



National Congress of American Indians

Summary of Proposed Changes and Comment Submission Details 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

On September 8, 2015, sixteen federal departments and agencies released a [notice of proposed rulemaking \(NPRM\)](#) to revise the Federal Policy for the Protection of Human Subjects, also known as the “Common Rule”. The proposed changes described in the NPRM follow the Advance Notice of Proposed Rulemaking (ANPRM), which began the revision process in 2011. Changes to the Common Rule will impact all research conducted in the US and likely inform research policy globally given the international role of US research policy.

What is the “Common Rule”?

The Federal Policy for the Protection of Human Subjects, originally published in four Subparts by the Department of Health and Human Services in 1991 (HHS 45 CFR 46), draws largely on three principles emphasized in the Belmont Report – justice, beneficence, and respect for persons – to protect living human participants in research. Subpart A is often referred to as the Federal Policy or the “Common Rule”, and it outlines basic requirements for Institutional Review Boards (IRBs), informed consent processes, and assurances of compliance with research regulations. Subparts B, C, and D provide further protections for pregnant women, fetuses, neonates, prisoners, and children. Fifteen additional federal departments and agencies subsequently codified regulations within their own Code of Federal Regulations (CFR) using language and section numbers identical to the HHS codification of Subpart A. Protections for human subjects are the cornerstone of research ethics and came about in response to egregious violations against humans during World War II, which were brought to light during the Nuremberg Trials.

Why Should Tribal Nations Care, and What Can They Do?

There are significant implications for research with tribal nations and American Indian and Alaska Native (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 a parallel process of tribal consultation. NCAI submitted various rounds of comments in response to previous requests related to the Common Rule revision process and will build upon this work to submit comments by the **January 6, 2016**, NPRM deadline. 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. Comments, especially those that provide specific examples of the implications within a tribal context, are important. To engage in this process, there are three suggested efforts for tribal nations to consider:

1. Submit tribal comments in response to the NPRM by **5pm EST on January 6, 2016** (see NCAI’s draft comments, which can be used in full or in part, and submission details below; NCAI will continue to update our draft comments until the deadline);
2. Share this resource and encourage organizations and scholars engaged in research with tribal citizens to submit comments in response to the NPRM;
3. Submit a call for tribal consultation on the proposed revisions to the Common Rule in the NPRM; and/or
4. Send comments and feedback to NCAI as we finalize these comments.

What are Some of the Proposed Changes in the NPRM?

Eight changes to the Common Rule are highlighted as “significant” in the NPRM. In sum, these changes aim to:

1. Improve informed consent by increasing transparency and by imposing stricter new requirements regarding the information that must be given to prospective subjects, and the manner in which it is given to them, to better assure that subjects are appropriately informed before they decide to enroll in a research study.
2. Require informed consent in a general way for the use of stored biospecimens in secondary research (for example, part of a blood sample from a living human that is left over after being drawn for clinical purposes), even if the investigator is not being given information that would enable him or her to identify whose biospecimen it is. That consent would generally be obtained by means of broad consent (*i.e.*, consent for future, unspecified research studies) to the storage and eventual research use of biospecimens.
3. Exclude from coverage under the Common Rule certain categories of activities that should be deemed not to be research, are framed as inherently low risk, or where protections similar to those usually provided by IRB review are separately mandated.
4. Add additional categories of exempt research to accommodate changes in the scientific landscape and to better calibrate the level of review to the level of risk involved in the research. A new process would allow studies to be determined to be exempt without requiring any administrative or IRB review. Certain exempt and all non-exempt research would be required to provide privacy safeguards for biospecimens and identifiable private information.
5. Change the conditions and requirements for waiver or alteration of consent such that waiver of consent for research involving biospecimens (regardless of identifiability) will occur only in very rare circumstances.
6. Mandate that US institutions engaged in cooperative research rely on a single IRB for that portion of the research that takes place within the United States, with certain exceptions. To encourage the use of IRBs that are otherwise not affiliated with or operated by an assurance-holding institution (“unaffiliated IRBs”), this NPRM also includes a proposal that would hold such IRBs directly responsible for compliance with the Common Rule.
7. Eliminate the continuing review requirement for studies that undergo expedited review and for studies that have completed study interventions and are merely analyzing data or involve only observational follow-up in conjunction with standard clinical care.
8. Extend the scope of the policy to cover all clinical trials, regardless of funding source, conducted at a US institution that receives federal funding for non-exempt human subjects research.

