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Rockville, MD 20852

RE: HHS-OPHS-2011-0005 (Advance Notice of Proposed Rulemaking) "Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Researchers"

Dear Dr. Menikoff,

On behalf of the University of North Carolina at Chapel Hill (UNC-CH), we are pleased to submit these comments in response to the above-referenced Advance Notice of Proposed Rulemaking (ANPRM).

INSTITUTIONAL BACKGROUND AND PERSPECTIVE: UNC-CH is the oldest public university in the country, and one of only a few that combines a liberal arts campus with a full complement of professional schools (medicine, law, public health, nursing, dentistry, pharmacy, social work, business). The University is a broad-based research institution with over 4000 active studies involving human subjects, ranging from unfunded social science surveys led by students to international interventional trials by some of the country's leading clinical scientists. We also have a long-standing commitment to human subjects protections, and have been active participants in many of the initiatives undertaken in recent years to examine and enhance this system. Our comments draw on this experience and commitment. More immediately, our comments draw from an outreach effort to inform our research community about the changes proposed in the ANPRM, and to solicit feedback. This included a series of Town Hall Meetings over the past two months, attended by an estimated 600 investigators, administrators, institutional review board (IRB) members and community partners. The perspectives that follow represent the aggregate input from these multiple sources.

GENERAL COMMENTS: We applaud the initiative and effort that led the Department of Health and Human Services (HHS) to issue the ANPRM, and agree with its underlying precepts. We acknowledge that the current framework of protections, codified as the Common Rule (Subpart A, 45 CFR 46) and largely unchanged since 1991, is overdue for a critical re-evaluation, with improvements and enhancements where warranted. In particular, we recognize that the nature and volume of research, as it is conducted today, has outpaced the system for overseeing that research.

At the same time, we advocate caution in implementing changes that may have unintended consequences. Several of the proposals contemplated in the ANPRM would have predictable consequences that run directly counter to the expressed goal(s). In other cases, the outcome is less predictable, but there is also a lack of evidence that we have a problem in need of “fixing.” Indeed, many of the issues that are rightly identified in the ANPRM as problems are not due to the regulations themselves, but to overly restrictive interpretations by enforcement agencies and institutions. This suggests that more guidance and clarity is needed, not only to permit but encourage institutions and IRBs to exercise more flexibility and discretion in the application of the existing regulations. We have made a conscious effort at UNC-CH over the past five years to bring a sense of proportionality and “risk-based protections” (in the words of the ANPRM) to the oversight of our research portfolio; were this being done more broadly and consistently, we suspect that the current concerns may not have reached this point.

We agree that intervention is needed to reverse current trends and practices, but are concerned that some of the proposed changes may trade one set of problems for another. Despite its deficiencies, one of the strengths of the current system is the flexibility to accommodate research scenarios and methodologies that could never be fully anticipated at the time of writing; attempts to proscriptively address these in advance, at the level of federal regulation, are destined to fail.

SPECIFIC COMMENTS: We have elected to address the issues raised in the ANPRM in the order outlined in the accompanying table provided by HHS, entitled “Comparison of Existing Rules with Some of the Changes Being Considered,” which we found to be a helpful framework for reviewing and commenting. These issues are enumerated as presented in that table. In each case we repeat the summary information from the table for context, and then provide our comments (*italics*).

ISSUE 1

Current rule: There are no specific data security protections for IRB-reviewed research: regulations require IRBs to determine, for each study, “when appropriate [that] there are adequate provisions to protect the privacy of subjects and to maintain the confidentiality of data.”

Changes being considered: Specified data security protections would apply to such research, calibrated to the level of identifiability of the information being collected.

UNC-CH Commentary: We support the establishment of uniform research-specific data security measures to assure appropriate privacy and confidentiality for research participants, provided these are feasible to adopt. We do not support the concomitant exclusion of IRBs from oversight of research that is theoretically limited to “informational risks.” The underlying presumption is that all informational risks are equivalent, and amenable to a universal set of protections that can be implemented independently by investigators. This belies the fact that some such studies may carry significant risk, and require additional protections and oversight. Moreover, the original collection of such data may present considerable risk to subjects, even before there is information to be put at risk of breach.

