological research, and not merely the result of inappropriate disclosure of information. Another example would be studies that involve asking individuals about potentially traumatic life events, self-injury, or suicide ideation. While informational risks are a concern for these types of studies, it should also be recognized that reporting on such events by research participants might also pose a psychological risk in that some individuals may become very distressed during the course of or after the interview. Furthermore, the probability and magnitude of this risk may vary by characteristics of individual participants, clinical expertise of the interviewer(s), as well as the risk-minimizing protections that are in place.

APA would also like to highlight the fact that the concept of psychological risk continues to be misunderstood by IRBs and other regulatory bodies and inclusion of a clear definition of the term in the NPRM would be beneficial. Any and all negative emotional reactions experienced by an individual participating in a study should not be classified as a “psychological risk.” Instead, the psychological risk of harm in research refers to the extent to which participating in the study may result in significant emotional distress, frustration, or aversion that persists after the study participation has ended and is not adequately addressed through debriefing or post-study psychotherapy or counseling. (Questions 9, 13, and 48)

(v) Vulnerable populations

In addition to addressing the need to clearly define psychological risks, APA would like to share our concerns regarding the expanding definition of “vulnerable populations” in research. Three specific requirements of the proposed rule at §___.107(a), §___.111(3) and (9)(b) list categories of subjects “vulnerable to coercion or undue influence, such as children, prisoners, pregnant women, physically or mentally disabled persons, or economically or educationally disadvantaged persons.” Assuming that merely by virtue of being physically disabled, or being economically or educationally disadvantaged, an individual is inherently vulnerable to coercion or undue influence is erroneous. In some instances, special characteristics of the study population (e.g., diminished capacity to consent) can require different accommodations to ensure that the rights, including autonomy, and welfare of the participants are protected (e.g., through a legally authorized representative and/or tiered consent process).

However, applying the concept of vulnerability to coercion and undue influence to broad categories of people raises serious ethical considerations – including violating the Belmont Principle of respect for persons by infringing on the individual’s right to choose, given that s/he is deemed “vulnerable.” Furthermore, such special characteristics could make specific populations ineligible for participation in research if those characteristics are seen as changing the risk metric relative to other “normal” participants in the study. For example, by using the broad, undefined term “mentally disabled”, it could become impossible to conduct a study evaluating the efficacy of therapy via telephone for such patients in rural areas, because the study
would require a waiver of documentation of consent, which an IRB will not approve as it will deem the study to be more than minimal risk.

We also believe that the concept of undue influence should be calibrated on a protocol-by-protocol basis taking into consideration such factors as the research topic, the context in which the research is being conducted, the level of risk of harm to participants, and the monetary compensation for participation, if any. (Questions 82, 83, and 84)

(vi) Lack of integration with other regulations that have impacts on the rights and welfare of human participants

APA is concerned that revisions to the Common Rule are being undertaken without taking into consideration other regulatory changes that intersect with the requirements of the Common Rule. For example, one unintended outcome of the White House Office of Science and Technology Policy (OSTP) directive requiring all federal agencies to implement policies for the sharing of data resulting from federally-funded research might be an exhaustive re-evaluation of the concept of “informed consent” in the research setting. While the requirements, in certain instances, for “broad consent” in the proposed regulations allude to such a reconceptualization of consent to research participation, APA believes that the evolving nature of consent needs to be more thoroughly explored. It would be beneficial if OHRP were to engage in sustained discussions with the public and the scientific community broadly to develop consensus on how “consent” in the research setting should be construed in today’s digital world and era of precision medicine. One key aspect of data sharing that may be of concern to participants is that absolute maintenance of confidentiality cannot be guaranteed in an era of increasingly sophisticated computer algorithms which may enable an individual’s identity to be determined in the absence of any obvious individual identifiers (“de-de-identification”).

