



NATIONAL CONGRESS OF AMERICAN INDIANS

January 6, 2016

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

Re: NPRM (Docket ID # HHS-OPHS-2015-0008) Comment Submission

Dear Dr. Menikoff,

The National Congress of American Indians (NCAI) is the oldest and largest national organization representing the interests of American Indian and Alaska Native (AI/AN) tribal governments in the United States. NCAI is a membership organization that serves the interests of the 566 federally-recognized tribes, state-recognized tribes, and AI/AN tribal citizens. As part of our work to affirm tribal sovereignty and secure our ability to continue to live as Native peoples, NCAI recognizes that research can add value to Native communities when it is driven by tribal leaders and developed and conducted in an ethical way.

Updates to the Federal Policy for the Protection of Human Subjects (the "Common Rule") are critically needed, and the public comment period is important for allowing diverse and meaningful responses to the Notice of Proposed Rulemaking (NPRM). The proposed changes may have significant implications for tribes, tribal organizations, and those who engage in research with tribal communities. As such, NCAI has developed the following comments on the proposed changes on behalf of our members and AI/AN citizens across the US. We expect that many of the tribes and organizations we engage with will do the same and hope that, together, our input on the potential impact of the proposed revisions on tribal nations will be fully considered and addressed within the revision process.

Sincerely,

Jacqueline Pata
Executive Director
National Congress of American Indians

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National Congress of American Indians

Comment Submission for the Notice of Proposed Rulemaking (NPRM) to Revise the Federal Policy for the Protection of Human Subjects (the “Common Rule”) Docket ID: HHS-OPHS-2015-0008

The National Congress of American Indians (NCAI) is the oldest and largest national organization representing the interests of American Indian and Alaska Native (AI/AN) tribal governments in the United States. NCAI is a membership organization that serves the interests of the 566 federally-recognized tribes, state-recognized tribes, and AI/AN tribal citizens. As stated in the Preamble to the NCAI Constitution, NCAI serves:

“to secure to ourselves and our descendants the rights and benefits [of] the traditional laws of our people to which we are entitled as sovereign nations; to enlighten the public toward the better understanding of the Indian people; to preserve rights under Indian treaties or agreements with the United States; to promote the common welfare of the American Indians and Alaska Natives.”

As part of our work to affirm tribal sovereignty and secure our ability to continue to live as Native peoples, NCAI recognizes that research can add value to Native communities when it is driven by tribal leaders and developed in an ethical, meaningful way. As such, NCAI established the National Congress of American Indians Policy Research Center (NCAI PRC) in 2003 to serve as a tribally-driven center, focusing solely on issues facing tribal communities. We assert that tribes have sovereignty over research that happens on their land and with their citizens and that research ethics must acknowledge the need to *both protect and benefit* Native people through research development.

NCAI advocates that all research conducted with AI/AN tribes and peoples should be developed in full consultation and in equal partnership with tribal leaders over the course of the entire research process, including: research design, data collection, data analysis, and reporting and dissemination. Tribal leaders have the best sense of what kinds of research and data would be most helpful to their citizens. Furthermore, given the diversity and uniqueness of AI/AN communities, the potential risks, benefits, and considerations related to participating in a research study will vary by tribe and by research study. For this reason, AI/AN individuals and tribes must have the opportunity to consent to participate in research in an informed and ethical way, and have the opportunity to engage in research regulatory activities.

The NCAI PRC provides the resources and tools necessary to inform public policy debates with meaningful information and assist in shifting the discourse in Native policy from a problem-focused approach to truly proactive, future-thinking strategy development. The NCAI PRC’s tribal research regulation work serves to support tribal leaders in ensuring research that is conducted on their lands and with their citizens is ethical, affirms tribal sovereignty, and contributes to community well-being. A major part of the work of the NCAI PRC has been to engage with tribal leaders and federal partners around data sharing and research, while also recognizing the long and challenging history of research in AI/AN communities.

AI/AN people are one of the most heavily-studied groups in the United States. Unfortunately, the long history of research in Indian Country has included some instances of harm to AI/AN tribes and peoples. Many Native peoples are wary of research and do not trust researchers. This is largely due to the fact that the term “research” generally reminds Native peoples of the myriad projects historically conducted that did not benefit Native communities, and even, in some cases, resulted in harm to these communities.

It is in the spirit of affirming tribal sovereignty, traditional laws, and the role of appropriate research that NCAI submits comments on the NPRM to Revise the Federal Policy for the Protection of Human Subjects (the “Common Rule”).

There are significant implications for research with tribal nations and AI/AN peoples within the NPRM and, while this revision process and call for federal comments has been ongoing since at least 2011, the federal government has not established an adequate, parallel process of tribal consultation – only recently scheduling a conference call for tribal consultation to occur one day prior to the NPRM comment submission deadline. NCAI submitted various rounds of comments in response to previous requests related to the Common Rule revision process and has built upon these comments in response to the NPRM. Within the rapidly evolving context of human subjects research, updates to the Common Rule are critically needed. The NPRM comment period and revision process provide an important window of opportunity to ensure protection of tribal sovereignty and the rights of tribal citizens who choose to participate in research.

With this in mind, our comments relate to nine overarching themes, including:

- Protection of human subjects framed as counterbalanced against promotion of scientific innovation;
- Proposed tradeoffs with principles of research ethics;
- Autonomy rationale coupled with promotion of broad consent;
- Responsibility placed on individual investigators more than research institutions;
- Focus on risk, rather than benefit;
- Commitment to tribal consultation;
- Reliance on “majority rule” in determination of research policy rather than a reasoned process where minority voices can be heard on matters of ethics and research burden;
- Acceptance of the “burden” of consent; and,
- Inclusion of specific language regarding tribal research oversight and approval.

Implications of the NPRM Revisions for Research with Tribal Nations and AI/AN People

Several areas within the NPRM have implications for research conducted with tribes and AI/AN people. Some areas, such as the protection of biospecimens from individuals who are no longer living, have been commented on previously by NCAI. Others are new and deserve careful attention to fully understand how their implementation will impact research in tribal contexts.

- *Tribal and individual consent for secondary research with biospecimens*: Proposed changes that include a broad consent for future, unspecified research use of biospecimens challenge the ongoing ability of both tribes and individuals to choose to remove their data from research, or to understand how their information is being used to benefit, or put at risk, themselves or others. Secondary research with biological data has violated individual AI/AN and tribal consent in our lifetime, and had consequences for other communities as well (e.g., Henrietta Lacks). At the same time, we need a deeper ethical conversation about the appropriate use of biological data for secondary research purposes, so that the discussion (and policy) is not limited to either allowing for violations of human subjects protections or engagement in secondary research.
- *Tribal and individual consent for research with biospecimens or other data from people who are no longer alive*: As part of comments submitted for the 2011 ANPRM (Appendix A) and the 2013 request for comments on the NIH Genomic Data Sharing Policy¹, NCAI emphasized the need to

¹ http://www.ncai.org/policy-research-center/research-data/priorities/2_2013_11_19_Comments_NIH_Genomics_Data_Sharing.pdf

address protections for biospecimens initially collected from living humans after those humans pass away. Although the revisions proposed in the NPRM provide a level of oversight that did not previously exist for secondary use of de-identified biospecimens, the revisions have yet to address use of biospecimens from individuals who are no longer alive.

- *Research oversight by tribal Institutional Review Boards (IRBs) and other tribal regulatory bodies:* By promoting the use of a single IRB in cooperative and multi-site research, these proposed revisions do not foster community-based governance and oversight of research that has the potential to improve outcomes for tribal and minority populations. Further, without specific regulatory language that directs research involving tribal nations to a process that includes at minimum an initial review by a tribal entity (e.g., tribal IRB, Research Review Board, or governing body), there is a continued risk that the sovereign rights of tribes will be circumvented. The promotion of a single IRB in multi-site research is also concerning in light of the fact that there is no support for tribal IRBs alongside other support for IRBs, and other proposed revisions seek to shift oversight and responsibility from research institutions to individual investigators. This has the potential to put tribes and other communities at greater risk due to a lack of community governance or enforcement of research ethics.
- *Research oversight for categories of research and activities important in tribal contexts:* Proposed changes related to the exclusion of certain categories of activities (e.g., oral history, biographies), addition of exempt categories of research (e.g., educational tests, surveys, interviews), and elimination of continuing review requirements for some studies will potentially remove research protections for activities that are common and important for the protection of sensitive information in tribal research contexts. Tribal research review often extends the scope of examination beyond individual-level protections to enact community-level protections important for maintaining the integrity of culturally significant information and practices. Some tribal research review boards do not even include exempt or expedited processes, preferring to review all proposed research activities for the protection of their community and citizens. Tribal review processes also frequently require review of presentations and publications as part of a continuing review. Given that all tribal nations do not have their own regulatory bodies to provide these additional protections, changes to excluded and exempt categories of research and elimination of some continuing review requirements, especially in the context of no clear mechanism for additional tribal oversight and input, are a cause for concern.

Overarching & Specific Comments on Proposed Revisions to the Common Rule

NCAI has prepared the following overarching and specific comments on the NPRM's proposed changes and justifications. Responses to individual questions posed in the NPRM can be found using a keyword search (e.g., "Question 1"). Note, however, that while the majority of the 88 questions posed in the NPRM have a response some questions are not addressed due to the need for expertise in specialized areas (e.g., prison populations, clinical or institutional practice) or local tribal context or practices.

- *Protection of human subjects framed as counterbalanced against promotion of scientific innovation:* The proposed revisions to the most important research policy in the federal code are based on a notion of governance as regulation as opposed to governance as stewardship. When we constrain governance to regulation, its purpose is framed as a balance between preventing against harm to humans and promoting scientific innovation through minimizing researcher burden. We see this throughout the proposed revisions in language such as:

"This NPRM seeks comment on proposals to better protect human subjects involved in research, while facilitating valuable research and reducing burden, delay, and ambiguity for

investigators. This proposed rule is an effort to modernize, simplify, and enhance the current system of oversight. The participating departments and agencies propose these revisions to the human subjects regulations because they believe these changes would strengthen protections for research subjects while facilitating important research” (p. 53936).

This framing is problematic for several reasons, including that it:

- o Can place the protection of humans at odds with the goal of fostering scientific innovation;
- o Does not explicitly speak to benefit;
- o Often places individual and community protections at odds; and
- o Can frame governance bodies as gatekeepers rather than stewards.

Perhaps most importantly, ethical violations and significant harm to humans has taken place as a direct result of the compromise of human subjects protections in the name of science and innovation – in places like Germany, Tuskegee, and Havasupai, to name a few. There is a minor nod in the proposed revisions to reduce burden in order to deliberate and seek stakeholder input on ethical challenges and the real risks and benefits of research (p. 53941), but the emphasis remains on reducing researcher burden while limiting institutional accountability for research oversight. It begs the question, who is responsible for protecting human subjects in research and generating meaningful research outcomes? Who are the stewards of ethical and meaningful research policy in the US?

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 1 & Question 54: 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. Public comment is sought on whether the NPRM’s proposal of exemption §____.104(f)(2) is the best way to balance respect for persons with facilitating research. [Framing the protection of human subjects as counterbalanced against the promotion of scientific innovation does not make the regulations more effective in protecting research subjects. Improvements in regulatory efficiency for the benefit of all stakeholders (e.g., research participants, researchers, and IRB members) are worthy of attention within the revisions; however, they should not be approached in a way that places the protection of research participants at odds with scientific progress.]*
- o *Question 50: Public comment is sought regarding whether the proposed exemption should be limited to research in which individuals had been informed of the potential future research use of their information, and given the opportunity to opt out of having their identifiable private information used for research. If the proposed exemption should be limited in this way, what information should be included in the opportunity to opt out? If the opportunity to opt out is made a condition of the exemption category how should it be structured (e.g., how long and under what circumstances should it remain in effect) and what, if any, impact should the opt out have on other provisions of the rule, such as the ability of an IRB to waive informed consent for a subsequent research study using the individual’s information? Are there other or alternative mechanisms that should be required to respect individuals’ autonomy and other interests? [If the proposed exemption is included in the revised policy, it should be limited to research in which individuals had been informed of the potential future research use of their information, and given the opportunity to opt out of having their identifiable private information used for research.*

The opportunity to opt out should remind individuals of the anticipated risks and benefits of allowing use of their identifiable private information for future research, and it should provide an opportunity to specify general types of research for which the data should not be used (e.g., research in a particular topic area).]