Current initiatives on our campus give us experience in applying data security standards in a more globalized manner, similar to that proposed; the reality is that this is challenging enough to implement within a single entity under centralized policies. Implementing uniformly across the country, while at the same time removing IRBs (and institutional control mechanisms) from the mix, would present an overwhelming challenge. An optimal system may offer several levels of security, commensurate with the level of identifiability and sensitivity of the information being collected.

Despite our general support for standards, these measures should NOT rely upon or be modeled after the HIPAA Privacy and/or Security Rules, which were established to govern protected health information (PHI) relating to clinical care. There is little evidence that HIPAA has provided additional benefit in the research to which it currently applies (in general, clinically-oriented research that relies upon access to PHI). On the contrary, it has encumbered this research by adding to the overlapping set of jurisdictions and forms, superimposed on Common Rule and/or FDA requirements that already address consent and privacy. Extending these procedures, restrictions and requirements to all research, including research in the social sciences and humanities, would only add burden without adding protections. We support recommendations from multiple sources (including the Institute of Medicine, Secretary's Advisory Committee on Human Research Protections, et al) that research uses should be exempted from HIPAA, as originally contemplated. Extending HIPAA to all research would be going in the wrong direction, and would be problematic on many levels.

ISSUE 2

Current rule: Research using existing biospecimens (clinical or from prior research) can be done without consent by stripping the specimens of identifiers.

Changes being considered: Reforms would require written consent for research use of biospecimens, even those that have been stripped of identifiers. Consent could be obtained using a standard, short form by which a person could provide open-ended consent for most research uses of a variety of biospecimens (such as all clinical specimens that might be collected at a particular hospital). This change would only apply to biospecimens collected after the effective date of the new rules.

UNC-CH Commentary: *We are strongly opposed to this proposed change. Requiring written informed consent for research use of biospecimens would create increased burdens across the country for little to no enhanced protections for participants. This requirement would be immensely harmful to scientific discovery. A great deal of high-value, low-risk research is currently conducted using biospecimens remaining from clinical procedures, after their original purpose has been served. This can occur either through de-identification (in which case the research may be considered to not involve a human subject) or with a waiver of consent (in which case oversight and control are maintained). We are aware of no body of evidence that suggests this research has resulted in harm to subjects. On the contrary, there is ample evidence of the enormous benefit that accrues to future patients and to society at large, from the responsible use of biospecimens.*

At our university alone, over 8 million lab specimens are collected per year, and the majority are discarded. Efforts to “recycle” these residual materials for scientific gain should be encouraged and facilitated, rather than inhibited. Arbitrary limitations will have a chilling effect on several levels. Obtaining consent from every patient would require enormous investment in terms of personnel and the electronic systems needed to track patient preferences. Many institutions will find the additional requirements too burdensome and expensive, and shut off any use of their biospecimens, resulting in the loss of a precious resource. Those research-intensive institutions that do elect to implement procedures will be forced to account for skewed populations in the final sample. Indeed, it can be predicted that the specimens (and data) that would be most important to include, because they reflect something less than optimal outcomes, would be the very ones most likely to be excluded. The end result will undercut scientific validity, and ultimately lead to harms to the very public this change is intended to help. Scientific advances based on incomplete or under-representative samples are a very real concern, far outweighing theoretical concerns that each of us has, as individual patients.

Moreover, we must question the meaningfulness of consent obtained in the manner proposed. The consent process would necessarily be shifted from the research setting to the clinical setting, because collection of biospecimens would routinely occur prior to the identification of any research purpose or involvement of research personnel. This would reduce the consent process to a pro forma signature, buried in the already-voluminous paperwork that patients encounter as they enter hospitals and clinics. The process would be administered in a similarly pro forma manner, by admissions staff or intake nurses who would not be well-positioned to address research questions, even if patients realized enough to ask. It is not likely they would, given the means by which this process would undoubtedly be implemented. The proposal threatens to dial back the clock several decades, to a time where one line in the hospital admission form was considered adequate to allow people to “do research on you.” This is an intellectually and ethically dishonest approach, which serves no one well, even if it (technically) puts us in position to say that patient-subjects gave their consent. This approach becomes even more problematic if subsequent uses of specimens obtained under this questionable form of consent are removed from any oversight or review, as proposed in other parts of the ANPRM.

