United States Department of Health and Human Services
Office for Civil Rights
Attention: Privacy 2
Hubert H. Humphrey Building, Room 425A
200 Independence Avenue, S.W.
Washington, D.C. 20201

Ladies and Gentlemen:

As a committee charged with advising the Secretary of the Department of Health and Human Services regarding human subjects research, the National Human Research Protections Advisory Committee ("NHRPAC") over the past several months has considered the difficulties in implementing the Privacy Regulations issued in December 2000 by the Department under the Health Insurance Portability and Accountability Act of 1996 ("HIPAA"). At NHRPAC's July 2001 plenary meeting, Ms. Julie Kaneshiro of the Office of Science Policy at the National Institutes of Health gave a detailed presentation on these issues. Further, in their own roles at their respective institutions and organizations, the individual members of NHRPAC have come to understand and appreciate, in a direct and first-hand way, some of the problems associated with the implementation of the HIPAA rules in the context of research involving human subjects. NHRPAC fully and strongly supports the Department's commitment to enhancing privacy protections for human research subjects, and notes that consideration of privacy issues has been a required part of the research application and approval process under the Common Rule. At this time, based our understanding of the Final Rule and our analysis of the amendments to that Rule proposed on March 27, 2002, NHRPAC writes to offer comments and suggestions to the Department in regard to the Notice of Proposed Rule Making ("NPRM").

1. <u>The Compilation of Data Preceding Approved Research</u>

   Many institutions, especially academic medical centers that treat large numbers of patients who have diseases of research attention and interest, currently maintain systems by which patient data are compiled, often by electronic means, and sorted by diagnosis, diagnosis codes, DRGs, procedure codes or other means. The purpose of this data compilation is not to conduct research at time of collection (nor is the compilation for treatment, payment or health care operations), but to facilitate the formulation of research

projects and to facilitate their implementation once approved by IRBs. Although the HIPAA regulations contain an allowable use and disclosure by researchers of protected health information ("PHI") for uses preparatory for research, both the regulations and the commentary accompanying the issuance of the regulations (the "Preamble") appear to contemplate the use and disclosure of existing data in the form as stored in the covered entity's Designated Record Set. Neither the regulations nor the Preamble contemplates a pre-research practice by which a covered entity may decide to compile PHI in systematic ways to assist researchers in their reviews preparatory to research and/or to make that research more efficient and less costly once conceptualized, submitted as an application, and approved. Further, many institutions use similar methods to compile human tissues, not in order to conduct research, but to have the tissue banks available so that future research studies might be possible, upon IRB approval. In compiling such tissue banks, information about patients is, in a HIPAA sense, used by health care staff, and yet such uses are not "operations" under a HIPAA definition and thus are not clearly allowed by patients' HIPAA consents.

Although the Guidance issued by the Department on July 6, 2001 includes a question and answer section that seems to have been intended to address these issues, and although the NPRM contains similar suggestions, we continue to be concerned that the recommended use of a Privacy Board, or of an IRB sitting as a Privacy Board, to approve these pre-research compilations of data is not consistent with the text of the regulations. Waiver or alteration of authorization requirements is allowed only, by the terms of the HIPAA regulations, for "research." For Common Rule and other research purposes, "research" signifies an actual research protocol, approved by an IRB, or exempt from IRB approval under specific categories, and would not include a data or tissue compilation that is undertaken to facilitate future approved protocols. For this reason, explicit amendment of the HIPAA regulations to allow privacy board approval of this additional pre-research use of data would give greater assurance to hospitals and other providers that these prevalent practices will continue to be allowed.

For the HIPAA regulations to be amended to allow such pre-research compilation and sorting of data (and similar practices for identified tissue bank compilations) would not seem to endanger or in any way undermine the HIPAA protections for PHI, since the data compiled would be neither used nor disclosed except for uses and disclosures allowed under applicable HIPAA regulations, such as in reviews preparatory to research, or in reviews authorized by patients/subjects or authorized by a HIPAA Privacy Board. Similarly, tissues and the data attached to those tissues could not be used or disclosed without both IRB and Privacy Board approvals. NHRPAC therefore suggests that such practices be allowed, either by amendment to the research authorization exception relating to reviews preparatory to research, or through a process by which the Privacy Board (or IRB sitting as a Privacy Board) might consider and approve applications to build and maintain such pre-research databases and/or tissue banks.

