

Citizens for Responsible Care and Research, Inc. (CIRCARE)
(A wholly independent, volunteer, non-profit, tax-exempt organization,
incorporated under the laws of the State of New York)

1024 North 5th Street
Philadelphia, Pennsylvania 19123-1404
www.circare.org; web@circare.org
215.627.5335

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Jerry Menikoff, M.D., J.D.
Office for Human Research Protections
1101 Wootton Parkway, Suite 200
Rockville, Maryland 20852

VIA: Federal eRulemaking Portal: <http://www.regulations.gov>

In re: Docket ID Number HHS-OPHS-2015-0008:

Notice of proposed rulemaking, Federal Policy for the Protection of
Human Subjects, Docket ID Number HHS-OPHS-2015-0008, 80 Fed.
Reg. 53,933-54,061 & 73,679-73,680 (2015).

This responds to the joint announcement by the Office of the Secretary of
the Department of Health and Human Services (HHS) and cooperating
departments and agencies of proposed rulemaking to amend the Common Rule,
human subjects protection regulations codified at 46 C.F.R. pts. 46, 160, and 164,
at 21 C.F.R. pts. 50 and 56, and in related regulations of other Federal entities.

Citizens for Responsible Care and Research, Inc. (CIRCARE) is the oldest
human research protection organization in the United States and is entirely
independent. We advocate conscionable research. We are a network of private
citizens dedicated to effective protection of human subjects in behavioral and
biomedical research. Our board members and officers are from science, law,
research policy, ethics, medicine, nursing, social work, education, and
care-giving. Some of have been voluntary subjects of research. Our experience
includes governmental and academic Institutional Review Board membership and
chairmanship and university faculty in national and international law and ethics of
human subjects research. We serve without pay. CIRCARE receives no support
from industry or government.

We address: (A) applicable law and legislative intent; (B) NPRM
numbered questions, and (C) general concerns in response to this NPRM.
Although this response is directed to the Department of Health and Human
Services, as the lead agency for this project, we intend it as applicable to all
Common Rule agencies. Repetitive questions in the NPRM necessitate some
repetitive answers; we cross-reference our responses where practical. Our

response to any one question applies to all related questions. We respond also to NPRM issues for which the notice poses no direct questions.

A. APPLICABLE LAW AND LEGISLATIVE INTENT.

STATUTORY AUTHORITY FOR THE COMMON RULE IS A MANDATE TO PROTECT THE RIGHTS OF HUMAN SUBJECTS OF RESEARCH.

THE LAW EXPRESSLY MANDATES PROTECTION OF THE RIGHTS OF HUMAN SUBJECTS OF RESEARCH WHETHER BIOMEDICAL OR BEHAVIORAL RESEARCH.

HHS' primary statutory authority for the current Common Rule is a mandate to protect the rights of human subjects of biomedical or behavioral research. Legislative intent is clear, at 42 U.S.C. sec. 289(a) (emphasis added):

Sec. 289. Institutional review boards; ethics guidance program

(a) The Secretary shall by regulation require that each entity which applies for a grant, contract, or cooperative agreement under this chapter for any project or program which involves the conduct of *biomedical or behavioral research involving human subjects* submit in or with its application for such grant, contract, or cooperative agreement assurances satisfactory to the Secretary that it has established (in accordance with regulations which the Secretary shall prescribe) a board (to be known as an "Institutional Review Board") *to review biomedical and behavioral research involving human subjects* conducted at or supported by such entity *in order to protect the rights of the human subjects of such research.*

OTHER RESEARCH-RELATED FEDERAL STATUTES SIMILARLY REFLECT PROTECTIVE INTENT.

Other federal statutes, directed to specific departments and agencies, similarly evince protective intent. See, e.g., the Family Educational Rights and Privacy Act (FERPA) (20 U.S.C. § 1232g), the Protection of Pupil Rights Amendment (PPRA) (20 U.S.C. § 1232h); the informed-consent requirement in the Newborn Screening Saves Lives Reauthorization Act of 2014, Pub. L. No. 113-248 (2014); and Department of Homeland Security organic legislation, the Intelligence Reform and Terrorism Prevention Act, Pub. L. No. 108-458 sec. 8306 (2004). The Homeland Security law defers to the Common Rule, 45 C.F.R. part 46, and implements its human subjects protection mandate in U.S. Dep't of Homeland Security, DHS Directive MD No. 026-05 rev. no. 00 (2007), Protection of Human Subjects, which reiterates the Common Rule. The legislative reference was to the then-extant Common Rule, not to some such formulation as whatever the Common Rule might be. See also the Intelligence Reform and Terrorism Prevention Act of 2004, Pub. L. No. 108-458 secs. 1061 et seq., evidencing

legislative intent to safeguard personal privacy and comply with the Privacy Act, 5 U.S.C. sec. 552a, even in operational intelligence work involving information technologies. The Privacy Act itself is intended as protective of personal privacy although as a practical matter is difficult to use and allows certain government data access.

THE LAW CONSISTENTLY EMPHASIZES FULLY VOLUNTARY INFORMED CONSENT AS A PRECONDITION FOR A RESEARCH INTERVENTION INTO SOMEONE’S LIFE. FEDERAL JURISPRUDENCE HAS APPLIED THIS REQUIREMENT TO SOCIAL AND BEHAVIORAL RESEARCH AS WELL AS TO BIOMEDICAL RESEARCH.

The law has long applied informed “knowing, intelligent, voluntary and aware consent,” which requires circumstances conducive to voluntariness, to social and behavioral as well as biomedical research. The law here is Constitutional. *Merriken v. Cressman*, 364 F. Supp, 913 (E. Pa. 1973).

THE UNITED STATES IS A STATE PARTY TO THE INTERNATIONAL COVENANT ON CIVIL AND POLITICAL RIGHTS, WHICH BARS NON-CONSENSUAL MEDICAL AND SCIENTIFIC RESEARCH ON HUMAN BEINGS.

THE UNITED STATES HAS ASSURED THE INTERNATIONAL COMMUNITY THAT NON-CONSENSUAL RESEARCH IS BARRED BY THE U.S. CONSTITUTION AS WELL AS BY THE INTERNATIONAL COVENANT ON CIVIL AND POLITICAL RIGHTS.

U.S. obligations under international human rights law apply to anyone operating under U.S. Government authority whether within or outside the United States.

The U.S. Government’s legal obligation to protect the rights of human subjects of research subject is expressed also in binding commitment to the international community. The United States is a state party to the International Covenant on Civil and Political Rights (ICCPR), Done at New York December 16, 1966, entered into force March 23, 1976; for the United States September 8, 1992, T.I.A.S., 999 U.N.T.S. 171 (168 ratifications as of 2015); see also: Restatement (Third) of the Foreign Relations Law of the United States sec. 702 (1986). The ICCPR provides in pertinent part:

No one shall be subjected to torture or to cruel, inhuman or degrading treatment or punishment. In particular, *no one shall be subjected without his free consent to medical or scientific experimentation.* Int’l Covenant on Civil & Political Rights, art. 7 (emphasis added).

“*No derogation*” from Article 7 may be made even in times of public

emergency.” Int’l Covenant on Civil & Political Rights, art. 4 (2) (emphasis added). In other words, the prohibition of medical or scientific experimentation of human subjects without their “free consent” is absolute (except where the intervention is for the direct medical benefit of an individual patient and no alternative is available).

The United States, officially reporting its ICCPR compliance, has assured the international community that it deems non-consensual experimentation on human beings Constitutionally impermissible. U.S., Initial reports of States parties [to the International Covenant on Civil and Political Rights] due in 1993; United States of America (CCPR Human Rights Comm., State Party Report CCPR/C/81/Add.4, 1994), <[http://www.unhchr.ch/tbs/doc.nsf/\(Symbol\)/da936c49ed8a9a8f8025655c005281cf](http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/da936c49ed8a9a8f8025655c005281cf)> (last visited Nov. 20, 2015). The U.S. position is that the ICCPR prohibition on non-consensual research applies very broadly, domestically as well as in transnational research:

178. Medical or scientific experimentation. Non-consensual experimentation is illegal in the U.S. Specifically, it would violate the Fourth Amendment’s proscription against unreasonable searches and seizures (including seizing a person’s body), the Fifth Amendment’s proscription against depriving one of life, liberty or property without due process, and the Eighth Amendment’s prohibition against the infliction of cruel and unusual punishment.