We do agree that ethical protections are necessary for biobanks and their research uses. Models that store and manage biospecimens in centralized facilities, established with “honest broker” mechanisms under IRB approved-protocols, have proven to be a workable means of balancing individual privacy concerns with societal benefits. While there are challenges, to be sure, these approaches provide an efficient and effective resource for genomic science, with appropriate ethical and procedural safeguards. A public education campaign, supplemented by notification of patients by institutions running these biobanks, would be a more meaningful way to protect their interests while promoting science. The public deserves to understand the benefits we all derive from this area of research.

Lastly, while we agree that evolving technology in the field of genomics has dramatically increased the amount and nature of information about individuals that can be obtained from their DNA, at the current level of analytical technologies, DNA is not inherently identifiable. We do not agree that biospecimens and data should be separated in the regulations, with separate rules for their handling and oversight. This is an area where codifying technical issues within the

regulations, which have functioned admirably as a flexible framework that did not try to anticipate or pre-empt future technologies, may not serve us well.

ISSUE 3

Current rule: Federal protections only apply to studies that are funded by certain federal agencies (Common Rule agencies), or to clinical investigations that involve products regulated by the FDA

Changes being considered: Regulations would apply to all studies, regardless of funding source, that are conducted by a U.S. institution that receives some federal funding for human subjects research from a Common Rule agency.

UNC-CH Commentary: *We support the underlying concept that all human subjects deserve the same level of protections, regardless of who is conducting or funding the research. We also recognize that the current regulatory structure comprises a “patchwork quilt” of jurisdictions that simultaneously creates overlap in some areas and gaps of coverage in others. Unfortunately, the proposed change does little to close the gaps that currently exist.*

Most FWA-holding institutions already apply the regulations to all research under their purview, in principle and in practice. At the same time, these institutions have the flexibility to accommodate research that would technically not be allowed, due to regulatory idiosyncrasies (e.g., applicability of subparts, continuing review). The proposed change would only penalize those institutions, while having no impact on the researchers and organizations that currently operate outside the regulations. Indeed, there are concerns that this change would have the unintended consequence of driving sponsors and collaborators away from the former and toward the latter. That is, non-regulated entities would now have incentive to avoid doing business with institutions that received some federal funding, and were therefore obligated to extend the Common Rule. A more meaningful and productive solution would work toward the goal of a truly comprehensive and uniform set of research regulations, via congressional legislative action.

ISSUE 4

Current rule: Adverse events and unanticipated problems occurring in research are reported to multiple agencies and with various time-lines, with no central database as a repository for such data.

Changes being considered: A single web site would be created for the electronic reporting of all such events: this would meet all federal reporting requirements and the collected data would be stored in a single database. Reporting requirements would be harmonized across agencies.

UNC-CH Commentary: *As a general principle, we are strongly supportive of efforts to harmonize across agencies and departments. We are also supportive and appreciative of the efforts in recent years (2007-9) to clarify and redirect the adverse event reporting practices that had resulted in much wasted effort for very little gain; these joint agency efforts are finally*

turning around what had been decades of counterproductive reporting. That said, it is unclear whether the proposed adverse event repository would be beneficial or confounding. It should not be taken for granted that merely “putting it on the web” will serve the public or the research community. Without additional information as to the people, process, and technology being deployed, it is difficult to know if this would be of any help.

ISSUE 5

Current rule: Current provisions of the Common Rule provide only basic information about the elements of informed consent and how consent documents should be written. Many consent forms are too long and hard to understand, and fail to include some of the most important information.

Changes being considered: The regulations would be revised to provide greater specificity about how consent forms should be written and what information they should contain. The goal would be consent forms that are shorter, more readily understood, less confusing, that contain all of the key information, and that can serve as an excellent aid to help someone make a good decision about whether to participate in a study.