2. Subject Withdrawal of HIPAA Authorization after Conclusion of a Research Project

Under the HIPAA regulations, subjects who consent to research involving treatment must also execute a HIPAA authorization to allow the investigators, the IRB, research administrators and others to use and disclose their PHI for research purposes. At the same time, under HIPAA rules relating to authorizations for use and disclosure, a person who has signed an authorization has the right, with few exceptions, to withdraw that authorization at any time. If such a withdrawal of an authorization occurs, no additional use or disclosure of that person's PHI is allowed. This is extremely problematic for human subjects research.

Under the Common Rule and under applicable standards for the ethical conduct of research, a subject is allowed to withdraw his or her consent to participate in the research at any time, and may not be compelled to continue participation in the project. Under pre-HIPAA practice, if a subject withdrew his or her consent to continue in the research, then there had been no question but that the researcher would still be allowed to compile, use and disclose the data that had previously been collected on the subject as described in the approved protocol. Thus, for example, if a subject terminated his or her participation after one stage of a multi-stage research project, that termination would not prevent the researcher from compiling, using and disclosing the subject's data in analyzing and reporting on the stage(s) of the project through which that subject had participated. Similarly, for those subjects who participated in a complete research project until its end, withdrawal of consent to the research after the research itself had terminated had no real meaning and no effect: in fact, under pre-HIPAA practice, for a subject to withdraw consent to the research after the collection of data had been completed would have been, for almost all purposes, nonsensical.[1]

Under the Final Rule as currently written, however, once research data collection has been accomplished (as, for example, after all clinical interactions with a subject have been completed during a clinical trial), a subject's withdrawal of authorization for the investigators and others to continue to use and disclose the already-gathered data could seriously affect the scientific validity of the research project. In the NPRM, the Department has tried to use the "reliance" exception to allow some limited uses by researchers of data after a subject's revocation of his or her HIPAA authorization, under a theory that researchers may need to use such data in order to report other data accurately. The difficulty with the use of this "reliance" exception, however, lies in the

[1] Please note, however, that in research in which consent may be gained from subjects in emergency circumstances (such as stroke or emergency cardiac conditions), IRBs may allow the subject to withdraw consent, and thus to end consent for use of data already collected, even after the clinical portion of the study has concluded. This option may be provided in order to mitigate the effect of any duress felt by the subject during the informed consent process that occurred under "emergency" medical conditions.

fact that some post-revocation uses of data may be indicated not simply due to the investigator's "reliance," but because the data themselves are unique and important. For example, if a subject experiences an adverse event during research and subsequently withdraws both informed consent and HIPAA authorization, the data relating to that adverse event may well not be essential to the reporting of other study data, and the investigator thus may not have the ability to argue "reliance" for use of the adverse event data. Moreover, the Department's suggested use of the "reliance" exception would place researchers and research institutions in a perilous position , as every post-revocation use of data could be the basis for a complaint from a research subject. (Indeed, these complaints might be quite likely, since the persons revoking their HIPAA authorizations are in fact the most likely of all subjects to utilize the HIPAA complaint process.) The burden of doubt thus would lie, in the Department's formulation, on researchers, and their likely reaction would be to forego use of data and thus avoid legal penalties. This could lead, very predictably, to the failure to use and analyze important research data that otherwise could increase knowledge, prevent injuries and even save lives.

To forestall this, NHRPAC would advise the Department to amend the regulations so that application may be made to a Privacy Board by an investigator that research data could continue to be used and disclosed after a withdrawal of a subject's authorization. Of course, under such an exception, a Privacy Board would not allow researchers to use or disclose data in ways that would publicly identify subjects, since after a subject's withdrawal of a research authorization, the researchers would remain subject to the limitations and restrictions on public disclosure contained both in the original authorization and in the IRB-approved research design. In making this determination, the Privacy Board should be charged with considering the circumstances of a subject's withdrawal of the authorization and the scientific need for the continued use of the data. Establishing a "safe harbor" process like this would remove the uncertainty inherent in the NPRM's suggested use of the "reliance" exception.

