

**Social and Behavioral Science White Paper on
Advanced Notice for Proposed Rulemaking (ANPRM)
Federal Register 44512-531 (July 26, 2011); ID Docket HHS-OPHS-2011-0005**

Introduction

On behalf of 22 research associations and over 350,000 members, we are pleased to provide this social and behavioral science (SBS) white paper in response to the Advanced Notice for Proposed Rulemaking (ANPRM) requesting comments regarding current regulations for the protecting human subjects in research, as set forth in 45CFR46, Subpart A (the “Common Rule”). We applaud your recognition of the need to modernize and provide for a more effective Common Rule in light of concerns, complexities, and challenges that have arisen during the 20 years since its adoption. We also commend the Department of Health and Human Services (HHS) and the Office of Science and Technology Policy (OSTP) for jointly taking on this task. We hope and urge that this direct collaboration continues not only to conclude successfully this process of rulemaking but also to develop a mechanism that engages the expertise of all relevant science agencies in the implementation, oversight, and evaluation of the regulations that issue. An interagency committee under OSTP would facilitate communication and planning across agencies as new issues arise and ensure that the focus is not predominately biomedical.

This white paper addresses the ANPRM from the vantage point of a very large community of concerned scientists with longstanding commitments to and engagement in the ethical conduct of research. In preparing this document, our aim is to foster revisions to the Common Rule that are consistent with the principles set forth in the Belmont Report in 1979 and to offer guidance that can serve to protect the interests of human subjects so that they can safely participate in research with genuine informed consent and a sense of their own interests in advancing knowledge. Although in this white paper we address specifically only social and behavioral science research, we believe much in this document is pertinent to all human subjects research that has found itself overshadowed and limited by regulations drafted with biomedical studies first in mind. We are, in particular, pleased to see specific attention to SBS research and ways that it differs from biomedical research whose potential for physical harm led to the development of the Common Rule.

Lest our specific criticisms be taken too broadly, we emphasize at the outset that we strongly support the aims and ambition of this project to revise the Common Rule. We believe that many of the proposed changes will facilitate quality research without diminishing, and in some cases further strengthening, the protections accorded human subjects. In structuring our guidance and comments, we follow the ANPRM systematically in sections II-VIII. Since our aim is to be educative with respect to the ethical conduct of research, this white paper addresses each topic generally in order to provide pertinent information and expertise and to better

situate our responses to the specific questions asked in ANPRM. In doing so we note that it is in the nature of white papers such as this to focus on points found to be problematic, but we shall also indicate strong support for certain proposed changes as set forth in the ANPRM. We trust that our comments and recommendations will allow for further improvement of 45CFR46 consonant with its fundamental purpose and intent and with furthering the goals that the drafters of ANPRM seek to achieve.

II. Ensuring Risk-Based Protections

We applaud the drafters for directly addressing and aiming to distinguish between the types of risks involved in human subjects research. We want to call to their attention the compelling need also to clarify the definitional language in 45CFR46 to meaningfully distinguish for IRBs the difference between and the implications of the probability or likelihood that a harm of a certain type might occur and the magnitude of the harm. The three types of harm (called risks in ANPRM) are physical, psychological, and informational.

The Social and Behavioral Sciences Working Group on Human Research Protections offered guidance on this subject in 2004 in a working paper on risk and harm (see <http://www.aera.net/humansubjects/risk-harm.pdf>), This guidance is important with respect to SBS and other human subjects research as it calls attention to the need to separately evaluate the probability of a harm and its likely severity. Moreover, both should be judged not in the abstract or by envisioned worst case scenarios, but in the context of actions that the researcher will take to reduce the likelihood of the harm and/or its severity if harm occurs.

More generally it should be made clear that the “ordinarily encountered in daily life standard” can include both high probabilities of minor inconveniences, harms, and discomforts when these are of a magnitude, although not necessarily of a kind, that characterize people’s daily existence and potentially even slightly more serious harms when the likelihood that these will occur is so extremely remote that they approximate the very low likelihoods of serious harms in daily life. While the SBS Working Group document was intended for the Office of Human Research Protection (OHRP) to guide and improve the operations of Institutional Review Board (IRB), altering 45CFR46 to language that conveys that the Common Rule addresses both the likelihood of harm and the magnitude of harm would allow for a richer understanding of both what kinds of research require full review and the importance of the steps that researchers can take and IRBs can consider to reduce the likelihood or probability that a given harm will occur.

We recommend the following: **Since the current regulations conflate the implications of likelihood or probability of harm and the magnitude of harm, the language in 45CFR46 should be revised to avert this confusion.**

A. New Mechanism for Protecting Subjects from Informational Risk

We support the recommendation to separate informational risks from physical and psychological risk and the proposed plan to remove evaluation of information risk from the purview of Institutional Review Boards (IRBs). It is possible to train IRB to assess the magnitude of information harm, but the ANPRM rightly observes that IRBs are overburdened with the assessment of other harm categories and that informational risk can be best be handled through mechanisms for ensuring data protection plans consonant with the magnitude of the informational harm and the probability of unauthorized access to the identities of research participants or information (of greater or lesser sensitivity) about them.

In July 2002, the National Human Research Protections Advisory Committee (NHRPAC), taking into consideration the advice of its SBS Working Group, approved recommendations on Confidentiality and Research Data Protections (advanced to the then DHHS Secretary) that emphasized that the potential harm that looms largest in a great deal of human subjects research relates to inadvertent disclosure of sensitive information and that this potential can be reduced through strong data protection plans and other mechanisms. The NHRPAC report noted that the level of informational harm varies from relatively minor information to highly personal information on sensitive topics and that data protection plans need to be calibrated to the level of potential informational harm. The report also notes that research data need to be protected from forced disclosures for non-research purposes (e.g., legal entities) and provides an Illustrative Overview of Federal Research Confidentiality Statutes and Codes. See the NHRPAC report and recommendation at <http://www.hhs.gov/ohrp/archive/nhrpac/doc-report.htm>.)

The NHRPAC recommendations on data security and reduction of information risk are consistent with the ANPRM, and we applaud attention to this issue in the plan for proposed rulemaking changes. **Consistent with the NHRPAC recommendations, however, we do not support a one-size-fit all solution for data security and data protection or basing mandatory standards for data security and information protection on the standards of identifiability specified under the HIPAA Privacy Act.** As discussed in greater length in section V below (Strengthening Data Protections to Minimize Information Risks), HIPAA's standards are unsuitable for several reasons: HIPAA is designed to provide privacy protection for administrative health records related to specific categories of Personal Identifiable Information (PII) and has failings even as a mechanism for permitting health research consonant with privacy protection (see 2009 IOM report on *Beyond the HIPAA privacy rule: Enhancing privacy, improving health through research*); HIPAA was not intended to identify data security and data protection mechanisms that would reduce risks of advertent or inadvertent data disclosure while allowing appropriate research use, nor is it well suited to this end; and, because HIPAA was drafted with an eye to protecting patient medical records, it is particularly ill suited to the kinds of data security and subject protection issues that SBS researchers encounter in wide-ranging research beyond health and beyond the use of administrative records (e.g., census data).

In its suggestion that HIPAA be consulted for definitive guidance, the ANPRM has not benefitted from the best scientific and ethical understandings of how to ensure data protection and data security at minimal cost to important research enterprises, particularly with respect to data, including health data, produced and used by the SBS sciences. For more than two decades, guidance has been produced and updated under the auspices of the National Academy of Sciences (through the National Research Council [NRC]) and the Institute of Medicine (see Appendix A). Other well thought-out guidance, including guidance for data protection, data security, data disclosure testing, and secure data access, is found in the work of federal statistical agencies. Also, data archives such as the Inter-University Consortium of Political and Social Research (ICPSR) have established rigorous standards and procedures for the dissemination and analysis of public-use data and for the conditions that allow for access, use, and analysis of restricted-data. In addition, codes of ethics of various professional and scientific associations address these issues (for example, the ethical standards of the American Educational Research Association on appropriate use of confidential data collected by others, or the American Statistical Association's statement on Data Access and Personal Privacy: Appropriate Methods of Disclose Control). Finally, federal regulations apart from HIPAA also confront the need to protect PII and do so using different mechanisms (e.g., federal data collections adhere to the Confidential Information Protection and Statistical Efficiency Act [CIPSEA]). These sources must be consulted in thinking about how best to protect the data security and privacy interests of research subjects. It would be good if the HIPAA definitions and regulations provided an adequate solution, but they do not.

Appendix A of this white paper is a report on *Protecting Research Participants and Facilitating Data Access—Recommendations prepared by the National Academies* prepared by the Academies staff to summarize the state of the knowledge and recommendations issued between 1985 and 2010 from approximately 20 study panels and committees. This work and in particular two of the foundational NRC reports—the *Protecting Participants and Facilitating Social and Behavioral Sciences Research* (2003) and *Expanding Access to Research Data: Reconciling Risks and Opportunities* (2005), suggest that HHS would be remiss if it revised 45CFR46 to put in place mandatory standards, whether based on HIPAA or otherwise, without building on extant, time-tested, and cumulative standards, methods, measures, and advisement for protecting personally identifiable information, ensuring data protection and security, and permitting access and use.

We recommend one of a number of immediate steps in the revision of 45CFR46:

- **Commit to (1) an examination of options available for researchers establishing data protection plans and for oversight of those plans that are efficient, flexible, and in accord with the data being collected; and (2) an independent study of these options drawing upon expert sources like those mentioned above (seeking guidance from the NRC would be particularly appropriate here);**

- **Meanwhile, permit researchers under a revision of 45CFR46 to provide information on data protection as part of the registration process for excused research subject to the conditions below.**
 - **Exempt from further specification, review, or registration of data protection plans, research using only data derived from public-use files that have been already vetted through a disclosure review board, data archives, survey/data centers, or federally approved data archives or other federally approved system of access.** This recommendation is consistent with the 2002 recommendations on public use data files of the National Human Research Protections Advisory Committee (see <http://www.hhs.gov/ohrp/archive/nhrpac/documents/dataltr.pdf>), the NRC 2003 report cited above, and growing practices at a number of institutions. It also recognizes the adequacy of the conditions that federal agencies themselves impose when providing research access to some of the most sensitive federally held data.
 - **Hold researchers who seek excused status for restricted-data use accountable in accord with their data security and protection plans. Require researchers using such data to register their research and information on access approval through a data use agreement. Require researchers using restricted data to adhere to the protection of private information and confidentiality agreements that were part of the original consent with human subjects, under penalty for violation.**

B. Calibrating the Levels of Review to the Level of Risk

We welcome and strongly support planned changes set forth in the ANPRM that will better calibrate IRB scrutiny of the risk of harm (better stated as the magnitude of harm) that a project might entail. Better calibration will allow IRBs to more closely review projects that pose greater than minimal levels of harm or otherwise raise serious ethical concerns. It will at the same time reduce delay and other costs that unnecessary scrutiny of low-risk projects imposes on IRBs and researchers alike. This commitment to strengthen the calibration necessarily needs to involve a parallel commitment to scrutinize what research can be included in excused or expedited review and to monitor the process to ensure that regulatory creep to full review is averted given the all too common migration to full review by IRBs over time.

1. Full Convened IRB Review

Turning to the specific suggestions, we believe that continuing review can be eliminated for all minimal risk studies that undergo expedited review, or, with

research involving greater than minimal risk (addressed in this section of the ANPRM), when the research is at the data analysis stage or when data are provided that are routinely collected and have been approved for the study. At this stage, any harm is informational and should be protected under appropriate data protection plans. Specifically:

- **We agree with the statement in the ANPRM that research that poses greater than minimal risk should be reviewed by a fully convened IRB and that 45CFR46 should not be changed in that regard.** Assuming increased attention and clarity about what can be classified as minimal risk research and qualify for expedited review (or in the case of information risk for being excused), we support the premise that IRB review should focus on research that involves greater than minimal risk.
- **We also agree with the statement in the ANPRM that, regardless of whether identifiers are retained, continuing review should cease when data analysis and report writing are the only remaining research activities or when additions to the data are part of routine data collection. We agree with the change in (i) about the data analysis stage, and we further recommend that the language in (ii) be broadened to include accessing follow-up data that are routinely obtained (e.g., test scores, salary information) in SBS research and for which there has been prior consent and approval.** There are social and behavioral science data that are equivalent to follow-up data that are part of the standard of care, and reference to such SBS data should be included in a revised ii.
- In the course of data analysis, SBS researchers more than occasionally find ways of improving their planned approach or that relationships that they had not planned to investigate are worthy of exploration. In all of science, data analysis is an iterative process where the entire analysis cannot be anticipated in advance. So long as informational risks remain minimal, such steps should not constitute changes triggering continuing review. **We agree that dropping the requirement of continuing review under these circumstances from the Common Rule would allow for more effective use of IRBs' time and also allow them to focus continuing review on issues requiring their attention.** Nothing in this change would alter the ethical obligation of researchers to ensure that their analyses and reporting did not violate obligations raised by the scope of informed consent or data protection plans.
- **As set forth in the ANPRM, we concur that researchers would still have the obligation to report significant unanticipated problems or issues.** For example, it would be expected that researchers would report if the data analysis reveals that human subjects were harmed in unanticipated ways,

that informed consent had been inadequate, or that risks to human subjects' exceeded those that had previously been brought to the IRB's attention.

2. Revise Approach to Expedited Review

We support all three areas of change (revising the criteria for expedited review, eliminating continuing routine review of expedited studies, and streamlining submission requirements) contemplated in the ANPRM under IIB2. The plan to expand the research activities appropriate for expedited and increase the clarity of what qualifies as minimal risk is long overdue.

- **We support updating the list of research activities that qualify a study for expedited review and for periodically considering further expansion based on empirical assessment of the levels of risk.**
- **We also support the default assumption that research that falls under one of the listed activities is by definition minimal risk and thus qualifies for expedited review.**
- **While we appreciate that there may be a need for reviewers to be able to determine that listed research should receive full IRB review, we strongly recommend that such decision should be documented and subject to auditing to avert the migration from expedited to full review.**

We strongly agree that a periodic review and update of the list of research eligible for expedited review is highly desirable, whether annually or every two years. We support the appointment of an inter-agency federal panel to be charged with this responsibility and urge strongly that SBS sciences be visibly present on that panel because of the preponderance of research in SBS fields that are appropriate for expedited review. **Such a federal panel should recommend that areas be added to or removed from the list, and the DHHS Secretary should seek public comment on the recommendations.**

As SBS research organizations we particularly applaud the goal of ensuring that updates to the list are based “on a systematic, empirical assessment of the level of risk.” Systematic empirical assessments sufficiently valid to drive policy may, however, be difficult to do, particularly when the presence or absence of undesired outcomes are not easily measurable. Unlikely deviant cases should not drive decision making. In revising 45CFR46, we want to avert circumstances where the empirical evidence is unspecified and might itself preclude additions to the list.

Empirical assessment might be facilitated in several ways. In addition to investment in systematic research, research communities with approved protocols might be invited to suggest candidates for the expedited-approved list. Another approach is to invite local IRBs to supplement the national list with their own lists so long as local additions and experience with these additions were reported to the Secretary.

The federal panel could be tasked with reviewing the suggestions from IRBs and research communities.

SBS scientists' experience leads us to strongly endorse the ANPRM observation that far too many SBS studies appropriate for expedited review nevertheless undergo full IRB review. A conservative bias is natural in a system that threatens to penalize insufficient scrutiny but that does not sanction unwarranted review. The proposed solution, the default that studies eligible for expedited review should receive it, may help, but the forces that make for hyper-regulation are such that more oversight is likely to be needed. Thus, as set forth in our recommendation above, **there should be written justification citing specific concerns when a study that is *prima facie* qualified for expedited review is referred to a full IRB panel. In addition, we recommend routine audits of the documentation in order to provide IRBs with feedback to better calibrate their decisions and to provide national policy makers with data to assess whether expedited review is working as intended.**

Finally, we endorse the proposal for reconsidering whether, when research is considered under expedited review, it is necessary to find that all of the criteria for IRB approval have been met. We address them in turn:

(1) Research activities listed for expedited review have met the minimal risk criterion and thus an additional finding should not be required. **We wish to emphasize that the language in 46.111a(1)(i) inviting IRBs to determine whether research procedures are “consistent with sound research design” should be stricken or modified to avert judgments beyond the expertise of IRBs and not directly germane to human subjects protections.** There needs to be strict scrutiny to ensure that IRBs do not stray from their regulatory purpose. In the context of expedited review, when risks are by definition minimal, design evaluation is best left to peer review and review by funders, mentors, advisors, or colleagues. Indeed, even when risks are more than minimal, unless design changes will reduce otherwise unacceptable risks, such changes should not be within the purview of the IRB.

(2) It is similarly unnecessary to require the IRB to weigh risks to subjects against anticipated benefits. Since the Secretary's list includes only research expected to be of minimal risk and since a reviewer can refer a protocol for full review where more than minimal risks appear possible, asking an IRB to strike a balance between risks and benefits in cases qualifying for expedited review is superfluous.

(3) The mandate that subjects be equitably selected is germane to over-inclusion of populations that might be exposed to more than minimal risk or denial on inclusion without good reason. While the principle of providing or denying benefits through research is important, further determination of whether, as a matter of human subjection protection, this criterion is met seems unnecessary with studies appropriately classified as expedited. The ANPRM addresses 45CFR46, Subpart A, and does not include the other Subparts related to designated categories of

vulnerable populations. We urge more attention to the other subparts of 45CFR46 in follow-up efforts. In this context (adult populations participating as human subjects in research eligible for expedited review), it seems unnecessary to undertake further review of the equitable selection of human subjects. The fact that additional review is not needed does not relieve researchers of other scientific or ethical responsibility related to research conduct.

(4) (5) The fact that research is listed as eligible for expedited review and meets the criteria for minimal risk does not by itself vitiate the need for informed consent. These criteria should remain in place. Elsewhere, we recommend revision of 45CFR46.116-117 to more fully reflect the nature of the informed consent process and the range of ways it can be appropriately and meaningfully obtained.

(6) If the research is eligible for expedited review, then the provisions for data security and data protection should be sufficient to protect human subjects.

(7) In the case of research classified as expedited, the same procedures for addressing informational risk should be applicable to ensure that data protection plans appropriate to the research are in place.