- o *Question 65: Public comment is sought on how the waiver criterion regarding “practicably” at §____.116(d)(3) could be explicitly defined or otherwise clarified. [If applied, the SACHRP’s recommendations have the potential to frame scientific validity at cross-purposes with research ethics. However, if at least two of the four items proposed were required to justify a practicable waiver that would be sufficient. To ensure ethical use of this criterion and adequate protections for human subjects, there should be a method to track waiver criterion over time, monitoring the rationales supplied and decisions made.]*

- o *Question 71: Public comment is sought regarding whether particular information security measures should be required for certain types of information or research activities and, if so, what measures and for what types of information or research. Specifically, should the safeguards be calibrated to the sensitivity of the information to be collected? [NCAI recommends that limited data sets should not be shared outside the original research team without permission from individual research participants and tribal nations involved in the study. This kind of data sharing without tribal authorization was part of the problem in the *Havasupai Tribe v. Arizona Board of Regents* case. Data sharing outside of the original research team falls under NCAI’s broader concern about secondary use of specimens. There are models for making data accessible to outside research teams without compromising tribal confidentiality, such as a data enclave – or a secure space for researchers to perform analyses that require a protected or controlled environment. The National Institutes of Health (NIH) has offered data enclaves as an option for the original research team to retain control over data, but to provide the aggregate results of secondary analyses to outside requesting research teams in an ethical way. NCAI supports the use of HIPAA Privacy Rule standards for identifiable and de-identifiable information and data sets. These standards are appropriate for most types of research studies and data. Employing different standards for different types of research could be confusing and lead to inconsistent application of those rules. For some social and behavioral research, individual participants may wish to be identified to “receive credit” for their contribution. In these cases, the informed consent form should explicitly have the option for participants to be identified or not be identified.]*

- *Proposed tradeoffs with principles of research ethics: As further evidence of the dangerous framework within which these proposed revisions emerge, there is explicit language that asks how best to “tradeoff” ethical principles that form the foundation of research ethics in order to revise the definition of *human subject*. Question 4 asks, “Which of the three proposals regarding the definition of human subject achieves the most reasonable tradeoff between the principles of autonomy (including transparency and level of trust) versus beneficence (as measured by facilitating valuable research)?” (p. 53946). While it may be important to balance a range of ethical principles, when we begin considering tradeoffs of our ethics, we not only constrain our ability to protect humans, but also open the possibility that harm to humans is allowable.*

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 4: Which of the three proposals regarding the definition of human subject achieves the most reasonable tradeoff between the principles of autonomy (including transparency and level of trust) versus beneficence (as measured by facilitation valuable*

research)? [It is not appropriate or ethical to accept any tradeoff between the principles within the Belmont Report. The protection of human subjects and groups in research demands that all three principles are upheld and review of the impacts of decision-making on individuals and communities be reviewed regularly.]

- *Autonomy rationale coupled with promotion of broad consent*: Enhancement of autonomy is provided as a rationale for extending human subjects protections to secondary use of de-identified biospecimens, yet a broad consent for future, unspecified research is promoted, stating:

“The proposed elements of broad consent are intended to ensure that the individual would be provided with sufficient information to make an informed decision about whether to agree to provide broad consent for a wide variety of research that may be unforeseen at the time which consent is being sought” (p. 53973)

Is consent for future, unspecified research, especially in the context of rapidly evolving technology, truly enhancing informed decision-making and autonomy? The additional protections for secondary use of de-identified biospecimens are an improvement; however, for many populations, including vulnerable populations and tribal and minority populations, where access to scientific advances are often limited and historical legacies of unethical research have resulted in mistrust, it is difficult to understand how broad consent for unspecified future research would be an acceptable revision.

The above comments are submitted in relation to the following specific questions in the NPRM:

- *Question 61, Question 69, & Question 70: Public comment is sought on whether broad consent to secondary research use of information and biospecimens collected for non-research purposes should be permissible without a boundary, or whether there should be a time limitation or some other type of limitation on information and biospecimens collected in the future that could be included in the broad consent as proposed in the NPRM. If a time limit should be required, is the NPRM proposal of up to 10 years a reasonable limitation? Would a limitation related to an identified clinical encounter better inform individuals of the clinical information and biospecimens that would be covered by a broad consent document? Public comment is sought regarding how likely investigators are to seek broad consent for the use of identifiable private information (as contrasted with biospecimens), given that there are provisions within the NPRM that would make it easier to do such research without consent. Public comment is sought on the proposed prohibition on waiving consent when an individual has been asked to provide broad consent under §____.116(c) and refused. [The proposed provisions about broad consent currently in the NPRM create confusion and slippery slope for investigators to navigate while removing institutional accountability from research organizations that have a responsibility to protect human subjects in research and uphold research ethics. NCAI recommends that a standardized general consent form or broad consent should not be used. “Blanket consent” or broad consent was used in the *Havasupai Tribe v. Arizona Board of Regents* case and harm resulted. NCAI recommends specific informed consent forms which detail how specimens and data can and will be collected and used. All secondary uses of collected specimens and data should require an additional consent process. Informed consent forms should also be clear, understandable, and specific enough to ensure an informed consent can be solicited. NCAI also recommends that options be provided for research participants on informed consent forms (e.g., checkboxes for what types of research they do and do not want their data used for) to ensure a clear, full-disclosure process. The Belmont Report’s principles of autonomy and respect for persons require honoring decisions and wishes of research participants, rather than blanket use of their specimens and data without their explicit consent for specific*

purposes. Many AI/AN peoples believe that specimens and blood are considered sacred as they contain a person's essence and spirit. For this reason, sharing specimens between investigators or moving them from facility-to-facility is worrisome and spiritually concerning for tribal nations and peoples. By providing a full detailed informed consent form, tribal participants will have the option to determine how their specimens and data can be used. NCAI reiterates its acknowledgement of the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. Tribal consultation on informed consent processes will be an important part of any decision-making about standardization of consent forms and generation of best practices in the context of research with AI/AN tribes and peoples. As such, there should not be a body or a process with the authority to waive someone's consent.]

- *Responsibility placed on individual investigators more than research institutions*: Where much of these proposed revisions seek to remove burden from investigators in order to facilitate more innovative research, they also appear to remove responsibility, oversight, and "liability" from research institutions. This can be seen in a few places, including:
 - Discussion of the introduction of a web-based "decision tool" designed to determine if a study should be exempt from IRB review or not:
 - "it is expected that in many instances the tool would be used by the investigators themselves, thus obviating both the need for further review and the concern that the institution might be subjecting itself to future liability by allowing investigators to use the tool" (p. 53936).
 - "Institutions may rely on use of the federally developed tool by investigators as a 'safe harbor' for this determination: So long as the information that was provided to the tool was accurate, result of the application of the tool will be presumed by the federal departments or agencies to be an appropriate determination of exempt status" (p. 53956).
 - Discussion of research excluded from human subjects oversight, (e.g., "By reclassifying certain research activities from being exempt to being excluded, the proposed rule would eliminate the need for any administrative or IRB review. All investigators performing excluded studies are expected to act in a way that is consistent with the principles outlined in the Belmont Report, even if the Common Rule does not impose requirements on excluded work. For instance, consistent with the spirit of respect for persons, investigators should tell prospective subjects the purpose of the information collection and, where appropriate, that they can choose to participate or not in these activities, although investigators are not explicitly required to do so. Designating certain research fully outside of the bounds of the Common Rule means that investigators are self-determining whether their own research is covered by the law. As such, the proposal to add these categories is based on the assumption that all investigators will be accurately determining whether their proposed activity is outside the scope of the Common Rule. There is no current proposal outlining how decisions will be made for determining whether a research activity is eligible for exclusion and by whom or how differences among collaborators would be handled") p. 53950.

This shift does not allow for sufficient oversight and protections for human subjects in relation to research practice. In our work with tribal nations, we consistently hear about ongoing violations of research ethics and protocols designed to protect human subjects in research, and the need for oversight to monitor and enforce the ethical and appropriate practice of research. These proposals will result in greater risk and harm to human subjects in research. They do not speak to whether there will be subsequent changes in the role of federal agencies to monitor and enforce federal research policy, or foster ongoing discussion of ethics in the practice of research.

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 5: Public comment is sought regarding any concerns that you have about each of the three proposals, including concerns about implementation or burden to investigators and institutions. [The proposed revisions appear to prioritize minimizing the regulatory burdens on investigators and institutions ahead of protections for human research participants. In our work with tribal nations, we consistently hear about ongoing violations of research ethics and protocols designed to protect human subjects in research, and the need for oversight to monitor and enforce the ethical and appropriate practice of research. These proposals will result in greater risk and harm to human subjects in research.]*

- o *Question 6 & Question 8: Public comment is sought for whether this excluded activity should simply be discussed in the text of the final rule's preamble, and guidance produced to assist investigators in making such determinations, or whether any other similar exclusions should be addressed? Public comment is requested on whether the parameters of the exclusions are sufficiently clear to provide the necessary operational guidance, or whether any additional criteria or parameters should be applied to clarify or narrow any of these exclusions. [Guidance and resources need to be provided to IRBs to implement these new provisions, and specifically to tribal IRBs who currently lack access to federal resources on this front. It may also be important to provide guidelines based in actual research oversight processes, with scenarios as part of the resources, to organizations stewarding federal research policy. Further, it would be useful to request that organizations providing research oversight share the results of some of their decisions and changes in policy as part of a searchable database or tool to build the capacity of oversight organizations over time.]*

- o *Question 11, Question 16, Question 20, Question 41, & Question 47: Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category. If so, should documentation of any kind be generated and retained? Public comment is sought on whether it is reasonable, for the purposes of this exemption, to rely on the exemption determination produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances. [Oversight needs to be provided by some research institution/group/organization to ensure accountability for preventing harm, recourse if harm does result, and support for researchers to develop ethical research, particularly in the case of research with tribal nations. As such, it is not reasonable to rely on investigators to make self-determinations in the case of research with tribal nations. Should this proposed change remain, however, documentation needs to be generated and retained, especially in the case of research with tribal nations.]*

- o *Question 27, Question 28, Question 29, Question 30, & Question 31: Public comment is sought regarding how likely it would be that institutions would allow an investigator to independently make an exempt determination for his or her own research without*

additional review by an individual who is not involved in the research and immersed in human research protection e.g., a member of the IRB Staff. Public comment is sought regarding whether an investigator would be able to contrive his or her responses to the automated exemption decision tool in order to receive a desired result i.e., an exempt determination, even if it does not accurately reflect the research activities. Public comment is sought on whether it would be more appropriate for some of the exempt categories than others to rely on the exemption determination produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances. Public comment is sought regarding whether relying on the exemption determination produced by the decision tool where investigators themselves input the data into the tool as proposed would reduce public trust in research. Public comment is sought regarding how likely it would be that institutions would rely on such a decision tool to provide a safe harbor for an investigator making a determination that the proposed research qualifies for an exemption, or whether developing such a tool would not be worthwhile, and whether institutions would be able to adequately manage exemption determinations without the use of the decision tool. [There are tribal research review bodies that do not allow for special categories of review (i.e., exempt or expedited) and opt to review all research proposed within tribal boundaries to ensure individual and community protections and address mistrust generated by past experiences of unethical investigator behavior. It is difficult to comment on the utility of a decision tool without review of its contents; however, it is unlikely that such a tool would adequately address the unique cultural concerns represented across the diverse AI/AN communities throughout the US.]

- o Question 32 & Question 33: Public comment is sought regarding what additional information should be required to be kept as a record other than the information submitted into the decision tool, for example, a study abstract, the privacy safeguards to be employed, or any notice or consent documented that will be provided. Public comment is sought regarding the value of adding an auditing requirement. [If a decision tool is used, the information submitted into the decision tool as well as a study abstract, privacy protocols, and consent documents should be kept on record for auditing purposes. Oversight needs to be provided by some research institution/group/organization to ensure accountability for preventing harm, recourse if harm does result, and support for researchers to develop ethical research, particularly in the case of research with tribal nations.]*

- o Question 43: Public comment is sought on the concept of requiring such minimum safeguards and limitations on disclosure, as well as whether the requirements of the proposed §____.105 would constitute a broadening of IRB responsibilities rather than a streamlining of the implementation of responsibilities that many IRBs already adopted. If an institution does view this as an inordinate broadening of responsibilities, does the institution currently have in place alternative mechanisms for ensuring data security and participant privacy in a research context? Suggestions for alternative approaches to meeting public expectation that federally sponsored research safeguard their data and protect privacy are sought during this public comment period. [The concept of requiring minimum safeguards and limitations on disclosure is important, and the final policy should clearly state that tribal research review bodies can require additional safeguards and limitations that extend beyond the agreed upon federal minimum standards. There are tribal research review bodies that opt to review all research proposed within tribal boundaries to ensure individual and community protections; therefore, the proposed changes may not be viewed as a broadening of IRB responsibilities in some cases. The*

capacity, infrastructure, and technical expertise necessary for implementing such requirements; however, could be a challenge given that many tribal research review bodies operate on limited budgets with few resources (e.g., no electronic management system or dedicated staff members) and members who hold multiple positions within their community. Additionally, research occurring in tribal communities may have limited access to the technology and resources necessary for meeting the minimum safeguards. If the minimum safeguards require specific skills or resources, development of training and educational tools will likely be needed to support implementation.]