3. Duration of a HIPAA Research Authorization

NHRPAC also notes, more generally, that a HIPAA authorization requires a time limit or defined limiting event for the duration of the authorization; after that time or event, which must be specified in the research authorization, additional uses and disclosures of PHI would not be allowed. This also is extremely problematic in the research context. Although the Preamble to the Final Rule and the NPRM suggest that a research authorization might specify the "end of the research project" as a permissible terminating event, in fact the termination of a research project might not be appropriate at all as a definable termination point for the use and disclosure of PHI. For example, in clinical research conducted to support an FDA application, even long after a research project has "terminated" and its results have been reported, the investigators, sponsors and the FDA itself may need to revisit, re-examine, re-use and re-disclose PHI to consider adverse

events, to analyze new use applications or new proposed clinical guidelines for the drug, device or biotech agent, or to investigate charges of research misconduct. In non-clinical research conducted by or in a covered entity, similarly, use and re-disclosure of PHI might well be necessary for academic or research integrity oversight purposes long after the study itself has "terminated" and its results have been published.

For these reasons, NHRPAC suggests that the Department review the acceptable definition of a "termination event" in a HIPAA authorization, to allow researchers to define that event as "the termination of the research project, or the extinguishing of the need to review, analyze and consider the data generated by a research project, whichever is later." Alternately, the Department could specifically provide for a process by which a Privacy Board could accept, even on an expedited review basis, applications for additional uses and disclosures of research data after that research has terminated.

4. Absence of Requirements for HIPAA Authorization in "Research Not Involving Treatment"

The HIPAA regulations make a distinction between research involving treatment and research not involving treatment, specifically requiring a researcher to obtain a HIPAA research authorization only in research that involves treatment. In this way, the final HIPAA Privacy Rules mark a departure from those rules as proposed, in which such an authorization would have been required for both categories of research. NHRPAC notes that this distinction among two categories of research may not be sufficiently protective of research subjects. Although the regulations appear to assume that research not involving treatment presents somehow less risk to privacy than research involving treatment, such an assumption may not be correct. For example, research involving extraction of blood or tissue specimens from subjects for genetic research may not involve treatment at all, but the results of such research – the data gathered during the research itself – may have great significance for subjects, either under current or future interpretations of those testing results. Therefore, NHRPAC supports the Department's suggested elimination in the NPRM of the distinction between research involving treatment and research not involving treatment..

5. Use and Disclosure of PHI for Consideration and Enrollment of Subjects into Research

Since the HIPAA regulations allow treating physicians, health professionals, and others in covered entities to use and disclose PHI only pursuant to a HIPAA consent (and thus only for treatment, payment and health care operations purposes), persons acting within covered entities cannot, strictly speaking, use or disclose PHI to investigators for the purpose of proposing a patient or client for a clinical trial or other types of research projects, or discussing with an investigator a patient's or client's suitability for a particular research study. In fact, as the Final Rule is now written, in order to have such

a conversation, a provider within a covered entity should have a HIPAA authorization from the patient or client before initiating any such discussion or inquiry. Even if the person within the covered entity fails to use the patient's or client's name, such a conversation might involve PHI that is not "de-identified" for HIPAA purposes, under HIPAA's strict requirements for such information. Moreover, a physician may not under HIPAA regulations are written even initiate a conversation with a patient about his or her enrollment in a clinical trial, since this would ab initio be a use of the patient's PHI for other than treatment, payment or operations purposes.

This state of affairs is not sustainable in the course of clinical practice with patients and clients, as it imposes a huge and unnecessary burden on clinicians and others acting in covered entities, who must have some latitude to propose patients and clients for study enrollment and to facilitate that enrollment for patients and clients who so desire, without gaining a separate HIPAA authorization.

There are, in fact, two schools of thought within NHRPAC in regard to this set of issues. To some NHRPAC members, as to others in academic medicine, the requirement for an authorization in these circumstances demonstrates the very real ways in which HIPAA will complicate, and ultimately undermine, clinical research. To these members, the Common Rule's requirement that IRBs consider privacy and confidentiality issues within the context of each research protocol adequately protects the rights of human subjects. Others within NHRPAC's membership, appreciate the need for application of more strict federal standards relating to the privacy of medical information within research, but also recognize that some major aspects of the HIPAA regulations unnecessarily and excessively complicate the research process, and also recognize this area as being one example.

Accordingly, if the Department is insistent upon requiring HIPAA authorizations as part of human subjects research, a more appropriate and efficient method of addressing any risk to privacy here would be to allow treating clinicians and others in a relationship with a patient or client that is governed by HIPAA to make research eligibility inquiries and to have such subject suitability and eligibility discussions with investigators, provided that (1) the information disclosed is the minimum necessary to accomplish the purpose of the use and disclosure (for example, not disclosing information such as name that would allow identification of the patient) and (2) the investigator with whom the discussion is held and to whom the PHI is disclosed is himself or herself subject to HIPAA regulations as acting for or within a covered entity.