UNC-CH Commentary: We generally support the changes being considered, provided such changes result in greater understandability of the consent form for research participants. We acknowledge that consent forms have become overly long and complex, undercutting and obfuscating their intended purpose. Informed consent documents are complex in part because of concerns about regulatory and legal liability, and existing regulations that mandate certain components. A compelling argument can be made for expanded use of "short form" consent documents, as allowed under 46 CFR 46.117. Published literature indicates increased comprehension and understanding by enrolled participants when the short form is used. Frequently, sponsoring groups insist on additional language in the consent document which is difficult to understand, particularly when it involves injury information and confidentiality measures. Further, if greater specificity about how consent forms should be written and what information they should contain was integrated into the approach inherent with a short(er) form the consent process and human research protections would be simultaneously improved. Provision of templates by the regulatory agencies, which demonstrate how required and relevant information can be presented in a manner that simultaneously supports subject understanding and complies with the regulations, could be helpful in modifying current practices. Without such directive (and corrective) action, it is likely that current trends will continue.

ISSUE 6

Current rule: Each site in a study requires IRB review. Although the regulations allow one IRB to carry out the review for multiple sites, it is common for a single study conducted at multiple sites to have many IRBs separately reviewing the study.

Changes being considered: For all of the U.S. sites in a multi-site study, the changes propose a single IRB of record.

UNC-CH Commentary: We are in favor of changes that make collaboration and communication between IRBs easier. This is particularly needed in multisite research, for the reasons noted in the ANPRM. We are increasingly making use of cooperative review agreements in our own collaborations. Nevertheless, despite its conceptual appeal, mandating one IRB of record and one review model for multisite studies may not be a viable proposition. At present, this proposal raises more questions than it answers. These must be addressed before any serious consideration could be given to such a mandate, including: Who will select the single IRB, if they are to serve as a “first among equals?” Who will pay for centralized review, and how? How will the system guard against “IRB shopping” that will predictably occur, as researchers or sponsors search for the fastest or most lenient IRB? How will accountability and liability issues be resolved, by institutions that have been forced to relinquish local oversight? How will local context be evaluated by the single IRB, across sites that may number in the dozens or hundreds? Does the federal government have the authority to mandate reliance on a single IRB?

ISSUE 7

Current rule: Each Common Rule agency, and the FDA, is authorized to issue its own guidance with regard to interpreting and implementing the regulations protecting human subjects. That guidance may substantially differ from agency to agency.

Changes being considered: The ANPRM does not propose a specific change but through questions, seeks to determine whether or not the differences in guidance from agency to agency are justified by differences in the applicable statutes or missions of those agencies, and if not, to determine how to make guidance more uniform.

UNC-CH Commentary: As above, we favor harmonization. We support uniformity of guidance among Common Rule agencies and the FDA when it is determined appropriate to eliminate current existing differences. Examples of harmonized efforts that have been helpful include the aforementioned guidance on adverse event reporting, and recent guidance on exculpatory language in consent forms, issued jointly by OHRP and FDA.

ISSUE 8

Current rule: Research involving more-than-minimal risk requires review by a convened IRB.

Changes being considered: This requirement would remain unchanged.

UNC-CH Commentary: We agree that research involving more-than-minimal-risk should continue to require review by a convened IRB.

ISSUE 9

Current rule: Research that requires review by a convened IRB requires continuing review at least annually.

Changes being considered: Continuing review would generally not be required after all subjects in the study have completed all study interventions, and the only remaining procedures are standard-of-care procedures that are used to obtain follow-up clinical information (e.g., standard annual CT scans to detect any spread of the patient’s cancer), and the analysis of the research data.

UNC-CH Commentary: We support the changes being considered, with the understanding that there would be specific guidance regarding acceptable measures by which investigators verify that all remaining interventions are routine care. Moreover, it should be clarified if/that this cessation of continuing review would equate to “closing the study” for the purposes of IRB record-keeping.

ISSUE 10

Current rule: Research that poses minimal risk and includes only research activities in a list approved by the HHS Secretary is eligible to be reviewed in an “expedited” manner (e.g., with one reviewer, instead of a convened IRB).