- *Focus on risk, rather than benefit*: While there is reference throughout the proposed revisions to “risks and benefits”, there is little discussion of benefits to communities beyond to “society as a whole” or to the “public” from these proposed revisions. There will be an increase in burden to human subjects participating in research as a result of these proposed revisions, especially to vulnerable populations and those from tribal and minority populations, yet there is no discussion of benefits to them. This violates the principle of beneficence that is foundational to the practice of ethical research in the US. Consider, for example, this excerpt from page 53952 of the proposed revisions: “The exclusion of this type of activity rests in large part on the idea that all individuals, regardless of the setting or context in which the activity will take place, are generally familiar with common forms of educational tests, survey and interview procedures which they experience in their daily lives, and do not need additional measures to protect themselves and their privacy from investigators who seek their involvement in research activities involving these procedures”. American Indian parents of students in public schools on tribal lands have expressed concerns to NCAI about inappropriate use of school-based research activities, and many AI/AN people are not “generally familiar with common forms of educational tests, survey and interview procedures” due to a variety of historical policies and events.

The above comments are submitted in relation to the following specific questions in the NPRM:

- *Question 34, Question 36, Question 39, Question 42, Question 46, Question 51, & Question 52: Public comment is sought on whether this exemption category should only apply to research activities in which notice that the information collected will be used for research purposes is given to prospective subjects or their legally authorized representatives as a regulatory requirement, when not already required under the Privacy Act of 1974. If so, comment is sought on what kind of information should be included in the notice, such as the research purpose, privacy safeguards, contact information, etc. Comment is also sought on how such a notice should be delivered, e.g., publication in a newspaper or posting in a public place such as the school where the research is taking place, or by individual email or postal delivery. Note that other requirements, such as those of the Family Educational Rights and Privacy Act (FERPA) or the Protection of Pupil Rights Amendment, may also apply. Would requiring a notice as a condition of this exempt research strike a good balance between autonomy and beneficence?...In many cases, it may be that individual notice or consent to all potentially affected persons before the research or demonstration commences is ordinarily impossible in the conduct of such studies. For example, if a research or demonstration project will affect all inhabitants of a large geographic area (e.g., a housing, a police patrol, a traffic control, or emergency response experiment), or all clients or employees of a particular program or organization or setting will be subject to a new procedure being tested (e.g. a new approach to improving student performance, a new anti-smoking or anti-obesity program, a new method for evaluating employee performance), would it be possible to make participation voluntary for all affected individuals, or even to identify and inform all affected individuals in advance? Should prospective subjects be given the explicit opportunity to opt out of such research? Public*

comment is sought regarding what should constitute notice for purposes of this exemption category. Given the many different types of data that would be covered by this provision...would it be possible to develop a uniform “notice” requirement? What type of notice, in terms of its dissemination and scope, should be considered to meet this requirement of the proposed exemption? With regard to the dissemination of the notice, should the notice requirement be permitted to be fulfilled through a general public notice, not specifically directed to individuals who are potential research subjects, such as the notice allowable under the Privacy Act?...Public comment is sought on whether, on the other hand, prior notice is necessary. Is the notice requirement proposed for this exemption a meaningful and important measure to respect individual autonomy, particularly if the notice requirement could be fulfilled through a general public posting?... [Efforts to be as transparent as possible regarding research-related activities and policies, especially in school settings, are needed to build trust among AI/AN populations and ensure that individual and community benefits of participation in research are achieved. Any notice should include information on the research purpose, possible risks and benefits of participation, privacy safeguards, and contact information (i.e., phone, email, and postal address). Tribal consultation will facilitate decisions around appropriate modalities for delivery of such notices; although, it should be noted that the rural nature of many AI/AN communities often requires longer lead-time and use of multiple modes of communication in order to reach the intended audience. Potential research participants should explicitly be given the opportunity to opt of research activities.]

- o *Question 35: Public comment is sought on whether the privacy safeguards of §____.105 should apply to the research included in §____.104(d)(1), given that such research may involve risk of disclosure of identifiable private information. [Disclosure of identifiable private information is a particular concern for research involving AI/AN participants given the small population size; therefore, the application of privacy safeguards to protect against disclosure of identifiable private information collected in educational settings among AI/AN youth is especially important.]*

- o *Question 45 & Question 48: Public comment is sought on whether the proposed exemption regarding the use of educational tests, survey procedures, interview procedures, or observation of public behavior (§____.104(e)(1)) should be applied to research involving the use of educational tests with children and whether it should also be applied to research involving the use of survey or interview procedures with children. If so, for research involving children, should the permissible survey or interview topics be limited in some way? Public comment is sought on whether this exemption category should be narrowed such that studies with the potential for psychological risk are not included. Are there certain topic areas of sensitive information that should not be covered by this exemption? If so, please provide exemplary language to characterize such topic areas in a manner that would provide clarity for implementing this Rule. [Due to the types of health disparities and issues present in AI/AN communities, research, especially research with tribal youth, is often focused on sensitive topic areas (e.g., suicide, alcohol and substance use, school drop out, adverse childhood experiences, and trauma). Interest in strengths-based approaches also means that research with tribal populations often includes a focus on culture and identity, which in many instances may be difficult to separate from standard health topics due the holistic worldview present in many AI/AN cultures. For these reasons, if the proposed exemption categories are adopted or applied, especially to research with children, language that explicitly allows tribal review of the proposed research should be added to the Rule. Tribal consultation would also facilitate development of a list of permissible*

survey or interview topics to be included within the exemptions should it become part of the final policy.]

- o *Question 88: Would protection to human subjects in research be enhanced if OHRP conducted routine periodic inspections to ensure that the membership of IRBs designated under FWAs satisfy the requirements of § ____ .107?* [OHRP has an ongoing responsibility to protect human subjects in research. It is essential to a process in place for monitoring individual and institutional accountability for the provisions ultimately approved as part of this NPRM, including those related to membership of IRBs.]
- ***Commitment to tribal consultation:*** As the predominant policy governing research practice and protection of human research subjects in the US, the Common Rule and this set of proposed revisions have significant tribal implications. Per the Memorandum issued by President Barack Obama in 2009, pursuant to Executive Order 13175, there must be a process of consultation with tribes. Consider this language from the 2009 Memorandum, “The United States has a unique legal and political relationship with Indian tribal governments, established through and confirmed by the Constitution of the United States, treaties, statutes, executive orders, and judicial decisions. In recognition of that special relationship, pursuant to Executive Order 13175 of November 6, 2000, executive departments and agencies (agencies) are charged with engaging in regular and meaningful consultation and collaboration with tribal officials in the development of Federal policies that have tribal implications, and are responsible for strengthening the government-to-government relationship between the United States and Indian tribes.” To adequately weigh the implications of revisions proposed in the NPRM and ensure that the core principles of ethical research – beneficence, justice, and respect for persons – are upheld in research with AI/AN tribal citizens, tribal consultation must take place. The Common Rule establishes a minimum standard of research regulation, and although tribal research regulation can expand and build upon the federal policy, efforts to generate compatible policy and processes that benefit all tribal peoples, including those residing in tribal communities without their own regulatory bodies, require full tribal consultation.

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 2, Question 3, & Question 66: Would providing a definition of biospecimen be helpful in implementing this provision? To what extent do the proposed issues raised in this discussion suggest the need to be clearer and more direct about the definition of identifiable private information? Public comment is sought on the proposed differences between the criteria for waiving informed consent for the research use of biospecimens versus identifiable information.* [Yes, providing a definition of biospecimen would be helpful, especially given different perspectives on what constitutes a biospecimen and its status as identifiable data. Additionally, clear and direct communication regarding identifiable private information is important given that genetic data is inherently identifiable, small tribal populations could result in easier triangulation of de-identified data, and even without individual identification, tribal identification could be a concern. Previously, NCAI submitted the following comment that is pertinent here, “NCAI recommends that DNA and biospecimens should be considered identifiable in and of themselves because genome sequencing technology is making it more possible to link DNA with an individual. NCAI is concerned about secondary use of data, so rigorous data protections should be applied to genetic information and specimens containing DNA. NCAI advocates specific informed consent be required for all studies in which an individual’s DNA or data are used, and that general informed consent not be allowed. NCAI recommends that future research use of data require informed consent and tribal consent for secondary

analysis. Regardless of whether the secondary data could be identifiable or not, some AI/AN peoples believe that human tissue, blood, and other biological specimens are sacred as they contain a person's essence and spirit. For this reason, sharing specimens between investigators or moving them from facility-to-facility is worrisome and spiritually concerning for tribal nations and peoples. Other potential harm may occur when tribal nations' names are linked to biological specimens, genetic material, or other kinds of data. Even when a sample or data point does not identify the individual participant, the tribal nation may be named. If specimens and data are then used for secondary analysis in ways not authorized by the tribe, there is the potential for group harm and stigmatization of the tribe in resulting publications and reports...Biospecimens that are collected outside of the research study such as "left-over" tissue and blood may be considered sacred by tribal nations and peoples and so sharing them between investigators or moving them from facility-to-facility may circumvent the human subject protection provided as part of informed consent processes." Further, any definition of biospecimen should include information on the ethical protocols and policies involving biological samples collected from humans who have since passed away (or who are now deceased).]

- o *Question 12, Question 21, Question 37, Question 38, & Question 49: Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions. Public comment is sought on whether this exemption category is appropriate based on the recognition that alternative processes are in place in which ethical issues raised by research in public benefit or service programs would be addressed by the officials who are familiar with the programs and responsible for their successful operation under state and federal laws, rather than meeting specific risk-based criteria, or whether risk limitations should be included, and if so, what those limitations should be...With regard to the issue of risks encountered by participants in such research or demonstration projects, comments are also sought regarding the argument that any and every demonstration project involving changes in public benefit or service programs (e.g., water or sewage treatment programs or pollution control programs, programs involving educational procedures, or programs involving emergency procedures related to extreme weather events, etc.) exposes those affected to possible risks of some kind... It is common for all Federal departments and agencies that regulate private or public organizations to impose conditions of participation in public programs providing for safety, program integrity, financial reporting, etc. Public comment is sought regarding whether there should be conditions (e.g., an individual notice or consent requirement) imposed on such research or demonstration projects involving public benefit or service programs which might lead to significant impediments or limitations on testing and evaluation before or after being imposed program-wide. Would the effect of imposing expensive or impracticable conditions on public benefits or services evaluations be to reduce the number of such evaluations and consequently to expose program participants to increased risk through exposure to untested reforms? Public comment is sought on whether the existing privacy safeguards for such activities, including the Privacy Act, HIPAA rules, and other federal or state privacy safeguards provide sufficient independent controls, or whether other safeguards such as the privacy safeguards of §____.105 should be applied. Public comment is sought on the types of research that should fall under the proposed exemption. Should the proposed exemption be available to all types of research using identifiable data collected for non-research purposes or should the exemption be available only to a more limited subset of research? For example, should the proposed exemption apply only for research using records and information already subject to comprehensive privacy and other protections in other Federal laws (e.g., records held by the Federal Government subject to the Federal*

Privacy Act, or records governed by HIPAA or FERPA)?... [There is a need for more specific provisions in the proposed revisions that address the authority and role of tribal nations in overseeing research on their lands and with their citizens. Echoing recommendations presented by the National Collaborative team in, "[Research Ethics Reconsidered in the Context of Community-Engaged Research: Proposed Revisions to the Belmont Report and Federal Regulations Guiding the Protection of Research Participants](#)"², tribal nations should be consulted about the vulnerabilities, or need for research protections, for individual members and for their nation. In many tribal contexts, data availability and access are important issues, and the need to maximize the value of information collected for other purposes is appreciated. That said, some tribal research review bodies do not allow for special categories of review (i.e., exempt or expedited) and opt to review all research proposed within tribal boundaries to ensure individual and community protections. Additionally, not all government policies have been developed through tribal consultation processes; therefore, to assume that "it does not seem that the delay imposed by obtaining a determination as "exempt" or "expedited" is likely to increase the protections provided to those who have already provided the government with information for other purposes", may mean that a study protocol deemed low-risk in a non-tribal review would be an inaccurate assessment of risk at the community-level. Tribal consultation would provide important insight into whether research conducted by a federal department or agency using government-generated information obtained for non-research purposes should be categorized as exempt or excluded. Tribal consultation would also allow leaders from tribal governments to provide input on the capacity and ability of public benefit or service programs to handle changes in regulation that would impact their primary responsibilities to community members.]