(8) If risks are genuinely minimal, if standards for data protection are in place, and if informed consent exists, as will be true of research eligible for expedited review, it may be unnecessary to introduce additional safeguards to protect the rights and welfare of human subjects likely to be vulnerable. Special rules delineating how informed consents may be secured from members of vulnerable populations are appropriate, and IRBs may wish to pay close attention to the consent process.

We agree that annual or continual review of expedited studies is not a good use of an IRB's (or a researcher's) time and strongly support eliminating continuing review of expedited studies.

We further support the continued requirement that researchers should report study changes or unanticipated problems as currently required, but that determination should continue to rest with the researcher.

We understand that there will be circumstances when a reviewer needs the latitude to require continuing review of expedited research, and we support the proposed change requiring the reviewer to justify the continuing review and to specify how frequently the review should take place. Our observations of the drift toward hyper-regulation lead us, however, to urge additional safeguards to ensure that continuing review of expedited studies is properly justified and to avert overuse. Such steps might include an annual review of all such requirements to ensure that continuing review is both well justified and well documented each time it is required.

We support the recommendation that there be streamlined documentation for expedited studies. It is important, however, that standard templates and forms

intended to expedite the process lead to greater flexibility and efficiency and not result in a one-size-fits-all template for minimal risk research. Documents based on materials appropriate to similar studies or previously approved for use in similar expedited research—whether approved at the same institution or not—should qualify as acceptable templates for expedited studies.

In addressing the specific questions (Q1-13), the SBS response is as follows:

Q1. It would help helpful to clarify the current definition so that so that the two elements of risk—magnitude of harm or discomfort in relation to daily life and the likelihood or probability of its occurrence—and their relationship to each other are fully understood. The confusion inherent in the language can lead to focusing more on the likelihood of the occurrence of the harm than on attention to the primary issue of whether the harm, if it were to occur, is minimal in magnitude and no more than would be encountered in daily life. Also, it would be useful in light of proposed changes in the ANPRM to state explicitly that research involving only informational risk meets the criteria for minimal risk research if information disclosure would produce harm no greater than the “everyday” standard, or if strong data protection plans are in place to minimize the risk of informational harm.

Q2. Yes. We support the proposed change establishing a strong presumption that research involving no more than minimal risk that qualifies for expedited review should not need to undergo continuing review. One exception might be where unanticipated problems or adverse events trigger researcher reporting. Such reporting might lead subsequently to introducing continuing review until at least the next reporting period. Overall, research that qualifies for expedited review does not need the routine monitoring envisioned by continuing review. The biggest need is to ensure that the shift to eliminate continuing review is not averted by risk-averse reviewers. There needs to be strong safeguards to ensure that reviewers have checks on their discretion to require continuing review through requirements to document and report on the reasons for such review and by at least an annual review of studies that although qualified for expedited review are required to have continuing review. In sum, rather than create exceptions to the no continuing review default, IRBs should retain discretion but be required to provide written justification for overriding the default and to state at the study’s conclusion whether the continuing review led to changes in research procedures or otherwise forestalled potential harms.

Q3. No. There is no need for annual review of research greater than minimal risk when the remaining stages of the research would be expedited or excused under the new ANPRM categories (e.g., when routine surveys are being completed or the research is in the data analysis phase). If continuing review is required by reviewers, they should provide justification. OHRP should also provide guidance to support IRBs transition to and implementation of the elimination of continuing review in these phases of the research.

Q4. Yes. The regulations should be changed to make clear that IRBs should only consider “reasonably foreseeable risks or discomforts.” The proposed language properly emphasizes that although IRBs should evaluate the likelihood that harms might be more than minimal, they should not speculate about every possible harm. If harm is not *reasonably foreseeable* (likely), then the probability of that harm is minimal. As emphasized earlier in this white paper, the language should speak of “harm” in the same way it speaks of “discomfort” rather than use the word “risk.” It is the possibility of harm and not risk that must be foreseeable. If, for example, the risk of harm is one in 10 million, the risk is reasonably foreseeable, but it would be unreasonable to foresee harm.

Q5. There is considerable ambiguity in the discussion of psychological risk in 45CFR46 creating a danger that IRBs will misjudge the nature of possible psychological harms and overestimate their likely magnitudes and risks. The result will be unneeded reviews and unnecessary regulation of important but low risk SBS research. Among the negative psychological risks labeled “psychological harms” that human subjects may experience are such emotions as boredom, worry, frustration, annoyance, stress, upset, guilt, and loss of self confidence. These may be minor in magnitude or transitory and may even stimulate new levels of personal insight or self awareness. The definition of minimal risk and the procedures for informed consent offer a framework, if appropriately applied, for meaningful analysis of psychological risk. In weighing such risk careful attention needs to be paid to the magnitude of the psychological harm and its likelihood of occurrence in comparison to psychological states encountered in ordinary life or in routine physical or psychological tests or procedures. Also important is the period for which the state can be expected to endure.

Developing an evidential basis for determining whether psychological or other non-physical risks are greater than minimal risk requires further research. Meanwhile, multiple factors (the topic of research, the study population, the methodology to be used) should be taken into account to assess whether the magnitude of harm and its likelihood exceed the definition of minimal risk. Considerations include (1) what stressors, if any, a subject will face; (2) the duration of any stress; (3) whether the experience is likely to produce transitory or enduring reactions; (4) whether the stress could have positive outcomes; (5) whether informed consent alerts persons to possible stressors and emphasizes options (including opting out) to reduce stress; (6) the likely effectiveness of post study debriefing; and (7) whether subject vulnerabilities are likely to interact with any of the preceding considerations to a subject’s detriment.

Risks should not be considered greater than minimal simply because deception is involved. Nor should questions that probe highly sensitive matters like sexual behavior or criminality be regarded as posing greater than minimal (non-informational) risks so long as (1) informed consent will be adequate; (2) subjects are clearly told that they can refuse to answer sensitive questions without penalty, including the forfeiture of promised incentives for study participation; and (3)

subject who refuse to answer questions are not pressured to answer beyond the later offering of a chance to rethink the refusal. Absent a sufficient research base, the rules should not presume that any particular study feature creates more than minimal non-physical risks, although some of the features mentioned above (not including deception) will appropriately trigger close inquiry.

Q6. Assuming informational risks are controlled, we do not think there are any types of survey instruments or questions administered to consenting individuals following adequate informed consent that should be prima facie classified as more than minimal risk. Respondent characteristics may figure in the determination of what is adequate informed consent or, if the respondent is incapable of giving informed consent, whether posing a question might create more than a minimal risk of harm.

Q7. There is useful guidance in existing documents about the research activities that should qualify for expedited review. For example, in 2008, the National Science and Technology Council issued a report on Expedited Review of Social and Behavioral Science Activities (see <http://www.nsf.gov/pubs/2008/nsf08203/nsf08203.pdf>) that includes an extensive list aligned with 9 categories for expedited review specified as part of 45CFR46. Such a list could now be expanded to include spatial or location information and observations of information made publicly available either by law or by a person's voluntary actions, including such information as tweets, Facebook entries, and reportable campaign contributions.

Q8. Neuroimaging techniques are central to investigations into brain mechanisms that underlie different behaviors. These investigations, particularly in conjunction with cognitive and behavioral measurement techniques, are the norm in a variety of areas across behavioral science research, and allow scientists to explore the brain mechanisms that, for example, may contribute to behavioral features of autism, such as differences in eye gaze and attention; that underlie the behavioral features of ADHD, such as differences in attention and inhibition; or that are related to the experience of cravings and addiction, where studies have shown that cues (e.g., an image of a cigarette) can elicit activation in areas of the brain related to reward processing. In other examples, researchers also have used neuroimaging to investigate the brain basis for visual and auditory hallucinations, reasoning and moral judgment, and whether brain differences underlie the many behavioral differences we see between children and adults, such as the differences in prefrontal activation that have been identified in children, adolescents, and adults when they engage in risk-taking tasks. As with other areas of research involving human subjects, the appropriate level of review for research involving radiological investigations should be calibrated to the level of risk involved. Establishing a threshold for the risk involved in radiological techniques is in keeping with this view and would likely be useful in determining the overall risk involved in a behavioral study involving imaging or other radiological techniques.

Q9. We support routinely adding to the list of presumptively minimal risk research, and the approach of doing so periodically (every year or two). We reiterate that, except where a clear pattern of harm has developed, removal from the list should be rare and only occur after notice about the proposed change and a comment period.

Q10. The answer to this question is provided in detail in 1-8 above on pages 8-9.

Q11. There may be gains from allowing expedited review by persons other than IRB members. A trained and experienced staff person, with relevant background, may be better equipped to do expedited reviews than an IRB member, especially a member recently appointed. A possible danger (under either scenario) is that, if a single person handles most expedited reviews, that person's misunderstandings or idiosyncratic judgments may be repeated in case after case. Also IRB members will be less familiar with cases that pose only minimal risk, and this may affect establishing a meaningful baseline of cases they review. The local IRB is perhaps best equipped to judge what training is necessary. A required element of training might be a certain number (say 10) of joint but independent research reviews to ensure the non-member is properly calibrated. (These could be reviews of files the IRB has passed on if the person trained does not know the decisions reached.) In addition, a sample of the staff person's decisions might be reviewed by the IRB twice each year to ensure that judgments are appropriate and that drift into risk-averse actions does not occur.

Q12. We support the recommendation of streamlining documentation and the use of standard templates to the extent that they facilitate the process for expedited studies. Caution is needed to ensure that that template documents not be confused with standardized forms that could become mechanistic and less useful.

Q13. We believe that a periodic reporting requirement when IRBs override expedited review defaults would have considerable value. First, it could identify recurring situations where full reviews were unnecessarily required and so support more specific guidance. Second, it could reveal situations where studies apparently suitable for expedited review are likely to pose more than minimal risk. To achieve these ends, IRB reports would have to explain decisions to opt for full review and the outcomes of review in some detail.

3. Moving Away from the Concept of Exempt

We have substantial concerns about the use of the ANPRM proposed new category of "excused" research to the extent it covers exempt research and imposes additional regulations relating to data protection and consent. The introducing of an excused category for research that, apart from possible information risks involves no more than minimal risk, is attractive because it largely removes from IRBs the burden and distractions of review tasks that do little if anything to protect human subjects. It also lessens burdens, especially the burden of delay, on the research enterprise. Indeed, we believe that much research that is now

subject to expedited review can be productively moved to the excused category, and we encourage consideration of additional types of research that can be classified as excused instead of expedited without risking harm to human subjects.

Our concern is with the functional abandonment of an exempt category for research activities that are best left as uncovered by 45CFR46. To relocate activities as excused that have previously been classified as exempt from 45CFR46 and then to introduce new requirements they must meet is potentially a step backwards. The logic that led to the original creation of the exempt category for activities that fall outside of the province of 45CFR46 is principled and compelling. Whether the current categories and classifications of exempt are all the right choices is not the issue. The point here is that to shift activities that have been determined to be outside of the purview of 45CFR46 so that they now fall within it may, no matter how limited the requirements for excused research, place new burdens on work that as a matter of policy or principle should be outside of the scope of human subjects research.

- **We recommend that any decision about exempt research be deferred from the planned and important revisions to 45CFR46 unless and until there is an independent study of (1) what exemption should mean and means in practice, (2) the appropriateness of exempting studies of various sorts from IRB review, (3) whether or not oversight under 45CFR46 is appropriate when research is exempt, and (4) what principles and procedures should be used in determining what research should be exempt.**
- **We further recommend that an independent entity (e.g., the National Research Council [NRC]) be asked to consider the above issues and that it be charged with constituting a committee to report with guidance on (1) how to define exempt research, including the implications of being so labeled, (2) how to determine what research should be classified as exempt, (3) the means or mechanisms by which exempt status is conferred, and (4) procedures for reviewing research that is or might be classified as exempt in order to shrink or expand the list as appropriate. In addition to focusing on what the exempt category means and how it is treated, the review should also address the standards that specific studies should meet and procedures that should be followed in determining whether a study in fact falls into the exempt category, including where primary responsibility for making that determination should lie.**

The issue of exemptions and how exemptions have been conferred or determined has been mired in confusion for some time. Because a great deal of research in the SBS sciences falls under one or more than one of the six of categories exempt from 45CFR46, our scientists and scientific societies understand and have been at the

forefront of concerns about the relationship between current practices under 45CFR46 and its legislative intent. For all practical purposes, at most institutions, IRBs make determinations about exemptions, though the OHRP guidance only discourages institutions from having researchers themselves determine whether their activities are exempt. OHRP (1) advises that institutions should have a clear policy in place on who shall determine what research is exempt under .46.101(b), and (2) allows for but does not require institutions to review all research under the auspices of the institution even if the research qualifies for exemption under .46.101(b). (See <http://www.hhs.gov/ohrp/policy/hcdc95-02.html> and see also <http://answers.hhs.gov/ohrp/categories/1564>.)

Just as there are appropriate cautions about researchers determining whether their research is exempt from review under 45CFR46, there are problems in having IRBs make this determination. There is danger of a slippery slope of hyper-regulation and decisions that do not reflect legislative intent but instead the risk-aversion of IRBs. The 2003 NRC report pointed to the vagaries in the provision of exemptions—reporting on empirical studies revealing the great reluctance of IRBs to use the exempt categories for otherwise exempt research (pp. 40-41). The Social and Behavioral Sciences Working Group on Human Research Protections issued a report and recommendations on Institutional Arrangements for Reviewing Exempt, Expedited, and Other Research and Research-Related Activities calling for institutions to consider how exempt determinations should be made and the criteria to be applied (<http://www.hhs.gov/ohrp/policy/protocol/index.html>).

The SBS community strongly urges that the revised regulations not further obliterate the distinction between exempt and other research by requiring activities outside of 45CFR46 to be monitored within the confines of 45CFR46. Data protection and consent for exempt research activities must exist as appropriate, but other authority exists and can guide these determinations. To the extent that any of the six currently exempt categories might be viewed as inappropriate for exemption or other categories might be seen as appropriate, that guidance could and should be a part of the NRC review called for and recommended above.

A few examples illustrate why the expansion of regulation under 45CFR46 and the erosion of the meaning of exempt proposed in the ANPRM should not occur without special attention to what is appropriately within and outside of the scope of this policy and the way determinations should be made:

Under 46.101(b)(2), research involving the use of educational tests, survey procedures, interview procedures or observations of public behavior are now exempt from review unless (1) information is recorded in such a manner that persons can be directly or indirectly identified, and (2) any disclosure of responses outside of the research could place subjects at risk of civil or criminal liability or damage a subject's financial standing, reputation, or employment. Under the ANPRM, the qualifier that limits the scope of the

exemption would be dropped—that is, everything after “unless,” the qualifier that makes the work exempt, would be eliminated. In its stead would be rules regarding data security, subject privacy protection and informed consent. The change in approach is substantial and the coverage of the two approaches does not completely overlap.

The same type conundrum is created in the ANPRM for exempt category 4, specified at 46.101(b)(4). This category was intended to exempt from the policy research “involving the collection or study of existing data, documents, records. . . if these sources are publicly available or if the information is recorded. . . in such a manner that subjects cannot be identified, directly or through identifiers linked to the subjects.” This exception puts outside of the purview of 45CFR46 public-use data and other information that meets the criteria of being unidentifiable. The ANPRM seeks not to limit researchers from recording or using identifiable data, and we support this affirmation. Such activities, however, now fall within 45CFR46. While we appreciate the ANPRM recognition of the value and importance of retaining identifiable information and using it, this exemption is specifically intended for public information and for information recorded without identifiers. By eliminating this qualifier, the ANPRM obliterates the distinction that both defines and justifies the exemption. (Note, as an aside, that we concur with the word clarification that “existing” is not intended to mean that information gathering is not ongoing.)

Under 46.101(b)(3)(i), the policy now provides an exemption for studies of public officials or candidates for public office. Under the ANPRM, research of this type would be reclassified as excused and the data identifying political actors would be subject to data security and privacy protection provisions. Yet, public officials and candidates for public office ordinarily have no right to claim anonymity in reports on their beliefs and actions. Indeed, we further recommend (when this issue is taken up) expanding the category to any person who has public figure status. Imposing data controls by converting this category of exempt to excused may raise significant First Amendment problems. Continuing to classify such research as exempt and thus uncovered by 45CFR46 does not mean that there are no constraints on a researcher’s behavior, including obligations to protect confidential data. Professional ethics, organizational policy, and the civil and criminal law appropriate apply to ensure ethical behavior in research of this nature. Being exempt under 45CFR46 offers researchers no protection against civil suits or criminal liability, nor should it control grant making or contracting entities.

We strongly caution against regulatory creep. We recognize that the ANPRM suggests a number of changes designed to guard against it, but the suggested elimination of the exempt category poses this danger. Moving now exempt research to the excused category functionally expands the scope of 45CFR46 when the intent of the ANPRM is to devise a streamlined and more ethically effective

system for the consideration of research under its purview. Until further independent consideration of this issue can be undertaken, we recommend that the exempt categories for activities outside of the domain of 45CFR46 remain intact and the new category of excused research be used only for types of research previously receiving or potentially now eligible for expedited review. **Our view is that exempt research should not be treated as covered by the regulations, for that was and is not the intent of having certain classes of activities outside of 45CFR46.** If there is a case for making a change of the kind proposed, that case has not been made. Time is needed to examine what types of research activities are appropriately exempt and how these determinations should be made going forward. As set forth above, we recommend that an NRC Committee be given this charge.

Tracking and Auditing Excused Research

Assuming that exemptions to 45CFR46 are appropriately defined and administered so that deservedly exempt research is not treated as excused, the ANPRM proposal to put in place registration mechanism for previously expedited research redefined as excused is a positive approach with the particular virtue that it provides a handle for research oversight while allowing research to proceed without costly and unnecessary wait and delay. Guarantees of subject safety are found both in the general nature of the research and in the requirements that researchers, in registering their studies, can be required to attest to the fact that their study poses only minimal risks, that informational risks are minimized by appropriate data security and data protection plans, and that, where applicable, certain consent requirements have been met. The fact that research of this genre can be registered subject to audit but without review should reduce unnecessary burdens on IRB and investigators. To reduce the likelihood of new burdens in excess of reasonable need, any revision to 45CFR46 should specify what registration would entail and what “certain consent requirements” means. We strongly favor expanding the list of study types eligible to be excused, including not just for research that involves only informational risk but also for studies where the magnitude of psychological harm is very low and of a transitory nature that is no more than one’s experience in everyday life.