179. Comprehensive control of unapproved drugs is vested by statute in the federal Food and Drug Administration (FDA). The general use of such drugs is prohibited, see 21 U.S.C. section 355(a), but the FDA permits their use in experimental research under certain conditions. 21 U.S.C. sections 355(i), 357(d); 21 C.F.R. section Part 50. The involvement of human beings in such research is prohibited unless the subject or the subject’s legally authorized representative has provided informed consent, with the limited exceptions described below. The FDA regulations state in detail the elements of informed consent. 21 C.F.R. sections 50.41-50.48.

180. An exception is made where the human subject is confronted by a life-threatening situation requiring use of the test article, legally effective consent cannot be obtained from the subject, time precludes consent from the subject’s legal representative, and there is no comparable alternative therapy available. . . .

181. The United States has also undertaken substantial efforts to diagnose and redress injuries that may have been caused by past exposure to potentially dangerous military agents. Thus, it continues to fund epidemiological studies in an attempt to resolve lingering scientific and medical uncertainty surrounding the long-term health effects of exposure to herbicides containing dioxin and to ionizing radiation. . . .

182. In December 1993, it became widely known that between 1944 and 1974 the United States Government conducted and sponsored a number of experiments involving exposure of humans to radiation. While certain experiments resulted in valuable medical advances including radiation treatment for cancer and the use of isotopes to diagnose illnesses, a number of the experiments may not have been conducted according to modern-day ethical guidelines. Moreover, the majority of the records of the experiments were kept secret for years. The United States Government has taken a number of steps to investigate the propriety of the experiments. . . . By executive order in January 1994, the President established the Advisory Committee on Human Radiation Experiments, which is charged with investigating the propriety and ethics of all human radiation experiments conducted by the Government, and determining whether researchers obtained informed consent from their subjects. . . .

183. Experimentation on prisoners is restricted by the Fourth, Fifth, and Eighth Amendments to the United States Constitution, by statutes, and by agency rules and regulations promulgated in response to such provisions. As a general matter, in the United States, "[e]very human being of adult years or sound mind has a right to determine what shall be done with his own body ...". *Schloendorff v. Society of New York Hospitals*, 211 N.Y. 125, 105 N.E. 92, 93 (1914). Accordingly, prisoners are almost always free to consent to any regular medical or surgical procedure for treatment of their medical conditions. Consent must be "informed": the inmate must be informed of the risks of the treatment; must be made aware of alternatives to the treatment; and must be mentally competent to make the decision. But due to possible "coercive factors, some blatant and some subtle, in the prison milieu", (James J. Gobert and Neil P. Cohen, *Rights of Prisoners*, New York: McGraw Hill, Inc., 1981, pp. 350-51) prison regulations generally do not permit inmates to participate in medical and scientific research.

184. The Federal Bureau of Prisons prohibits medical experimentation or pharmaceutical testing of any type on all inmates in the custody of the Attorney General who are assigned to the Bureau of Prisons. 28 C.F.R. section 512.11(c).

185. Moreover, the federal government strictly regulates itself when conducting, funding, or regulating research in prison settings. An Institutional Review Board, which approves and oversees all research done in connection with the federal government, must have at least one prisoner or prisoner representative if prisoners are to be used as subjects in the study. Research involving prisoners must present no more than a minimal risk to the subject, and those risks must be similar to risks accepted by non-prisoner volunteers. See 28 C.F.R. Part 46. Furthermore, guidelines established by the Department of Health and Human Services

provide that the research proposed must fall into one of four categories:

- "(1) Study of the possible causes, effects, and processes of incarceration, and of criminal behaviour, provided that the study presents no more than a minimal risk and no more than inconvenience to the subject;
- (2) Study of prisons as institutional structures or of prisoners as incarcerated persons, provided that the study presents no more than minimal risk and no more than inconvenience to the subject;
- (3) Research on conditions particularly affecting prisoners as a class;
- (4) Research on practices, both innovative and accepted, which have the intent and reasonable probability of improving the health and well-being of the subject."

45 C.F.R. section 46.306(a)(2).

186. Similar standards have been developed within the broader correctional community that strictly limit the types of research conducted in prisons, even with an inmate's consent. For example, in its mandatory requirements for institutional accreditation, the American Correctional Association (ACA) stipulates that:

"Written policy and practice prohibit the use of inmates for medical, pharmaceutical, or cosmetic experiments. This policy does not preclude individual treatment of an inmate based on his or her need for a specific medical procedure that is not generally available (emphasis added)."

Mandatory Standard 3-4373, Section E, "Health Care", in Standards for Adult Correctional Institutions, 3rd ed., Laurel, Maryland: American Correctional Association, January 1990, p. 126.

The commentary accompanying this mandatory regulation reads:

"Experimental programmes include aversive conditioning, psychosurgery, and the application of cosmetic substances being tested prior to sale to the general public. An individual's treatment with a new medical procedure by his or her physician should be undertaken only after the inmate has received full explanation of the positive and negative features of the treatment."

(Id.)

187. Non-medical, academic research on inmates is normally allowable in federal and state prisons with the inmate's express consent. This type of research normally consists of inmate interviews and surveys. Inmates are not required to participate in any research activities other than those conducted by correctional officials for purposes of inmate classification, designation, or ascertaining inmate programme needs (e.g., employment preparation, educational development, and substance abuse and family counselling).

U.S., Initial reports of States parties [to the International Covenant on Civil and Political Rights] due in 1993; United States of America (CCPR Human Rights Comm., State Party Report CCPR/C/81/Add.4, 1994), <[http://www.unhchr.ch/tbs/doc.nsf/\(Symbol\)/da936c49ed8a9a8f8025655c005281cf](http://www.unhchr.ch/tbs/doc.nsf/(Symbol)/da936c49ed8a9a8f8025655c005281cf)> (last visited Aug. 24, 2011).

EXECUTIVE ORDER REQUIRES U.S. DEPARTMENTS AND AGENCIES TO IMPLEMENT U.S. HUMAN-RIGHTS TREATY COMMITMENTS.

All U.S. Government departments and agencies long have been under Presidential order to implement the Covenant and other human rights treaties to which the United States is a state party. Exec. Order No.13,107, 63 WEEKLY COMP. PRES. DOC. 68,991 (Dec. 15, 1998).

WORLD HEALTH ORGANIZATION REGULATIONS REITERATE OBLIGATIONS TO RESPECT INTERNATIONAL HUMAN RIGHTS LAW.

The International Health Regulations (2005) declare that implementation "shall be with full respect for the dignity, human rights and fundamental freedoms of persons." The implication is that no shortcuts may be taken in protections for human subjects of public health research. World Health Organization, International Health Regulations (2005) (2d ed. 2008), art. 3 para.1.

U.S. OBLIGATIONS FOR HUMAN-SUBJECTS SAFEGUARDS UNDER INTERNATIONAL HUMANITARIAN LAW.

U.S. obligations under humanitarian law apply to anyone operating under U.S. Government authority whether within or outside the United States.

REFUGEES AND OTHER DISPLACED PERSONS.

The United States has relevant international legal obligations also as a state party to the 1967 Protocol Relating to the Status of Refugees, 19 U.S.T. 6223, T.I.A.S. No. 6577, 606 U.N.T.S. 267.

The Protocol obligates the United States to cooperate with the U.N. High Commissioner for Refugees (UNHCR) in conduct of the UNHCR's mission. The UNHCR's protective mission in turn requires deference to UNHCR administrative interpretations, including the paramount principle of personal security. "The personal security of refugees is an essential element of international protection. Unless the fundamental rights of refugees as human beings . . . are safeguarded, other rights . . . are of little use. Ensuring the safety of refugees and asylum seekers . . . has consequently been a major preoccupation of UNHCR and an important component of the Office's field activities." UNHCR, *The Personal Security of Refugees*, EC/1993/SCP/CRP.3, <http://www.refworld.org/docid/3ae68cd10.html> (5 May 5, 1993).