- o Question 18: Public comment is sought on whether this or a separate exclusion should also include research involving information collected for non-research purposes by non-federal entities where there are comparable privacy safeguards established by state laws and regulations, or whether such non-federally conducted research would be covered by the proposed exemption..." [There is a need for a separate exclusion here as there are other safeguards to establish to protect members of tribal nations beyond privacy. Safeguards are necessary to ensure benefit and minimize risk. Further, there need to be specific provisions to acknowledge the authority and role of tribal nations, especially when state law is referenced, and many states have a demonstrated record of working against the interests of tribal nations within their catchment area and developing policies that explicitly result in harm to tribes.]*

- o Question 43: Public comment is sought regarding whether the proposed Rule's information security requirements for biological specimens and identifiable private information are highly technical and require a level of expertise not currently available to most IRBs. Do these security requirements unrealistically expand IRB responsibilities beyond current competencies? [The capacity, infrastructure, and technical expertise necessary for implementing such security requirements for biological specimens and identifiable private information could be a challenge given that many tribal research review bodies operate on limited budgets with few resources (e.g., no electronic management system or dedicated staff members) and members who hold multiple positions within their community. Development of easily accessible training and educational tools will likely be needed to support implementation.]*

² https://ccph.memberclicks.net/assets/Documents/PapersReports/research_ethics_reconsidered_final.pdf

- o *Question 60: What topics should be addressed in future guidance on improving the understandability of informed consent?* [Tribal consultation would allow for important input on areas that should be addressed in future guidance around informed consent. Topics that might be of particular interest to tribes include incorporation or acknowledgment of community level implications of research activities and findings, as well as clarification around the handling of biospecimens after a study participant is deceased.]

- o *Question 62 & Question 68: Public comment is sought on whether all of the elements of consent proposed at §____.116(c) should be required for the secondary use of biospecimens or identifiable private information originally collected as part of a research study that was conducted without consent because either the original research study met an exclusion or exempt category of research, or a waiver of consent was approved by an IRB. Public comment is sought on the proposal to permit an IRB to waive consent for the secondary use of biospecimens or information originally collected for research purposes, even if the original research study required subjects' informed consent.* [NCAI recommends that consent should be required for research involving secondary use of biospecimens. It does not matter if existing data and specimens were collected originally for research or other purposes. All secondary use of data and specimens should require informed consent by research participants. NCAI is concerned with the secondary use of these specimens without informed consent due to potential for harm of the individual participants and tribal communities as groups. Biospecimens that are collected outside of the research study such as "left-over" tissue and blood may be considered sacred by tribal nations and peoples and so sharing them between investigators or moving them from facility-to-facility may circumvent the human subject protection provided as part of informed consent processes. *Havasupai Tribe v. Arizona Board of Regents* is a perfect example of an instance of unauthorized secondary use that can clearly result in harm of research participants when the full intention of a study is not disclosed. Under current tribal laws, there are some instances in which consent for secondary use is required from both the tribal nation and individuals due to the sovereign status of AI/AN tribal nations, as they have the jurisdiction to regulate research including specimen and data use. NCAI asserts that there is no circumstance in which it would be appropriate to waive the requirement to obtain consent for additional analyses of biospecimens for the reasons stated above.]

- o *Question 67: Public comment is sought on whether the proposal to permit an IRB to waive consent for research involving the use of biospecimens should be included in the regulations.* [NCAI recommends that consent should be required for research involving the use of biospecimens. As such, IRBs should not have the authority to waive consent. All use of data and specimens should require informed consent by research participants. NCAI is concerned with the use of these specimens without informed consent due to potential for harm of the individual participants and tribal communities as groups. *Havasupai Tribe v. Arizona Board of Regents* is a perfect example of an instance where waiving consent clearly resulted in harm of research participants when the full intention of a study is not disclosed. NCAI asserts that there is no circumstance in which it would be appropriate to waive the requirement to obtain consent for analyses of biospecimens for the reasons stated above.]

- o *Question 72: Are the proposed limitations on re-disclosure more or less restrictive than necessary? Are there additional purposes for which re-disclosure of biospecimens or identifiable private information should be permitted?* [Because the current proposed

revisions to the Common Rule have not included a process for tribal consultation, do not address the balance of responsibility for research institutions (alongside those for researchers), and do not include protections for tribal information or protections for vulnerable populations, these proposed limitations on re-disclosure are less restrictive than necessary.]

- o *Question 75: What areas of guidance would be needed for institutions to comply with this requirement? Is there something that OHRP could do to address concerns about institutional liability, such as the development of model written agreements?* [Tribal consultation would allow for important input on areas that should be addressed in future guidance around compliance with this requirement and topics that could be added to model written agreements. Research review through IRBs is a relatively new concept in tribal communities, and many tribes without their own research regulatory bodies are interested in the possibility of developing them in the future. Full consultation with tribes will assist with development of a process that will result in the effective and efficient review of research involving AI/AN populations.]
- o *Question 79: How often should the Secretary's list of minimal risk activities be updated? Should advice be solicited from outside parties when updating the list?* [This list should be updated every two to five years in order to keep up with changing technology and research methodologies. Tribal nations should be consulted to ensure adequate protections for tribal citizens in research.]
- o *Question 87: Public comment is sought on whether the definition of clinical trial (NPRM at § ____ .102(b)) should include additional explanation of what is encompassed by the term behavioral health-related outcomes.* [A large amount of research conducted in AI/AN communities and with AI/AN people focuses on behavioral health-related outcomes. Any additional clarification that can be provided within the policy to aid in implementation and understanding will be beneficial to the research review process.]
- Reliance on “majority rule” in determination of research policy rather than a reasoned process where minority voices can be heard on matters of ethics and research burden. Throughout the proposed revisions, 28 separate references are made to the “majority” of comments received at various points in the process of amending the Common Rule. This suggests that research institutions with greater capacity and investment in certain types of research that submit comments may overrule other institutions with just as much stake, but less capacity, such as community-based institutions. Within the four-year timeline since release of the ANPRM, NCAI has submitted comments at least twice and, in addition, met with federal partners on aspects of the revisions. Yet, most of our comments are not reflected in the NPRM. We continue our calls for transparency in the process of establishing federal research policy, federal responsibility for monitoring the impact and outcomes of these policies, and a commitment to tribal consultation on policies with significant tribal implications.
- Acceptance of the “burden” of consent: Throughout the proposed revisions, there is a concern that unnecessary burdens on researchers (or “investigators”) constrain research innovation, but we are left wondering about the nature of these burdens – is it too much burden to expect that potential research participants be asked for their consent to use their information and biospecimens? When did consent become such a burden? Was it when research with large or “big” datasets became a priority? When information technology advanced in significant ways? According to the rationale

presented for “modernizing the Common Rule” on page 53938 of the NPRM, advances in technology create much of the need for these proposed revisions:

“Evolving technologies, including imaging, mobile technologies, and the growth in computing power have changed the scale of information collected in many disciplines. Computer scientists, engineers, and social scientists are developing techniques to integrate different types of data so they can be combined, mined, analyzed, and shared. Research has also increased, evolved, and diversified in other areas, such as national security, crime and crime prevention, economics, education, and the environment, using a wide array of methodologies in the social sciences and multidisciplinary fields. The advent of sophisticated computer software programs, the internet, and mobile technology has created new areas of research activity, particularly within the social and behavioral sciences. In biomedical science, the Human Genome Project laid the foundation for precision medicine and promoted an environment of data sharing and innovation in analytics and technology, and drew attention to the need for policies that support a changing research landscape. New technologies, including genomic sequencing, have quickly led to exponential growth in the data to which investigators have access. The sheer volume of data that can be generated in research, the ease with which it can be shared, and the ways in which it can be used to identify individuals were simply not possible, or even imaginable, when the Common Rule was first adopted”.

Yet, we would rather promote a revised policy that diminishes responsibility for protecting human subjects and ethical tradeoffs instead of using this advanced technology to facilitate consent? By removing the burden of asking for permission, will the gateway to research innovation somehow be opened? This rationale echoes a time in the past when the research community made the most severe violations against humans and prompted the very policy that we now aim to revise.

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 18: Public comment is sought on whether this or a separate exclusion should also include research involving information collected for non-research purposes by non-federal entities where there are comparable privacy safeguards established by state laws and regulations, or whether such non-federally conducted research would be covered by the proposed exemption...* [There is a need for a separate exclusion here as there are other safeguards to establish to protect members of tribal nations beyond privacy. Safeguards are necessary to ensure benefit and minimize risk. Further, there need to be specific provisions to acknowledge the authority and role of tribal nations, especially when state law is referenced, and many states have a demonstrated record of working against the interests of tribal nations within their catchment area and developing policies that explicitly result in harm to tribes.]

- o *Question 74: Is mandated single IRB review for all cooperative research a realistic option at this time? Please provide information about the likely costs and benefits to institutions. Will additional resources be necessary to meet this requirement in the short term? Should savings be anticipated in the long run?* [NCAI recommends that there should not be a requirement for only one IRB of record for multi-site studies, especially when AI/AN tribal nations and peoples are research participants in the study. The same survey instrument or types of questions might be considered minimal risk in one population, but greater than minimal risk with another group. For example, questions about topics that have been historically sensitive in AI/AN communities, such as alcohol use or genetic risk, may be considered higher risk than if the same questions were asked of other groups. Individual

studies should be assessed by local IRBs or review boards to determine the level of risk posed to potential study participants. Notably, tribal nations have a variety of research review structures. Some tribal nations have their own formal IRBs, while others have developed alternative forms of research review committees or processes. The local research review process a tribe has developed, regardless of its form, can help to ensure risks specific to the population will be minimized. Tribal IRBs and other review boards may have more insight about potential participants' ways of life, cultures, languages and community traditions that could inform decisions about human subject protection and research risk. They may also know and understand more about the issues and disparities the community faces and have ideas of how to be proactive and best address these issues.

University and federal review boards should also be encouraged to include AI/AN peoples and researchers to serve on research review bodies, especially when research with AI/AN tribes and peoples have been put forth. This is particularly important in the case of research review in an urban Indian context, where there may not be a formal tribal governance mechanism to provide research review. All participating tribal nations who have active IRBs or review processes should be provided with the opportunity to review the study. If tribal nations choose to defer to one IRB for a multi-site research study of which they are participants that is their option. However, there should not be any mandate for one IRB of record for multi-site studies because local tribal IRBs and research review boards have unique knowledge about a community's history that is important to consider. Therefore, a tribal nation IRB might have different and/or more restrictive guidelines than the federal guidelines. In order for successful collaboration and trust of research studies with AI/AN tribal nations, tribal sovereignty should be respected and tribal government IRBs should be provided the opportunity to review multi-site research studies.

NCAI holds that a local tribal IRB or research review board is vital to the review process because these committees generally consists of members from the community or those that are actively engaged in the best interests of the community. Local IRBs add to the protection of research participants through an understanding of the unique knowledge of local context, including history of research in the tribal community and past harms resulting from research – about which nearly every AI/AN tribal nation would have stories. Historically, federal IRBs do not have adequate representation of tribal members. Although there may be inefficiencies with multiple IRB reviews or local tribal IRB review along with a university review, the benefit of research participant protection is worth the extra time and process. When it comes to research with AI/AN tribes and peoples, NCAI advocates that it is better to have a thorough review of a research study by a tribal IRB than to rush the process without community or tribal involvement. Not having local IRB review increases the risk of harm to research participants later in the project, when effects are irreversible as occurred in the *Havasupai Tribe v. Arizona Board of Regents*.

NCAI recommends that if only one IRB of record is allowed for multi-site studies with AI/AN tribal nations, that the study team be required to use the tribal IRB as the one of record. Alternatively, the research team could submit their research proposal to a university IRB in addition to, but not in place of, an application to a tribal IRB. Allowing the option for only one IRB of record could allow some researchers to engage in "IRB shopping" and bypass tribal research regulation processes in order to avoid community involvement in publications, ownership of data, and data analyses. NCAI reiterates its acknowledgement of the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of

responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. This may work to prevent inconsistencies across research review processes that contribute to “IRB shopping”.]