In addition, while the NPRM proposes to revise the Common Rule, there are numerous instances in which it seeks to amend sections of other subparts of 45CFR 46. For example, §___101(b)(2) describes exclusions designed to be applied to subparts B, C and D, which cover pregnant women, prisoners, and children, respectively, and are not under consideration at this time. To truly simplify the oversight of research, while affording subjects the highest level of protections, APA believes that there should be a more systematic effort to amend all the regulations related to research with human participants, including 45CFR46 subparts B, C, and D, as well as other statutes and regulations that intersect with the Common Rule, such as the Family Educational Rights and Privacy Act (FERPA) and Protection of Pupil Rights Amendment (PPRA). (Questions 25, 26, 45, 57, 58, and 59)

B) 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 human research participant protections are commensurate with the risks of harm associated with participation in the research. 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.

(i) Categories of activities excluded from the policy

Although APA is supportive of the proposal to expand the list of types of research activities that do not need to meet the requirements of the Common Rule, we believe that the addition of the new category of "exclusions" alongside the old and new exemptions is confusing. Only those activities that do not meet the definition of “research with human participants” (program improvement, quality assurance/quality improvement, public health surveillance, biographies, etc.) should be explicitly excluded from the requirements of the Common Rule. In addition, instance §.101(b)(1)(ii) is particularly problematic because it conflates broad disciplines (journalism) with methodologies (oral history).

With regard to §.101(b)(2)(i), as we stated in our comments on the 2011 Advance Notice of Proposed Rulemaking (ANPRM), focusing solely on methodology to determine the level of risk of harm is misguided and provides insufficient protection for participants in some cases. 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 rather than the methodology used. Therefore, APA recommends that if §.101(b)(2)(i) is retained as an exclusion then it be revised such that specific procedures, namely interview and survey, are not explicitly listed.

In summary, our suggestion would be to retain §.101(b)(1)(i) and (iii)-(vi) as well as §.101(b)(2)(iii) and §.101(b)(3) as exclusions. If survey and interview procedures are deleted from §.101(b)(2)(i), it could be retained as an exclusion, and a similar requirement that incorporates those deleted procedures can be listed as an exemption in §.104. Alternatively, §.101(b)(2)(i) could be considered exempt and be moved as is to §.104.

With reference to §.101(b)(2)(ii), which is a modified version of the exemption at § 46.101(b)(4) in the current Common Rule, the OSTP data sharing directive, noted above, will render virtually all federally funded research data publically available. In addition, with increasing support for openness and transparency in science, which encompasses data sharing through repositories as a requirement for publication in scientific journals, even data from non-federally-funded research will likely become widely available. Without knowing the exact nature and characteristics of the data, it is impossible to determine whether or not it constitutes “low-risk research.” Thus, to provide some level of protection to research participants while reducing ambiguity for IRBs (which in turn might translate to burden on researchers and unnecessary delays in conducting the research), APA recommends that §.101(b)(2)(ii) be moved back to the exempt category, as it is in the current Common Rule.

To reiterate, we suggest moving parts of §.101(b)(2)(i) and (ii) to the exempt category because it reduces ambiguity without additional burden on researchers or IRB, but stress that in
order to do so clear instructions for making exempt determinations must either be specified by the rules or issued as guidance by OHRP. (Questions 9 and 15)

(ii) Categories of research exempt under the policy

In terms of improving clarity and reducing ambiguity in the regulations, APA recommends that the exemptions at §__.104(f), which require limited IRB review of the procedures for obtaining broad consent, be moved to the list of research activities eligible for expedited review. The mere fact that IRB review is required, however limited, by definition renders it ineligible for the exempt category.