UNHCR thus cautions: "In the context of standard programming in refugee settings it is not recommended to do research on prevalence figures of mental disorders because this is methodologically complicated, requires specific resources and, most importantly, the research outcomes are not essential to design services." UNHCR, *Operational Guidance: Mental Health & Psychological Support Programming for Refugee Operations*, <http://www.refworld.org/docid/53a3ebfb4.html> (2013).

ADDITIONAL RESEARCH PROHIBITIONS IN WAR AND OTHER ARMED CONFLICTS.

The Geneva Conventions and Additional Protocols bind entire governments, not just their military, and apply at home and abroad in addition to, not in lieu of, international human rights law and other humanitarian law.

Common articles of the 1949 Geneva Conventions prohibit biological experiments for wounded or sick military at sea or in the field and prohibited medical or scientific experiments on prisoners of war unless justified by the individual prisoner's medical need and conducted in this individual prisoner's interests. The 1977 Additional Protocols to the Geneva Conventions apply to victims of armed conflicts. The Additional Protocols prohibit medical or scientific experiments on these persons even with their consent and for interned, detained, or otherwise held persons prohibit medical procedures not indicated by the individual's medical status and inconsistent with medical standards for free persons. Convention (I) for the amelioration of the condition of the wounded and sick in armed forces in the field. *Dated at Geneva August 12, 1949. Entered into force October 21, 1950; for the United States February 2, 1956.* 6 UST 3114; TIAS 3362; 75 UNTS 31. Convention (II) for the amelioration of the condition of the wounded, sick, and shipwrecked members of armed forces at sea. *Dated at Geneva August 12, 1949. Entered into force October 21, 1950; for the United States February 2, 1956.* UST 3217; TIAS 3363; 75 UNTS 85. Convention (III) relative to the treatment of prisoners of war. *Dated at Geneva August 12, 1949. Entered into force October 21, 1950; for the United States February 2, 1956.* Convention (IV) relative to the protection of civilian persons in time of war. *Dated at Geneva August 12, 1949. Entered into force October 21, 1950; for the*

United States February 2, 1956. 6 UST 3516; TIAS 3365; 75 UNTS 287. Protocol Additional to the Geneva Conventions of 12 August 1949, and relating to the Protection of Victims of International Armed Conflicts (Protocol I), 8 June 1977, done at Geneva June 8, 1977, and signed by the United States December 12, 1977; Protocol II Additional to the Geneva Conventions of 12 August 1949, and relating to the Protection of Victims of Non-International Armed Conflicts, done at Geneva June 10, 1977, and signed by the United States December 12, 1977 (Treaty Doc.: 100-2).

The International Committee of the Red Cross, charged with enforcement of the Geneva Conventions and Additional Protocols, provides this additional commentary: The “three pillars of healthcare ethics” are:

- “respect for the autonomy and dignity of the individual”;
- “maintaining confidentiality”; and
- “ensuring genuine and valid consent for any procedure.”

International Committee of the Red Cross, Health Care in Danger: The responsibilities of health-care personnel working in armed conflicts and other emergencies (August 2012) at 39
<https://www.icrc.org/eng/assets/files/publications/icrc-002-4104.pdf> (last viewed Nov. 21, 2015).

B. NPRM NUMBERED QUESTIONS.

The proposed rule would change the current rule substantially while retaining some of its weaknesses. Our comments address the NPRM questions and the entire rule as proposed.

I. The Rationale for Modernizing the Common Rule

C. Guiding Principles for Proposed Changes

1. Question for Public Comment

1. Public comment is sought on whether the proposed changes will achieve the objectives of (i) decreasing administrative burden, delay and ambiguity for investigators, institutions, and IRBs, and (ii) strengthening, modernizing, and making the regulations more effective in protecting research subjects.

We question the logic and contest the premises of the rationale presented in the preamble in the Notice of Proposed Rulemaking (NPRM). The NPRM preamble ignores critical points of law and fact and misrepresents critically important documents, and the proposed rule would be contrary to law.

The regulatory rationale presented in this NPRM would not satisfy long-standing juridical criteria for rulemakings. The NPRM does not relate the draft rule to the legal mandate for human subjects protections and does not scrutinize alternatives to the draft rule. See Statement of Basis and Purpose, in American Bar Association, Guide to Federal Agency Rulemaking (Jeffrey S. Lubbers, ed., 3d edition, 1998) at 216-268.

The NPRM rationale does not take into account highly relevant responses to the NPRM. The ANPRM proposed that behavioral and social scientists decide for themselves whether to be subject to IRB scrutiny. We responded that researchers could not be expected to be objective in excusing their own research from IRB scrutiny and that limiting IRB scrutiny in this regard would weaken human subjects protections and would contravene relevant law. The NPRM rationale disregards that portion of the record.

THE NPRM REGULATORY RATIONALE DOES NOT TAKE INTO ACCOUNT THE LAW'S PROTECTIVE INTENT OR ITS COVERAGE OF HUMAN SUBJECTS OF BEHAVIORAL AND SOCIAL AS WELL AS BIOMEDICAL SCIENCE.

The NPRM rationale does not consider protective obligations under law. In particular, HHS is required by 42 U.S.C. sec. 289a to ensure that biomedical and behavioral research on human subjects is reviewed for the purpose of protecting the rights of human subjects. The Federal agencies have no authority to exclude some or much of social and behavioral research from relevant Constitutional protections. See *Merriken v. Cressman*, supra. But the NPRM does not examine this issue either.

The NPRM rationale that removing or sharply curtailing some extant human subjects research protections, especially for behavioral and social science, would strengthen human subjects research protections over-all by allowing more emphasis on biomedical interventions is self-contradictory. The stated “risk-based” goal of providing stronger protections where warranted makes sense in itself. But the rationale and proposed rule would accomplish this by weakening or removing protections that are nonetheless required by law and warranted by fact. The drafters explained that there is a larger volume of research now. A sensible reading of that fact is that the required protective regulations should be applied accordingly; the NPRM does not consider this alternative.

Promulgating broad categories of research as a priori minimal risk or not worth review but re-examining the list every eight years do not substitute for weighing the ethical merits and drawbacks of individual research projects involving circumstances, subjects, and research activities that may differ significantly. But the NPRM rationale does not consider these issues.

The proposed Sec. ____102 amendment does not solve the problem. We have observed from IRB members' and administrators' discussions that IRB compliance may be desultory, and IRBs have been advised to do only the minimum absolutely required, and one result is an erroneous belief subjects are vulnerable only if in a group identified in the Common Rule subparts. The NPRM amendment provides for review of the minimal-risk list at intervals of no more than eight years. The NPRM says the default position is that anything on the list is in fact minimal risk and that IRBs may consider other categories as minimal risk if they see fit to do so. That is not protective.

THE NPRM MISREPRESENTS THE BELMONT REPORT, THE BASIC AND WIDELY FOLLOWED REGULATORY RATIONALE FOR THE CURRENT COMMON RULE.

The Belmont Report: Ethical Principles and Guidelines for the Protection of Human Subjects of Research (National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research, 1978) long has been the central statement of regulatory intent in Federal human subjects research regulation. Belmont's drafters declined to recommend specific policies for social experimentation, i.e., evaluations of social programs, but otherwise addressed social, behavioral, and biomedical research. The statement of regulatory intent for the original Common Rule incorporated Belmont by reference. The NPRM invokes Belmont but highly selectively. The NPRM drafters endorse Belmont's stated ethical principles—respect for persons; beneficence; and justice—as appropriate for compliance with the law. But then the drafters without explanation ignore the principles' content and implications and Belmont points that conflict with the proposed rule. Indeed, the drafters assert that reduction or elimination of certain protections is a way to promote the Belmont principles.

Belmont was more than a statement of principles. Application of those principles, the Belmont drafters said, would require *inter alia*:

- Informed consent:

“Respect for persons requires that subjects, to the degree that they are capable, be given the opportunity to choose what shall or shall not happen to them. This opportunity is provided when adequate standards for informed consent are satisfied.”

Elements of the consent process: “information, comprehension and voluntariness.”