- o *Question 77: Are the exceptions proposed appropriate and sufficient, or should there be additional exceptions to this mandate for single IRB review than those proposed in the NPRM? If additional exceptions should be included, please provide a justification for each additional exception recommended.* [The exceptions are not sufficient. There must be considerations for research with tribal nations and tribal citizens, as well as for research with vulnerable populations.]
- o *Question 81: What should IRBs consider when reviewing the plans for returning research results, for example, what ethical, scientific, or clinical concerns?* [IRBs should consider both the benefits and risks involved in returning research results. There is often a need to ensure research balances the need to protect individuals and groups in returning results – for instance, if individuals were guaranteed confidentiality, but data is returned to an organization in a way that individual information could be identified, ethical principles are at risk; though commitment to communities or organizations that data will be returned in such a way that it can benefit their needs must also take into consideration how individual data will be held confidential. A transcript where so much text has been removed to protect individual confidentiality that it is unintelligible is of no benefit to the community. IRBs should also consider the process of oversight and management of that data to be returned.]
- o *Question 82 & Question 84: Is the §____.111(a)(3) and (b) focus on issues related to coercion or undue influence in research with vulnerable populations, and not other considerations related to vulnerability, appropriate? Should populations be considered vulnerable for reasons other than vulnerability to coercion or undue influence? Are the proposed categories appropriate?* [These considerations are important, however, there are other considerations as well, including those related to risk and benefit to the individuals and population group. NCAI recommends that populations be considered vulnerable as a result of being historically marginalized. Group stigmatization and harm is a very real risk of research conducted in Indian Country as is shown in the past case of the Barrow Alcohol Study. In this case, researchers stigmatized the community by stating that the tribe was “practically committing suicide” due to alcohol abuse, and there were resulting painful economic and social implications for the community. IRBs should be directed by federal regulations to consider group risks when dealing with AI/AN tribal nations and communities and other similarly distinct groups and communities.]
- o *Question 85: Public comment is sought on whether there might be unintended consequences from the clinical trials expansion proposed in the NPRM in §____.101(a)(2)(i).* [There is a concern that without adequate engagement of tribal consultation and acknowledgement of the role of tribal oversight of research in the proposed revisions in the NPRM, there could be confusion about human subjects protections for tribal citizens participating in clinical trials.]
- *Inclusion of specific language regarding tribal research oversight and approval:* In prior comments submitted in response to the 2011 ANPRM and 2013 NIH Genomic Data Sharing Policy, NCAI

outlined the need for active tribal approval for research involving tribal data as well as the inclusion of tribal IRBs and other research review processes in any revisions to federal policy. Explicit policy language indicating the need for tribal oversight will provide clear guidance for researchers and institutions engaged in research-related activities with tribal nations, rather than relegating this important process to the navigation of loopholes or dependence on the goodwill and persistence of others. In many AI/AN communities, well-designed, ethical research is vitally important for addressing the health and wellbeing of tribal nations. Clarification of the role of tribal research review processes within revisions of the federal policy will eliminate confusion, facilitate more timely review of research, and ensure that research occurring with tribal nations and AI/AN peoples truly meets ethical standards – a benefit to tribes, the researchers who partner with them, and the institutions who fund research and/or assist in the regulatory process. Moreover, clear language regarding tribal oversight will allow tribes to negotiate aspects of community consent and protection that are not provided within the focus on individual-level protections in the Common Rule.

The above comments are submitted in relation to the following specific questions in the NPRM:

- o *Question 1: 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.* [Policy language that explicitly addresses the role of tribal review within research regulation will eliminate confusion, facilitate more timely review of research, and ensure that research occurring with tribal nations and AI/AN peoples truly meets ethical standards. With respect to research with tribal populations, the proposed revisions without such language will not result in decreased administrative burden, delay and ambiguity for investigators, institutions, and IRBs. In fact, moving forward with the proposed revisions as-is misses an opportunity to strengthen and modernize the Common Rule in a way that recognizes tribal sovereignty and ensures protection for AI/AN research participants.]

- o *Question 7: Public comment is sought for whether biospecimens should not be included in any of these exclusion categories, and if so, which ones.* [Without more specific provisions in the proposed revisions that speak to the essential role of tribal nations in providing research oversight in relation to the use of biospecimens in federally supported research, NCAI does not support any use of biospecimens being included in any exclusion category. There is a need, however, for more specific provisions in the proposed revisions that address the authority and role of tribal nations in overseeing research on their lands and with their citizens.]

- o *Question 9: Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects.* [There are instances in each of these proposed areas where research conducted has resulted in harm to humans and whole communities, including members of tribal nations. When there is a specific tribal research code, policy, or set of provisions in place to address research oversight in any of these areas of activity, those standards should stand. When these do not exist, but there are tribal members involved in research or implications from research for tribal nations, there should be a process to oversee this research rather than an automatic ruling that it is exempt. Echoing recommendations presented by the National Collaborative team in, [“Research Ethics Reconsidered in the Context of Community-Engaged Research: Proposed Revisions to the Belmont Report and Federal Regulations Guiding the Protection of Research Participants”](#),

research with members of tribal nations should be considered research with vulnerable populations in the absence of more clear federal policy and protections developed in consultation with these nations to prevent future harm and protect our Nation's first peoples while ensuring their inclusion as participants in research and potential benefits should they choose to participate.]

- o *Question 10: Public comment is sought on whether this exclusion should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement.* [There is a need for more specific provisions in the proposed revisions that address the authority and role of tribal nations in overseeing research on their lands and with their citizens. There is also a need for specific provisions related to what consequences researchers and research institutions/groups/organizations face when harm resulting from research practice has been documented and reported, rather than narrow considerations about notice at the outset.]

- o *Question 12: Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions.* [There is a need for more specific provisions in the proposed revisions that address the authority and role of tribal nations in overseeing research on their lands and with their citizens. Echoing recommendations presented by the National Collaborative team in, "[Research Ethics Reconsidered in the Context of Community-Engaged Research: Proposed Revisions to the Belmont Report and Federal Regulations Guiding the Protection of Research Participants](#)", tribal nations should be consulted about the vulnerabilities, or need for research protections, for individual members and for their nation.]

- o *Question 13: Public comment is sought regarding whether these exclusions should be narrowed such that studies with the potential for psychological risk are not included.* [Research has contributed to significant benefit and significant trauma for members of tribal nations and whole communities. Any research with psychological risk for members of tribal nations must include provisions for oversight and consultation with tribal nations; they should not be excluded from oversight, as this would add greatly to the potential for harm to members of tribal nations from research.]

- o *Question 14: For activities captured under the third element of this exclusion, do the statutory, regulatory, and other policy requirements cited provide enough oversight and protection that being subject to expedited review under the Common Rule would produce minimal additional subject protections? If so, should the exclusion be broadened to also cover secondary analysis of information collected pursuant to such activities?* [There is a need for more specific provisions in the proposed revisions that address the authority and role of tribal nations in overseeing research on their lands and with their citizens. Secondary research with biological data has violated individual AI/AN and tribal consent in our lifetime, and had consequences for other communities as well (e.g., Henrietta Lacks). As such, NCAI is concerned about secondary use of data, so rigorous data protections should be applied to genetic information and specimens containing DNA. NCAI advocates specific informed consent be required for all studies in which an individual's DNA or data are used, and that general informed consent not be allowed. NCAI recommends that future research use of data require informed consent and tribal consent for secondary analysis. Regardless of whether the secondary data could be identifiable or not, some AI/AN peoples believe that human tissue, blood, and other biological specimens are sacred as they contain a person's essence and spirit. For this reason, sharing specimens between

investigators or moving them from facility-to-facility is worrisome and spiritually concerning for tribal nations and peoples. Other potential harm may occur when tribal nations' names are linked to biological specimens, genetic material, or other kinds of data. Even when a sample or data point does not identify the individual participant, the tribal nation may be named. If specimens and data are then used for secondary analysis in ways not authorized by the tribe, there is the potential for group harm and stigmatization of the tribe in resulting publications and reports. With this in mind, there is a need for further discussions about honoring ethics in the use of secondary data, both with the use of biological and non-biological data. On its face, the use of secondary data is not unethical if there is a process in place to uphold principles of respect, beneficence, and justice for both individuals and communities. The use of secondary data has begun to develop a characteristic of being taboo in some communities as a result of an unwillingness to develop ethical processes specific to use of these data – this does not benefit anyone, nor does it prevent harm.]

- o *Question 15: Public comment is requested on the extent to which excluding any of these research activities from the Common Rule could result [in] actual or perceived reduction or alteration of existing rights or protections provided to human research subjects. Are there any risks to scientific integrity or public trust that may result from excluding these research activities from the Common Rule?* [There is documented mistrust of research by AI/AN people and communities (see for example the rationale for establishing the Native American Research Centers for Health). Without specific provisions acknowledging the authority and role of tribal nations in overseeing research that happens on their lands and with their citizens, this trust will be further undermined – especially given that these are proposed revisions to the most significant research policy in the nation. Proposed revisions having to do with the use of biospecimens, secondary data, exclusions from research oversight, and use of a single IRB have significant implications for the sovereignty of and protections for tribal nations in research.]

- o *Question 17 & Question 19: Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects.* [Many federally funded programs are awarded to tribal nations and have mandated requirements about sharing data that results in tribal data being public even though these requirements to do so acknowledge the authority and role of tribal nations as sovereign governments. Covering these activities under the Common Rule would add protections to members of tribal nations in a research context.]

- o *Question 18: Public comment is sought on whether this or a separate exclusion should also include research involving information collected for non-research purposes by non-federal entities where there are comparable privacy safeguards established by state laws and regulations, or whether such non-federally conducted research would be covered by the proposed exemption...* [There is a need for a separate exclusion here as there are other safeguards to establish to protect members of tribal nations beyond privacy. Safeguards are necessary to ensure benefit and minimize risk. Further, there need to be specific provisions to acknowledge the authority and role of tribal nations, especially when state law is referenced, and many states have a demonstrated record of working against the interests of tribal nations within their catchment area and developing policies that explicitly result in harm to tribes.]

- o *Question 76 & Question 78: Would it be useful for this requirement to include criteria that Federal departments or agencies would need to apply in determining whether to make exceptions to the use of a single IRB requirement? If so, what should these criteria be? Is three years appropriate timing to establish compliance with this provision?* [Yes, this requirement should include criteria that Federal departments or agencies would need to apply in determining whether to make exceptions to the use of a single IRB requirement. Language should be added to the policy to clarify that cooperative, or multi-site, studies with tribal nations must be reviewed by a tribal entity and, if requested by the tribal entity, not be subject to the single IRB requirement. The inclusion of specific language regarding tribal research oversight and approval will facilitate more effective and efficient review of research involving AI/AN peoples. It is also likely that, with addition of this language, compliance could be established within a three-year timeline.]

Concluding Remarks and Recommendations

Thank you for the opportunity to provide comments in response to the NPRM to Revise the Federal Policy for the Protection of Human Subjects (the “Common Rule”). AI/AN communities face significant health disparities relative to other populations in the US and recognize the important role that research with human participants can play in efforts to improve the health and wellbeing of tribal nations and citizens. If the Common Rule is intended to serve as a baseline policy for stewarding research with human subjects, it should:

1. Include language that specifies the rights of tribal nations to provide protections and processes that go beyond the Common Rule provisions in order to protect tribal nations and citizens engaged in human subjects research, and
2. Ensure an adequate level of protection for tribal nations and citizens regardless of whether a tribal research review process (i.e., local tribal IRB or other research review body) exists to provide additional oversight.

NCAI reiterates our prior recommendation for formal tribal consultation on the proposed Common Rule revisions, as they stand to have significant, lasting effects on the integrity of research with AI/AN tribal nations and peoples. Consultation with tribal nations should be held in a manner consistent with the Department of Health and Human Services’ tribal consultation policy and on a government-to-government level. NCAI is willing to facilitate such a tribal consultation regarding OHRP’s proposed regulatory changes. For more information about these comments, please contact Dr. Deana Around Him, NCAI PRC Fellow, at daroundhim@ncai.org.

APPENDIX A

**NCAI Comment Submission on the Advanced Notice of Proposed Rulemaking (ANPRM) for
“Human Subjects Research Protections: Enhancing Protections for Research Subjects and
Reducing Burden, Delay, and Ambiguity for Investigators”**

Docket ID: HHS-OPHS-2011-0005



National Congress of American Indians

Comments on

Advanced Notice of Proposed Rulemaking (ANPRM) for “Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Investigators”

October 25, 2011

The National Congress of American Indians (NCAI) appreciates the opportunity to provide comments and other information to the U.S. Department of Health and Human Services (DHHS), Office for Human Research Protections (OHRP) on the proposed rulemaking (ANPRM) regarding how current regulations for protecting human subjects who participate in research might be modernized and revised to be more effective. NCAI seeks to better protect American Indian and Alaska Native tribes and peoples who participate in research.

NCAI is the oldest and largest national organization representing the interests of American Indian and Alaska Native tribal governments in the United States. It is a membership organization that serves the interests of the 565 federally-recognized tribes, state-recognized tribes, and American Indian and Alaska Native citizens. In 2003, NCAI established the National Congress of American Indians Policy Research Center (NCAI PRC) to serve as a tribally-driven center, focusing solely on issues facing tribal communities. The NCAI PRC provides the resources and tools necessary to inform public policy debates with meaningful information and assist in shifting the discourse in Native policy from a problem-focused approach to truly proactive, future-thinking strategy development. The NCAI PRC’s tribal research regulation work serves to support tribal leaders in ensuring research that is conducted on their lands and with their citizens is ethical, affirms tribal sovereignty, and contributes to community well-being.