As mentioned above, APA also recommends that some of the research activities listed in §__.101(b)(2)(i) and (ii) be included in the list of exemptions. Although we recognize that the excluded category is meant to reduce regulatory burden and delay, we strongly believe that some activities should remain exempt, and the goal of reducing regulatory burden and delay can be achieved just as effectively by implementing a more streamlined process for making exempt determinations. Again, the provision of a tool that researchers can use for making exempt determinations, so long as the tool is well-designed and validated, is one potential way to streamline the process. To deal with studies that require more nuanced and subtle judgements, OHRP should issue guidance in the form of alternate methods for making exempt determinations that are not cumbersome for the investigator or the IRB. (Questions 29, 31 and 47)

(iii) Eliminating continuing review

APA endorses the new rule that studies initially approved using the expedited review mechanism should not require continuing review. APA also supports the caveat that on the recommendation of the designated reviewer, the IRB would have the authority to require continuing review of specific expedited studies with a strong justification. APA therefore recommends that the regulations include a requirement for institutions to report to OHRP on an annual basis on all such deviations from the default “no continuing review” requirement. This reporting requirement could help discourage institutions/IRBs from continuing to insist on going above and beyond the regulations. This insistence, often more for the protection of the institution than the research participants, could defeat the spirit of these newly proposed changes to reduce burden and delay in the approval and conduct of safe and ethical research. Moreover, information provided in reports could help OHRP to refine its interpretations and guidance regarding the “no continuing review” requirement.

APA also supports elimination of the annual continuing review of studies approved by a convened IRB and recommends the same approach be taken as described above for expedited studies. Given that the regulations require that investigators submit an amendment or revised protocol when there have been major changes to the originally approved protocol, or there is new information (e.g., interim results, safety data) that has implications for the rights and welfare of the participants, it is unclear what additional information can be gleaned from a continuing review.

To address further the potential for regulatory creep, 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. Guidance in this regard would discourage 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 interpretation and implementation of the regulations to be fine-tuned. Such a reporting mechanism would serve a dual purpose of easing IRBs’ fears of non-compliance and deterring IRBs from overreaching in response to institutional pressures.

In keeping with the intended goals of the proposed rules to reduce burdens without compromising participant protections, the requirement for the investigator to provide the IRB with an annual confirmation that a study is still in progress should also be eliminated. We believe requiring annual confirmation by the investigator is unnecessary given that the study has already been approved and the researcher is required to submit an amendment if changes are made to the protocol or if interim findings suggest an increase in the probability or magnitude of harm posed to participants. Instead of the annual reporting, investigators should be required to report when data collection is complete to the IRB, so that the study can be designated as closed for administrative purposes. To account for rare instances of greater-than-minimal-risk research in which participant enrollment rates are so low as to require a reassessment of the risk-benefit ratio and justification for the study, the regulations should allow IRBs to periodically check on the status of the study through direct communication with the investigator. The IRB could make the determination that a periodic check is necessary for a specific protocol during the initial review.

C) Reducing administrative burden without compromising protections

APA appreciates OHRP’s efforts to enable better utilization of limited research resources by reducing institutions’ administrative burden while ensuring the protections for participants in research. One of the most important and most complex concepts in research ethics is that of informed consent. APA perceives the current revision of the Common Rule to be an excellent opportunity to re-evaluate the concept – its meaning and its practical implications for oversight of research with human participants. Similarly, the NPRM reflects the changing nature of research, including the move towards collaborative team science, as well as the need to reduce unnecessary regulatory costs with duplicative reviews of research studies that may have little impact on the protections already afforded to research participants.

(i) Informed consent requirements

As was initially described in the 2011 ANPRM, changes for improving informed consent proposed in the NPRM are focused entirely on the consent form and not the consent process. Criticisms about the length and complexity of consent forms are legitimate. 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, as well as from lack of attention to the research participant's perspective. Thus, APA strongly urges that the proposed new regulations for the protection of human participants focus on the consent process and not just the form. Such an approach would highlight the fact that the primary purpose is to provide prospective research participants with information at a level they can clearly comprehend so that they can make voluntary and informed decisions about participation in a study – rather than to protect the institution from liability or to meet a pro forma regulatory requirement.
APA recognizes that, in general, the eight required elements of informed consent are necessary for ensuring that prospective participants are making a genuinely 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. 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 is irrelevant in a specific study). Thus, the required elements in the proposed new rules could well 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. In addition, prescribing required elements runs counter to the stated goal of reducing the length of consent forms. Thus, APA recommends that, before issuing a final rule, OHRP get extensive input from stakeholders to determine what a “reasonable person” would consider critical information for research consent.