The plan to register excused research and conduct sample audits also makes sense and should not prove to be unduly burdensome if audits are initially based only on registration forms. To provide an accurate picture, with a known margin of error, of the appropriateness of excused designations, the forms audited should be chosen at random. A wider audit might be triggered if the proportion of misclassifications exceeds a certain level. Requiring that a specific portion of audits be conducted is poor policy because it is poor statistics. Rather, the number should be determined by the sample size needed to determine if misclassified applications exceed a certain threshold with a specified margin of error.

We understand the rationale for IRBs having an option to review some excused submissions at the time they are filed. We generally approve of such flexibility. We

fear, however, that bureaucratic routine and conservatism might make this number higher than it need be and that it will rise over time as new reasons for review are added. **Hence, we suggest that, if an IRB chooses to review an excused submission, it be required to explain in writing why that submission was chosen for review. Without a specific good reason, excused submissions should not be reviewed unless recent audits have indicated ongoing problems with how researchers have applied the excused designation and met the other conditions for excused research.**

Consent Rules for Excused Research

We have substantial concerns about the consideration of consent with respect to existing data as set forth in IIB3(c) and with reference to IIB(a)(3) at page 44519 of the Federal Register. The consent process as specified in 45CFR46 is directed to ensuring that human subjects agree to participate with sufficient information and understanding to ensure that decisions to participate are informed and voluntary. As part of the process, subjects are typically assured that their identities and private information about them will be protected through data security measures and confidentiality agreements. Attention is directed mainly to issues related to the data collection or intervention rather than on the details of how the researchers will use or disseminate the data or the benefit of making it accessible for other research use. The ANPRM, as indicated earlier in this white paper, does not build on the expertise or decades of guidance and experience in considering the relationship between consent, data protection, and appropriate data access and use. **Overall, we strongly recommend that any revisions to the consent rules with respect to use of pre-existing data focus on the objectives of the consent process and confidentiality protections put in place and on whether researchers using existing data do so consonant with consent agreements, rather than seeking to assess on a project by project basis the extent to which consent sufficiently anticipates the scope of scientific uses by the initial researcher or subsequent researchers (see NRC, 2007, Appendix B).**

The most serious problems raised by the ANPRM for the excused category involve the imposition of consent requirements where research involves pre-existing data or biospecimens. Imposing these requirements on SBS research would significantly harm not just the ability to do such research but also the integrity of the SBS research process. Our principal and principled concerns are the following:

(1) We question the need for written general consent (or for that matter consent more broadly) for research using biospecimens under conditions that preclude identifying the person who supplied the specimen. While identity information specific to a person can be extracted from a biospecimen no matter why it was secured, this does not mean that the biospecimen will allow the person to be identified. Re-identification from a research biospecimen can only occur if another specimen that has been similarly analyzed has the donor's identity attached to it and is in a data base accessible to those with access to the original data. There is already

strict legal and ethical guidance governing the linkage of data sets. This guidance that protects biospecimens or other unique identifiers (see, e.g., NRC2005, 2007, 2010) and defines conditions of data use can be referenced in a revised 45CFR46 to regulate research that requires biospeciman analysis. Under most circumstances, when researchers have no information that would identify a person attached to the specimen, there is no need for written consent. In SBS research, biospecimens are used to identify genetic or other variables (e.g., cortisol levels) that along with survey responses or other SBS data may help explain a phenomenon under study or clarify the impact of an observation or experimental condition. If biospecimens are taken with consent, requiring written general consent when the biospecimen is not linked to identifiable information does not add to the informational protection provided to a subject.

(2) The rule requiring consent if pre-existing data are obtained with identifiers will seriously impede some SBS research without corresponding benefits. As surveys and other data collections have become more robust and as there has been growing appreciation of the benefits to people, science, and society of cumulative knowledge built through data sharing (see NSF and NIH policies on data sharing), pre-existing data, most often collected for research purposes, has become an increasingly important SBS resource. Considerable research can meaningfully be undertaken using de-identified data, if de-identification is defined as the removal of direct and obvious indirect identifiers. There is growing appreciation, however, that some of the most important scientific questions require the use of micro-level, often longitudinal, data, where identifiers may exist or identifications can be easily deduced. In addition to data collected directly for research and statistical purposes, there is increasing attention to promising uses of administrative records that have direct or indirect personally identifiable information (e.g., related to education, health, or employment). For both *research* and *non-research* data sets, if identifiers are found in the data access to and uses of such information are governed by strict rules with harsh penalties for violation of privacy protection and the confidentiality agreements in place. Standard procedures call for the stripping of direct identifiers even when data are stored as well as their removal from data sets used in analysis. Where re-identification is possible additional information may be removed or blurred depending on the data sensitivity and those who may have access, and with certain very sensitive data special access rules and other security protections are imposed.

The AMPRM seeks to make fine-grained distinctions that do little if anything to advance the goals of informed consent or to ensure that data use will be consonant with maximum feasible PII protection or the terms of confidentiality agreements. In IIB3(c)(a) and (b), the ANPRM addresses the use of pre-existing data originally collected for *non-research* and for *research* purposes, respectively. Uses of *non-research* data would require written consent only if there is information that can identify persons. Uses of *research* data would require consent whether or not there are identifiers or data that allow re-identification. The latter provision could have a devastating effect on much SBS and other large sample research where contacting

subjects for additional consent will often be difficult, never complete, and not practically possible if in the interest of subject privacy identifiers and contact information was not originally collected or, if collected, retained in the data set.

If the research data are identifiable, any additional protections provided by recontact for further consent is unlikely to add anything to protections already in place through conditions of use and confidentiality agreements and a guarantee that data protection requirements will be at least as stringent as they were in the study for which consent was given. A subject's dignitary interests are similarly unlikely to be offended. Their original willingness to participate in a research study suggests a willingness if not a desire to contribute to science through their cooperation. There is thus good reason to believe that, if research subjects could be recontacted, they would consent to future research use, particularly since nothing further would be asked of them. Moreover, it is hard to take offense when one does not know one's de-identified data is being used, and this will most often be the case. Earlier, we addressed the fact that data that have been certified as de-identified and thus classified as public-use data were exempt under 45CFR46. The contemplated rulemaking in IIB3(c)(b) to obtain consent for de-identified data seems inconsistent with that important exemption.

In considering this issue, the drafters of the revised policy need to keep in mind that the risks involved here are informational risks which the ANPRM wisely removes from IRB purview, noting that the typical IRB lacks expertise on matters of confidentiality and security. These risks are handled by separate rules protecting subject identities which we have already discussed. Requiring informed consent for the use of existing *research* and *non-research* records with identifiable information would preclude many SBS studies that would otherwise qualify for excused status from being treated as such. This would defeat the purposes behind the separation of informational from other risks and the very creation of the excused category. For non-identifiable information, it would also needlessly undermine classes of exempt research and place undue burdens back on researchers (in this case researchers who use extant de-identified data) and IRBs. Applying the proposed new rules prospectively would help and is essential to many SBS endeavors if the proposed requirements are adopted, but this would not preclude serious future problems.

In revising 45CFR46 and balancing issues of (1) the scope of data use anticipated in consent by human subjects and (2) the protection of personally identifiable information from disclosure, the ANPRM drafters are right in attending to informational risk. In taking up this topic as part of consent requirements, we strongly recommend that the emphasis be placed on the registration process that certifies that researchers will adhere to confidentiality agreements and privacy protections consonant with or greater than that guaranteed in the original human subjects consent. We further recommend that the entities furnishing such data (typically data repositories or governmental agencies) retain their authority to establish data use agreements and that their proven successful data stewardship not be

constrained or micromanaged by IRBs or new mechanisms within 45CFR46 specifying what is needed for adequate identity protection or for assurances that researchers will adhere to consent agreements. Expertise, flexibility, and adaptability are important ingredients here, and neither IRB judgments nor any fixed set of regulations can adequately substitute for these strengths of the strong SBS data stewards.

(3) In addressing issues of consent in the manner that we have, we are sensitive to and supportive of the rationale and purposes of informed consent and the central importance of consent in the respectful and trustworthy relationship between researchers and those who give voluntarily and knowingly of their time and themselves in research. We are seeking here to avert a new set of informed consent requirements about prior human subjects that are not based on empirical study but on potentially misleading if not erroneous, assumption about the likely intentions of human subjects and their wishes in agreeing to participate in research. It would be unfortunate if the limitation of language in prior or future consent agreements limited the later capacity to undertake important research.

Data protection and security under restricted use agreements that are at least as strong as those that existed when the data were collected should be sufficient to meet any informational concerns research subjects had, and we believe it is safe to assume that almost all research subjects would, if they could be asked, feel gratified to know that their original cooperation was likely to yield greater returns to science and society than they anticipated when they gave their consents. We further emphasize the benefits for human subjects and for society that come from supporting openness in scientific inquiry, replication, testing falsifiable hypotheses, asking important questions that could not have been foreseen at the time of the initial data collection, and the other gains that derive from data sharing and reducing and discouraging the privatization of data production and use.

We strongly recommend requirements for future data use that ethically and legally obligate other researchers to adhere to all information protections in prior agreements with human subjects but do not require them to obtain new consent agreements. These same obligations apply when research involves the integration or linkage of more than one data set. Researchers must have authorization to use these data and also must adhere to license provisions or data use agreements with respect to use. (Consent or waiver of consent is needed if there are additional waves of data collection; such research would not ordinarily be classified as excused.) The SBS sciences have years of experience in approaching data use in this manner without breaches and with success. Indeed, we believe that further attention to the experiences and expertise developed in the SBS sciences can help inform those drafting the revision of 45CRR46.

The ANPRM does not anticipate major problems. The announcement posits that in most instances consent requirements would have been met through human subjects having agreed to a standard, brief general consent form (or the equivalent through

oral consent). The ANPRM also postulates the expectation that future consent procedures should generally be sufficient to allow for future research use.

- **In revising 45CFR46, we recommend that the expectation of subsequent data use by researchers be the default and that procedures set forth for exceptional circumstances when it is necessary and appropriate for human subjects to specify their agreement to particular types of usage.**
- **In revising 45CFR46, we further urge that a guidance document be prepared that would offer examples of standard consent forms that would meet the requirements for future use.**

We agree that under no circumstance should participation in a study be conditioned on agreement to allow for future unknown data uses. Since this section is about consent rules for researcher use of pre-existing data, as long as there are not or were not explicitly stated limitations on future use, pre-existing data should be eligible for use and can be in the excused category as long as the researcher complies with data use requirements, including confidentiality agreements.

The ANPRM in this section acknowledges that oral consent will continue to be allowed where now permitted and that no additional requirement of written consent will be imposed for future research uses. We agree with this judgment. Also, this section notes that waiver of consent will be allowed under specified circumstances. We support this as well. Also, while we agree that the possibility of consent waiver should be retained in 45CFR46, we are uncertain of the scope of this power in the context of use of pre-existing data where we are recommending that additional consent not be required. As we have emphasized, permission for the future research use of identity-protected data should be regarded as implicit in the original agreement to provide the data except in rare circumstances. If there are foreseeable situations in which ethical considerations preclude the reanalysis of research data without further consent, these should be specifically defined. Other reuses should be permitted consonant restricted-use requirements.

Overall Consequences for Current Review Practices

We strongly support the provision to allow work on excused research projects to start once a project is registered. The drafters sought to create a category of excused research just for this reason—to allow research to be undertaken without additional administrative burden on IRBs or researchers. While we reiterate the importance of not eliminating the category of exempt research for activities falling outside of 45CFR46, we agree that the current practice of delaying the start of exempt research until exempt research has been certified by a reviewer unnecessarily delays the initiation of research without adding to research protections. We similarly believe that otherwise excused research should not be beset by the delays than have been experienced with exempt studies. We strongly

agree that the regulations should discourage administrative review of registration forms, but we believe that it needs to be made clear what would happen were any review to question the excused status. We further suggest that, when such review occurs, it should be incumbent on the reviewer to state specifically in writing what aspect of a registration document leads to doubt a project's excused status and to refrain from review where it finds none.

In addressing the specific questions (Q14-29), our response is as follows:

Q14. The proposed expansions of types of studies for the excused category are welcome. With respect to SBS research we do not see expansion of the excused category along the lines proposed as likely to discourage individuals from research participation, reduce needed subject protections, or diminish attention to the principles of respect for persons, beneficence, and justice.

Q15. As we noted above, there needs to be independent study of the category of exempt research and the status of activities intended to be uncovered by 45CFR46. The ANPRM proposed reclassification of the six exempt categories as excused with the additional requirements for excused research means that 45CFR46 would no longer define any of these research activities as uncovered by the regulations. We find this problematic with respect to certain kinds of research and believe an expert body should be asked to report on the matter. Among possible additions to the excused category is research where access to a location or to subjects is given by a person entitled to give access to a research setting and where the data will be collected by observation or by other methods that themselves qualify as excused so long as the data collected will not be linked to named persons. A business might, for example, provide a researcher access to observe and analyze how plant architecture affects worker interactions, or a police department may allow researchers to ride in police cars to observe exchanges between police and citizens.

Q16. Research involving surveys and related methodologies on adult populations that involve emotionally charged topics may qualify for the excluded category. Surveys or related methodologies seeking opinions, views, observations, or attitudes on emotionally charged topics could readily be classified as excused as long as the informed consent procedure alerts human subjects that they should only answer questions they wish to answer and can skip topics or stop their participation at any time without penalty. Surveys or related methodologies directed to human subjects' own personal experiences that may have the potential for emotional or reputational harm would not ordinarily qualify as excused but may be highly appropriate for expedited review. In the first type of study, the IRB might require a researcher who seeks excused status to include with the registration document the consent form or script that provides information about the survey and makes clear that questions may be skipped or participation discontinued.

We urge and recommend that it would be wise to define and list emotionally charged criteria or topics to avert broad-based exclusions of research that can be

excused or receive expedited review. The vague language of “emotionally charged” is unsatisfactory because topics that elicit no strong emotional reaction from most persons will be emotionally charged for some. A question about the war in Iraq might be emotionally charged for a parent who has recently lost a son there, and a question about the economy may be emotionally charged for someone who cannot find work. It is in part because what is emotionally charged can vary greatly from person to person, that we believe the best solution is to empower human subjects to refuse to answer specific questions or questions addressed to certain topics and to allow subjects to terminate participation at any time and to excuse surveys and related methodologies when the research is not directed to personal experiences.

An illustrative list of criteria for presumptively disturbing inquiries might include research that: (1) seeks information that because of its emotional valance most people are willing to share only with helping professionals or with a small group of close friends and family able to provide emotional support or (2) exposes the subject to emotionally charged information of a kind seldom voluntarily encountered in daily life. The latter category might include pictures depicting sexual activity, extreme violence, or serious disfigurement due to accident or disease. Whatever the ultimate scope, surveys or related methodologies on topics that fall outside of such criteria should qualify as excused whether they ask about human subjects’ personal experience or seek views, attitudes, and opinions.

Q17. Methodology alone cannot fully define whether a study qualifies as excused or exempt or whether expedited or full review may be necessary. Therefore, we urge that further thought be given to a more nuanced and robust definition. Some methodologies which are presumptively excused may, however, be indicated. SBS methodologies that can readily fall within the excused category, if the risks are essentially informational, include but are not limited to surveys, focus groups, interviews, observations, and oral histories. Note again that research activities exempt from 45CFR46 should remain so until this matter is separately addressed.

Deception, explicit information, or the provision of incomplete information is used in different kinds of SBS research. Scientific validity may require keeping the purpose behind a survey or experiment initially concealed from human subjects because knowing the purpose will change subjects’ behavior. Or an experiment may require the participation of a “stooge” or other actor cooperating in the experiment. If, for example, in the famous Asch line experiment which laid the foundation for behavioral compliance research, naïve subjects knew that those group members who claimed the shorter line was longer were in Asch’s employ, the experiment would have been impossible. In addition, outright deception may be necessary. In a game theory experiment a person playing with a computer might be told that the opponent is a person because in games people respond differently to computer moves than they do to human ones. Or subjects may be told that if they do not perform at a certain level they will not be paid, when they will be paid regardless. Sometimes experiments end just when subjects thought they were to begin because the variable of interest was the subject’s behavior while waiting for a supposed

experiment to start. Deception in these and many other circumstances poses no threat of harm to subjects and is essential for an experiment to proceed. Moreover, debriefing can be educational, giving subjects insight into behavior or psychological processes that they would not otherwise gain. Hence, depending on how it is defined and the form it takes, deception or the withholding of information does not per se bar excused treatment. The test of whether deception should trigger greater review than that associated with excused studies should be whether deception places a subject at risk of suffering psychological distress or even minimal harm that might endure after the deception is revealed.

Q19. Ordinarily there will be no need for a post-registration waiting period before research on an excused project may commence, for it is the rare study that upon approval will immediately engage human subjects. IRBs should, however, have the option of requiring up to a seven day waiting period after registration before the human subjects portion of a research project can begin. Seldom will such a waiting period impose costly delay and where it does, as in post disaster research where getting immediately to a disaster site is essential, there can be an opportunity to file for 24-hour turn around.

Q20. We have no strong view about whether the nomenclature for what the ANPRM called “excused” might be better termed “registered.” Excused might very well be the right term since it is our belief that excused should be intended for studies that can be excused from expedited review because any harms they risk are primarily informational and so subject to specific standards..

Q21. It is appropriate to require institutions holding Federalwide Assurances to conduct retrospective audits of excused studies. Such audits will (1) tell IRBs whether researchers are applying correct standards in declaring their projects “excused;” (2) provide feedback that allows researchers to hone their judgments of what research is excused; and (3) potentially reveal kinds of research that are poor candidates for the excused designation even if they appear to meet its general requirements. As indicated above, it is a mistake to mandate that a specific percentage of excused studies to be reviewed. Cases should be drawn at random from the list of registered studies, and a power analysis should be used to determine the desired sample size. Cases where the IRB has reason for concern might also be reviewed (e.g., subjects raising issues about the time burdens of a survey), but these cases should not be considered in estimating overall compliance rates unless they are also selected for review as part of the random sample.