There has been a long and challenging history of research in American Indian and Alaska Native communities. American Indian and Alaska Native people are one of the most heavily-studied groups in the United States. Unfortunately, the long history of research in Indian Country has included some instances of harm to American Indian and Alaska Native tribes and peoples. Many Native peoples are wary of research and do not trust researchers. This is largely due to the fact that the term “research” generally reminds Native peoples of the myriad projects historically conducted that did not benefit Native communities, and even, in some cases, resulted in harm to these communities.

The most recent, public example of harmful research in Indian Country is described in the now-infamous lawsuit the Havasupai Tribe filed against the Arizona Board of Regents. In February 2004, the Tribe filed the lawsuit, charging that researchers from Arizona State University (ASU) misused blood samples taken from tribal members. The Tribe claimed that tribal members were told their blood samples would be used for a study on the genetics of diabetes. However, the samples were also used for studies on schizophrenia, inbreeding, and possible migration patterns of the tribe’s ancestors from Asia to America. The case was recently settled out of court. This case sent waves throughout Indian Country and the research world, with many tribes and American Indian and Alaska Native organizations, including NCAI, passing resolutions

expressing support for the Havasupai Tribe's lawsuit against the Arizona Board of Regents. This case also caused many American Indian and Alaska Native communities to seek new ways to protect themselves from being deceived about the purposes of research projects and to control how their communities are portrayed in publications or presentations by researchers.

NCAI recognizes the critical need for meaningful and clear Institutional Review Board (IRB) regulations to protect human subjects. Yet, NCAI has concerns that these proposed changes would have major implications for research conducted with American Indian and Alaska Native tribes and peoples. As such, in our comments below, NCAI advocates that the sovereignty of tribal governments, as nations, be acknowledged in all aspects of research regulation and IRB rules. Specifically, NCAI submits comments that call for:

- Initial and continuing review of research with American Indian and Alaska Native tribes and peoples by IRBs;
- Continued oversight of and protection over informed consent processes in all research involving American Indian and Alaska Native tribes and peoples;
- Specific oversight in instances where informed consent processes must consider both individual and tribal consent;
- Oversight of any proposed secondary uses or analyses of data collected;
- Acknowledgement of the complexities around de-identification of data due to the small size of communities and unique characteristics of American Indian and Alaska Native tribes and peoples in the larger population;
- The inclusion of tribal IRBs and other research review processes in the revised regulations; and
- Coordination across tribal, community-based, regional, institutional, and national research review bodies to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty.

NCAI urges DHHS to be conscious of the challenging and complex history that American Indians and Alaska Natives have faced and continue to face with regards to research, as well as to be mindful of the opportunity DHHS has to foster a meaningful research ethic going forward so that research can have a positive impact in American Indian and Alaska Native contexts. NCAI advocates that all research conducted with American Indian and Alaska Native tribes and peoples should be developed in full consultation and in equal partnership with tribal leaders over the course of the entire research process, including: research design, data collection, data analysis, and reporting and dissemination. Tribal leaders have the best sense of what kinds of research and data would be most helpful to their citizens. Furthermore, given the diversity and uniqueness of American Indian and Alaska Native communities, the potential risks, benefits, and considerations related to participating in a research study will vary by tribe and by research study. For this reason, American Indian and Alaska Native individuals and tribes must have the opportunity to consent to participate in research in an informed and ethical way.

American Indian and Alaska Native tribal nations are recognized sovereign nations with the authority to regulate all affairs on their lands, including research. A tribe's sovereignty is critical to consider as part of examining IRBs and research regulation policy in Indian Country. The

Obama Administration has specifically committed to direct government-to-government dialogue with tribal nations through the President's 2009 Executive Memorandum directing all federal agencies to comply with Executive Order 13175. This type of direct consultation is necessary for major proposed policy changes, such as those related to human subjects protections in research. NCAI recommends formal tribal consultation by DHHS regarding the proposed changes to IRB regulations so that tribes can directly express their views to OHRP.

NCAI offers the following comments and responses to the DHHS's questions on proposed changes to the IRB regulations to help inform the process that is being conducted. Our responses below are grouped by theme, with references to the relevant questions from the ANPRM. These themes are noted in boldface and emerge from the NCAI Policy Research Center's work related to tribal research regulation. These comments reflect NCAI's best experience and insight to date given our work in the tribal research regulation domain, but we also acknowledge that we continue to consult with tribal leaders and researchers to shape ongoing best practice toward protecting American Indian and Alaska Native tribes and peoples and encouraging meaningful research.

A. Continuing and close review on a consistent and regular schedule by Institutional Review Boards (IRBs) should be required for studies conducted with American Indian and Alaska Native tribal nations and communities.

Question 2: Would the proposals regarding continuing review for research that poses no more than minimal risk and qualifies for expedited review assure that subjects are adequately protected? What specific criteria should be used by IRBs in determining that a study that qualifies for expedited initial review should undergo continuing review?

NCAI recommends that studies conducted with American Indian and Alaska Native tribes and peoples require some form of continuing review. The timeframe should be agreed upon by the American Indian and Alaska Native tribal nation or community at the beginning of the project development. NCAI recommends this review happen at least every two years and in the project's final year. In the Havasupai Tribe's case mentioned above, the university IRB did not review the study after the first approval. Secondary data analyses were conducted that were not authorized by the original consent process. Ongoing review by the IRB might have identified the unapproved secondary use of the data and residual harm to the tribe.

IRBs should consider continuing review for studies that qualified for expedited initial review in cases where research is being conducted where issues related to individual and tribal consent are involved, where anonymity and confidentiality have been guaranteed to research participants and/or tribes, or where any secondary analyses of data are being proposed.

Question 3: For research that poses greater than minimal risk, should annual continuing review be required if the remaining study activities only include those that could have been approved under expedited review or would fall under the revised exempt (Excused) category described in section 3, below (e.g., a study in which a physical intervention occurred in the first year, all subjects have completed that intervention, and only annual written surveys are completed for the next five years)?

NCAI recommends that all studies conducted with American Indian and Alaska Native tribal nations and communities that pose greater than minimal risk should be required to have continuing review annually regardless of whether the remaining study activities only include those that could have been approved under expedited review or would fall under the revised exempt status. As stated in our response to Question 2, we believe that continuing review of research studies will ensure that secondary analyses are not being conducted without consent and that the rights of American Indian and Alaska Native tribes and peoples are being protected throughout the research process.

Question 10: Which, if any, of the current criteria for IRB approval under 45 CFR 46.111 should not apply to a study that qualifies for expedited review?

NCAI recommends that all of the criteria for IRB approval under 45 CFR 46.111 should apply to expedited studies. NCAI advocates that regulations should not be “relaxed” in the revised proposed rules. Protection of human research participants should still be robust and clearly defined given history of cases with harms in research studies in American Indian and Alaska Native and other communities whose rights have been disregarded by researchers and who have been negatively impacted by insufficient human subject protection within the realm of research review and regulation.

Question 11: What are the advantages of requiring that expedited review be conducted by an IRB member? Would it be appropriate to instead allow such review to be done by an appropriately trained individual, such as the manager of the IRB office, who need not be a member of the IRB? If not, what are the disadvantages of relying on a non-IRB member to conduct expedited review? If so, what would qualify as being appropriately trained”? Would the effort to make sure that such persons are appropriately trained outweigh the benefits from making this change?

NCAI recommends that expedited review be conducted by an IRB member and not a trained staff member in an IRB office. Official IRB members are tasked with the ethical responsibility to uphold their duties and responsibilities in their role for the protection of human subject and the ethics and integrity of the science. A staff member may not have the same duty of care that is necessary to protect the rights of American Indian and Alaska Native tribes and peoples as part of a human subjects protocol.

B. Institutional Review Boards (IRBs) should make the decision about whether a study is “exempt” or “excused;” researchers should not be allowed to just register their studies and then proceed with the study without IRB approval.

Question 19: Regarding the Excused category, should there be a brief waiting period (e.g. one week) before a researcher may commence research after submitting the one-page registration form, to allow institutions to look at the forms and determine if some studies should not be Excused?

NCAI recommends that the IRB should determine whether a research study is exempt or excused rather than allowing researchers to register their studies involving American Indian and Alaska Native tribes and peoples as “exempt” or “excused”. Periodic audits do not substitute for initial IRB review prior to when a study commences. NCAI recommends a waiting period longer than

one week before a researcher may commence research after submitting the one-page registration form. This waiting period should be the full time period that the IRB needs to actually review the application and not just the one-page registration form. Essentially, the IRB should still be required to review applications for “excused” research – even if only one IRB member reviews it. Reviewing the entire application will allow a research project to begin only if approved and not cause a situation where damage could be done to the study participants with no recourse. When harm has already occurred (e.g., the Havasupai case), rectifying the problem is much harder than preventing it in the first place.

Question 21: Is it appropriate to require institutions holding a Federalwide Assurance to conduct retrospective audits of a percentage of the Excused studies to make sure they qualify for inclusion in this category? Should the regulations specify a necessary minimum percentage of studies to be audited in order to satisfy the regulatory requirements? Should some other method besides a random selection be used to determine which Excused studies would be audited?

NCAI does not recommend retrospective audits of research projects when this process serves to replace initial review of research studies. A retrospective audit cannot reverse harm or adequately protect research participants. Rather, there should be an IRB review of all studies involving American Indian and Alaska Native tribes and peoples.

Question 22: Are retrospective audit mechanisms sufficient to provide adequate protections to subjects, as compared to having research undergo some type of review prior to a researcher receiving permission to begin a study? Might this new audit mechanism end up producing a greater burden than the current system? Do researchers possess the objectivity and expertise to make an initial assessment of whether their research qualifies for the Excused category? By allowing researchers to make their own determinations, without prospective independent review, will protections for some subjects be inappropriately weakened? If allowing researchers to make such determinations without independent review would generally be acceptable, are there nonetheless specific categories of studies included in the proposed expansion for which this change would inappropriately weaken protections for subjects? And will the use of a one-page registration form give institutions sufficient information to enable them to appropriately conduct the audits?

NCAI believes that retrospective audit mechanisms are not sufficient to provide adequate protections to subjects, as compared to having research undergo some type of review prior to a researcher receiving permission to begin the study. This new proposed audit mechanism will create a greater burden on research subjects and communities that are the focus of the research when studies are found to violate human subjects ethics protocols. Retrospective audits do not adequately protect research participants. A one-page registration form will not give sufficient information to enable them to conduct audits. A brief paragraph abstract may not highlight all methods of research to allow the institutions to make an informed decision on the ramifications of the research study.

C. Secondary use of data or specimens holds potential for harm to individuals and communities.

Question 14: Are these expansions in the types of studies that would qualify for this Excused category appropriate? Would these changes be likely to discourage individuals from

participating in research? Might these changes result in inappropriately reduced protections for research subjects, or diminished attention to the principles of respect for persons, beneficence, and justice?

NCAI does not recommend expansions in the “Excused” category as they are not appropriate. NCAI does not feel that secondary analysis (i.e., use of “preexisting specimens or data”) should be allowed without IRB approval for specific secondary studies. Our reasoning is that potential for harm exists if research is conducted without IRB review and/or American Indian and Alaska Native tribal nation authorization of secondary studies (e.g. Havasupai case).

Question 23: Under what circumstances should it be permissible to waive consent for research involving the collection and study of existing data and biospecimens as described in Section 3(a)(3) above? Should the rules for waiving consent be different if the information or biospecimens were originally collected for research purposes or non-research purposes? Should a request to waive informed consent trigger a requirement for IRB review?

NCAI recommends that waiving consent should not be permissible under any circumstances for research involving collection and study of existing data and biospecimens. It does not matter if existing data and specimens were collected originally for research or other purposes. All secondary use of data and specimens should require informed consent by research participants. Again, *Havasupai Tribe v. Arizona Board of Regents* is a perfect example of an instance of unauthorized secondary use that can clearly result in harm of research participants when the full intention of a study is not disclosed. Under current tribal laws, there are some instances in which consent for secondary use is required from both the tribal nation and individuals due to the sovereign status of American Indian and Alaska Native tribal nations, as they have the jurisdiction to regulate research including specimen and data use.

Question 45: Under what circumstances should future research use of data initially collected for non-research purposes require informed consent? Should consent requirements vary based on the likelihood of indentifying a research subject? Are there other circumstances in which it should not be necessary to obtain additional consent for the research use of currently available data that were collected for a purpose other than the currently proposed research?