- Review for validity of the research, for possible alternatives; for assessment of risks and benefits; for fair and valid selection of research subjects; and for unlikelihood of voluntariness:

“Thus, there should first be a determination of the validity of the presuppositions of the research; then the nature, probability and magnitude of risk should be distinguished with as much clarity as possible. The method of ascertaining risks should be explicit, especially where there is no alternative to the use of such vague categories as small or slight risk. It should also be determined whether an investigator's estimates of the probability of harm or benefits are reasonable, as judged by known facts or other available studies.”

“Risk can perhaps never be entirely eliminated, but it can often be reduced by careful attention to alternative procedures. . . . When research involves significant risk of serious impairment, review committees should be extraordinarily insistent on the justification of the risk (looking usually to the likelihood of benefit to the subject - or, in some rare cases, to the manifest voluntariness of the participation).”

“When vulnerable populations are involved in research, the appropriateness of involving them should itself be demonstrated. “

“Many kinds of possible harms and benefits need be taken into account. There are, for example, risks of psychological harm, physical harm, legal harm, social harm and economic harm and the corresponding benefits. While the most likely types of harms to research subjects are those of psychological or physical pain or injury, other possible kinds should not be overlooked.”

- Fairness and scientific justification for selection of subjects, and concern for the vulnerability of subjects:

“Risks and benefits of research may affect the individual subjects, the families of the individual subjects, and society at large (or special groups of subjects in society).”

Insofar as the NPRM rationalizes reduction or elimination of these protections, it contradicts its own assertion of faithful adherence to the Belmont principles, and it ignores the law's clear protective intent.

THE REGULATORY RATIONALE FAILS TO TAKE ACCOUNT OF THE DIFFERING IMPACTS OF BEHAVIORAL AND SOCIAL SCIENCE RESEARCH ON HUMAN SUBJECTS.

The NPRM drafters assume that the risk of particular categories of behavioral and social science research will be somewhat the same for all subjects and little or none for most subjects save perhaps for certain categories of persons deemed especially vulnerable. This approach conflicts with Belmont's

conclusions (1) that risk depends not only on the activity but also on the circumstances and vulnerabilities of individual subjects and their families and social groups, and (2) that claims of little or no risk should be scrutinized.

THE NPRM RATIONALE MISREPRESENTS THE NATIONAL RESEARCH COUNCIL BEHAVIORAL AND SOCIAL SCIENCE WORKSHOP SUMMARY ON WHICH IT RELIES HEAVILY.

For its treatment of issues of behavioral and social science research, the NPRM rationale relies heavily on assertions by behavioral and social scientists and their organizations. The NPRM rationale accords special weight to the National Research Council workshop document, Proposed Revisions to the Common Rule: Perspectives of Social and Behavioral Scientists: Workshop Summary (National Academies Press 2013). That reliance and the document therefore necessitate attention. In short, the document is not what the NPRM drafters said it is and on the critical issue of privacy does not say what the NPRM drafters reported.

The NPRM drafters asserted that the document is a National Research Council “consensus report . . . commissioned to ensure that the issues related to research involving human subjects in social and behavioral research would be addressed appropriately” It was a summary, by project organizers, of a workshop convened by a National Research Council committee and sponsored by social and behavioral science organizations. It does not reflect consensus among participants. According to the NPRM drafters, “The Panel made numerous recommendations, including recommendations about what research studies should not undergo review, about calibrating the level of IRB review to the level of risk, about the desirability of privacy and confidentiality protections in social and behavioral research other than those of the Health Insurance Portability and Accountability Act of 1996 (HIPAA), and about improving informed consent by placing greater emphasis on the process of consent.” The document, which has its strengths and weaknesses, actually says:

This report is a summary of the presentations and discussions that took place at the two-day workshop and does not offer additional comment, interpretation, or analysis. During discussion periods, speakers, committee members, and audience members commented on the presentations, and some of their comments are included in this summary. Although the perspectives of a broad range of behavioral and social scientists were provided at the workshop, some topics may not have been covered in sufficient depth. Among these are privacy issues and disclosure risks presented by advances in technology, such as data mining and tracking of individuals. The workshop also did not cover the full body of evidence on the functioning of the Common Rule and IRBs, particularly questions related to the evidence for over-regulation or under-regulation of human participants in social and behavioral sciences research. . . .

Proposed Revisions to the Common Rule: Perspectives of Social and Behavioral Scientists: Workshop Summary, at 3.

THE REGULATORY RATIONALE IS DISMISSIVE OF INSTITUTIONAL AND RESEARCHER LIABILITY EXPOSURE.

The regulatory rationale notes that responses to the ANPRM prompted questions of likely increase in institutional and researcher liability exposure. The drafters seem to interpret the term “liability” as meaning no more than being within the scope of this particular regulation. But liability means far more. It means accountability under the whole of the applicable law, including the law of torts. The rationale for the current proposal deals with such issues wrongly or not at all. For examples:

Proposed elimination of continuing review:

The regulatory rationale notes but does not respond to concerns that eliminating or curtailing this oversight mechanism could increase institutional and researcher liability exposure because of long-continuing, un-reviewed, often non-consensual research activities.

Proposed required reliance on central institutional review boards:

The regulatory rationale notes but does not respond to concerns that requiring reliance on central institutional review boards raises problems of accountability and increased institutional liability exposure.

Proposal that researchers determine for themselves that their work in some categories are not subject to institutional review board oversight:

The rationale says “it is expected that in many instances” an exemption decision tool, to be promulgated by the Department of Health and Human Services, “would be used by the investigators themselves, thus obviating both the need for further review and the concern that the institution might be subjecting itself to future liability by allowing investigators to use the tool.” But the Common Rule agencies have no legal authority to relieve any entity or person of legal liability exposure. The legal mandate is not to shield research entities and researchers from liability but to protect the rights of research subjects,

SHORT-CUTTING FULL CONSENT IS LIKELY TO IMPEDE BIOTECHNOLOGY DEVELOPMENT.

Contrary to the regulatory rationale, short-cutting full consent procedures for the taking and uses of biospecimens is likely to impede rather than help accelerate developments in biotechnology. The rationale is that research, development, and potential beneficial exploitation of biotechnology ought not to

be slowed by fully informed consent in circumstances conducive to voluntariness. But the rationale does not address the likelihood that ownership questions will arise—perhaps not so much involving persons whose biomaterials and related data were taken or donated—but rather involving secondary and subsequent uses, including use of these materials in commercial development. The slowing-down begins when these materials and rights to their use are transferred or sold (or if not sold, then transferred for a service fee) and there may be multiple claimants to ownership. How the problem originates is easy to see. As we learned from an ethics consult experience, a patient may go to more than one hospital, each of which routinely takes biospecimens and related data and there is little or no personal explanation and no opportunity to opt out. Perhaps the materials and data are for the patient’s care, perhaps not. Ultimately, there may be secondary, tertiary, and yet further uses. Research institutions and hospitals are entering into joint commercial agreements. It may be, then, that the one individual’s tissue or commercially interesting molecule or molecular fragment or sequence has many potential claimants in a patent-hungry industry.

Materials transfers involving publicly supported work at research institutions are thorny; in the commercial world they are yet more complex and expensive. It seems to us, therefore, that a recorded, clear, fully voluntary, consensual understanding, with discussion of ownership and choices, at the outset is a necessary protection not only for the person whose materials and data are taken but also for all subsequent users. “Sign here” and a poster on the wall do not suffice; this passive approach to “notice” presents a huge potential for backlash from subjects who did not understand what they were supposed to have agreed to.

ESSENTIAL REGULATORY IMPACT ANALYSES ARE LACKING.

The Regulatory Impact Analyses in the NPRM omit some highly relevant issues and fail to consider alternatives. Burdens of the proposal on human subjects of research, on research institutions, and on the Government itself are not considered.

Under the proposed rule the burdens on human subjects would include:

- Costs of recovery from losses incurred directly and indirectly from wrongful uses of their private information; and
- Injury and costs resulting from unaccountability for errors of omission and commission by private central institutional review boards operated for or as limited-liability entities.

But the Regulatory Impact Analyses do not acknowledge these burdens.

Nor do the Regulatory Impact Analyses consider increased tort liability exposure and possible losses from vulnerability to errors of omission and

commission by external IRBs. Government IRBs cannot indemnify in these situations, and commercial IRBs may have insufficient assets or be protected as limited-liability entities.