Q22. Retrospective audits coupled with informational protections, informed consent requirements, and limitations on the research methods that qualify for excused status should provide subjects with the protections from harm they need and deserve. Researchers can for the most part be trusted to make fair initial assessments so long as they must register their studies and know they risk being audited. In implementing the new rules and procedures, it would help if web or written materials were available to provide researchers with guidance, including

perhaps interactive modules to help researchers understand the implications of a study's characteristics for its status within 45CFR46. At the time revised regulations are introduced, IRBs might examine an initial sample of registrations to ensure that the members of the local research community and its IRB(s) are properly calibrated. Ordinarily the registration document should be designed to provide sufficient basis for an audit, and one page seems at the outset desirable and doable. If registration information is found to be incomplete or otherwise problematic, the auditor should be able to request additional information. As long as audits are based on data in registration forms, unless there is cause to dig deeper, the proposed system should not place undue burdens on researchers or IRBs, and overall lessened burdens can be expected.

Q23. We have indicated above why we recommend that research on pre-existing identifiable data (whether originally collected for research or non-research purposes) should not require further consent if the data are being provided and used in accord with data security and confidentiality protections and under penalty for violations. In registering use of such data, researchers should provide information that certifies that they have received permission to use the data and have met the conditions for use. Data that has been vetted for public use by a certified entity (e.g., a data archive or agency of the federal government), or information provided by persons without any interest in or requirement of confidentiality should not require approvals for use or have any consent requirements. Consent should be required when any new data collection is sought or planned with human subjects who are part of pre-existing data sets.

If our advice is accepted, waiver of consent for existing identifiable data should not be necessary under these circumstances. In the rare circumstance where access is provided for some forms of existing data and there are no provisions in place to have authorized use under specified agreements, research may still be excused if the risk is essentially informational, but researchers may need to seek waivers of consent in line with the stipulated conditions for seeking waivers and also attest to the data security and information protection plan in place.

Q24. This question speaks directly to the issue of what types of research activities are appropriately exempt from 45CFR46, the process by which that exemption should be determined, and in what way exempt research should be handled. The ANPRM would seemingly now place more of such activities under the purview of 45CFR46. We have at several places indicated our substantial concerns about the usefulness and appropriateness of doing so. The very illustrations in this question—quality improvement work—point to the need to reconsider how exempt is defined and what this status should mean going forward. There are current categories of exempt research akin to quality improvement and organizational evaluation. For example, 46.101(b)(1) related to research on educational practices intentionally and for good reason exempts research activities that provide information, feedback, or evaluation that can help improve teaching, curriculum, and other educational objectives. This exemption has, however, been administered with ambiguity,

uncertainty and inconsistency regarding the activities that are not covered by 45CFR46. We suggest that it is time to seek guidance on 46.101—to define with greater specificity the activities to which this policy does and does not apply. More broadly, given similar confusion about aspects of 46.102(d) and 46.102(f), we recommend that attention to these portions too be included within the scope of any such examination. We encourage that an independent body that draws upon research expertise in these areas be charged with taking up this task.

Q25. This issue too calls out for independent expert review and could be part of the kind of independent study that we believe would provide the best basis for determining the types of activities that should be considered exempt (under 46.101) and the types of activity that fall within the definitions of covered research (46.102[d]) involving human subjects (46.102[f]). We suggest that rather than focus on what does or does not contribute to generalizable knowledge (which in fields of science and scholarship can be a rather insulting task) or making judgments based solely on the disciplinary identification of researchers, it would be wiser to define the categories of research activities that 45CFR46 should cover adhering to the explicit definition of human subjects, as is relied on in exemptions 46.101(b)(2), (b)(3), and (b)(4), for example.

Q26. Our recommendation here parallels our recommendation in response to questions 24 and 25. The ANPRM drafters raise questions that have been festering for some time about what is and should be exempt and how determinations should be reconciled with the definitions as set forth for research in 46.102(d) and for human subject in 46.102(f). We recommend not only that an independent body address these areas of ambiguity but that they do so from the premise that the burdens to IRBs and to researchers are major and costly impediments to socially valuable research and that much of the impulse for this long overdue review is a sense of the need to divest IRBs of regulatory obligations that distract them from focusing on research that involves more than minimal risk. While covered and uncovered research needs to be undertaken in an ethically responsible manner by all involved, we urge that in revising 45CFR46, in establishing the excused category, and in revising the expedited category, the predominant goal be to ensure that IRBs can focus their attention on research where the magnitude of harm and the likelihood of its occurrence is more than minimal.

Q27. We support the interpretation of the province and scope of 45CFR46 as set forth in the ANPRM. The focus should remain squarely on human subjects protection for the identified subjects in the research and not on the long-range effects of knowledge on policy or related issues.

The interests of human subjects should be the paramount consideration for 45CFR46 so as to ensure that those who participate in research are not diminished or made more vulnerable by virtue of their willingness to participate in research. Consideration of other factors can limit research that needs to be done and chill the freedom of inquiry that scientists need to advance knowledge. We are concerned

that factors other than human subjects protection not creep into the work of IRBs. It is of paramount importance that other considerations do not color the work or judgment of IRBs and that policy considerations do not interfere with academic freedom and the pursuit of knowledge. In addition, we urge emphasizing the core principle, perhaps with examples, to make its intention inescapably clear.

Q28. We strongly support the requirement of an appeals process. The consequences of an IRB's denying or substantially limiting how research can proceed could be severe, affecting those who might reap the benefits of the research, the immediate interests of the researcher, and the interests of institution or society over the longer run. When consequences are great, the fallibility of judges suggests the desirability of an appeals mechanism. Appeal procedures would need to be developed, but this in itself would not be a formidable task.

An appeals panel might consist of two permanent members from different segments of the research community, an ad hoc member appointed from the IRB whose judgment is being appealed, and two ad hoc members drawn from study-relevant field(s). Under such an approach, one person could present the reasons that motivated the IRB's decision, and two members could give the perspectives of researchers with expertise in the relevant discipline. Even if these three differed in predictable ways, which often might not be the case, neither side could prevail without persuading one or two neutral members chosen for their wisdom and breadth of knowledge and for their experience in hearing appeals. Conflicts of interest would have to be defined and avoided, even if that entailed bringing in outside specialists. An appeal process not only offers a second chance to researchers whose plans had not met with IRB approval, but also strengthens the IRB because by giving them feedback on the quality of their decisions.

Q29. Yes. We support the ANPRM's identification of a potential need here. Having a mechanism requiring IRBs to identify each time actions are taken that are not required under 45CFR46 would promote transparency, discourage hyper-regulation, and highlight sources of inconsistency between different IRBs.

III. Streamlining IRB Review of Multi-Site Studies

We support the ANPRM proposed change to allow the use of one IRB of record for multi-site studies. The term "multi-site" is, however, unclear. A single investigator or institution may conduct a study with data collection or other human subject interventions at multiple sites. To avoid confusion we suggest that the rules distinguish on the basis of researcher affiliation between single institution, multi-site research and multi-institution research whether at a single site or many. If both situations are to be covered this should be clearly stated.

Multi-site/multi-institution studies are common not just in clinical trials but in social and behavioral science research as well. Moreover, multi-site/multi-institution SBS studies are often low-risk. Hence, the application of the proposed

change to research that undergoes expedited review is welcome. The benefits are obvious. Streamlining IRB review of multi-site/multi-institution studies by creating a central IRB for multi-site studies or allowing one institution to conduct the review for all institutions will reduce the burden on IRBs and investigators, provide considerable savings in cost and time, and allow science to advance without adding risks to human subjects.

Specifically, we support the mandatory use of a single IRB in research that is funded by the federal government. We similarly support the use of a single institution of record to receive and have oversight of an excused registration when the research qualifies as involving only minimal informational risks. For other research, the federal government should encourage the use of a single IRB if by institutional or other policy IRB review is required. Doing so will remove a regulatory hurdle that hinders research even when protocol changes are minor and risks to human subjects do not change.

Without a rule change and appropriate guidance, institutions that have grown increasingly concerned about federal oversight and liability issues associated with their investigators' research conduct are likely to continue to put into place and maintain unnecessary barriers in the review of research protocols. Hence a particularly important aspect of the ANPRM is the proposed change in enforcement practices including the determination of who is responsible for any failures of compliance. Concerns about local control or liability may still arise once federal regulatory hurdles are removed, but institutions will be free to address any concerns through other mechanisms (e.g., inter-institutional agreements that allow for local input).

We support a process that allows institutions/investigators to choose which IRB will serve as the IRB of record. Applications for federal funding could state which institution's IRB will serve as the IRB of record, requiring institutions/investigators to work out the details in advance. Alternatively, a default position could provide that the principal PI's institution serve as the IRB of record.

Q30. The advantage of mandating rather than simply encouraging the use of one IRB of record is that this practice will become institutionalized and uniform. Given how the culture of IRB review has developed at some institutions and given the conservatism of attorneys who advise on how best to avoid legal problems, merely encouraging the use of one IRB of record may not lead to quick or widespread adoption of the recommendation. A mandate is more likely than encouragement, however strongly phrased, to achieve the following goals:

- Removing a barrier to scientific progress that does little to advance ethical research or increase human subject protections;

- Reducing the time and paperwork burdens on IRBs and investigators that result from multi-site reviews for a single study and amended protocols;
- Reducing ambiguity for institutions that want to simplify the IRB review process; and
- Increasing the predictability of research start dates, which will facilitate investigator involvement and coordination across investigators and teams. For faculty, it could provide more efficient course scheduling and the employment of graduate students, while allowing important research to begin and conclude sooner.

Beyond these evident benefits, if single (or central) IRB review is mandated rather than just encouraged, the liability/compliance protections extended to research institutions will be on more solid ground since decisions to forego additional review will not be subject to second guessing.

Q31. Local IRB review can add to human subject protections in multi-site research if conditions at the different sites or the likely research participants at different sites differ substantially in ethically relevant ways *and* a local IRB but not a more distant IRB is likely to know why special precautions are needed at the local research site. Where these conditions plausibly exist, various approaches may be taken beginning with guidelines that indicate situations when consultation with a distant site IRB is likely to be of value. Alternatively or in addition, the information provided the IRB of record might be circulated to the IRBs at the all participating research institutions, and these IRBs might be given the opportunity to express any local site specific concerns. The IRB of record could then follow-up and seek more information if necessary. If investigators and institutions are given the flexibility to work out agreements in advance of the research, which we strongly support, details on whether local input is needed and, if so, how it will be obtained can be tailored to any issues that exist or arise.

Q32. Institutional practices surrounding human subjects regulations are increasingly driven by regulatory and legal liability concerns, rather than concerns for the welfare of human subjects. The ANPRM changes alleviate a significant concern that has fed the reluctance on one institution to accept the judgments of another's IRB.. This will be more certain if single or central IRB review is mandated rather than encouraged and if the rules clearly spell out and delineate the situations in which institutions and researchers are responsible or not responsible for IRB decision making and regulatory compliance.

Q33. In many institutions, there are backlogs of protocols waiting for IRB review. The proposed change would reduce the burden on IRBs and allow them to use the time saved on high-risk protocols or protocols for which they are the IRB of record.

Hence, the contemplated change promises to increase the overall efficiency of the IRB process.

Q34. There should be flexibility in the process, and the best solution is likely to be giving institutions/investigators the option of choosing which IRB will serve as the IRB of record. Applications for federal funding could state which institution's IRB will serve, requiring institutions/investigators to work out the details in advance. Alternatively, a default position could provide that the lead PI's institution or the institution whose researchers will be most deeply involved in interactions with human subjects serve as the IRB of record, We expect that the problem of cherry picking an IRB to avoid serious scrutiny is one that exists more in theory than in practice. Given the regulatory and liability hurdles associated with serving as the IRB of record, institutions are not likely to approve studies without proper scrutiny.

IV. Improving Informed Consent

We commend the ANPRM drafters for their interest in examining and improving informed consent for human subjects. The current process has become burdensome for researchers, time-consuming for IRBs, and has also added to the complexity for research participants.

Informed consent is a process whereby potential human subjects are provided with relevant information (e.g., goals, risks, benefits) needed to make an informed decision about whether to participate in a study. Current regulations as well as the proposed changes continue to assume a one-dimensional mental model of written consent at one point in time. In general, the informed consent process could benefit from more research (e.g., what do human subjects want to know, what do they comprehend, what kinds of information are most relevant to making a decision about participation) so that any changes to the regulations are evidence-based.

The best way to fully inform human subjects depends on numerous factors such as the participants themselves (e.g., literacy, native language), the setting (e.g., cultural considerations), and the method (e.g., self-administered questionnaire, interview, experiment). It therefore follows that the best process for informing human subjects may be written, oral, or implicit, and it may occur at the beginning of the research, in advance of it, or repeatedly during various steps of the research. Specific mandates regarding the structure of informed consent forms and what they must or must not include may be poorly suited to the goal of ensuring informed consent in some instances and/or they may promote uninformed denials of consent.

We strongly recommend that a revised 45CFR46 set forth what needs to be accomplished through the consent process and the alternative approaches to obtaining meaningful consent, rather than emphasizing the default of written forms as the requirement. We encourage thinking broadly about the informed consent process in redrafting the policy to make real progress. Below we respond to the specific questions raised.

A. Improving Consent Forms

Q35. One of the primary factors contributing to the length and complexity of informed consent forms is the perceived need for institutions (through their IRBs) to require researchers to identify and mention every conceivable risk to human subjects, however remote. We assume institutional concerns with federal regulatory compliance and liability issues drive this requirement. However, in doing so, human subjects are presented with mounds of information that aid neither in comprehending their role in the research effort nor in assessing the risks and benefits associated with participation.

We recommend that relevant information on the risks and benefits of research participation be separated from remote risks or risks that are mentioned primarily to protect the institution from liability. Risks that are both remote and speculative are likely to fall in the latter category and should not be included in informed consent forms. Language that is non-threatening should be crafted and used that notes the current and future benefits of their participation and qualify as a brief general consent.

Q36. It is far from certain that more rather than less is needed. The requirement for disclosure of appropriate alternative procedures or treatments should be focused on providing information that is meaningful and relevant to human subjects at a level that they can understand. Without care, other additional requirements may add complexity to the informed consent process. This requirement makes great sense in certain contexts, such as clinical trial where research participation may preclude using an existing treatment, but in other research, such as social science surveys, it may simply confuse human subjects. The rules should make clear that, when the only alternative to participating in research is not participating, discussion of alternative procedures or treatments is neither required nor good practice. The same is true if the only reason research participation may not be in a human subject's best interest is the time involved. In addition, the requirement in 46.116 (a)(1) that subjects be explicitly alerted when procedures are experimental should not apply when this information might affect a human subject's behavior unless this fact bears on risks that the subject may face. For example, notification of experimental involvement should not be required in a survey experiment which seeks to determine whether question order will affect responses, nor should there be a need for a researcher and an IRB to spend time processing a waiver.

Q37. It appears that there are five contemplated modifications to consent forms that are intended to improve their quality: (1) prescribing appropriate content, with greater specificity, that must be included in the forms; (2) restricting inappropriate content; (3) limiting the length of sections of a consent form; (4) prescribing how information should be presented (e.g., introduction, main body, appendix); (5) reducing institutional boilerplate in consent forms; and (6) making available standardized consent form templates that satisfy regulations.

We enthusiastically endorse the proposal to make available standardized consent form templates that meet regulatory requirements, but **we explicitly recommend that required language be avoided and flexibility be retained.** Guidance can serve as an aid to researchers as well as IRBs that spend excessive time reviewing consent forms. **We encourage in the objectives to devise straightforward language that satisfies the requirements for a general consent that allows for future data use.**

Additionally, as noted in the response to Question 35, separating relevant information on the risks and benefits of research participation from either remote risks or risks that primarily protect the institution from liability will improve the quality of informed consent forms. Reducing, rather than separating, institutional boilerplate language should also improve the quality.

Beyond these two proposed changes, it is difficult to determine, without additional detail, whether the other proposed changes to informed consent forms would add additional burdens and complexity to a process that is sorely in need of improvement. We urge caution. This issue is, we might add, an area ripe for research and evidence-based improvements. Changes could be evaluated experimentally before they are imposed by law. The use of technologies like interactive video can be explored. For example, it might be difficult to explain certain elements of a research project in language that someone reading at the 8th grade level or a non-native English speaker could easily comprehend, but the same information presented by video with the use of graphics might be comprehended. Communication methods other than print should not be mandated now or in the foreseeable future, but studies about such approaches should be encouraged and funded and their effectiveness evaluated.

Q38. This topic is also ripe for research. It is definitely the case that improving comprehension as a predicate to consent is a positive goal and an area where research can help. That step is far different than concluding that human subjects should be tested to ensure that their comprehension is sufficient to participate as a human subject. The task itself could be anxiety arousing or stressful for human subjects if they perceived that they were being screened or appraised as to their cognitive capacities to agree to participate. Q.38 is delimited; it suggests that classes of studies may require a particular level of comprehension. More details are needed on the types of studies that would require that step. Instead of such a change, we recommend that research on comprehension and modes of inviting consent be aggressively pursued, and, for studies where there are imminent concerns about whether comprehension is sufficient, multiple approaches be offered to human subjects for explaining the study and obtaining their consent.

Q39. We have no specific comments here but wish to note our understanding that any HIPAA changes would involve HIPAA conforming more closely to 45CFR46 rather than vice versa. We have already expressed our concern about using HIPAA

requirements to shape what the Common Rule requires. HIPAA was adopted for purposes far removed from many issues the Common Rule confronts, and its standards are too closely linked to medical privacy needs to fit well the requisites of SBS and other non-clinical research.

Q40. We are in general reluctant to recommend that new requirements be added to the consent process absent research and compelling rationale. The one example noted in the ANPRM might be an exception. It seems appropriate for human subjects to be informed of any financial relationships investigators have with study sponsors.

B. Waiver of Informed Consent or Documentation of Informed Consent in Primary Data Collection

We note at the outset that we support the proposed classification of most studies that involve surveys, focus groups, and interviews of competent adults as excused with only oral consent required.

Question 41. Under current regulations, an IRB may waive the requirement to obtain informed consent if it finds and documents that: (1) the research involves no more than minimal risk to the subjects; (2) the waiver or alteration will not adversely affect the rights and welfare of the subjects; (3) the research could not practicably be carried out without the waiver or alteration; and (4) whenever appropriate, additional pertinent information is provided after participation. In interpreting these requirements it makes sense to take advantage of the consideration that SACHRP has already given these issues. In order:

Sec. 46.116 (d)(1). We agree with SACHRP's recommendation that IRBs should interpret minimal risk using a uniform standard of not greater than the harms and discomforts ordinarily encountered in daily life or during the performance of routine medical and psychological examinations or tests for the average person in the general population. This will clarify that the standard is not tied to the harms of daily life encountered by the proposed research subjects.