NCAI recommends that future research use of data initially collected for non-research purposes require informed consent for secondary analysis or research conducted on data and specimens. NCAI is concerned about the precedent of secondary use due to the potential for harm on research participants, such as in the *Havasupai Tribe v. Arizona Board of Regents* case, where participants were not made aware of, let alone asked to consent to, the secondary use of specimens collected from them for another study. Regardless of whether the secondary data could be identifiable or not, some American Indian and Alaska Native peoples believe that human tissue, blood, and other biological specimens are sacred as they contain a person’s essence and spirit. For this reason, sharing specimens between investigators or moving them from facility-to-facility is worrisome and spiritually concerning for tribal nations and peoples. Other potential harm may occur when tribal nations’ names are linked to biological specimens, genetic material, or other kinds of data. Even when a sample or data point does not identify the individual participant, the tribal nation may be named. If specimens and data are then used for secondary analysis in ways not authorized by the tribe, there is the potential for group harm and stigmatization of the tribe in resulting publications and reports.

NCAI acknowledges the Alaska Area Specimen Bank as a potential model of tribal oversight of research that ensures ethical and informed collection and management of biological specimens in a way that provides crucial data to researchers. The Alaska Area Specimen Bank includes biological specimens donated by nearly 92,000 people, most of whom are Alaska Native. The Arctic Investigations Program of the Centers for Disease Control (CDC) in Anchorage, Alaska, houses the specimen bank. The biological specimens in the bank have been collected from Alaska Native people who have participated in research studies, public health investigations, and clinical testing over the last half century. Oversight of the Specimen Bank is now provided by the Alaska Area Specimen Bank Working Group, which includes representatives from the CDC and Alaska Native tribal and community organizations. This Working Group is responsible for the development of policies and procedures governing the collection, storage, and reuse of specimens. Researchers wishing to use specimens contained in the bank must obtain permission to use stored specimens from the Tribal Health Organization of the area where the study participant's specimens were collected and the Alaska Area IRB. Research study proposals must have tribal approval before any research activities are allowed to begin.

Question 46: Under what circumstances should unanticipated future analysis of data that were collected for a different research purpose be permitted without consent? Should consent requirements vary based on the likelihood of indentifying a research subject?

NCAI recommends that any future use of data that were collected whether anticipated or not require consent for secondary analysis or research conducted on data and specimens for the reasons stated above under question 45. Unanticipated harm to individuals or tribal communities may result from secondary use of biological specimens and other data. Therefore, informed consent should be required for any proposed secondary use of data. Even if an individual is not identifiable in the data, a tribe may be. As sovereign nations, tribes have jurisdiction over research conducted using information collected on their land and from their citizens; and, as such, their rights must be considered as part of the informed consent, data reporting, and data ownership processes.

Question 47: Should there be a change to the current practice of allowing research on biospecimens that have been collected outside of a research study (i.e. "left-over" tissue following surgery) without consent, as long as the subject's identity is never disclosed to the investigator?

NCAI recommends that the regulations be clarified regarding the current practice of allowing research on biospecimens that have been collected outside the research study to require consent, regardless of whether a research participant's identity is never disclosed to the investigator. NCAI is concerned with the secondary use of these specimens without informed consent due to potential for harm of the individual participants and tribal communities as groups. Biospecimens that are collected outside of the research study such as "left-over" tissue and blood may be considered sacred by tribal nations and peoples and so sharing them between investigators or moving them from facility-to-facility may circumvent the human subject protection provided as part of informed consent processes.

Question 48: What, if any, are the circumstances in which it would be appropriate to waive the requirement to obtain consent for additional analysis of biopspecimens?

NCAI asserts that there is no circumstance in which it would be appropriate to waive the requirement to obtain consent for additional analyses of biospecimens for the reasons stated above.

Question 52: Should the new consent rules be applied only prospectively, that is, should previously existing biospecimens and data sets be “grandfathered” under the prior regulatory requirements? If so, what are the operational issues with doing so?

NCAI believes there are several operational issues with regulating research projects under two sets of regulations. In an effort to allow for the fullest clarity and least ambiguity, NCAI recommends that regulations related to previously existing biospecimens and data sets require consent for any secondary use.

Question 53: In cases in which consent for future research use is not obtained at the time of collection, should there be a presumption that obtaining consent for the secondary analysis of existing biospecimens or identifiable data would be deemed impracticable, such that consent could be waived, when more than a specified threshold number of individuals are involved? (SACHRP provided the Secretary with recommendations on this issue.) If so, what threshold number should constitute impracticability? Is the number of potential human subjects the only measure of impracticability?

NCAI recommends that no presumption should be made that obtaining consent for analysis of existing specimens is impractical; secondary use of specimens should not be allowed without informed consent from research participants. Secondary use of data without proper informed consent of research participants holds potential for harm as in the *Havasupai Tribe v. Arizona Board of Regents* case.

Question 62: If investigators are subject to data security and information protection requirements modeled on the HIPAA Rules, is it then acceptable for HIPAA covered entities to disclose limited data sets to investigators for research purposes without obtaining data use agreements?

NCAI recommends that limited data sets should not be shared outside the original research team without permission from individual research participants and tribal nations involved in the study. This kind of sharing of data without tribal authorization was part of the problem in the *Havasupai Tribe v. Arizona Board of Regents* case. The sharing of data outside the original research team falls under NCAI’s broader concern about secondary use of specimens. There are models for making data accessible to outside research teams without compromising tribal confidentiality, such as a data enclave – or a secure space for researchers to perform analyses that require a protected or controlled environment. The National Institutes of Health has offered data enclaves as an option for the original research team to retain control over data, but to provide the aggregate results of secondary analyses to outside requesting research teams in an ethical way.

Question 64: For research involving de-identified data, is the proposed prohibition against a researcher re-identifying such data a sufficient protection, or should there in some instances be requirements preventing the researcher from disclosing the de-identified data to, for example, third parties who might not be subject to these rules?

NCAI recommends that IRBs work to ensure that researchers abide by data sharing, use, review, and dissemination agreements stated in research review applications; and that IRBs pay particular attention to the complexities around de-identification of data due to the small size of tribal communities and unique characteristics of tribal nations and peoples in the larger population that may require initial and continued research review.

D. Potential harms to certain groups should be considered by IRBs, not just the risks to individual participants.

Question 4: Should the regulations be changed to indicate that IRBs should only consider “reasonably foreseeable risks or discomforts”?

NCAI recommends that IRBs should consider potential group harms to historically marginalized populations and other vulnerable groups, including American Indian and Alaska Native tribal nations and communities. Group stigmatization and harm is a very real risk of research conducted in Indian Country as is shown in the past case of Barrow Alcohol Study.¹ In this case, researchers stigmatized the community by stating that the tribe was “practically committing suicide” due to alcohol abuse, and there were resulting painful implications for the community. IRBs should be directed by federal regulations to consider group risks when dealing with American Indian and Alaska Native tribal nations and communities and other similarly distinct groups and communities.

Question 27: The Common Rule currently states (45 CFR 46.111(a)(2)) that an IRB “should not consider possible long-range effects of applying knowledge gained in the research (for example, the possible effects of the research on public policy) as among the research risks that fall within the purview of its responsibility.” Do IRBs correctly interpret this provision as meaning that while they should be evaluating risks to the individual subjects participating in the a study, it is not part of their mandate to evaluate policy issues such as how groups of persons or institutions, for example, might object to conducting a study because the possible results of the study might be disagreeable to them? If that is not how the provision is typically interpreted, is there a need to clarify its meaning?

NCAI recommends that IRBs should consider potential group harm to historically marginalized populations and other vulnerable groups, including American Indians and Alaska Native communities. Group stigmatization and harm is a very real risk of research conducted in Indian Country as discussed above.

E. Tribal research review is important because tribal IRBs and other research review boards have unique knowledge about tribal and local contexts that should be respected.

Question 6: Are there survey instruments or specific types of questions that should be classified as greater than minimal risk? How should the characteristics of the study population (e.g. mental health patients) be taken into consideration in the risk assessment?

The same survey instrument or types of questions might be considered minimal risk in one population, but greater than minimal risk with another group. For example, questions about topics that have been historically sensitive in American Indian and Alaska Native communities, such as alcohol use or genetic risk, may be considered higher risk than if the same questions

were asked of other groups. Individual studies should be assessed by local IRBs or review boards to determine what level of risk is posed to potential study participants. Notably, tribal nations have a variety of research review structures. Some tribal nations have their own formal IRBs, while others have developed alternative forms of research review committees or processes. The local research review process a tribe has developed, regardless of its form, can help to ensure risks specific to the population will be minimized. Tribal IRBs and other review boards may have more insight about potential participants' ways of life, cultures, languages and community traditions that could inform decisions about human subject protection and research risk. They may also know and understand more about the issues and disparities the community faces and have ideas of how to be proactive and best address these issues. University and federal review boards should also be encouraged to include American Indian and Alaska Native peoples and researchers to serve on research review bodies, especially when research with American Indian and Alaska Native tribes and peoples have been put forth. This is particularly important in the case of research review in an urban Indian context, where there may not be a formal tribal governance mechanism to provide research review.

Question 29: As noted above, IRBs sometimes engage in activities beyond those that are required by the regulations. For example, an IRB might review some studies for the purpose of determining whether or not they qualify for exemption (the new Excused category), or might review studies involving the analysis of data that is publicly available. Would it be helpful, in furtherance of increased transparency, to require that each time an IRB takes such an action, it must specifically identify that activity as one that is not required by the regulations?

It would be important to use information about the activities IRBs engage in that are beyond those required by the regulations in understanding how that IRB understands its role and regulatory authority. It may also foster coordination across tribal, community-based, regional, institutional, and national research review bodies as part of a more comprehensive initiative to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. In addition, it may encourage other research review bodies and tribal and community organizations to put forth recommendations that an IRB may consider when it next convenes on issues beyond its regulatory scope.

Question 13: Given the problems with the current system regarding wide variations in the substance of IRB reviews, would it be appropriate to require IRBs to submit period reports to OHRP in the instances in which they choose to override the defaults described in Sections B(1), B(2)(a)(ii), and B(2)(b) above? Should IRBs have to report instances in which they require continuing review or convened IRB review of a study which involves only activities identified as being on the list of those eligible for expedited review? If an IRB that chose to override these defaults was required to submit a report to OHRP, would this provide useful information about any lack of appropriate consistency among IRBs so that clarifying guidance could be provided as needed, or provide useful information to OHRP about the possible need to revise the expedited review list or the continuing review requirements?

NCAI acknowledges the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and

reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. This sort of reporting could contribute to such a dialogue. However, NCAI would also note that this reporting may need to be voluntary as American Indian and Alaska Native tribal governments are sovereign nations who have the authority to impose their own IRB regulations that may be different from federal regulations. They should not be required to report to OHRP if they choose to impose regulations different from federal ones, which require continuing review or convened IRB review of the study or expedited items.

Question 30: What are the advantages and disadvantages of mandating, as opposed to simply encouraging, one IRB of record for domestic multi-site research studies?

NCAI recommends that there should not be a requirement for only one IRB of record for multi-site studies, especially when American Indian and Alaska Native tribal nations and peoples are research participants in the study. All participating tribal nations who have active IRBs or review boards should be provided with the opportunity to review the study. If tribal nations choose to defer to one IRB for a multi-site research study of which they are participants that is their option. However, there should not be any mandate for one IRB of record for multi-site studies because local tribal IRBs and research review boards have unique knowledge about a community's history that is important to consider. Therefore, a tribal nation IRB might have different and/or more restrictive guidelines than the federal guidelines. In order for successful collaboration and trust of research studies with American Indian and Alaska Native tribal nations, tribal sovereignty should be respected and tribal government IRBs should be provided the opportunity to review multi-site research studies.

However, NCAI reiterates its acknowledgement of the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. This will aid researchers who have to coordinate across several research review boards – and where some of their efforts may be duplicated – as part of multi-site studies because there is not enough coordination on the part of research review boards themselves.

Question 31: How does local IRB review of research add to the protection of human subjects in multi-site research studies? How would mandating one IRB of record impair consideration of valuable knowledge that enhances protection of human subjects? Should the public be concerned that a centralized IRB may not have adequate knowledge of an institution's specific perspective or knowledge of an institution's specific perspective or the needs of their population, or that a centralized IRB may not share an institution's views or interpretations on certain ethical issues?

NCAI holds that a local tribal IRB or research review board is vital to the review process because these committees generally consists of members from the community or those that are actively engaged in the best interests of the community. Local IRBs add to the protection of research participants through an understanding of the unique knowledge of local context, including history of research in tribal community and past harms resulting from research – about which nearly every American Indian and Alaska Native tribal nation would have stories.