The Regulatory Impact Analyses fail to acknowledge the likelihood of investigatory and legal costs of ascertaining ownership of biomaterials and related data where the same individual has had biospecimens taken or has donated biospecimens at different facilities.

The Regulatory Impact Analyses fail to account for increased direct financial and personnel time costs to the Government for centralizing institutional review boards. Indiscriminate reliance on a single IRB for each multi-site human subject study within the NPRM definition of clinical trial would impose substantial operational burdens of time, costs, and personnel for the cognizant Federal agencies and Federal IRBs and would incur substantial costs for the use of commercial IRBs. Are the requisite conflict-of-interest standards, audit protocols, and audit procedures in place? How, for example, do National Institutes of Health staff ascertain and verify fitness and costs when an awardee institution hold investments in corporate parent of a commercial IRB? These questions involving subrecipients and subawards are not hypothetical. Uniform Administrative Requirements, Cost Principles, and Audit Requirements for Federal Awards, 2 C.F.R. pt. 200.

At the same time, IRB capabilities would have to be duplicated where institutions maintain IRBs for their other human subjects research and must continue to have to train and vet their researchers in the ethical conduct of research on human beings.

The NPRM assumes that coverage by the Privacy Act, 5 U.S.C. sec. 552a, justifies excluding certain currently covered social and behavioral research from any scrutiny. This is a no-cost-to-the-Government proposal if it is assumed that non-consensual behavioral and social research on identified individuals will never be discovered or, if discovered, will generate no inquiries. If the drafters deem the Privacy Act a realistic protection, then the Regulatory Impact Analyses should take into account likely costs to the Government and likely costs to individuals in connection with Privacy Act inquiries.

In sum, the conclusions of the Regulatory Impact Analyses to support curtailment or elimination of human subjects protections are based on the NPRM premises, not on disinterested consideration of significant legal and factual issues raised by this proposed rule.

INCREASED COMPLEXITY, INCREASED BURDENS

The proposed rule is extremely complex, replacing a relatively simple and well-established regulatory regime. The draft is a tangle that is perhaps amenable to checklists but not to serious judgment. The proposed rule imposes

on researchers and their institutions an additional burden of legal interpretation, and it expands liability exposure while making it more difficult for research institutions to manage their own activities. The ultimate burdens fall on research subjects, whether they fit the definitions or not. The proposed system is less transparent and as a practical matter less accountable. It expands the gulf between research and the necessary ethical and scientific reflection that should characterize conscionable, valid science.

II. Major Proposals To Modernize the Common Rule

A. Proposed Changes to the Scope and Applicability of the Regulations

1. Expanding the Definition of Human Subject to Cover Research With Non-identified Biospecimens (NPRM at Sec. Sec. __.102(e) and __.101(b)(3)(i))

f. Questions for Public Comment

2. Would providing a definition of biospecimen be helpful in implementing this provision?

We share concerns for stronger, clearer human subjects protections in connection with human biological materials and gene sequences. We suggest an easier approach:

The touchstone should be respect for persons, and data-mining technologies already are available. Therefore, the rule should be based on a rebuttable presumption that human biological materials and gene sequences when acquired are identifiable to individual persons and therefore are human subjects research and subject to the precondition of consent to their uses. This approach is far more realistic and far simpler than the primary proposal and alternatives presented.

Human biological materials and gene sequences that are not identified to an individual should be assumed to be identifiable and therefore subject to the human subjects protection rule upon any attempt or proposal to link them with any person or the records of any person. Problems arising can be handled with agency guidance.

3. . . . How . . . appropriate is the current modifier . . . ?

See above. The “may be” and “readily” terminology has been outdated by events.

4. Which of the three proposals regarding the definition of human subject achieves the most reasonable tradeoff between the principles of autonomy (including transparency and level of trust) versus beneficence as measured by facilitating valuable research)?

See above.

Autonomy “versus” beneficence is a false dichotomy that embraces (1) diminution of dignity and rights, and (2) an unsupported assumption that such activity is beneficent.

Much research is beneficent in intent, some in result; much is not. The drafters here harbored a version of the therapeutic misconception.

An allowable possibility of *sub rosa* use of such materials destroys trust.

5. Public comment is sought regarding any concerns that you have about each of the three proposals, including concerns about implementation or burden to investigators and institutions.

See above. A plainly written, easy-to-see regulation conducive to good-faith compliance is less burdensome than the proposed complicated latticework of narrow definitions, exclusions, exceptions, and exemptions.

2. Explicit Exclusion of Activities from the Common Rule

a. Exclusion of Activities That Are Deemed Not Research (NPRM at Sec. __.101(b)(1))

i. Program Improvement Activities (NPRM at Sec. __.101(b)(1)(i))

(2) Questions for Public Comment

6. Public comment is sought for whether this excluded activity should simply be discussed in the text of the final rule's preamble, and guidance produced to assist investigators in making such a determination, or whether any other similar exclusions should be addressed.

First, the institutional review board and not the investigator should make the determination of whether a specific collection or use of personal data or biological materials for other than direct care of the individual patient is excluded from Common Rule coverage.

This proposed exclusion is for a range of activities that do not readily fit a single category. Collection and analysis of biospecimens differ considerably from asking a patient about hospital meals.

These qualifiers are unclear: “if the data collection and analysis is limited to the use of data or biospecimens originally collected for any purpose other than the currently proposed activity, or is obtained through oral or written communications with individuals (e.g., surveys or interviews).” This implies that these data, analyses, and specimens can be used without real consent if the rationale for use is quality improvement no matter what the purpose of the original collection and no matter what restrictions have been imposed by the individual subject for primary and subsequent use, and no matter what the ethical and legal adequacy of the consent process if any.

A lot of research is done in the guise of administration or quality-improvement. Medicare has allowed some clinical trials as demonstration projects. This proposed exclusion is an open invitation to evasion of human subjects protection, even though the projects may put primary subjects and third parties at risk. While some hospital-based projects might pose relatively low hazard to primary subjects they may pose considerably more hazard to other parties, e.g., patients. This exclusion proposal should be stricken. If personal data and biological are to be collected and analyzed for other than the individual patient’s care, then that activity should be subject to the Common Rule.

In an appropriate section the rule can make plain the intent that administration and quality improvement not be a cover for research activities that would normally come within the purview of the Common Rule. Then agency guidance can deal with the arguments.

All work undertaken in whole or in part with research funding or to fulfill academic or other research requirements or for which research credit is claimed should be covered by the Common Rule.

7. Public comment is sought for whether biospecimens should not be included in any of these exclusion categories, and if so, which ones.

See above. Biospecimens should not be excluded from Common Rule coverage. They are often collected in circumstances not conducive to fully informed, voluntary consent.

ii. Oral History, Journalism, Biography, and Historical Scholarship Activities (NPRM at Sec. ____101(b)(1)(ii))

iii. Criminal Justice Activities (NPRM at Sec. 101(b)(1)(iii))

iv. Quality Assurance and Quality Improvement Activities (NPRM at Sec. ____101(b)(1)(iv))

v. Public Health Surveillance (NPRM at Sec. 101(b)(1)(v))

(2) Question for Public Comment

8. Public comment is requested on whether the parameters of the exclusions are sufficiently clear to provide the necessary operational guidance, or whether any additional criteria or parameters should be applied to clarify or narrow any of these exclusions.

Our response to Question 8 refers to NPRM items II.A.2.a.ii, iii, iv. & v. as well as to exclusions generally. Our comments here apply also to item II.A.2.a.vi., regarding intelligence and national security, although the NPRM does not request comment on this provision specifically.

Our responses to Questions 6 and 7 apply to the idea of exclusions generally and to Question 8 as well. Investigators are not disinterested and should not make the decision as to whether their projects do or do not come within the ambit of the Common Rule. All work undertaken in whole or in part with research funding or to fulfill academic or other research requirements or for which research credit is claimed should be covered by the Common Rule. The “the parameters of the exclusions” are not clear. These subtopics necessitate additional comment:

Oral History, Journalism, Biography, and Historical Scholarship Activities: If the activity includes the use of data or information for which original acquisition was subject to the Common Rule it should not be excluded from Common Rule coverage. The rule text itself doesn’t raise this problem; rather, the statement of intent does: The NPRM “does propose to explicitly exclude oral history, journalism, biography, and historical scholarship activities that focus directly on the specific individuals about whom the information or biospecimens is collected.” That’s an unclear but very big escape hatch. If there is a link to data gathered under the Common Rule or which should have been subject to Common Rule oversight, then the activities should not be excluded from Common Rule coverage.