What are the 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 tribal nations 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, however, 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 data 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 and the 2013 request for comments on the Genomics Data Sharing Policy, NCAI emphasized the need to 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.

What are NCAI's Overarching Comments on Proposed Revisions to the Common Rule?

NCAI has prepared the following overarching comments on the NPRM's proposed changes and justifications:

- *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 can place the protection of humans at odds with the goal of fostering scientific innovation;
- It does not explicitly speak to benefit;
- It often places individual and community protections at odds; and
- It 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:

- *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. [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.]*
- *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:

- *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)?*
- *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 would be an acceptable revision.

- *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:

- *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.*

 - *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.

 - *Question 11, Question 16, & Question 20: 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?* [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, there needs to be documentation generated and retained, especially in the case of research with tribal nations.]
- ***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.

- *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:

- *Question 2 & Question 3: 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?* [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 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...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).]

- *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.]
- *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.]
- *Question 21: Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions.* [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 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.]
- *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:

- *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.]
- Inclusion of specific language regarding tribal research oversight and approval: In prior comments submitted in response to the 2011 ANPRM and 2013 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:

- *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.]

- *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.]

- *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 arenas 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 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.]

- *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.]*

- *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.]*

- *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.]*

- *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 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. 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.]

- *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 American Indian and Alaska Native 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.]

- *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.]

- *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.]

How Can Comments be Submitted in Response to the NPRM?

NCAI will submit comments on the proposed changes on behalf of our members. We encourage tribal nations, tribal organizations, and those who engage in research with tribal communities to do the same.

- The current deadline to submit comments is **5pm EST on January 6, 2016**. Requests to extend the comment period are being made by NCAI and other institutions, but not guaranteed.

- Comments, identified by docket ID number HHS-OPHS-2015-0008, must be submitted either online at the Federal eRulemaking Portal (<http://www.regulations.gov>) or in hard copy to:

Jerry Menikoff, M.D., J.D.
OHRP
1101 Wootton Parkway, Suite 200
Rockville, MD 20852

Where Can Additional Information and Resources on the NPRM be Found?

The length and significance of changes in the NPRM require careful review and processing. Information on the location of the full document as well as several resources geared toward understanding the proposed changes appears below.

- The NPRM can be found in full at: <https://federalregister.gov/a/2015-21756>.
- Public comments already submitted in response to the NPRM can be viewed at <http://www.regulations.gov> by searching for “HHS-OPHS-2015-0008”, then clicking on “Open Docket Folder” and “View all documents and comments in this Docket”.
- The Office of Human Research Protections (OHRP) has six webinars covering key aspects of the NPRM available for free at: <http://www.hhs.gov/ohrp/education/training/nprmwebinars.html>.
- An archived webcast of the NPRM Town Hall Meeting held at the Department of Health and Human Services (DHHS) on October 20, 2015, can be found at: <https://www.youtube.com/playlist?list=PLrI7E8KABz1HThmKd6A5viE3c8aeH7-uQ>.
- The Quorum Review IRB’s regulatory attorneys created a summary and description of the eight most significant Common Rule changes proposed in the NPRM available for download at: http://pages.quorumreview.com/nprm-updates-to-the-common-rule/?utm_source=qr-website&utm_medium=referral&utm_campaign=nprm-2015&utm_content=banner-nprm-2015-whitepaper.
- Public Responsibility in Medicine & Research (PRIM&R) has a webpage dedicated to NPRM resources available at: http://www.primr.org/publicpolicy/nprmresources/?utm_source=MagnetMail&utm_medium=email&utm_term=mvillegas@ncai.org&utm_content=NPRM%20Resource%20Page%209-17-15&utm_campaign=PRIM%26R%27s%20NPRM%20Resources%20page%3A%20The%20information%20you%20need%20all%20in%20one%20place.

For more information, please contact Deana Around Him, Collaborative Research Center for American Indian Health Fellow at the NCAI Policy Research Center, at daroundhim@ncai.org.