Changes being considered: This list would be updated now, and at regular intervals, using appropriate data about risks to the extent possible.

UNC-CH Commentary: We support the proposed changes regarding regular maintenance and updating of the expedited review list.

ISSUE 11

Current rule: Research that is eligible for expedited review requires continuing review at least annually.

Changes being considered: Continuing review would not be required of studies that are eligible for expedited review unless the reviewer, at the time of initial review, determines that continuing review is required, and documents why.

UNC-CH Commentary: We support the proposed changes, with caveats. For much research that is deemed eligible for expedited review at the time of initial review, there is little benefit of conducting continuing review when no significant changes or events occur over the course of conducting the study. For these studies, annual continuing review adds little more than paperwork. The requirement that the reviewer, at the time of initial review, make a protocol-specific determination that continuing review should (or should not) be required should allow for the necessary protections (e.g., the protocol is likely to generate new information that could affect subjects’ willingness to participate, the protocol is in a particularly sensitive domain, the protocol involves risks that are rapidly evolving). Further, major protocol amendments or adverse events/unanticipated problems that could potentially alter the risk/benefit ratio will continue to receive IRB review at the level deemed appropriate by the reviewer.

ISSUE 12

Current rule: For a research study to be eligible for expedited review, an IRB member must determine that it is minimal risk.

Changes being considered: The “default” assumption will be that a study otherwise eligible for expedited review will be considered minimal risk unless a reviewer documents the rationale for classifying the study as involving more than minimal risk.

UNC-CH Commentary: While we do not view this as a major source of current problems, we support the changes being considered. Presumption of expedited eligibility for research meeting the approved list of requirements (coupled with updating the current list of research activities that qualify as minimal risk) would streamline approval processes without increasing risk to subjects. With technological advances that better protect research subjects' identities during data collection (especially survey data or limited/de-identified data sets), new and ongoing reassessments of risk of research activities is appropriate. Additional specificity that serves to clarify and not restrict appropriate application of expedited categories will aid reviewers in conducting quality review of minimal risk research.

ISSUE 13

Current rule: For a research study to be approved, even if it qualifies for expedited review, the same approval criteria must be met as for studies that are approved by a convened IRB.

Changes being considered: The ANPRM does not propose a specific change, but through questions seeks to determine whether some approval criteria do not meaningfully increase protections for subjects (i.e., in the case of studies that otherwise would qualify for expedited review).

UNC-CH Commentary: We do not support the premise that approval criteria should be different for expedited review. Regardless of the level of risk posed by the research, all possible risks and discomforts should be considered in order to provide optimal protection of research participants. Assurance that all risks are considered occurs by comprehensively addressing the required approval criteria outlined in 45 CFR 46.111 for all human subjects research. The research is then reviewed at a level commensurate with the risk. We believe that the approval criteria are essential as principles; their application and depth of review is protocol-specific. We also believe that current concerns stem more from over-application of the regulations or presumption of hypothetical worst case scenarios (in the absence of evidence-based risks), than from the regulations themselves. That is, all research has risks and benefits, and it is appropriate to weigh them for every protocol; problems come from over-applying these straightforward criteria. Accordingly, concerns in this area might better be addressed through education and guidance, than through regulatory change that may only result in confusion.

ISSUE 14

Current rule: Six categories of studies qualify as “exempt” from the regulations, meaning that they do not have to comply with any of the requirements of the regulations.

Changes being considered: These studies would no longer be fully exempt from the regulations. In particular, they would be subject to the new data security protections described above; and for some studies (e.g., those using biospecimens) new consent requirements would apply.

UNC-CH Commentary: We do not support the proposed changes to eliminate the option for studies meeting any of the six categories to be exempt from the regulations. The changes conflict with the overall spirit of the exemption categories, which is to allow low-risk research studies to proceed without unnecessarily cumbersome oversight. If there is adherence to the exemption categories, as currently written, there is no practical need to eliminate the flexibility afforded by exemption from the Common Rule. Only when it is determined that the research poses informational and/or other risks should the data security measures be applied and subsequently reviewed at a level commensurate with the identified risk. Similarly, only when it is determined that consent is warranted should consent requirements be applied, and then in a manner commensurate with the need.