Criminal Justice Activities: Investigations in pending and specific cases would not be funded as research. Research, development, and testing of technologies and methods relating to law enforcement and penology should not be excluded from the Common Rule when they seek or acquire data or biological material for identifiable individuals and are funded as research. An example of a technique-development activity was funded as research jointly by the National Science Foundation, Defense Advance Research Projects Agency, and the McDonnell Foundation. This is the recently published Indiana University-based non-consensual use of Twitter message content and metadata to track sources, dispersion, and destinations of political ideas in the Occupy Wall Street movement down to the individual, identified mobile telephone. Michael D. Conover et al. Geospatial Characteristics of a Social Movement Communication Network, PLOS ONE, <http://www.plosone.org/artile/info:doi/10.1371/journal.pone.0055957> (March 6, 2013). It seemed that researchers, perhaps assuming that Twitter users had agreed that anyone could use their data and metadata even if identifiable, could do what the U.S. Government itself was not supposed to do.

Individual cases and programs of government surveillance which the Committee examined raise questions concerning the inherent conflict between the government's perceived need to conduct surveillance and the citizens' constitutionally protected rights of privacy and dissent. It has become clear that if some lose their liberties unjustly, all may lose their liberties. The protections and obligations of law must apply to all. Only by looking at the broad scope of questionable activity over a long period can we realistically assess the potential dangers of intrusive government. For example, only through an understanding of the totality of government efforts against dissenters over the past thirty years can one weigh the extent to which such an emphasis may "chill" legitimate free expression and assembly.

Senate Select Committee to Study Governmental Operations with Respect to Intelligence Activities, Final Report: Foreign and Military Intelligence, Book I, 94th Cong., 2d sess. (1976) at 6-7.

Our concerns here apply as well to item II.A.2.a.vi., regarding intelligence and national security.

This proposed law enforcement and national security exclusions should be stricken as too fraught with ethical and legal hazard and with necessity to distinguish between research and operations.

Quality Assurance and Quality Improvement Activities: This exclusion proposal should be stricken. See our response to Question 6.

Public Health Surveillance: The NPRM statement of intent regarding this provision is nearly unexceptionable. The problem is that implementation of the apparent regulatory intent here is difficult.

The fields of public health and social programs are replete with technique-development research projects, ranging from small to large projects and from one-time to longitudinal. The subjects of these activities often are disadvantaged and highly vulnerable, and even if their consent is sought the circumstances are not conducive to voluntariness. These activities are often justified as operational rather than research although not part of any established or prototype series or immediate disease surveillance, and often gathering highly personal information from and about specific, identified individuals. Some persons are tracked from infancy on and are never informed that they are tracked. One troubling use of the public health rationale is the long-continuing School Associated Violent Death Study, a Centers for Communicable Diseases and Prevention (CDC) project in which telephone interviewers promise informants confidentiality and ask them to name and characterize “suspects,” who may not have been charged and who are never told of these inquiries, let alone that they are its real subjects.

In some instances there has been IRB oversight, however inadequate; in others, involving the same kinds of activities, there has been none.

vi. Intelligence Surveillance Activities (NPRM at
Sec. __.101(b)(1)(vi))

This proposed exclusion should be stricken, for the reasons given concerning law enforcement. Intelligence and national security have been used to rationalize experiments with dubious surveillance technique research. James Risen, *Pay Any Price: Greed, Power, and Endless War* (2014) Rachel Levinson-Waldman, *What the Government Does with Americans’ Data*, Brennan Center for Justice at New York University School of Law (2013). And the intelligence and national security rationale has been used for research and experimentation with unlawful interrogation techniques. David J. Hoffman, et al. Report to the Special Committee of the Board of Directors of the American Psychological Association: Independent Review Relating to APA Ethics Guidelines, National Security Interrogations, and Torture (Sidley Austin LLC 2015); Senate Committee on Armed Services, Report: Inquiry into the Treatment of Detainees in U.S. Custody, 110th Cong. 2d sess. (2008), passim; Senate Select Committee on Intelligence, Report: Committee Study of the Central Intelligence Agency’s Detention and Interrogation Program, S. Rep. 113-288, 113th Cong., 2d sess. (1914), passim; Steven H. Miles, *Oath Betrayed: America’s Torture Doctors* (2009) & *Doctors Who Torture* (2015).

In the national security area the line separating operations from research subject to Common Rule scrutiny evidently has not been clear enough. An example here is the Comprehensive-Fitness project, which we understand did not

undergo Common Rule scrutiny inasmuch as it was deemed training and not subject to Common Rule review. But progenitors of this project, which has gathered highly personal data on hundreds of thousands of military personnel and their families, have characterized it this way also:

One million soldiers taking the [Global Assessment Tool] is an unprecedented database for the prospective longitudinal study of the effects of psychological variables on physical health, mental health, and performance. The Soldier Fitness Tracker is the backbone of this longitudinal study, and we predict that this database will become a national treasure for psychological and medical research.

Martin P. Seligman & Raymond D. Fowler, Comprehensive Soldier Fitness and the Future of Psychology, 66 American Psychologist No. 1 (January 2011) at 85.

The Comprehensive Soldier Fitness program, at the critical research-or-operations border of 10 U.S.C. sec. 980, Limitation on Use of Humans as Experimental Subjects. It is yet another illustration of why such activities require case-by-case ethical and legal scrutiny, not categorical exclusion from oversight.

Where there is a Government-approved research purpose, there should be no categorical exclusions from the Common Rule. It is a failure of respect for persons and is contrary to law to deny the right, among others, to fully informed consent, in circumstances conducive to voluntariness, contravenes the law.

b. Exclusion of Activities That Are Low-Risk and Already Subject to Independent Controls (NPRM at Sec. __.101(b)(2))

iii. Educational Tests, Survey Procedures, Interview Procedures, or Observation of Public Behaviors (NPRM at Sec. __.101(b)(2)(i))

(2) Questions for Public Comment

9. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects.

As we have shown above, adducing examples of research activities at or across the ethical and legal borderline, categorical exclusions are inappropriate also for educational tests, survey procedures, interview procedures, and observations of public behavior.

These activities are not necessarily low risk. Case-by-case analysis is required. An educational test may be highly intrusive and subject to pupil privacy requirements. Surveys, opinion polling, and focus groups may be harmless in some settings but not where prospective respondents or third parties would be endangered by disclosures. Two examples of essential IRB protection: (1) Blocking a focus group of high school students who would be promised confidentiality but would be asked to reveal details of violent encounters; (2) blocking a court-appointed psychiatrist's proposal to use court-referred persons as research subjects without informing them that everything they did or said would have to be reported to the court. In some anthropology projects the researcher may witness the planning or commission of a violent crime.

Whether behavior is public or not is arguable; vacuous cant about lack of expectations of privacy is not dispositive. In this electronic information age, acquiescence to interference with privacy is not necessary informed or voluntary; it may just be a price paid grudgingly or unwittingly to participate in the modern economy. Generalization about low risk is inappropriate to broad categories and locational assumptions.

The existence of independent controls raises the question of which controls are meaningful in what settings. The Paperwork Reduction Act is not remedial, and Federal Register notices pursuant to that act are unlikely to come to the attention of prospective or actual research subjects. The Federal pupil privacy laws do not give rise to private remedy. The Privacy Act, for which there are many exceptions, requires Federal Register publication of the existence of certain sets of records maintained by Government agencies, but there are many exceptions and no details. Individuals who feel aggrieved under the Privacy Act can initiate inquiries, but there is a very short statute of limitations and almost no remedy. To vindicate rights under the Privacy Act, a private individual must suspect there is a record, be able to identify the agency, record, and record system, be outside the exceptions, and make his or her inquiries and submit corrections, and do it all quickly. A Privacy Act information chase is all the more difficult because of extensive increases in research-data sharing, non-research data-matching systems, and automated computer-matching programs.