In assessing whether risks of harm are minimal, SACHRP also recommended:

- IRB evaluations of the harms and discomforts of the research should consider the nature of the study procedures, other study characteristics, subject characteristics, and steps taken to minimize risk.
- In judging research-related risk, the IRB should consider subject susceptibility, vulnerability, resilience, and experience in relation to the anticipated harms and discomforts of research involvement.
- Although minimal risk should be applied in a manner that recognizes that risks are procedure-specific and population dependent, the notion of "acceptably-low" risk [what is necessary to justify expedited review or waiver of consent] is fixed.

We believe these are appropriate considerations, but SACHRP's language as summarized in the last bullet is problematic. The first recommendation regarding the interpretation of minimal risk" provides: *"The regulatory intent of minimal risk is to define a threshold of anticipated harm or discomfort associated with the research that is "acceptably-low" or "low enough" to justify expedited review or waiver of consent."* The 6th and last recommendation provides: *In summary, minimal risk should be applied in manner that recognizes that risks are procedure-specific and population-dependent, but that the notion of "acceptably-low" risk is fixed. When the harms and discomforts of the proposed research as they are anticipated to impact the study participants are judged to fall below this acceptably-low risk threshold, the research is said to be "minimal risk."* There is confusing circularity here. To enable expedited review or waiver of consent, risks must be minimal, but to be considered "minimal" the risk must be low enough ("acceptably low") to justify expedited review or waiver of consent.

We suggest that the SACHRP guidelines do not provide the guidance needed. Rather the focus should be on the definition of minimal risk as an estimated risk of harm not greater than *"the harms and discomforts ordinarily encountered in daily life or during the performance of routine medical and psychological examinations or tests."* In considering whether a risk meets this test, IRBs should realize that a risk of harm may be procedure specific and population dependent.

Sec. 46.116(d)(2). SACHRP recommended that IRBs consider the following three points when determining whether a waiver or alteration of consent would adversely affect the rights and welfare of subjects:

- (1) *Whether federal, state, or local laws provide rights to potential participants that require informed consent, SACHRP recommended that IRBs seek advice from their legal counsel to help the IRB.* It goes without saying that state and federal laws must be obeyed by researchers and institutions, but to make such consultation routine is unlikely to add much in the way of protections to research participants, and will further burden IRBs. Shifting the burden for determining legal requirements to investigators is not a workable solution because they typically have fewer resources and less general legal knowledge than IRBs.
- (2) *Whether the subject population in general would object if they knew of the waiver and its intent in facilitating research.* We are concerned that this recommendation would encourage unfounded speculation regarding prospective human subjects' perspectives that could result in uneven protections for them. Researchers might, however, be invited to provide evidence on this matter where the issue is deemed close.
- (3) *Whether the subject population in general would consider that the waiver has the potential to cause adverse consequences for their welfare or general well-*

being. Again, here we are concerned that this recommendation would encourage unfounded speculation regarding prospective human subjects' perspectives that could result in uneven protections for research participants. We also reiterate the possibility that investigators might be invited to furnish evidence gathered from existing sources to illuminate this issue.

Sec. 46.116(d)(3). SACHRP recommended that IRBs consider the following points when determining whether research could not practicably be carried out without a waiver or alteration of informed consent:

- *Whether it is impracticable to perform the research, not just impracticable to obtain consent.* This reading of the term “impracticable” strikes us as self contradictory. If consent is required to do research and it is impracticable to secure that consent, then it is impracticable to do the research. We suggest that this distinction be discarded.
- *Whether scientific validity would be compromised if consent were required.* For example, the sample size is so large (e.g., population-based studies, epidemiology trials) that including only samples/records/data for which consent can be obtained would prohibit conclusions to be drawn or bias the sample such that conclusions would be skewed. This is an issue to be considered, though the example is unfortunate since it appears to make waiver in these circumstances turn on sample size.
- *The subjects for whom records would be reviewed are no longer followed or may be lost to follow up (e.g., a significant percentage may have relocated or died such that the results would not be meaningful if consent were required).* This is a particularly important consideration, especially when follow up relies on administrative records.
- *The disclosure of the study purpose as part of the consent process would bias the research subjects so that the results would not be meaningful.* We agree with the SACHRP judgment that this makes research impracticable.
- *There is a risk of creating additional threats to privacy by requiring consent that links individuals to de-identified data.* We agree.
- *There is a risk of inflicting psychological, social, or other harm by requiring consent.* We agree.
- *There is a scientifically and ethically justifiable rationale why the research could not be conducted with a population from whom consent can be obtained.* We agree.

- *Practicability should not be determined solely by considerations of convenience, cost, or speed. We agree, but emphasize that, while these are not the sole considerations, they may be taken into account.*

Sec. 46.116(d)(4). SACHRP recommends that IRBs consider the following points in determining when it would be appropriate for investigators to provide participants with additional pertinent information after participation:

- *In appropriate cases informed consent waivers may be granted without requiring the researcher to provide additional information to subjects after their participation. We agree and point out that often the same circumstances that precluded securing informed consent will preclude providing subjects with additional information.*
- *It may be ethically required or respectful to provide additional pertinent information after the research (e.g., with deception research). We agree.*
- *Under most circumstances, this criterion does not apply to retrospective research (e.g., review of existing records) conducted under a waiver. We agree, and emphasize the importance of this exception to the SBS research community.*

Q42. We agree with the ANPRM recommendation to allow oral consent for studies that only involve surveys, focus groups, and interviews with competent adults. Researchers should be required to provide to prospective human subjects a verbal description that essentially covers 46.116(a); that is, (1) a statement of the study and what is involved and expected from participation, (2)/(3) reasonably foreseeable risks and benefits, (5) how the confidentiality of the data will be maintained, (6) the voluntariness of participation overall or to any part, and (7) who to contact for questions regarding participation. The topics that can be dropped are (4) alternative treatments, and (6) information on compensation or medical coverage for injury as well as those additional elements classified under 46.116(b). (Note with oral or written consent, there are rare occasions where confidentiality is affirmatively not sought or provided.)

Q43. Yes, research using public use data files does not require and is exempt from 45CFR46. Thus, technically there should not be a need for a waiver since this is uncovered research. Researchers who use existing identifiable data under the requirement that they adhere to the data security and information protections in place should not need additional consent as long as they comply with the original consent agreements. Also, waivers of consent and documentation of waiver should be obtained in research where a written record of consent may increase risk for human subjects.

Q44. There are no ready a priori criteria that could or should be put in place to guide when oral consent would not be appropriate with surveys, focus groups, or similar procedures. Researchers should have the latitude to set forth review procedures that they believe will best provide for informed consent and minimize the likelihood of risks of harms due to the consent process. IRBs should likewise be able to preclude oral consent depending on the situation. For example, in the case of spouse abuse, victims may more readily seek to participate in a study if there are no identifiable records of their agreement to participate. Therefore, a requirement of written consent for all studies greater than minimal risk would not necessarily have been the desired outcome in that instance.

C. Strengthening Consent Protections Related to Reuse or Additional Analysis of Existing Data and Biospecimens

Many of the questions in this section are similar to or variants of issues raised with respect to consent rules for excused research that uses *research* and *non-research* data that are de-identified or identifiable. See text and answers to questions under IIB(3)(C) above. These issues are also covered from a somewhat different vantage in ANPRM Section V on Strengthening Data Protection to Minimize Information Protection that is addressed following this discussion.

Q45. We think the ANPRM was right in focusing on informational risk in the consideration of subsequent use of non-research as well as research data. We think the emphasis should be on strict prohibitions against re-identification for de-identified data and safeguards for the protection of advertent or inadvertent disclosure of identifiable information in the use of restricted data.

De-identified information (whether biospecimens or other forms of data) collected for non-research purposes should not require a process of additional consent as long as researchers protect and use this information in a means and manner that does not permit re-identification. In the SBS sciences, de-identified, data even if collected for non-research reasons, are public-use data and research should proceed without further consent (e.g., see also page 18 above).

In the SBS sciences, such non-research data that are public (as in the case with public records and information systems), there also should be no requirement of using these data that are otherwise available and have not been retained with any promise of privacy protection. For publicly available administrative data (e.g., court records), requiring consent for research purposes adds an unnecessary burden for researchers that is not required of others who might access and use the same data. No consent should be required for the use of publicly available data for research purposes, including information that pertains to public figures.

For non-research data that includes personal identifiable information, the question of appropriate access and use should depend on researchers adhering strictly to data security plans and conditions for use that honor confidential agreements with

severe penalties for violation. It would seem that similar requirements could be equally applicable for use of biospecimens so that such use does not require recontact of persons to obtain their consent for each and every research use. For data that are identifiable, do not pertain to public figures, and are not publicly available, researchers should be able to obtain approved access to such data as long as the confidentiality protections are commensurate with the risk of identification, meaning that researchers go beyond the original conditions for protecting the data. The likelihood of identifying a research subject should not trigger consent requirements, but instead, should trigger the need for confidentiality protections equivalent to that originally provided for the data.

Researchers need to adhere to requirements or develop mechanisms that ensure the confidentiality of the data, and IRBs, in turn, should evaluate the degree to which effective confidentiality protections are in place. Confidentiality protections should be a major component of the study plan and should describe the methods and procedures for each stage of the research. This approach will provide concentrate scarce resources where they are needed most—that is, in protecting the data, including identifying information about human subjects. Further, OHRP should develop guidance on good practices for analyzing disclosure risk and implementing appropriate confidentiality protections. The guidance should be based on state-of-the-art methods from reputable resources, including federal statistical agencies, NRC and IOM reports, and relevant research communities.

Q46. Federal agencies are increasingly calling for the sharing of data by researchers. While some future analyses of data may be anticipated and can be incorporated into the consent process, many future research uses, including by the initial researcher or research team, will have been unanticipated when the data were collected. We have discussed the basic issue at several places in our comments (e.g., page 19), including in our response to Question 45. For minimal risk SBS research, future analysis of data collected for a different research purpose should be permitted without requiring consent, assuming the IRB determines that data security and information protections plans are in place commensurate with the risk of identifying human subjects (in the case of excused research that approved plans are reported as part of the registration process). Ordinarily confidentiality protections described in the original study should be carried forward in all future research uses, unless additional protections are warranted, and no additional consent should be required. As with administrative data, the likelihood of identifying human subjects from research data should determine the level of confidentiality protections, but should not trigger the requirement for informed consent.

Q48. Biospecimens relevant to SBS research will typically have been collected as an adjunct to survey studies or similar research. As new capacities to learn from biospecimens develop, further analysis of collected specimens may allow important increments to prior knowledge, as when a study which explores links between genes and behavior is able to consider genetic information that was not extracted or coded in the original research. So long as the level of informational risk remains

more or less the same, the original research consent should be construed so as to allow further research without need for waiver unless guarantees were given that no information from the biospecimens would be extracted beyond that originally specified. Included in the carryover of consent should be carryovers in the guarantees of confidentiality at the level originally promised or at a higher level if appropriate. If the additional information increases the risk level, an IRB should be authorized to waive informed consent contingent on additional confidentiality protections sufficient to reduce informational risk to the original level. IRBs should also be allowed to waive informed consent even when the original consent was limited, as long as any increment in subject risk is minimal, and it is reasonable to suppose that a reasonable subject would not have objected to the new use of extracted data.

Q49. We support the development of standardized general consent language (rather than a form) permitting future research on data collected for other research purposes would reduce the burden on investigators and IRBs in determining whether adequate consent has been provided. According to some research, IRBs tend to use a considerable amount of time reviewing informed consent forms, and the development of standardized language could facilitate the review. We caution, however, that one size is unlikely to fit all. Thus, researchers should be able to choose standard language relevant to the study they are conducting, and they should be able to deviate from suggested language where this will improve the consent process. Also, as we suggest elsewhere, research should proceed on what makes for an effective consent process including the context specific value of proposed standardized approaches.

Q50. If human subjects were given the option of identifying broad categories of research for which their data could or could not be used, there would likely be disagreements in the interpretation of the categories, causing delays, burdening IRBs and researchers and potentially opening up liability issues for investigators and institutions. Although giving individuals an opportunity to consent for the use of their data in future research with a blanket “yes-or-no” option might be appealing, it has the potential to skew data and yet offer no meaningful additional protections for research participants. In these circumstances, the biases introduced by dissenters could prevent the effective use of data by subjects who would very much want to contribute to future research uses. Moreover, if dissenters could be contacted regarding specific reuse, which will often be impracticable, they might have no qualms about participating in the research although they originally did not want to give blanket permissions.

Q52. If new consent rules for the future research use of identifiable data are adopted, this will significantly limit a large amount of SBS research that is currently conducted. Consent requirements should not be extended to secondary analysis of data; rather, investigators and IRBs should focus on ensuring an adequate level of data security and information protection. If, despite our concern that limitations on researcher access to SBS data sets would stifle some of the most important ongoing

and contemplated SBS research, an extension of informed consent requirements to existing research data sets is enacted, the new rules should not be applied to data that has already been collected. Even with this provision, however, looking ahead to SBS scientific advances, such restrictions would limit research without evident gains to human subjects by returning to them to seek to seek agreement for use.

Q53. Additional consent for subsequent research, whether on de-identified or identified data should be addressed by data security and data protection plans and stringent penalties for reidentification in the case of de-identified data or disclosure in the case of use of restricted data. This position, the rationale underlying it, and how we recommend it be addressed in revising 45CFR46 consonant with human subjects protections are discussed elsewhere (see, e.g., pages 19-20). In the case of deidentified data, researchers are examining public-use data and, as long as these data are certified as public use, there should be no requirements under 45CFR46. For identifiable data, the steps set forth for excused research in most instances will be sufficient to guide researchers and IRBs.

Consent for secondary analysis of data that contains identifiable information should be waived when the same level of confidentiality protections are afforded. Although SACHRP recommended that a waiver of consent for secondary analysis of existing data be allowed under conditions when the sample size is large (e.g., population-based studies, epidemiology trials) or when the subjects are no longer followed (significant percentage have died or relocated) in order to meet the definition of “impracticable” in the current regulations—we disagree.

This example is poorly chosen for possibilities of bias do not depend on sample size but on attrition from it. Moreover, the possibility of recontacting human subjects to secure later consent depends on what contact information is available, where members of the original sample are located, and the resources available to find them. In some circumstances, it may be easier to recontact 90% of a 1000 person sample than it is to recontact 75% of those in a 50 person sample. Equally important is whether the loss of subjects through an inability to recontact is at random or whether those who cannot be recontacted differ in study-relevant ways from those who are accessible. If loss is at random (e.g. some address records were inadvertently destroyed), a numerically small study will be more threatened by an inability to recontact than a study with far more subjects. But all this should beside the point. As we have indicated in our comments, in almost all cases pre-existing data, whether collected for research or non-research purposes, should be reusable without consent as long as risks to human subjects are minimal and sufficient confidentiality protections are in place.

V. Strengthening Data Protections to Minimize Information Risks

Overall Observations on Suggested Uses of HIPAA

As we indicated in our comments on Section II above, the SBS community supports the ANPRM goals of strengthening data protections to minimize informational risk and ensure risk based protections. To that end, we also support the separation of informational risks from other risks and their regulation by standard setting rather than through IRB review. We take these positions because we share the ANPRM judgment that these issues need dedicated expertise. IRBs are experts in research ethics, but seldom are experts in data security and data protection.

We understand why the drafters of ANPRM might think that HIPAA can provide the right foundation to address data protection standards and procedures. HIPAA is a privacy protection act well known in the DHHS community; thus, adopting (or essentially adapting) it to meet the needs of data security and data protection is a familiar solution with the apparent additional virtue of enhancing uniformity across different spheres.

We have grave reservations, however, about the use of HIPAA as model for privacy protection and data security practices under the Common Rule. HIPAA has a very specific purpose—to alleviate privacy concerns about identifiable information in administrative health records. Hence, in dealing with research uses of health data, its central concern is ensuring that data sets are fully or partially de-identified, and regardless of use it is concerned with preventing data breaches and redressing any that seriously threaten a person’s interest. Moreover, HIPAA’s regulatory targets are “covered entities,” most of which share certain organizational interests, capacities and characteristics.

Any one privacy act is ill-suited to serve as a standard for protecting all confidential data and for allowing appropriate access and use in all settings. Of much longer standing, for example, is the Family Educational Rights and Privacy Act of 1974 (FERPA) established to protect the privacy of education records and now in the process of revision. The revision is expected to increase accountability and transparency as well as expand access and use, including the use of identifiable micro-level data under secure conditions coupled with data use agreements and enforcement mechanisms. Privacy acts like FERPA or HIPAA have their place for protecting administrative record systems under their aegis, but they fall short as guidance for preparing, storing, protecting data or stipulating conditions for public access or restricted data use. Other sources of guidance (e.g., the National Center for Education Statistics *Restricted-Use Data Procedures Manual* or the ICPSR *Guide to Social Science Data Preparation and Archiving, Data Use Agreement, or Instructions for Preparing the Data Protection Plan*) are more relevant, nuanced, and better adapted to the range of data protection issues that researchers confront.

As noted earlier, Appendix A of this white paper, *Protecting Research Participants and Facilitating Responsible Use*, provides extensive information on relevant NRC reports. Importantly, the Appendix includes a brief summary of why an NRC committee determined that HIPAA was not the appropriate framework for guiding

health research. It also sets forth eight recommendations for protecting privacy in all health research. As a privacy act, HIPAA's attention is understandably on protecting privacy and not on the relationships among privacy, confidentiality, and security.

The limitations of HIPAA for health research and for the SBS sciences in all areas, including health, can be readily highlighted:

- **HIPAA's de-identification standards are both too broad and too narrow.**
 - HIPAA focuses on direct identity disclosure and not on other attribute disclosures that can inadvertently lead to identification in research. Surveys, for example, may collect information not on the HIPAA list of identifiers that in combination with publicly available data might produce re-identification. Conversely, some data, like facial images, that must be removed to construct a HIPAA limited or de-identified data base is essential for certain kinds of SBS research (e.g., efforts to learn if microfacial expressions are valid indicators of attempts to deceive).
 - HIPAA authorizations, which allow the use of personal identifiers, are only a partial solution. They pertain only to the specific research study and do not allow for unanticipated data uses or analyses by different investigators.
 - IRB consent waivers allowed under HIPAA bring IRBs back into an area where most lack expertise and impose the kinds of hurdles that the promulgation of data protection standards aims to obviate.
- **Data security standards and information protection are important, but in HIPAA they are underspecified and do not offer guidance on the specific ways to protect identifiable data from inadvertent access, use, or disclosure or unauthorized use.**
 - A nuanced approach with respect to mechanisms of data security will not readily or easily map on to HIPAA. Field researchers, for example, taking notes by hand or with the use of recording devices will seldom be able to encrypt their data upon collection, and opportunities for physical secure storage to ensure access control may be limited.
 - HIPAA notes encryption requirements. The use of such methods should, however, be based not just on the identifiability of information but also on its sensitivity, on the availability and appropriateness of other modes of identity protection such as restricted-data use and

confidentiality agreements and on whether encryption will significantly impede desired data uses and data sharing .