ISSUE 15

Current rule: The categories of studies that qualify as “exempt” are not very clearly defined. As a result, it is sometimes difficult to determine whether a study qualifies as exempt.

Changes being considered: The criteria for determining whether a study is exempt would be more clear-cut and less open to interpretation.

UNC-CH Commentary: We agree that the current exemption categories can be difficult to apply, and agree with the proposed changes. These changes are favorable to the extent they serve to clarify, not restrict, the exemption categories. Please note, however, that overly defining these could be counterproductive in removing necessary flexibility to accommodate the considerable diversity and variability among individual studies. It is suggested that pragmatic examples be provided to allow more guidance for investigators and IRBs.

ISSUE 16

Current rule: Although the regulations do not require administrative review before a study is determined to be exempt, most institutions follow current federal recommendations and carry out such an administrative review.

Changes being considered: The recommendation that all such studies undergo administrative review would be eliminated. Researchers would file a brief “registration” form with their institution or IRB, and would be permitted to commence their research studies immediately after filing the form. Audits of a small percentage of studies would take place to ensure appropriate application of and compliance with the revised regulation.

UNC-CH Commentary: We have serious reservations regarding this proposal. Just as the rationale provided for this change draws on many other components in the ANPRM, so do our concerns.

Even with the proposed clarifications (issue 15), the ability of researchers to apply the exemption criteria has not been established. Beyond any regulatory or interpretational nuances, the more fundamental concern involves inherent conflict of interest. Any of us, when wearing the hat of investigator, is conflicted when it comes to assessing our own work. We routinely underestimate the risks of procedures with which we are comfortable, and over-estimate the importance. That does not reflect negatively on our investigators, nor on investigators in general. It is simply reflective of the human condition, and a major reason IRBs came to be in the first place.

Equally questionable is the argument that self-applied security protections (issue 1) are all that is needed to assure subject protections in these exempted activities. We acknowledge that the major risk in many exempt studies is limited to breach of confidentiality. While many survey and interview studies may, indeed, be limited to these “informational risks,” there is an important subset that involve more direct (and less controlled) risks. Procedures used to identify, approach, recruit and interview subjects can carry significant risk in selected cases. The difficulty is to identify these in advance and implement appropriate protections, if all surveys and interviews are uniformly and pre-emptively excluded from review via self-granted exemptions.

We do not support the creation of a new category or terminology for “excused” research, which will only add to the current confusion. Clarification and expansion of existing categories, combined with a strong signal that encourages their use, would go far toward making appropriate use of exemptions, as originally intended.

We do not support the imposition of post hoc audits, either as a regulatory mandate or a practical means to oversee research. Establishing efficient procedures to briefly vet such projects and grant exemptions proactively is much preferable to “catching them” after the fact, by relying on random audits.

Finally, the proposed changes will ultimately be unfair to researchers. While the opportunity to grant ourselves exemptions (i.e., “excuse” ourselves from review) may be appealing to investigators, this freedom will necessarily come with responsibility. Institutions may be less willing to stand behind investigators who misapply the regulations or subsequently have problems with their research, if the institution has had no previous role or opportunity to review. Thus, there will be an inappropriate shifting of responsibility to investigators, both in terms of applying the regulations and accepting the consequences.

At our university, exemptions are reviewed by staff within 1-2 days, and the vast majority proceed without any delays or problems. The goals of the ANPRM are already achievable within the current regulations, if only institutions are willing to make use of the flexibility they provide. The federal agencies can help by empowering institutions to exercise discretion, rather than over-reviewing out of generic concerns over regulatory liability.

ISSUE 17

Current rule: One of the six exempt categories applies to research using educational tests, survey procedures, or observation of public behavior, but not if both (i) information is recorded in a way that allows subjects to be identified, and (ii) disclosure of the subjects' responses outside of the research could reasonably place subjects at risk of criminal or civil liability or cause damage to financial standing, reputation, or employability.