10. Public comment is sought on whether this exclusion should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement.

Because so many of these activities raise ethical and legal problems, none should be excluded categorically from Common Rule coverage save public opinion polling, where safe for pollsters and respondents, and for ordinary classroom teaching clearly unassociated with research.

If so, please comment on what kind of information should be included in the notice such as the research purpose, privacy safeguards, contact information, ability to opt-out, etc.

For opinion polling as covered research, prospective respondents first should be informed of the research purpose, sponsorship, privacy safeguards, what personally identifiable information is to be retained, anticipated subsequent uses of that information, and contact information, after which they may be asked to opt in. For teaching methods research in ordinary classroom settings where data are not identified or identifiable to the subject and no adverse effects on subjects can be anticipated, then the federal educational privacy rules should suffice.

Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence?

As we note above, exemption is inappropriate, because a seemingly innocuous activity in one setting and with some human subjects may pose considerable hazard in other settings and with other subjects. Privacy and ability to safeguard data that should be confidential can be critically important. This is not a matter of weighing autonomy against beneficence. Beneficence of purpose is not the same as beneficence of the activity or beneficence of result (which cannot be assured). The NPRM notion of “a good balance between autonomy and beneficence” ignores the pivotal question of who is burdened for whose benefit.

Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category.

Common sense, the Belmont admonitions, the possibility that investigators can make mistakes, and investigator conflicts of interest make it unreasonable to rely on investigators to exempt themselves and their projects from Common Rule scrutiny—whether or not their projects are within the exclusion categories proposed here.

If so, should documentation of any kind be generated and retained?

This question exposes contradictions within the NPRM proposal. If categorically excluded, then there is no authority, because the IRB has no way to determine whether a self-exclusion is legally valid. If the IRB must keep track of

what is outside its purview, then the result is regulatory burden without actual regulation or oversight.

11. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category.

No. See our responses to Question 10, above.

If so, should documentation of any kind be generated and retained?

No. See our responses to Question 10, above.

12. Public comment is sought regarding whether some or all of these activities should be exemptions rather than exclusions.

The proposed categorical exclusions are contrary to law. The categories proposed in the NPRM warrant case-by-case Common Rule scrutiny whether treated as exclusions or as exemptions.

13. Public comment is sought regarding whether these exclusions should be narrowed such that studies with the potential for psychological risk are not included.

There should be no exclusions. See our response to Questions 10-12, above. This question (13) shows that exclusions and exemptions can be dangerous. Even the possibility of psychological risk implies a danger from disclosure as well.

Are there certain topic areas of sensitive information that should not be covered by this exclusion?

Even intra-familial disclosures may be dangerous. Special scrutiny should be given to any project seeking any information for which unwanted disclosure would put the prospective or actual subject at risk in any way, ranging from physical danger to criminal or civil liability and including the consequences of unwanted disclosure of information pertaining to health, personal finance, employment history, personal relationships, educational and job performance, and lifestyle.

If so, please provide exemplary language to characterize such topic areas in a manner that would provide clarity for implementing the Rule.

The rule should continue to require careful judgment in good faith, recognizing serious consequences of unwanted disclosures and recognizing individual vulnerability, as in this language in the current rule:

- (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
- (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

45 C.F.R. pt. 46 sec. 101(b)(2).

Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

45 C.F.R. pt. 46 sec. 111(3).

14. For activities captured under the third element of this exclusion, do the statutory, regulatory, and other policy requirements cited provide enough oversight and protection that being subject to expedited review under the Common Rule would produce minimal additional subject protections?

The proposed exclusion and the rationale for it rest on explicit assumptions that informational risk is unimportant, that current privacy protections are adequate, that watching and tracking people without their knowledge is consistent with respect for persons, and that an IRB cannot provide meaningful protections.

As we have pointed out above and as the current rule accepts, informational risks are real, and they are consequential. We pointed out in response to Question 9, above, that neither the Paperwork Reduction Act nor the Privacy Act is protective in these contexts. They involve no risk assessment, no

risk minimization, no fairness considerations, no consent. Current privacy protections are far from adequate:

Risks to cyber assets can originate from unintentional and intentional threats. These include insider threats from disaffected or careless employees and business partners, escalating and emerging threats from around the globe, the ease of obtaining and using hacking tools, the steady advance in the sophistication of attack technology, and the emergence of new and more destructive attacks. The ineffective protection of cyber assets can result in the loss or unauthorized disclosure or alteration of information. This could lead to serious consequences and result in substantial harm to individuals and to the federal government. The security of these systems and data is vital to public confidence and the nation's safety, prosperity, and well-being. Safeguarding federal computer systems and the systems that support critical infrastructures—referred to as cyber critical infrastructure protection—is a continuing concern. The security of our federal cyber assets has been on our list of high-risk areas since 1997. In 2003, we expanded this high-risk area to include the protection of critical cyber infrastructure. This year, we added protecting the privacy of personally identifiable information (PII)—information that is collected, maintained, and shared by both federal and nonfederal entities.

Regarding PII, advancements in technology, such as new search technology and data analytics software for searching and collecting information, have made it easier for individuals and organizations to correlate data and track it across large and numerous databases. In addition, lower data storage costs have made it less expensive to store vast amounts of data. Also, ubiquitous Internet and cellular connectivity facilitates the tracking of individuals by allowing easy access to information pinpointing their location. These advances—combined with the increasing sophistication of hackers and others with malicious intent, and the extent to which both federal agencies and private companies collect sensitive information about individuals—have increased the risk of PII being exposed and compromised. Furthermore, the number of reported security incidents involving PII at federal agencies has increased significantly in recent years and a number of high-profile breaches of PII have occurred at commercial entities.

For these reasons, we added protecting the privacy of PII to this high-risk area.

Government Accountability Office, High-Risk Series: An Update, Report to Congressional Committees, GAO-15-290 (February 2015) at 235-236 (annotations omitted). A few months later, Congress learned:

On June 4, 2015, the U.S. Office of Personnel Management (OPM) revealed that a cyber intrusion had impacted its information technology systems and data, potentially compromising the personal information of about 4.2 million former and current federal employees. Later that month, OPM reported a separate cyber incident targeting OPM's databases housing background investigation records. This breach is estimated to have compromised sensitive information of 21.5 million individuals.

Congressional Research Service, Cyber Intrusion into U.S. Office of Personnel Management: In Brief, CRS Report 44111 (July 17, 2015).

Nor has personal health information been sufficiently protected generally. See Pro Publica, Policing Patient Privacy, <https://www.propublica.org/series/patient-privacy> (Dec. 11, 2015).

The NPRM drafters asked what an IRB can do that would be more protective. Our answer is that where and when warranted an IRB can and should say no.

15. Public comment is requested on the extent to which excluding any of these research activities from the Common Rule could result an actual or perceived reduction or alteration of existing rights or protections provided to human research subjects.

Protections are a precondition for agency support of human subjects research and for marketing approvals for drugs, biologics, and medical devices. The legal basis for the human subjects regulations is the legal mandate to protect the rights of human subjects indirectly. As a legal matter, rights do not change; they are inherent or recognized in positive law. The human subjects regulations cannot accord or diminish rights; they are supposed to be protective of rights.

We point out above, in response to Questions 9-14, that the proposed categorical exclusions disregard rights and eliminate or weaken mandated protections. Allowing essentially unlimited, unchecked mining and cross-linking of stored data, including biosamples, raises severe problems of violation of confidentiality and trust. Might the proposed exclusions be perceived as eliminating protections? Yes. For example, visualize a possible news report that the Government has chosen to allow researchers to mine data or track individuals in ways that would be forbidden to the Government itself.

Are there any risks to scientific integrity or public trust that may result from excluding these research activities from the Common Rule?

Yes. The proposed exclusions show that the Government declines its mandate to protect research subjects and that it defers to some researchers who consider themselves above ethical scrutiny.

iv. Research Involving the Collection or Study of Information That Has Been or Will Be Collected (NPRM at Sec. __.101(b)(2)(ii))

(4) Questions for Public Comment

16. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category.

No. Investigators have conflicts of interest; they are not disinterested, and they do not come to these issues from the standpoints of the rights and concerns of prospective and actual subjects.

If so, should documentation of any kind be generated and retained?