In light of the OSTP directive, the new required element of informed consent at §___.116(a)(9) is problematic. If all data from federally-funded research (and with the open science movement rapidly gaining momentum, potentially non-federally funded research as well) will be publically available in some form, then a statement that subjects’ de-identified data will be used or distributed for future research [§___.116(a)(9)(ii)] could be redundant. This is another instance of the need for an interim-final rule that more fully takes into consideration both other regulatory and policy changes that are being implemented as well as an evolving paradigm shift within science with respect to openness and transparency. (Questions 49, 50, 60, 61, 62, 69, and 70)

As elaborated above, before issuing a final rule, OHRP should consult with the scientific community as well as the public at large to better define the concept of consent to research participation in today’s advanced digital research environment. APA believes that it is premature to develop, for instance, a template to obtain broad consent, in the absence of general consensus on its meaning and significance. The NPRM itself seems to reflect conflicting notions of consent. While respect for persons’ autonomy is cited as underlying the requirement for broad consent for research with biospecimens, the only consideration for excluding or exempting broad categories of research is the level of risk of harm with little, if any, regard to respecting the autonomy of potential participants.

Lastly, the varied use throughout the NPRM of terms such as “consent,” “informed consent,” broad consent,” and “notice” renders many aspects of the proposed regulations unclear and thus difficult to implement. (Question 1)

(ii) Review of cooperative research/multi-site studies

APA agrees that inefficiencies arising from having multiple reviews are considerable: the duplicative efforts are a waste of scarce resources and can unnecessarily slow the conduct of research. To that extent, we welcome the proposed new regulation mandating single-IRB review of multi-site studies, with certain exceptions. However, we are concerned by language in the preamble, which states that “[The proposed new rule would not] prohibit institutions from choosing, for their own purposes, to conduct additional internal IRB reviews, though such reviews would no longer have any regulatory status …. “ Mentioning the possibility 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). The regulations should not encourage such internal reviews, which 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.

We also want to emphasize the importance of OHRP issuing clear guidance to institutions that clarify the roles, responsibilities, and obligations of all the institutions involved in a multi-site study. To address concerns about institutional liability, we recommend that OHRP publish model written agreements. *(Questions 74 and 75)*

**Conclusion**

In summary, APA is pleased that OHRP has undertaken this long-overdue revision of the Federal Policy for the Protection of Human Subjects. We believe that many of the proposed revisions do indeed have the potential to reduce burdens on institutions, IRBs, and investigators, without compromising protections for human participants in research. These include the explicit exclusion of activities deemed not to be research, the expansion of categories of research that are exempt from the requirements of the regulations as well as a proposal for streamlining the process for making exempt determinations, “no continuing review” as the default for most studies, and single IRB review of multi-site studies. Many, if not most, of these proposals, however, have yet to be fully developed and vetted with the research community, and as such, APA does not believe that the NPRM can be the penultimate step before a final rule is issued by the agencies that are signatories to the Common Rule.

We recognize the importance of the Common Rule in ensuring protections for participants in behavioral, biomedical, and social research and we offer our concerns and suggestions in order to help ensure that the Common Rule retains its current flexibility and remains applicable to all types of research. Given that important elements of the proposed new rule were not available for review and comment (the exempt determination tool, broad consent template, and measures for meeting the new data and information protection standards), APA requests that OHRP publish an interim-final rule for additional public comment before issuing the final rule.

APA thanks OHRP for this opportunity to share our comments on proposed changes to the Common Rule. If you have any questions, or if we can provide any further information, please feel free to contact me at 202-336-5939 or hkurtzman@apa.org.

Sincerely,

Howard S. Kurtzman, Ph.D.
Acting Executive Director for Science