Changes being considered: This exempt category would be broadened by eliminating criteria (i) and (ii) for studies that involve competent adults, i.e., such research would be exempt even if the information was recorded in an identifiable way and the disclosure could pose such risks to the subject.

UNC-CH Commentary: We have serious reservations about the changes being considered. We do acknowledge that the qualifying criteria (i) and (ii) under 45 CFR 46.101(b)(2) are among the elements that make the exemptions difficult to apply. However, eliminating these criteria, such that an identifiable survey on sensitive topics (e.g., illegal drug use, sexual behavior, criminal activity) would now be exempt would appear to fly in the face of reason and experience. Moreover, the absence of any institutional oversight or IRB review (per proposed change in issue 16) would combine to elevate the likelihood of problems. As above, we believe it is a fallacy to expect that enhanced data security measures (presumably to be implemented independently by investigators, since the institution has been removed from the process) would be sufficient to guard against mishaps, inadvertent or otherwise.

ISSUE 18

Current rule: Currently, research studies in the social and behavioral sciences that do not qualify for exemption category 2, but that involve certain types of well-understood interactions with subjects (e.g., asking someone to watch a video and then conducting word association tests), require IRB review.

Changes being considered: The ANPRM does not propose a specific change, but seeks public comment on whether a broad subset of studies using common social and behavioral science methodologies can be identified that should be eligible for exemption 2.

UNC-CH Commentary: We agree with the changes being considered and would welcome expansion of this and other exemption categories. We are particularly cognizant that much social and behavioral science research could be exempted, were it easier for researchers and IRBs to make appropriate use of the regulatory categories. Toward that end, we suggest that actual examples of other types of research that would qualify for this category are needed. Because it is possible that survey instruments, specific questions, and even otherwise benign types of questions in studies addressing particularly sensitive issues could pose more than minimal risk, behavioral and social science researchers should contribute to the development and periodic updating of such examples to provide guidance that can help IRBs and investigators identify these components in any study.

ISSUE 19

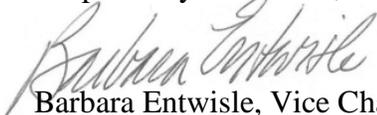
Current rule: One of the six exempt categories applies to research involving the use of existing data, documents, records, and pathological or diagnostic specimens, but only if the sources are publicly available or if the information is recorded by researchers in such a manner that subjects cannot be identified, directly or through identifiers linked to them.

Changes being considered: The requirements in this category that (1) all the data or specimens must exist as of the time that the study commences, and (2) the researcher cannot record and retain information that identifies the subjects, would be eliminated. If a researcher chooses to obtain and record identifiable information, the subject's consent would generally be needed (as required by the current rules), but that could be obtained at the time the materials are collected by using a general, open-ended consent to future research. With regard to studies using existing biospecimens, see Issue 2 above.

UNC-CH Commentary: As with exemption category 2, we acknowledge that the qualifying criteria for the exemption under 45 CFR 46.101(b)(4) make it difficult to understand and apply, and welcome clarification. Specifically, we recognize the desirability of expanding the exemption to cover data, records or specimens obtained prospectively for non-research purposes, as well as existing. Similarly, we recognize the desirability of eliminating the restriction on investigators "recording" identifying information, which creates a tenuous scenario in which they can access/see information so long as they don't write it down; in practice, this element creates confusion that is difficult for investigators and IRBs to navigate. Simplifying and clarifying exemption category 4 would be helpful. As above, we do not support (a) the mandating of written consent for all biospecimens, including leftover, de-identified clinical samples; (b) the arbitrary and artificial separation of data and specimens; (c) the sole reliance on data security measures to protect subjects; and (d) the self-granting of exemptions by investigators.

Thank you for the opportunity to comment. Once again, we appreciate the initiative undertaken by HHS, and look forward to participating as the rulemaking process moves forward.

Respectfully Submitted,



Barbara Entwisle, Vice Chancellor for Research

Daniel Nelson

Daniel K. Nelson, Director, Office of Human Research Ethics