Another alternative perhaps more acceptable to privacy advocates would be to allow the physician or other provider to acquire a HIPAA authorization allowing the use of the patient's PHI for seeking enrollment of the patient into clinical trials, without specifying in the HIPAA authorization the persons to whom the PHI would be disclosed and the

exact information to be disclosed, but retaining the authorization requirements of specified duration and purpose, and adding the requirement for the minimum necessary disclosure. (In this alternative, the Department likely should require that the physician disclose to the patient any remuneration received by virtue of referral of the patient into a clinical trial or other research study.) This would allow the patient, prospectively, to discuss with his or her physician clinical trial enrollment, and the patient could choose whether to execute such an authorization.

In any event, for the Department not to remedy this problem would result in enormous inefficiencies in the research enrollment process, and might even deter some clinicians from proposing patients or clients for studies, and some patients from having ready access to protocols in which they would like to enroll.

6. The Standards for Privacy Board Consideration of Waiver or Alteration of HIPAA Authorization Requirements

One of the aspects of the Privacy Rule that has provoked great concern has been the eight criteria that a Privacy Board, or IRB sitting as a Privacy Board, must consider when addressing applications for waiver or alteration of HIPAA authorization requirements in research. The eight criteria are, in fact, vague and uncertain, especially when one considers the lack of precedential standards that such an entity or committee might use in evaluating privacy interests and risks to privacy. There does seem to NHRPAC to be an essential ambiguity in the standards, for while the HIPAA regulations and Preamble indicate that a Privacy Board should evaluate only subjects' privacy interests, those interests are most often interwoven with and intimately connected to subjects' overall safety and welfare. Further, although it is likely that some of the apprehension with which covered entities now view these privacy criteria will dissipate with actual experience, there is a real risk that Privacy Boards may be so strict in their application of these eight criteria that their judgments will significantly handicap the conduct of clinical research, which already must abide by privacy parameters set by IRBs under Common Rule requirements. Those parameters invariably include the requirement that research be reported publicly only in ways that would not identify subjects, thus already providing a bedrock of privacy protection to subjects.

NHRPAC therefore supports the Department's suggestion revision of the eight criteria, so that those eight become more refined and are limited to three. The ultimate goal of a Privacy Board review must be to assure that waiver or alteration of authorization requirements is granted only in cases in which there is a real need for such waiver or alteration (due to efficiency and practicability concerns) and in which the privacy interests of subjects are not in any significant or material way compromised by the use and disclosure of PHI in the research context. NHRPAC also suggests that in light of the lack of precedent in this area, the Department issue guidance built around case examples

in which the final criteria are applied in ways that the Department finds acceptable. Among the features of such case examples should be measures that might be required by Privacy Boards of researchers to safeguard subjects' rights when a waiver or alteration of authorization requirements is granted.

NHRPAC also would suggest that the Department clarify whether an IRB, if sitting as a Privacy Board, may hold its meetings simultaneously both as an IRB and as a Privacy Board, and whether unified minutes, with required findings under both the Common Rule and the HIPAA regulations, would be acceptable. Further guidance by the Department on these matters would assist the national research community greatly in its implementation of the Final Rule.

7. Standards for De-Identification of Data

NHRPAC strongly suggests that the Department review the standards for de-identification of data in order to reduce the number of data categories that must be eliminated for data to be regarded as de-identified and thus not protected as PHI under HIPAA standards. Among those data categories that should be strongly considered for deletion from the de-identification standards are zip codes and geographic subdivisions. While the specific addresses of persons should not be included in de-identified information, their areas of residence, work or origin, may, in fact, be essential to epidemiologic and other studies of, for example, cancer incidence. For the efficiency of essential research, NHRPAC encourages the Department to reconsider its de-identification standard, reduce the number of data categories to be eliminated, and focus regulatory attention on the safeguards that researchers using such information should respect in recording and publishing data. A "goal-oriented" revision of the regulation could protect subjects' privacy while not rendering critical research excessively costly and troublesome to undertake.

NHRPAC thanks the Department for its consideration of these comments and suggestions as it proceeds with the issuance of its Notice of Proposed Rule Making for the HIPAA Privacy Rules. NHRPAC stands ready to assist the Department and to offer other help as requested.

Respectfully,

Mary Faith Marshall, Ph.D.
Chairperson, NHRPAC

cc: Dr. Eve Slater
Dr. Greg Koski
Kate Gottfried
NHRPAC Members