- A full consideration of the options for data protection, depending on the level of risk, can include institutional approaches (e.g., licensing, data enclaves) and technical approaches such as data limitations (e.g., not releasing all the data, cell suppression or aggregation) and data alteration (e.g., swapping, masking). HIPAA provides no such guidance for reviewing or approving data protection plans.
- **Application of HIPAA rules for breach notification is problematic for the breadth of SBS research.**
 - Patient records typically contain contact information that makes breach notification straightforward, but SBS researchers, as a matter of sound data protection, seek to separate and secure information and, depending on the nature of the study (e.g., cross-sectional or longitudinal), may not retain contact information without reason to do so. The use of recreated or aged contact information could do more harm than good by reaching persons other than human subjects.
 - The HIPAA option of substitute notification through web postings or media alerts when contact information cannot be secured is likely to be futile at best and counterproductive at worst. Unlike patients who might have reason to regularly visit a health provider's web site, SBS subjects other than students have little reason to visit a university's or a researcher's web site.

Beyond the specific limitations of HIPAA, we have additional severe doubts that a workable single data security and protection plan can or should be established. The range of research and types of data, the levels of informational risk, and the provisions of informed consent are too varied for a generalized one-size-fits-all approach. We think requirements could be specified for data protection plans appropriate for different forms of data carrying different levels of risk and for studies that differ on whether they involve data collection or the reuse of data.

Our suggestion that neither HIPAA nor any other extant set of legal standards is the place to turn to for data security and privacy standards should not obscure the fact that we think that appropriate data security and information protection are core elements of responsible research ethics. Researchers registering their studies for excused status (or for the preparation of protocols for expedited or full review) need to address data security and information protection plans aligned with the level of risk, the conditions of use, and the nature of the data to be collected or obtained. We strongly endorse the goal of providing data protection standards appropriate to the research. As stated earlier in this white paper:

- **We do not support a one-size-fit all solution for data security and data protection or basing mandatory standards for data security and information protection on the standards and approaches of HIPAA.**
- **We recommend that, instead of turning to HIPAA, the drafters revising 45CFR46 (1) commit to examining options available for researchers establishing data protection plans and for oversight of those plans in ways that are efficient, flexible, and in accord with the data being collected, (2) plan to consult experts for guidance.**

Before taking up the questions, we should note that the heavy emphasis in the ANPRM related to biospecimens and health data comes at a cost. The biomedical emphasis eclipses attention to the characteristics and properties of SBS data, the wide overlap between health data and SBS data, and the need to consider identifiability issues in a context that balances considerations of data security, confidentiality protection, and appropriate access and use.

A. Consistently Characterizing Information With Respect to Potential for Identification

Q54. This question, insofar as it pertains to the suitability of applying HIPAA standards to the types of research done in SBS science, is addressed above. Therein we note and illustrate the availability of standards that would be appropriate for data security and information protection for SBS research, including health research. We also reference sources that contain the best scientific thinking about these and other standards (see also the Appendix).

The HIPAA standards are not appropriate for use in all types of research studies, especially much social and behavioral science research. When data are collected for research, regardless of research type, the organizational settings, ethics codes, and uses to which data are put will differ substantially from the patient practice settings that HIPAA regulates.

Q55. Studies on changing possibilities of re-identification and new means for de-identifying information have been ongoing for some time. There have, from time to time, also been helpful reviews by the National Research Council and other non-governmental and governmental bodies of these studies, and continuing investment in them would be desirable. Extant and new research should be monitored on a regular basis through independent periodic study or the commissioning of papers or reports directed to summarizing the state of knowledge and an updated set of best practices. Neither de-identification nor re-identification should be treated as if the only issues were technological. A full understanding of when data should be considered de-identified for research purposes should include attention to the incentives people with access to the data have for re-identification, as well as ways to affect those incentives, including confidentiality agreements and the ease of

theoretically possible re-identification. Finally, an adequate study of issues in this area would look closely at known instances involving the re-identification of de-identified data to learn why they happened and how this might have been prevented. If they are few and far between, their theoretical possibility should not control standard setting.

Q56. With rare exceptions de-identified biospecimens should not be considered identifiable in and of themselves. Unless they can be matched with bioinformation in a data set that contains links to a person's identity, the specimen remains effectively anonymous. The question is how to protect against data linkage without approval. Strong sanctions can and should be placed on researchers for unauthorized re-identification. Federal regulations can also enhance research protections by providing that biospecimens collected for research cannot be used for non-research purposes (as CIPSEA provides with respect to federal statistical data) and that measures such as certificates of confidentiality can help protect such information from forced disclosure by legal and other entities.

Q57. See generally responses to questions 55 and 56.

B. Standards for Data Security and Information Protection

Q58. Any new rules/standards implementing privacy protections should apply only prospectively. To do otherwise would devalue important SBS resources and threaten policies that depend on them. At the heart of the SBS data infrastructure are large survey research investments. Many of the scientifically most valuable repositories allow current data to be compared with similar data collected at earlier points in time. Applying proposed new rules to existing data would not only impose substantial compliance costs, some of which might not be fundable, but it could also hamper replication research and comparisons between past and present. Moreover, there have been no demonstrated problems with the human subjects protections and data security and protection plans now in place for informational risk sufficient to commend retrospective efforts.

Q59. This question is addressed in detail in Section II A and in our general discussion of the issues posed by Section V. Our response to Question 54 above is also relevant here. HIPAA standards are not designed for research data and depending on the data may over- or under-protect. Whether one is concerned with health or non-health data there exist excellence guidance for data security and information protection that go beyond the purposes and usefulness of HIPAA.

Q60. Absent instances of serious harms associated with survey interviews or other means of data collection, we see no need to require standardized means of data security and information protection at the data gathering phase. We urge strongly against further consideration of this additional burden with no obvious benefit. Appropriate guidance is well known and accessible to researchers and buttressed by strong pronouncements in codes of ethics in the SBS sciences. Moreover, ways of

gathering SBS information are so diverse that no simple set of rules or standards could be applied without unnecessarily interfering with important scientific research. SBS scientists, for example, often work in the field, recording information in field notes or by using video and audio recording devices. Requiring data de-identification or other protections in field settings may not be appropriate or possible or may interfere with the effectiveness and efficiency of the research efforts. The obligation to keep data secure and to protect the confidentiality of information is already well recognized by those SBS, medical and other researchers who collect data from human subjects by whatever means and mechanisms.

Q61. We do not recommend additional mandatory data security and information standards, modeled on the federal government or otherwise. As noted above, institutions or data providers exercise oversight, and researchers have the ethical and legal responsibility to adhere to data use agreements or secure their data consonant with guidance at their institutions. While some federal agencies are leaders in establishing data security measures, the best practices change over time and may not be suitable for every situation. The referenced NIST report, for example, is a valuable resource for government agencies and asserts some principles, like tailoring the level of protection to the level of risk, that apply generally, but it was not intended to regulate research data uses and protections. In addition, much of what it advises would impose substantial costs and impediments, without evident benefits, and other advice and directives lack the specificity needed for guidance. Better guides for new standards may be found in National Research Council reports, in the ethics codes of professional associations, and in the practices employed by entities like the ICPSR which are responsible for storing and disseminating SBS data varying in sensitivity.

Q62. We do not believe that data security and information protections under the 45CFR46 should be modeled on HIPAA. We do think that, if equally protective requirements for data security and information protection are in place under 45CFR46, HIPAA covered entities should be allowed to provide de-identified, public-use data to researchers without data use agreements; provide data to appropriate data archives delegating to them responsibility for setting conditions of access to restricted-use data to researchers consonant with the degree of de-identification; and provide researchers with identifiable data where it is necessary for research purposes so long as the information is protected by appropriate data use agreements and other conditions to ensure confidentiality and data protection.

Q63. Researchers using de-identified data should be prohibited from re-identification of the data unless the data provider has agreed to re-identification. A change in the research from public-use, de-identified data to identifiable restricted use data should trigger review under 45CFR46, even if the only risk is informational and the research may otherwise be excused.

Q64. Third-parties should be able ordinarily to obtain data from the same provider who is otherwise making available such public-use (de-identified) information.

There should be no stricture on sharing data that are de-identified, including to researchers who may be in organizations not subject to these rules. Scientists in such organizations should be able to have access to de-identified public-use data just as do those who are in institutions covered by 45CFR46.

Q65. Requiring registration for analyses of de-identified datasets seems unnecessary. As discussed elsewhere, data that have been certified as de-identified meet the test of being appropriate for public use.

Q66. If there are to be audits for re-identification, institutional flexibility in allocating this responsibility is likely to work better and be less costly than a single mandated approach.

Our critical comments notwithstanding, we reiterate what we said at the outset. We *strongly* support the establishment of separate standards for information protection coupled with the exclusion of informational risk from the purview of the IRB. This removes from IRB scrutiny matters that are typically outside of their expertise and allows researchers to know when they begin research planning what data protection standards they will have to meet. Introducing and expanding the use of the excused category has the additional benefit of reducing burdens on IRBs while not diminishing human subject protections (as long as additional requirements are not imposed). The burden of our more critical responses to the proposed change is to ensure that the standards are well chosen and respond to the experience, expertise, needs, and concerns of SBS scientists.

VI. Data Collection to Enhance System Oversight

The suggested changes are intended to simplify reporting, promote consistency within and across agencies, and allow for a better understanding of the human research protection process and unanticipated problems that arise in research. Since many of the regulations in human research protections are driven by a biomedical model, including the reporting of adverse events and unanticipated problems, creating a system that works well for biomedical researchers and SBS researchers will be complex.

We encourage creators of such a system to include non-DHHS agency representatives and SBS researchers in the development so that concerns may be addressed at the outset. Similarly, attempts to standardize forms should involve agencies who have signed on to the Common Rule and a wide range of research approaches, including SBS research. An evaluation of reporting requirements (time, ease, etc) under the current and any new system would be worthwhile.

We caution that movement to electronic submission could lead to broader reporting requirements by making it easy for an agency to request and process new information. In addition, electronic submission could serve to frustrate investigators if situations do not fall neatly into the response categories or the entire form (even

where irrelevant) must be completed. Proposed changes in reporting methods and the substance of what must be reported should be announced in advance with requests for comment from relevant research communities. In addition, we recommend that draft forms should be distributed and prototypes made available for testing on the web.

Q67. With regard to the scope of events that must be reported, we urge that any new reporting requirement be narrowly tailored such that only that information which is needed to determine the safety of human subjects in a particular study is requested or required. We fear that a new reporting requirement could irresistibly lead to more requests for information unrelated to assessing adverse or unintended events, thereby increasing administrative burdens on researchers, IRBs, and supporting institutions. The returns from collecting new information should be evaluated through careful cost-benefit analyses informed by input from affected research communities.

Q68 (a). Although it would be interesting to know the number of participants in federally funded research, it is worth considering how much value it will in fact have, especially relative to the costs. It is unclear from the ANPRM who would be responsible for reporting the number of human research participants—institutions, IRBs, or investigators. In some instances (e.g., some ethnographic research), the precise number of human subjects may not be known until the end of a study.

Q68 (b). Although the goal of enabling “an empirically based assessment of the risks of particular areas of human subjects research or of human subjects research globally” is laudable, we are not certain that a new reporting requirement is the best way to accomplish that end. More information does not necessarily lead to more informed policy, and, simple statistics may hide more than they reveal, providing policy makers with misleading guidance. The detailed information needed to tease out the conditions under which risks exist and what works or does not work is not likely to be obtained through new reporting requirements. A better empirical understanding of risk in particular areas of research is worth pursuing, but we recommend independent lines of inquiry that can capture the subtleties needed.

Q68(c). See 68(b).

Q69. Subject to security concerns, a central repository for collected data is a good idea as it will facilitate administrative access and research. To maximize its value the data should be made accessible to responsible researchers.

Q70. We do not believe that the clinical trial data should be used to inform the public of the overall safety of human subjects. Risks of harm in SBS research and in much biomedical research are likely to differ greatly from what they are in FDA-regulated Phase II-IV clinical trials. In almost all SBS research, the risks of serious harm will be less than in FDA regulated trials. Instead, we urge the opposite—the

public should be cautioned that they should not use information from clinical trials to judge the safety of other research involving human participants.

It would be unwise to attempt to draw from any data source a general estimate of the risks to human subjects from federally funded research. This is more likely to mislead potential research participants than to help them. What concerns subjects are the risks of the research they are being asked to participate in. It will be only by coincidence that these risks are close to the overall average risk, but having an average in mind may lead subjects to give less than optimum scrutiny to the specific risks they might face.

VII. Extension of Federal Regulations

Q71. We agree with the underlying premise that ethical protections should extend to all human subjects research, regardless of how the research study itself is funded. However, **we disagree with the assumption that extension of the federal regulations or specifically the Common Rule is necessarily the best way to achieve the protections that are desired or that all human subjects research should receive oversight through a common mechanism.**

While we see the logic to an integrated human research protection system, we are mindful of the complexities and challenges that the current system has faced. Our observation is that the ANPRM is seeking to stimulate a very ambitious set of reforms that will require considerable work to implement, even within the current scope of the regulations. **Thus, we recommend that attention be directed to the federal system as now defined under 45CFR46-Subpart A.**

Continuing to give institutions the latitude under the Federalwide Assurance of Compliance (FWA) that they now have to determine the scope of research under 45CFR46, we believe should be retained as is. Giving institutions some leeway to experiment with subject protection mechanisms that differ from those in the Common Rule may reduce costs, increase subject protection and perhaps suggest new mechanisms that might be incorporated into the Common Rule. For example, the Social and Behavioral Sciences Working Group of the National Human Research Protections Advisory Commission recommended to DHHS that student research involving human participants be reviewed at the departmental level, rather than the IRB and similar procedures might be applied to low-risk research with the possibility of reference to the IRB if needed. Approaches like this involving mainly low-risk research would reduce burdens on IRBs while the proposed extension of jurisdiction would expand those burdens considerably.

In providing alternative mechanisms, institutions and fields of SBS science would not be ethically unmoored. They would be guided by their knowledge of when IRB review has worked well and worked poorly as well as by the law, by the ethical codes of the various disciplines and fields, and by the considerable thinking of scientists and ethicists regarding human subjects protection and the ethical conduct

of research. In short, we believe there is great value in retaining *more* flexibility at the local level so that institutions can experiment with different models of review with the aim of improving the efficiency and effectiveness of the overall human research protection system.

Ethical decision making is an ongoing, dynamic process that requires extrapolation and translation of ethical principles to address new technologies, new issues, or new understandings. It requires a consideration of broader ethical principles apart from the regulations. Best practices can be developed if alternative models are explored and evaluated without requiring an extension of the regulations. Beyond the logic of this mend it don't extend it philosophy, there are other principles at stake. One of the foundational aspects of the Common Rule is to allow for institutional autonomy and flexibility. We see continuing that model and averting a shift to consolidation is how the federal government should proceed at this time.

At a minimum, the Common Rule should not be extended without further research. The fact that some institutions now extend the Common Rule to non-federally funded research and others do not allows for a powerful empirical design that can shed light on the need for and potential value of extending the Common Rule as well as reveal ways in which Common Rule procedures work less well than alternatives or have other shortcomings that counsel against expanding the Common Rule's jurisdiction. We urge that any decision to expand the Common Rule be evidence-based, and that research be funded to provide needed evidence.

VIII. Harmonizing Regulatory Requirements and Agency Guidance

Uniformity is a goal often worth striving for, but unless a uniform rule is carefully drawn and finely nuanced, its consistent application can subvert the benefits it is designed to achieve. Well-considered tailoring will usually do more than surface uniformity to advance the twin goals of protecting human subjects and facilitating valuable research.

The fact that a rule is labeled “Common” does nothing to make a compelling case for consistency across Federal agencies. One can just as easily argue that the failure of some federal agencies to subscribe to the “Common Rule” means that there is concern that uniformity could do more harm than good. Our position is that uniform regulation, where it makes sense, is desirable. Determining where uniformity makes sense is the problem to be tackled, and the medical principle—“First, do no harm”—is as applicable here as in medicine.

Q72. Without data, it is unclear whether differences in agency guidance strengthen or weaken human subjects protections. Differing agency guidance, however, increases the burden on investigators and yet, provides a measure of flexibility—without harming subjects—that both agencies and investigators appreciate. Indeed, we are unaware of situations involving SBS research where human subjects

were harmed because the guidance of one agency rather than another was mistakenly applied.

To the extent that some agencies provide tailored protections that go beyond what the Common Rule requires, the risks to human subjects are diminished. Tailored guidance is particularly important where guidance that fits some studies well would impose unjustified costs or allow unnecessary risk if applied in different circumstances. For example, the confidentiality and data protection requirements that must be met by researchers who wish to use certain IRS and Census non-microdata would unnecessarily restrict research with other data sets, and rules and guidance appropriate to less sensitive data would impose excessive risk if they set a ceiling on the protection accorded highly sensitive data.

Q73. SBS researchers have been concerned—and remain so—about the dominance of the biomedical model for ensuring human research protections with DHHS as the sole interpreter of the regulations. Moreover, something may be lost in the compromises needed to procure interagency agreements on guidance. Furthermore, at NSF and NIJ specific guidance on the application of the Common Rule has helped researchers gain approval for important studies without adding to the risks their human subjects experienced or faced.

Human research protections may be improved precisely because agencies and investigators are using the flexibility that they have under the current system. For example, special security rules for sensitive data have enabled breakthrough research using Census, IRS and other microdata whose use two decades ago seemed unthinkable. Techniques for encrypting and anonymizing data and guaranteeing subject confidentiality have enabled the creation and dissemination of restricted use and public use data sets that have advanced significantly SBS understandings of causal relationships and social life. We recommend harmonizing regulations where possible to reduce burden on investigators, while also allowing flexibility. We also recommend that a human subjects committee be created under OSTP that will give all federal agencies an equal voice in working to align the regulations on human subjects protection that will allow flexibility where needed.