Historically, federal IRBs do not have adequate representation of tribal members as evidenced by the creation of the American Indian and Alaska Native Health Research Advisory Council.

Question 33: How significant are the inefficiencies created by local IRB review of multi-site studies?

Although there may be inefficiencies with multiple IRB reviews or local tribal IRB review along with a university review, the benefit of research participant protection is worth the extra time and process. When it comes to research with American Indian and Alaska Native tribes and peoples, NCAI advocates that it is better to have a thorough review of a research study by a tribal IRB than to rush the process without community or tribal involvement. Not having local IRB review increases the risk of harm to research participants later in the project, when effects are irreversible as occurred in the *Havasupai Tribe v. Arizona Board of Regents*.

Question 34: If there were only one IRB of record for multi-site studies, how should the IRB of record be selected? How could inappropriate forms of “IRB shopping” – intentionally selecting an IRB that is likely to approve the study without proper scrutiny – be prevented?

NCAI recommends that if only one IRB of record is allowed for multi-site studies with American Indian and Alaska Native tribal nations, that the study team be required to use the tribal IRB as the one of record. Alternatively, the research team could submit their research proposal to a university IRB in addition to, but not in place of, an application to a tribal IRB. Allowing the option for only one IRB of record could allow some researchers to engage in “IRB shopping” and bypass tribal research regulation processes in order to avoid community involvement in publications, ownership of data, and data analyses.

NCAI reiterates its acknowledgement of the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. This may work to prevent inconsistencies across research review processes that contribute to “IRB shopping”.

F. Informed consent should be required for all studies and standardized, general consent forms should be avoided.

Question 49: Is it desirable to implement the use of a standardized, general consent form to permit future research on biospecimens and data? Are there other options that should be considered, such as public education campaigns combined with a notification and opt-out process?

NCAI recommends that a standardized general consent form should not be used. “Blanket consent” or general consent was used in the *Havasupai Tribe v. Arizona Board of Regents* case and harm resulted. NCAI recommends specific informed consent forms which detail how specimens and data can and will be collected and used. All secondary uses of collected specimens and data should require an additional consent process. Informed consent forms should also be clear, understandable, and specific enough to ensure an informed consent can be solicited. NCAI also recommends that options be provided for research participants on informed consent forms (e.g., checkboxes for what types of research they do and do not want their data

used for) to ensure a clear, full-disclosure process. The Belmont Report's principles of autonomy and respect for persons require honoring decisions and wishes of research participants, rather than blanket use of their specimens and data without their explicit consent for specific purposes. Many American Indian and Alaska Native peoples believe that specimens and blood are considered sacred as they contain a person's essence and spirit. For this reason, sharing specimens between investigators or moving them from facility-to-facility is worrisome and spiritually concerning for tribal nations and peoples. By providing a full detailed informed consent form, tribal participants will have the option to determine how their specimens and data can be used.

NCAI reiterates its acknowledgement of the need to generate an ongoing dialogue across research review boards at the tribal, community-based, regional, institutional, and national levels to clarify issues of responsibility for protection of human subjects; oversight authority; application expectations and reporting requirements for investigators; and how research review regulation coordination serves to protect and advance tribal sovereignty. Tribal consultation on informed consent processes will be important as part of any decision-making about standardizing consent forms and generating best practices in the context of research with American Indian and Alaska Native tribes and peoples.

Question 50: What is the best method for providing individuals with a meaningful opportunity to choose not to consent to certain types of future research that might pose particular concerns for substantial numbers of research subjects beyond those presented by the usual research involving biospecimens? How should the consent categories that might be contained in the standardized consent form be defined (e.g. an option to say yes-or-no to future research in general, as well as a more specific option to say yes-or-no to certain specified types of research)? Should individuals have the option of identifying their own categories of research that they would either permit or disallow?

As noted in our response to question 49, NCAI recommends that all secondary uses of collected specimens and data should require an additional consent process. Additionally, clearly defined choices or checkboxes should be incorporated into the informed consent form for participants to specify which types of studies and how they would or would not like to participate. With respect to the last subquestion, individuals should have option to identify their own categories of research they would permit or disallow. The ability of participants to self identify their own categories of research they would permit or disallow should be clearly explained and defined in the informed consent process. However, NCAI cautions against using consent processes to garner blanket consent before future and secondary aspects of research design and data use have been determined. While many members of the general population may have a better sense today than in past about research and their rights, researchers and research review bodies should not transfer responsibilities around consent processes to potential participants. Researchers and research review bodies have significant responsibilities to ensure consent processes are informed and that human subjects are protected throughout the entire research process.

Question 51: If the requirement to obtain consent for all research uses of biospecimens is implemented, how should it be applied to biospecimens that are collected outside of the U.S. but are to be used in research supported by a Common Rule agency? Should there be different rules for that setting, and if so, what should they be? Should they be based on the relevant requirements in the countries where the biospecimens were collected?

NCAI recommends that the requirements of individual countries be followed for specimens and data collected outside the United States. However, if those countries do not have regulations or standards, then the minimum ethical requirements adhered to in the United States should still be followed. The sovereignty of international governments should be respected, just as tribal nations' sovereignty is important to consider in research regulation. NCAI requests and recommends that the new OHRP regulations specifically include language that explicitly recognizes the value of local American Indian and Alaska Native tribal nation review in all research projects. Implementing this specific language in the new IRB regulations will help researchers to understand that both international governmental sovereignty and American Indian/Alaska Native tribal sovereignty impact research regulation and review processes.

G. The proposed data protections will help prevent harm to research participants and tribal communities.

Question 54: Will use of the HIPAA Privacy Rule's standards for identifiable and de-identified information, and limited data sets, facilitate the implementation of the data security and information protection provisions being considered? Are the HIPAA standards, which were designed for dealing with health information, appropriate for use in all types of research studies, including social and behavioral research? If the HIPAA standards are not appropriate for all studies, what standards would be more appropriate?

NCAI supports the use of HIPAA Privacy Rule standards for identifiable and de-identifiable information and data sets. For some social and behavioral research, individual participants may wish to be identified to "receive credit" for their contribution. In these cases, the informed consent form should explicitly have the option for participants to be identified or not be identified.

Questions 59: Would study subjects be sufficiently protected from informational risks if investigators are required to adhere to a strict set of data security and information protection standards modeled on the HIPAA Rules? Are such standards appropriate not just for studies involving health information, but for all types of studies, including social and behavioral research? Or might a better system employ different standards for different types of research? (We note that the HIPAA Rules would allow subjects to authorize researchers to disclose the subjects' identities, in circumstances where investigators wish to publicly recognize their subjects in published reports, and the subjects appreciate that recognition.)

As noted above, NCAI supports the use of HIPAA Privacy Rule standards for identifiable and de-identifiable information and data sets will help with data security. These standards are appropriate for most types of research studies and data. Employing different standards for different types of research could be confusing and lead to inconsistent application of those rules.

Question 56: DNA extracted from de-identified biospecimens can be sequenced and analyzed in other ways, with the results sometimes being linked to other available data than may allow a researcher to identify the persons whose specimens were being studied. How should Federal regulations manage the risks associated with the possibility of identification of such biospecimens? Should a human biospecimens be considered identifiable in and of itself? What are the advantages and disadvantages of considering all future research with biospecimens to be research with identifiable information?

NCAI recommends that DNA and biospecimens should be considered identifiable in and of themselves because genome sequencing technology is making it more possible to link DNA with an individual. As noted above, NCAI is concerned about secondary use of data, so rigorous data protections should be applied to genetic information and specimens containing DNA. As noted above, NCAI advocates specific informed consent be required for all studies in which an individual's DNA or data are used, and that general informed consent not be allowed.

Question 63: Given the concerns raised by some that even with removal of the 18 HIPAA identifiers, re-identification of de-identified datasets is possible, should there be an absolute prohibition against re-identifying de-identified data?

NCAI recommends there should not be an absolute prohibition from re-identifying data sets that were previously de-identified. Sometimes it is necessary to link back to individuals to share with them test results found in research related to their health. There may also be a future need to go back to individuals for new informed consent for secondary use of specimens and data in future studies.

Question 64: For research involving de-identified data, is the proposed prohibition against a researcher re-identifying such data a sufficient protection, or should there in some instances be requirements preventing the researcher from disclosing the de-identified data to, for example, third parties who might not be subject to these rules?

NCAI recommends there should be a prohibition on sharing data sets with third parties, regardless of whether they are subject to the HIPAA rules or not. Sharing data sets with individuals outside the original research team is very concerning to NCAI given the *Havasupai Tribe vs. Arizona Board of Regents* case. Sharing of this information is fine if tribal or individual participant consent is given but such tribal government consent should be sought and required in the new regulations.

H. Consultation on IRB regulations with American Indian and Alaska Native tribal nations is vital for any future data collection by the federal government regarding local IRB review and approval and human subjects protection.

Question 68: With regard to data reported to the Federal government: a. Should the number of research participants in Federally funded human subjects research be reported (either to funding agencies or to a central authority)? If so, how? b. What additional data, not currently being collected, about participants in human subjects research should be systematically collected in order to provide an empirically-based assessment of the risks of particular areas of research or of human subjects research more globally? c. To what types of research should such a requirement apply (e.g., interventional studies only; all types of human subjects research, including behavioral and social science research)? In addition, are there other strategies and methods that should be implemented for gathering information on the effectiveness of the human subjects protection system?

NCAI acknowledges that it may be helpful to collect more data about participants in human subjects research, including number of participants being reported to a central authority. NCAI also agrees that it may also be helpful to collect data on adverse events for central database. However, NCAI recommends that before any such data collection is mandated or conducted,

there should be formal consultation with tribal governments under the tribal consultation policy. American Indian and Alaska Native tribal nations are sovereign governments and are often reluctant to engage in research studies and share their data when there has not been prior consultation about the research process. For more information on NCAI's recommendations for effective federal data collection in American Indian and Alaska Native communities, please see the white paper, "Federal Data Collection in American Indian/Alaska Native Communities." For a copy of the paper, please contact Emily White Hat, Program Manager, at ewhitehat@ncai.org.

Question 69: There are a variety of possible ways to support an empiric approach to optimizing human subjects protections. Towards that end, is it desirable to have all data on adverse events and unanticipated problems collected in a central database accessible by all pertinent Federal agencies?

Empiric data on adverse events in research studies would be a helpful resource. In particular, having such data sorted by study population, with separate data collected explicitly from research studies including American Indian and Alaska Native communities, would be very useful. However, as noted above, any such data collection should be preceded by formal consultation with American Indian and Alaska Native tribes, which have a government-to-government relationship with the federal government. The DHHS American Indian and Alaska Native Health Research Advisory Council (HRAC), which includes tribal leaders from diverse regions, would be an excellent resource for beginning such consultations.

I. Other Issues

Question 9: How frequently should a mandatory review and update of the list of research activities that can qualify for expedited review take place? Should the list be revised once a year, every two years, or less frequently.

NCAI recommends that the list of research activities that can qualify for expedited review should take place every two to five years.

Question 71: Should the applicability of the Common Rule be extended to all research that is not Federally funded that is being conducted at a domestic institution that receives some Federal funding for research with human subjects from a Common Rule agency?

NCAI recommends that protections provided to research participants under the Common Rule should be applied to all research projects not just federally funded studies. Establishing a standard for research protections regardless of the funding sources helps to prevent harm to research participants.

Question 74: If all Common Rule agencies issued one set of guidance, would research be facilitated both domestically and internationally? Would a single set of guidance be able to adequately address human subjects protections in diverse populations and contexts, and across the broad range of research context (including biomedical, national security, education and other types of social and behavioral research)?

NCAI recommends coordination between federal agencies on regulations regarding the protection of research participants. A single guidance document would be helpful and would help to ensure consistency in protections for research participants. NCAI also recommends formal

consultation with American Indian and Alaska Native tribal nations before such a guidance is developed. Tribal consultation would help ensure that the unique concerns and contexts of tribal nations are included in the guidance document. Different types of research may involve unique considerations as well. However, a single guidance document could include such exceptions where they may exist (e.g., for surveys or interviews as used in education or behavioral research) while still including a uniform minimum ethical standard for all types of research.

III. Conclusion

Thank you for the opportunity to provide comments. NCAI recommends formal tribal consultation on the proposed IRB regulation changes because they are significant and will have lasting effects on the integrity of research with American Indian and Alaska Native tribal nations. Consultation with tribal nations should be held in a manner consistent with the Department of Health and Human Services' tribal consultation policy and on a government-to-government level. NCAI is willing to facilitate such a tribal consultation regarding OHRP's proposed regulatory changes. For more information about these comments, please contact Emily White Hat, Program Manager, at ewhitehat@ncai.org.

http://www.uaf.edu/irb/readings/BAS_Case_Study.pdf