Q74. Although there is some room for harmonizing guidance across the Common Rule agencies or subsets of them, converging on one set of guidance would most likely hamper rather than facilitate domestic and international research without concomitant gains in human subject protection. The diversity of human subjects, research methods and relevant data is so great as to preclude drafting uniform guidance that will, on the one hand, be clear and concise and on the other, adequately protect and a facilitate across the range of human subjects research.

Highly nuanced guidance might achieve the aim of uniformity, but it would be unified in name only, for adequate nuance would necessitate mapping guidance closely to study characteristics, at the cost of conciseness and clarity. Allowing different agencies to assert somewhat different interpretations of Common Rule

protections or to incorporate other requirements, perhaps imposed on them by statute, is an approach that is easier to accomplish and allows agencies to tailor guidance to of different research.

IRBs often look to the agency guidance with which they are most familiar rather than to the guidance provided by the sponsoring agency. SBS researchers, for example, often encounter IRBs that look only to guidance developed with biomedical research in mind even when the guidance is poorly suited to the proposed SBS research. We have heard, for example, numerous reports of IRBs seeking to impose informed consent rules that potentially compromise SBS research designs without adding to human subject protections or meaningfully promoting their autonomy.

There is also room for consultation among federal agencies and with researchers regarding ways that agency guidance can be better harmonized even if not always made identical. An interagency human subjects research committee under the auspices of OSTP would facilitate this, assuming that all agencies have an equal voice and stake in the outcome.

Indeed, efforts to reach common solutions where it makes sense have long been happening, in both direct interchanges and through joint contributions to National Research Council and IOM best practice investigations. To achieve uniformity through this regulatory process without the aid of other agency voices could impose great costs on human subjects research than any risks it might curtail or any benefits it might bring.

Overview and Recapitulation

To recapitulate briefly, the following capture some of the more important positions and concerns mentioned in this white paper.

We strongly support:

- the recommendation to separate informational risks from physical and psychological risk and the proposed plan to remove the evaluation of information risk from the purview of Institutional Review Boards (IRBs)
- changes set forth in the ANPRM that will better calibrate IRB scrutiny to the risk of harm that a project might entail.
- the suggestion in the ANPRM that, regardless of whether identifiers are retained, continuing review should cease when data analysis and, we would add, report writing are the only remaining research activities. The same should be true when additions to the data are part of routine data collection and should extend to accessing follow-up data that are routinely obtained (e.g., test scores, salary information) in SBS research and for which there has been prior consent and approval.

- updating the list of research activities that qualify a study for expedited review and periodically considering further expansion based on empirical assessment of the levels of risk.
- ANPRM's endorsement of a default assumption that research that falls under the list of activities is by definition "minimal risk" and qualifies for expedited review, if not otherwise excused.
- RESTATE requiring that decisions to refer for full IRB review studies that are prima facie expedited review qualified be documented and subject to audit.
- the suggestion for periodic review of the expedited review approval list. We also urge that although additions to the list might be allowed at any time, deletions should be subject to a public comment period.
- the goal of ensuring that updates to the expedited review list are based on a systematic, empirical assessment of the level of risk.
- recognizing that when research is considered under expedited review it is should not be necessary to find that all of the criteria for full IRB approval have been met.
- streamlined documentation for expedited studies. (Standard templates and forms intended to expedite the process should allow for flexibility and promote efficiency. No one-size-fits-all template for minimal risk research will achieve the goals.)
- regulatory language emphasizing that IRBs should only consider "reasonably foreseeable risks or discomforts."
- considering whether there may be gains from allowing expedited review by persons other than IRB members and sponsoring pilot programs or other research to provide empirical evidence.
- a periodic reporting requirement when IRB's override expedited review defaults.
- an independent expert study of the exempt research category, including what it means in theory and practice, whether it should be maintained, (if it should be maintained) what research should remain uncovered by 45CFR46, and whether current procedures for determining exempt status should be reformed.
- The proposed creation of the new category "excused," provided this is not accompanied by the abolition of the exempt category and the recharacterization of all now exempt research as excused or impose regulations relating to data protection and consent
- the registration of studies claiming excused status and audits of registration statements. (We do not believe excused submissions should be reviewed by the IRB unless recent audits have indicated ongoing problems.)

- the proposal to allow research on excused studies to proceed once a study has been registered as excused.
- requiring institutions holding Federalwide Assurances to conduct retrospective audits of excused studies.
- taking advantage of the substantial SBS expertise on issues relating to data security, subject privacy and informed consent.
- incorporating institutions and procedures to protect subject data and privacy into any list of standards created with these goals in mind. (These practices and procedures are being continually used and updated by researchers in the SBS and other sciences and have a long history of providing the data and privacy protection that human subjects deserve.)
- making the expectation of future research uses of subject-provided data the default assumption when subjects' consent to research do not address future use, presuming the original privacy and confidentiality protections remain in place.
- reminding IRB's that their focus should remain squarely on the protection of human subjects and not on the long-range effects of knowledge on policy or related issues.
- instituting an appeals process for IRB judgments.
- requiring IRBs to identify each time actions are taken that are not required under 45CFR46.
- allowing the use of one IRB of record for multi-site studies and requiring this for federally funded research.
- empirical research into the informed consent process so that so that any changes to the regulations, including changes related to subject comprehension, are evidence-based.
- revising 45CFR46 to set forth what needs to be accomplished through the consent process and allowing alternative approaches to obtaining meaningful consent rather than an emphasis on a small set of written forms as the default procedure.
- making available standardized consent form templates that meet regulatory requirements, so long as required language is avoided and flexibility retained.
- eliminating from the information that must be given subjects a discussion of speculative or remote risks and risks mentioned primarily to protect institutions from liability.
- many but not all of SACHRP's recommendations regarding waiver of informed consent, including its recommendation that IRBs should interpret minimal risk using a uniform standard of not greater than the harms and

discomforts ordinarily encountered in daily life or during the performance of routine medical and psychological examinations or tests for the average person in the general population.

- the proposed classification of most studies that involve surveys, focus groups, and interviews of competent adults as excused with only oral consent required.
- clarifying the inapplicability of waiver requirements when research is exempt from coverage under 45CFR46.
- the ANPRM's focus on informational risk in considering requirements for the subsequent use of non-research as well as research data.
- strictly prohibiting re-identification for de-identified data and safeguards against the advertent or inadvertent disclosure of identifiable information retained in restricted use data sets.
- allowing de-identified information collected for non-research purposes to be used without additional consent as long as researchers protect and use this information in ways that prevent re-identification.
- ensuring that when existing data are used for research purposes data security and privacy protections are at least as protective as they were when the data was first secured.
- the development of standardized general consent language (rather than a form) permitting future research of data collected originally for research purposes.
- applying rules requiring new consents when existing research data are used in other research only prospectively if, contrary to our advice, such a requirement is instituted.
- applying any new data security and information protection requirements only prospectively.
- considering how best to promote data security and subject privacy drawing on such sources as National Research Council reports, the ethics codes of professional associations, and the practices of entities like the ICPSR which are responsible for storing and disseminating SBS data of varying sensitivity.
- allowing HIPAA covered entities to provide de-identified, public-use data to researchers without data use agreements.
- prohibiting researchers using de-identified data from re-identifying the data unless the data provider has agreed to re-identification.
- allowing institutional flexibility in the design and management of audits aimed at checking for unauthorized data re-identification and improper claims of excused status.

- advance announcement of proposed changes in reporting methods and the substance of what must be reported to allow for comment from relevant research communities.
- narrowly tailoring any new reporting requirement so that only information which is needed to determine the safety of human subjects in a particular study is requested or required.
- a secure central repository for collected data that is accessible to responsible researchers.
- retaining flexibility at the local level so that institutions can experiment with different models of review and contribute to improving the efficiency and effectiveness of the overall human research protection system.
- maintaining the current system that allows agencies to tailor their Common Rule guidance to the kinds of research they fund even if it means that different agencies may provide somewhat different guidance.
- the creation of a human research protections committee under OSTP that will consider the broad range of agency perspectives in making any changes to the regulations and make recommendations for future changes. This will provide a voice for many scientific areas outside biomedical research. Consideration of expert bodies such as the National Research Council in addressing the full range of human research protection issues such as data security, exemptions, de-identifying data (including concerns with HIPAA as a model)
- proposed changes to the Common Rule (Subpart A) where there is a strong consensus, and urge similar reviews of other Subparts that address special populations

We do not support:

- a one-size-fit all solution for data security and data protection.
- the use of HIPAA as a model for privacy protection and data security practices under the Common Rule.
- broad implementation of HIPAA's encryption requirements.
- application of HIPAA's rules for breach notification.
- importing rules and guidance from other federal agencies (e.g., NIST) as requirements under the Common Rule.
- the language in 46.111a(1)(i) and referenced in the ANPRM inviting IRBs to determine whether research procedures are "consistent with sound research design." (We believe this language should be stricken or modified to avert judgments beyond the expertise of IRBS and not directly germane to human subjects protections.)

- ANPRM’s proposed new category of “excused” research to the extent it covers exempt research and imposes regulations relating to data protection and consent. (We feel strongly that before changes are made to the exempt category, an independent panel should be created to evaluate and report on the wisdom of the change and whether some types of research are properly exempted from the structures of 45CFR46.)
- the distinctions the ANPRM proposes between existing research and non-research data.
- imposing re-consent requirements on further research uses of existing research data. (This requirement could threaten both the quality and integrity of large amounts of SBS research.)
- a requirement of written general consent for the future research use of biospecimens under conditions that preclude identifying the person who supplied the specimen.
- the designation of research involving deception or biospecimens as per se ineligible for excused or expedited status.
- a general mandate to apprise subjects as part of the informed consent process of alternatives to treatment or why it may be in their best interest not to participate. (Such requirements are sometimes appropriate, but add complexity and foster confusion where they are not.)
- any but the most limited (confined to high risk studies) requirements to assess subject risk comprehension as part of the informed consent process until an adequate research base exists.
- the ANPRM’s assumption that when existing data were collected for research purposes more is ethically required in the way of informed consent than when the data were collected for non-research purposes; only in exceptional circumstances will this be true.
- inviting participants to specify categories that they would either permit or disallow for future research use of the data.
- requiring standardized means of data security and information protection at the data gathering phase.
- requiring registration for analyses of de-identified datasets.
- adopting a reporting requirement to enable “an empirically based assessment of the risks of particular areas of human subjects research or of human subjects research globally.” (Although the goal is laudable, a reporting requirement is unlikely to produce data rich enough to provide answers of the quality needed for a reliable assessment.)
- using clinical trial data to inform the public of the overall safety of human subjects research.

- mandating the extension of Common Rule requirements to all federally funded research at institutions that do any federally funded Common Rule research.
- imposing uniformity across Federal agencies for its own sake rather than with careful attention to where uniformity may help meet subject protection and research facilitation goals and where allowing diversity has more to offer.

Conclusion

The ANPRM reflects a quite serious, major, and overdue attempt to examine and improve 45CFR46-Subpart A, a significant and longstanding regulation for the protection of human subjects. The social and behavioral science community sees much commendable in the proposed changes and urges that a revision be prepared that builds upon the quite promising areas ripe for reform. We also, however, have areas of concern detailed in this white paper and reflected in the recommendations set forth in the section on overall guidance.

The SBS sciences value the time and investment of HHS and OSTP and in particular the OHRP staff for taking on such a major project that was long overdue. We continue to be at a crucial turning point. While the comment period ends on October 26, 2011, the hard work resumes not just to perfect those areas where reforms are ripe but also to reflect on issues that need to be altered or require fresh expertise and consultation to realize the aspiration motivating this task.

We believe that the revision of 45CFR46 can be crafted as a series of meaningful regulatory reforms. As this white paper makes clear, in the near-term the major changes around which we believe there will be a strong consensus can dramatically improve the federal system of human research protection as we know it. To that end we wish you well and offer our support and continuing engagement in this task.

Endorsing Organizations¹

American Educational Research Association
Federation of Associations in Behavioral and Brain Sciences
Consortium of Social Science Associations
American Political Science Association
American Sociological Association
Association of Psychological Science
Association of Population Centers
Cognitive Science Society
Council of Professional Associations on Federal Statistics
Human Factors and Ergonomics Society
Inter-university Consortium for Political and Social Research
Law and Society Association
National Academy of Neuropsychology
National Communication Association
NORC
Population Association of America
Social Science History Association
Society for Behavioral Neuroendocrinology

¹ This white paper was prepared on behalf of the scientific societies and organizations listed. It reflects over a decade of work by behavioral and social scientists on panels, commissions, committees, conferences, courses, working groups, and most recently, a day-long meeting of numerous society representatives and experts on human research protections to discuss the specific changes proposed by DHHS and OSTP.

A writing team—Felice J. Levine, Richard O. Lempert, and Paula R. Skedsvold—took the lead in preparing this white paper based on that meeting and ongoing discussions with scientists and scholars as well as scientific organization and societies. The writing team has served in numerous roles that intersect with human research protection issues.

Levine, AERA Executive Director, has served on the National Human Research Protections Advisory Committee, co-chaired the Social and Behavioral Sciences Working Group on Human Research Protections, served as a member of the panel that produced the 2007 NRC report on protecting confidentiality with linked social-spatial data, and chaired the NRC workshop on protecting student records and facilitating education research. She also had leadership responsibility for the development of two SBS society ethics codes.

Lempert, AERA consultant, is the Eric Stein Distinguished University Professor of Law and Sociology Emeritus of the University of Michigan and more recently served as Division Director of the Social and Economic Sciences at the National Science Foundation and as Chief Scientist in the Human Factors Division of the Science and Technology Directorate of the Department of Homeland Security, during which time he co-chaired the NSTC interagency subcommittee on the Social, Behavioral and Economic Sciences.

Skedsvold, Executive Director of Federation of Associations in Behavioral and Brain Sciences, is trained in experimental psychology and law, served as Science Policy Analyst at NIH's Office of Behavioral and Social Sciences Research, and previously staffed the Social and Behavioral Sciences Working Group of the National Human Research Protections Advisory Committee.

Society for Computers in Psychology
Society of Experimental Social Psychology
Society for Industrial and Organizational Psychology
Society for Judgment and Decision Making

Appendix A – SBS White Paper on ANPRM Re 45CFR46 Protecting Research Participants and Facilitating Responsible Data Access—Recommendations from the National Academies*

The social and behavioral sciences rely on data collected from people (human subjects in the language of the Common Rule) for much of their work. Detailed information about individuals (microdata) is critically important for research and essential in studies based on surveys. Social and behavioral sciences (SBS) modeling aimed at understanding relationships among complex phenomena is hampered without microdata because of the loss of information that occurs in aggregation. There is, however, an inescapable tension between providing access to microdata and the ethical obligation to protect the confidentiality of those who provided the data. This tension is not new and continues to evolve. On one hand, there is increased opportunity to develop greater understanding of the human condition and evidence-based solutions to some of the nation’s most pressing problems by exploiting in more detail and in new ways the fruits of the nation’s highly decentralized apparatus of data collection and research activities, which include data collected by federal statistical, research, and operating agencies, academic institutions, state and local governments, and the private sector, including social media. On the other hand the challenge of protecting data confidentiality has grown, principally because the proliferation of available data coupled with software developments and high speed computing have substantially increased the potential for re-identifying individuals in a data set even after direct or obvious identifiers have been removed (*Expanding Access to Research Data*, 2006:1-2).

For this reason government agencies and others involved with the SBS research communities have on several occasions turned to the National Academy of Sciences and its operating arm, the National Research Council (NRC), and to the Institute of Medicine (IOM), for guidance. This brief note summarizes relevant recommendations of expert study panels and committees commissioned by the NRC and IOM to assess and make recommendations on data access and confidentiality protection (a complete bibliography of relevant NRC/IOM reports is attached). These reports capture state of the art thinking about ethical and technical issues at the time of their writing. The burden of these recommendations is that there is no “one size fits all” regime for accomplishing the desired protection of confidential data while facilitating research access; that the issues in this area will continue to evolve; and that responsible organizations, including federal statistical agencies and major social science data archives, have been and should remain at the forefront in determining appropriate guidance, protocols, and methods for data access and confidentiality protection. The efforts of such agencies and archives provide models for protecting research data sets funded by the

federal government. Hence, a theme running through the reports is that federal rules for data protection should not just allow for but encourage continual governmental and nongovernmental review and modification of existing standards in order to promote simultaneous progress toward both easier data access and greater subject protection. In this connection, a 2009 Institute of Medicine report makes clear that the HIPAA Privacy Rule (final 2002 version) proposed for possible use in a revision of the Common Rule (45 *CFR* 46, Part A) is not well suited for protecting data confidentiality and at the same time is a barrier to responsible research.²

SHARING RESEARCH DATA (1985)

This early, pathbreaking report of the Committee on National Statistics made a detailed case for responsible sharing of research data at a time when such practices were not widespread. The report noted (p. 3) that: “Data are the building blocks of empirical research, whether in the behavioral, social, biological, or physical sciences. To understand fully and extend the work of others, researchers often require access to the data on which that work is based. Yet many members of the scientific community are reluctant or unwilling to share their data even after publication of analyses of them.” To correct this situation the report included the following recommendations:

Recommendation 1: Sharing data should be a regular practice.

The advantages of data sharing [reinforcement of open scientific inquiry; verification, refutation, or refinement of original results; promotion of new research through existing data; encouraging more appropriate use of empirical data in policy formulation and evaluation; improvements of measurement and data collection methods; development of theoretical knowledge and knowledge of analytic technique; encouragement of multiple perspectives; provision of resources for training in research; protection against faulty data] are sufficient to warrant considerable attention to ways to share data without imperiling privacy or breaching the confidentiality promised to data providers.

Recommendation 2: Investigators should share their data by the time of publication of initial major results of analyses of the data except in compelling circumstances.

Recommendation 3: Data relevant to public policy should be shared as quickly and widely as possible.

Recommendation 4: Plans for data sharing should be an integral part of a research plan whenever data sharing is feasible.

Recommendation 8: Funding organizations should encourage data sharing by careful consideration and review of plans to do so in applications for research funds.

²See “Advance Notice of Proposed Rule-Making for Human Subjects Research Protections: Enhancing Protections for Research Subjects and Reducing Burden, Delay, and Ambiguity for Researchers,” *Federal Register*, 76 (43), Tuesday, July 26, 2011.

Recommendation 9: Organizations funding large-scale, general-purpose data sets should be alert to the need for data archives and consider encouraging such archives where a significant need is not now being met.

Recommendation 10: Journal editors should require authors to provide access to data during the peer review process.

Recommendation 11: Journals should give more emphasis to reports of secondary analysis and to replications.

Recommendation 13: Journals should strongly encourage authors to make detailed data accessible to other researchers.

Twenty-five years later, the recommendations in this report have been widely adopted by research funding organizations and scientific journals. As a result, the availability of rich microdata, often from longitudinal panels, has greatly expanded, making possible more in-depth analysis of important topics in basic and applied SBS research. The case for data access has been made; the challenge is to identify responsible practices for data sharing that do not result in intentional or inadvertent breaches of data confidentiality and that do not make data access more onerous than necessary.

PRIVATE LIVES AND PUBLIC POLICIES (1993)

This report, prepared under the aegis of the National Research Council's Committee on National Statistics and the Social Science Research Council, focused on (p. 1): "developing recommendations that could aid federal statistical agencies in their stewardship of data for policy decisions and research. Three areas were of paramount concern . . .: protecting the interests of data subjects through procedures that ensure privacy and confidentiality, enhancing public confidence in the integrity of statistical and research data, and facilitating the responsible dissemination of data to users."

Recommendation 4.2: Federal statistical agencies should seek to improve the access of external users to statistical data, through both legislation and the development and greater use, under carefully controlled conditions, of tested administrative procedures.

Recommendation 5.1: Statistical records across all federal agencies should be governed by a consistent set of statutes and regulations meeting standards for the maintenance of such records including . . . a guarantee of confidentiality for data.

Recommendation 5.3: There should be legal sanctions for all users, both external users and agency employees, who violate requirements to maintain the confidentiality of data. [This recommendation was subsequently endorsed in *Expanding Research Data* (2005), recommendation 8.]

Recommendation 6.1: The Office of Management and Budget's Statistical Policy Office should continue to coordinate research work on statistical disclosure analysis Major statistical agencies should actively encourage and participate in scholarly statistical research in this area.

Recommendation 6.2: Statistical agencies should determine the impact on statistical analyses of the techniques they use to mask data. They should be sure that the masked data can be accurately analyzed by a range of typical researchers.

Recommendation 6.4: Statistical agencies should continue widespread release, with minimal restrictions on use, of microdata sets with no less detail than currently provided.

This report was completed in a time when there was a large and growing body of microdata collected by statistical and other agencies of the federal government with great value for research; a growing recognition of the challenges in adequately protecting data confidentiality while not rendering data unusable for research; and a sense that well-thought-out guiding principles and practices and stronger legislation were needed because of the differences in statutes and practices then existing across agencies.

The 2002 Confidential Information Protection and Statistical Efficiency Act (CIPSEA) responded to the report's recommendations for legislation guaranteeing confidentiality for all federal statistical collections and providing penalties for breach of confidentiality applicable not only to agency staff, but also researchers who were provided access to microdata as agents of a statistical agency. The U.S. Office of Management and Budget (OMB) and many statistical agencies acted to develop best practices for data access and confidentiality protection and to establish or enhance different mechanisms for providing access under appropriate conditions to data that could not be provided in the form of public use microdata. Such mechanisms include research data centers, remote data access arrangements, and licensing of principal investigators at universities. See further discussion below under *Expanding Access to Research Data* (2005) and *Protecting and Accessing Data from the Survey of Earned Doctorates* (2010).

PROTECTING PARTICIPANTS AND FACILITATING SOCIAL AND BEHAVIORAL SCIENCES RESEARCH (2003)

This report of the National Research Council's Committee on National Statistics and Board on Behavioral, Cognitive, and Sensory Sciences responded to a growing concern in the social science community that (p. 1), "The U.S. system for protecting people who volunteer to participate in research is widely perceived to need improvement. A major concern is that the linchpins of the protection system—institutional review boards (IRBs)—are overloaded and underfunded and so may not be able to adequately protect participants from harm in high-risk research. . . . [while] the review process may delay research or impair the integrity of research designs, without necessarily improving participation protection, because the type of review is not commensurate with risk—for example, full board review for minimal-risk research that uses such methods as surveys, structured interviews, participant observation, laboratory experiments, and analyses of existing data." The report documented the variability in IRB workloads and practices (for example, treatment of expedited review that ranged from "never allowed" to "always allowed"). In addition to issues of informed consent and appropriate handling of minimal-risk research, the report gave substantial attention to the challenges of providing data access and protecting confidentiality of responses.

Recommendation 5.1: Because of increased risks of identification of individual research participants with new methods of data collection. . . federal funding agencies should support research on techniques to protect the confidentiality of SBES data that are made available for research use; and the Office for Human Research Protections should regularly promulgate good practices in analyzing disclosure risks and limiting those risks.

Recommendations 5.2 and 5.3: To facilitate secondary analysis of public-use microdata files, the Office for Human Research Protections . . . should establish a new confidentiality protection system for these data. . . . Participating [statistical agencies] and archives in the new public-use microdata system protection system should certify . . . whether data sets are sufficiently protected against disclosure to be acceptable for secondary analysis. IRBs should exempt such secondary analysis from review on the basis of the certification provided. [This recommendation was subsequently endorsed in *Expanding Access to Research Data* (2005), recommendation 6.]

Since the issuance of this report, several university IRBs have adopted a policy whereby microdata files that are released from statistical agencies and established data archives for public use are exempt from IRB review because they do not represent identifiable “human subjects”. For example, the Purdue University IRB exempts from IRB review public use data sets from the following sources (<http://www.purdue.edu/research/vpr/rschadmin/rschoversight/humans/docs/101Existing Public Use Datasets.pdf>):

- Inter-University Consortium for Political and Social Research (ICPSR)
- Better Access to Data for Global Interdisciplinary Research (BADGIR)
- National Center for Health Statistics
- National Center for Education Statistics
- National Child Development Study
- National Election Studies
- Roper Center for Public Opinion Research
- University of Wisconsin-Madison Data and Information Services Center (DISC)
- U.S. Bureau of Census
- U.S. Bureau of Labor Statistics
- The University of Michigan Health and Retirement Study (HRS) (unrestricted data sets only)
- Panel Study of Economic Dynamics (PSID)
- Survey of Consumers (SCA)
- Integrated Public Use Microdata Samples – International (IPUMS-i)
- Luxembourg Income Study Project Archive

EXPANDING ACCESS TO RESEARCH DATA: RECONCILING RISKS AND OPPORTUNITIES (2005)

This report of the Committee on National Statistics was issued in response to a request from the National Institute on Aging for an assessment of “competing approaches to promoting exploitation of the research potential of microdata—particularly linked longitudinal microdata—while preserving confidentiality . . . and how microdata should be optimally (from a societal standpoint) be made available to researchers.”

“The panel concludes that no one way is optimal for all data users or all purposes. To meet society’s needs for high-quality research and statistics, the nation’s statistical and research agencies must provide both unrestricted access to anonymized public-use files and restricted access to detailed, individually identifiable confidential data for researchers under carefully specified conditions” (p.2).

Recommendation 2: Data produced or funded by government agencies should continue to be made available for research through a variety of modes, including various modes of restricted access to confidential data and unrestricted access to public-use data altered in a variety of ways to maintain confidentiality.

Recommendation 3: The National Science Foundation, the National Institutes of Health, and major statistical agencies should support research to guide more efficient allocation of resources among different data access modes.

Recommendation 5: Agencies that sponsor data collection should conduct or sponsor research on techniques for providing useful, innovative public-use data that minimize the risk of disclosure . . . [including]: (1) developing measures for quantifying disclosure risk; (2) estimating the effect on disclosure risk of adding selected variables from confidential data files to public-use files; (3) estimating and improving the utility-disclosure limitation tradeoffs of alternative disclosure limitation methods, including synthetic data

Recommendation 9: To achieve the research potential and cost-effective operation of the Census Bureau [research] data centers, the Census Bureau should (1) broaden the interpretation of the criteria for assessing the benefits of access to data; (2) maintain the continuous review cycle; and (3) take account of prior scientific review of research proposals by established peer review processes.

Recommendation 10: Statistical agencies and other agencies that sponsor data collection should conduct or sponsor research on cost-effective means of providing secure access to confidential data by means of a remote access mechanism, consistent with their confidentiality assurance protocols.

Recommendation 11: Statistical and other agencies that provide data for research and do not yet use licensing agreements for access to confidential data should implement such an access mechanism. . . .

Since the issuance of this report, statistical and research agencies have expanded not only their use of innovative techniques for producing suitably anonymized public use files, but also their arrangements to provide access to identifiable confidential information through research data centers and/or licensing and/or remote access. For example, confidential data sets from the Health and Retirement Study sponsored by NIA are available on a restricted access basis at the University of Michigan, and the Census Bureau has expanded its RDC network and added data files from other agencies to the RDC holdings. This report recognized that what constitutes identifiable and not identifiable data is evolving and that different mechanisms are necessary to provide different kinds of access—for example, the provision of public use data sets with geographic identifiers may require perturbation of other data fields to safeguard against breach of confidentiality,

while some confidential data can only be provided under restricted conditions such as through a license with stiff penalties for disclosure or other means.

PUTTING PEOPLE ON THE MAP: PROTECTING CONFIDENTIALITY WITH LINKED SOCIAL-SPATIAL DATA (2007)

This report of the National Research Council's Committee on the Human Dimensions of Global Change responded to the interests of the National Science Foundation, National Institute of Child Health and Human Development, and National Aeronautics and Space Administration in addressing the added challenges for providing data access and protecting confidentiality when very accurate spatial data (from remote sensing or GPS location devices) are included in social science data sets. The report concluded and recommended that:

Conclusion 1: Recent advances in the availability of social-spatial data and the development of geographic information systems (GIS) and related techniques to manage and analyze those data give researchers important new ways to study important social, environmental, economic, and health policy issues and are worth further development.

Conclusion 2: The increasing use of linked social-spatial data has created significant uncertainties about the ability to protect the confidentiality promised to research participants. Knowledge is as yet inadequate concerning the conditions under which and the extent to which the availability of spatially explicit data about participants increases the risk of confidentiality breaches.

Recommendation 7: Data enclaves deserve further development as a way to provide wide access to higher-quality data while preserving confidentiality. This development should focus on the establishment of expanded place-based enclaves, "virtual enclaves," and meaningful penalties for misuse of enclaved data.

Recommendation 8: Data stewards should develop licensing agreements to provide increased access to linked social-spatial datasets that include confidential information.

The value of and issues raised by linked social-spatial data are obvious. Substantial additional research is needed to determine the risks of confidentiality and privacy breaches and to develop techniques for reducing those risks.

CONDUCTING BIOSOCIAL SURVEYS: COLLECTING, STORING, ACCESS, AND PROTECTING BIOSPECIMENS AND BIODATA (2010)

This report of the National Research Council's Committee on National Statistics and Committee on Population responded to the request of the National Institute on Aging to consider the added challenges for data access and confidentiality protection from the addition of biospecimens, such as blood, urine, and saliva, as part of large-scale household surveys intended for SBS research. The report cites best practice reference documents, including *Best Practices for Repositories: Collection, Storage, Retrieval, and Distribution of*

Biological Materials for Research, prepared by the International Society for Biological and Environmental Repositories (2008); *National Cancer Institute Best Practices for Biospecimen Resources* (2007); and *OECD Best Practice Guidelines for Biological Resource Centres* (2007) and makes recommendations for data sharing plans and confidentiality protection for biosocial data sets:

Recommendation 3: [NIH] should publish guidelines for principal investigators containing a list of points that need to be considered for an acceptable data sharing plan. In addition to staff review, Scientific Review Panels should read and comment on all proposed data sharing plans. In much the same way as an unacceptable human subjects plan, an inadequate data sharing plan should hold up an otherwise acceptable proposal.

Recommendation 4: NIA and other relevant funding agencies should support at least one central facility for the storage and distribution of biospecimens collected as part of the research they support.

Recommendation 7: Both rich genomic data acquired for research and sensitive and potentially identifiable social science data that do not change (or change very little) with time should be shared only under restricted circumstances, such as licensing and (actual or virtual) data enclaves.

Recommendation 8: [NIH] should develop new standards and procedures for licensing confidential data in ways that will maximize timely access while maintaining security and that can be used by data repositories and by projects that distribute data.

PROTECTING AND ACCESSING DATA FROM THE SURVEY OF EARNED DOCTORATES: A WORKSHOP SUMMARY (2010)

This summary of a workshop convened by the Committee on National Statistics responded to a request of the NSF National Center for Science and Engineering Statistics for expert discussion of confidentiality protection techniques for tabular data from the NSF Survey of Earned Doctorates. While not designed to produce consensus conclusions or recommendations, the workshop highlighted the issues. It also identified and discussed valuable guidance on disclosure protection from:

- U.S. Office of Management and Budget, *Implementation Guidance for Title V of the E-Government Act, Confidential Information Protection and Statistical Efficiency Act of 2002* (June 2007, http://www.whitehouse.gov/sites/default/files/omb/assets/omb/fedreg/2007/061507_cipsea_guidance.pdf);
- U. S. Office of Management and Budget, *Report on Statistical Disclosure Limitation Methodology*, Federal Committee on Statistical Methodology, Statistical Working Paper #22 (2006, http://www.fcsm.gov/working-papers/SPWP22_rev.pdf); and
- Professional association guidelines, such as the American Statistical Association's statement, *Data Access and Personal Privacy: Appropriate Methods of Disclosure Control* (December 6, 2008, <http://www.amstat.org/news/statementondataaccess.cfm>).

BEYOND THE HIPAA PRIVACY RULE: ENHANCING PRIVACY, IMPROVING HEALTH THROUGH RESEARCH (2009)

This report of the Institute of Medicine responded to a request from the National Institutes of Health, the National Cancer Institute, the Robert Wood Johnson Foundation, the American Cancer Society, the American Heart Association/American Stroke Association, the American Society for Clinical Oncology, the Burroughs Wellcome Fund, and C-Change for a study committee to undertake two tasks:

- (1) to assess whether the HIPAA Privacy Rule is having an impact on the conduct of health research, defined broadly as “a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge”; and
- (2) to propose recommendations to facilitate the efficient and effective conduct of important health research while maintaining or strengthening the privacy protections of personally identifiable health information.

The committee concluded the following:

The HIPAA Privacy Rule does not protect privacy as well as it should, and that, as currently implemented, the HIPAA Privacy Rule impedes important health research. The committee found that the Privacy Rule (1) is not uniformly applicable to all health research, (2) overstates the ability of informed consent to protect privacy rather than incorporating comprehensive privacy protections, (3) conflicts with other federal regulations governing health research, (4) is interpreted differently across institutions, and (5) creates barriers to research and leads to biased research samples, which generate invalid conclusions.

Recommendation I. Develop a New Approach to Protecting Privacy in All Health Research

The committee’s first and foremost recommendation (Recommendation I) is that Congress should authorize HHS and other relevant federal agencies to develop a new approach to protecting privacy in health research that would apply uniformly to all health research. When this new approach is implemented, HHS should exempt health research from the HIPAA Privacy Rule. The new approach should enhance privacy protections through improved data security, increased transparency of activities and policies, and greater accountability, while also allowing important health research to be undertaken with appropriate oversight. The new approach should do all of the following:

- Apply to any person, institution, or organization conducting health research in the United States, regardless of the source of data or funding.
- Entail clear, goal-oriented, rather than prescriptive, regulations.
- Require researchers, institutions, and organizations that store health data to establish strong data security safeguards.
- Make a clear distinction between the privacy considerations that apply to interventional research and research that is exclusively information based.

- Facilitate greater use of data with direct identifiers removed in health research, and implement legal sanctions to prohibit unauthorized reidentification of information that has had direct identifiers removed.
- Require ethical oversight of research when personally identifiable health information is used without informed consent. HHS should develop best practices for oversight that should consider:
 - o Measures taken to protect the privacy, security, and confidentiality of the data;
 - o Potential harms that could result from disclosure of the data; and
 - o Potential public benefits of the research.
- Certify institutions that have policies and practices in place to protect data privacy and security in order to facilitate important largescale information-based research for clearly defined and approved purposes, without individual consent.
- Include federal oversight and enforcement to ensure regulatory compliance.

*NOTE: The material in this document was prepared by National Academies staff from published reports of study panels and committees. It is faithful to those reports and does not go beyond them.

Reports on Privacy and Confidentiality and Access to Research Data from the National Academies

The challenge of providing for data access while protecting privacy, ensuring confidentiality, and minimizing risk of advertent or inadvertent disclosure has engaged the attention of federal agencies, the National Academies, and the scientific community for over three decades. Below is a chronological list of major reports from the National Research Council and the Institute of Medicine.

National Research Council. (1979). *Privacy and confidentiality as factors in survey response*. Washington, DC: National Academy of Sciences.

National Research Council. (1985). *Sharing research data*. Washington, DC: National Academy Press.

National Research Council. (1993). *Private lives and public policies: Confidentiality and accessibility of government statistics*. Washington, DC: National Academy Press

National Research Council. (2000). *Improving access to and confidentiality of research data: Report of a workshop*. Washington, D.C.: National Academy Press.

Institute of Medicine. (2000). *Protecting data privacy in health services research*. Washington, DC: National Academy Press.

Institute of Medicine. (2002). *Responsible research: a systems approach to protecting research participants*. Washington, DC: The National Academies Press.

National Research Council. (2003). *Protecting participants and facilitating social and behavioral sciences research*. Washington, DC: The National Academies Press.

National Research Council. (2005). *Expanding access to research data: Reconciling risks and opportunities*. Washington, DC: The National Academies Press.

Institute of Medicine. (2006). *Effect of the HIPAA privacy rule on health research: Proceedings of a workshop presented to the National Cancer Policy Forum*. Washington, DC: The National Academies Press.

National Research Council. (2006). *Improving business statistics through interagency data sharing: Summary of a workshop*. Washington, DC: The National Academies Press.

National Research Council. (2007). *Putting people on the map: Protecting confidentiality with linked social-spatial data*. Washington, DC: The National Academies Press.

National Research Council. (2007). *Engaging privacy and information technology in a digital age*. Washington, DC: The National Academies Press.

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