For their own legal protection, research institutions ought to monitor what its agents do, and the Government has its audit requirements. If the activity is excluded from Common Rule scrutiny but human subjects protection documents are required, then what should or could the IRB do? The proposed exclusions open but do not settle difficult ethical and administrative questions.

17. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects.

See our response to Question 9, above. Coverage under the Common Rule would (1) provide for independent review and oversight that otherwise would not occur, and (2) would provide sponsor agencies a way to fulfill their responsibilities.

Is there a way in which this exclusion should be narrowed?

All exclusions of putative research categories should be eliminated. Note: This is not the same as saying that some activities are outside the scope of legislative intent and thus would not be covered in the first place—although perhaps covered under state law, such as Maryland's, that emulates the Common Rule but applies to all human subjects research within state jurisdiction.

Public comment is also sought regarding whether activities described here should appear as an exclusion or as an exemption.

For reasons given above, there should be no exclusions. Exclusions as proposed in the NPRM leave the Government ignorant as to whether legal and ethical requirements are addressed and whether subjects are protected. Building exclusions into the rule contravenes the law and leaves subjects at risk

Because of the considerable confusion that occurs with the term “exemption,” we urge that there be no exemptions either. We recommend instead that the agencies use the guidance mechanism for analyzing what issues should be considered by the IRB in determining extent of review.

v. Research Conducted by a Government Agency Using Government-Generated or Government-Collected Data (NPRM at Sec. __.101(b)(2)(iii))

(2) Questions for Public Comment

18. Public comment is sought on whether this or a separate exclusion should also include research involving information collected for non-research purposes by non-federal entities where there are comparable privacy safeguards established by state laws and regulations,

No. As we point out above, this would amount to refusal to carry out the protective legislative mandate and would open the door to unlimited privacy violations. As we point out above also, current privacy law and enforcement lag far behind the problem.

or whether such non-federally conducted research would be covered by the proposed exemption at Sec. __.104(e)(2).

No. For reasons that we state above, there should be neither exclusion nor exemption.

19. Public comment is requested on the extent to which covering any of these activities under the Common Rule would substantially add to the protections provided to human research subjects.

As we said above, in response to Question 17, coverage under the Common Rule would (1) provide for independent review and oversight that otherwise would not occur, and (2) would provide sponsor agencies a way to exercise their responsibilities.

20. Public comment is sought regarding whether it is reasonable to rely on investigators to make self-determinations for the types of research activities covered in this particular exclusion category.

No, as we said above, in response to Question 16. Investigators have conflicts of interest; they are not disinterested, and they do not come to these issues from the standpoints of the rights and concerns of prospective and actual subjects.

If so, should documentation of any kind be generated and retained?

As we said above, in response to Question 16: For their own legal protection, research institutions ought to monitor what its agents do, and the Government has its audit requirements. If the activity is excluded from Common Rule scrutiny but human subjects protection documents are required, then what should or could the IRB do? The proposed exclusions open but do not settle difficult ethical and administrative questions.

21. Public comment is sought regarding whether some or all of these activities should be than exclusions.

As we say above, in response to Question 12: The proposed categorical exclusions are contrary to law. The categories proposed in the NPRM warrant case-by-case Common Rule scrutiny whether treated as exclusions or as exemptions.

vi. Certain Activities Covered by HIPAA (NPRM at Sec. __.101(b)(2)(iv)

(3) Questions for Public Comment

22. Public comment is requested on whether the protections provided by the HIPAA Rules for identifiable health information used for health care operations, public health activities, and research activities are sufficient to protect human subjects involved in such activities,

The HIPAA rules are insufficient; they are administrative, allow numerous exceptions (including for law enforcement), and neither protect rights nor provide remedy. HIPAA's Privacy Board provisions do not substitute sufficiently for good-faith Common Rule scrutiny. HIPAA provides no research protections.

and whether the current process of seeking IRB approval meaningfully adds to the protection of human subjects involved in such research studies.

HIPAA provides neither for voluntariness nor for fair selection nor for subject safety. As we say in response to Question 14: Our answer is that where and when warranted an IRB can and should say no.

23. Public comment is sought regarding to what extent the HIPAA Rules and HITECH adequately address the beneficence, autonomy, and justice aspects for the collection of new information (versus information collected or generated in the course of clinical practice, e.g., examination, treatment, and prevention).

Exclusion of these data from Common Rule coverage where they are used for research violates the protective mandate. As we state above, the records provisions of HIPAA are administrative. HIPAA's coverage is narrow, and it does not address or reflect research ethics concerns. HITECH addresses technical aspects of data security for covered Personal Health Information, and it has some teeth. Where there is overlap between HIPAA-covered data and research, HITECH standards already should be in effect for the health-care side but not necessarily for research if the data have been taken or sent elsewhere; they should be extended accordingly for HITECH-protected data used for research.

Should this exclusion be limited to data collected or generated in the course of clinical practice?

For reasons stated above, research use of these data should not be excluded from Common Rule coverage. Where these data are used for research, they should be subject to HITECH data security standards.

If additional data collection is allowable, should it be limited to what is on the proposed Secretary's list of minimal risk activities (discussed in more detail below in II.F.2 of this preamble)?

For reasons stated above in response to Question 14, unwanted disclosures should not be considered either unlikely or of minimal consequence.

24. Public comment is requested on whether additional or fewer activities regulated under the HIPAA Privacy Rule should be included in this exclusion.

As stated above in response to Question 23, HIPAA affords no effective protection for human subjects of research and should not be regarded as an excuse for exclusion from mandated protection of human subjects.

c. Applicability of Exclusions to the Subparts

iii. Questions for Public Comment

25. Should research involving prisoners be allowed to use any or all of the exclusions found at Sec. __.101(b)(2) and (3), as currently proposed?

No. Guidance should make clear: Anyone whose liberty interests are impeded or at risk should not be denied Constitutional rights or Common Rule protection of his or her rights in research. The term “prisoner” is insufficient. The same consideration should apply to detainees, to persons held without charge, to probationers, to persons who are parties at interest in law enforcement cases, to parolees, to persons under arrest, defendants, suspects, and others under or facing a legal disability under criminal law.

Prisoners, including those awaiting trial, are Constitutionally protected against forced medication except in rare circumstances. *United States v. Sell*, 539 U.S. 166 (2003) (6-3, forced medication of prisoner Constitutionally impermissible except in rare cases combining medical necessity, absence of less intrusive alternatives, and important state interest). That is for medication. Non-consensual research does not begin to satisfy that kind of Constitutional standard.

Note also that the Geneva Conventions and Additional Protocols prohibit research on individuals caught up in war, whether or not they have prisoner status.

26. Are there certain provisions within the broader categories proposed at Sec. __.101(b)(2) and (3) to which the subparts should or should not apply?

The subparts should continue to apply and should be interpreted broadly in guidance, as we suggest immediately above for persons whose liberty interests are impaired or at stake.

3. Proposed Exemptions (NPRM at Sec. __.104)

a. Making Exempt Research Determinations (NPRM at Sec. __.104(c))

v. Questions for Public Comment

27. Public comment is sought regarding how likely it would be that institutions would allow an investigator to independently make an exempt determination for his or her own research without additional review by an individual who is not involved in the research and immersed in human research protection e.g., a member of the IRB Staff.

We have no way to know, because the system is secretive. Research institutions vary in oversight of their investigators and in their support for Common Rule compliance. We have seen IRB accreditation advice to read the Common Rule narrowly, avoiding any review not absolutely required. We are aware also of institutions that try to adhere assiduously to the spirit and letter of the rule. The PLOS ONE publication reporting surreptitious tracking of Occupy Wall Street political communication (see our response to Question 2, above, mentioned no ethics concerns, IRB review, or exemption. Major research universities have had their rogues and their merely oblivious. A Midwest university IRB chair received this complaint from the director of a local refugee assistance center: University student researchers, having never taken their projects to their IRB, were wandering through the center without anyone's permission and interviewing refugees without regard for their subjects' privacy or vulnerability to consequences of unwanted disclosures.

Relying on IRB staff to make exemption determinations does not solve the problem. Some institutions are very serious in ensuring highly competent IRB staff. Many try to do it on the cheap, viewing the job as largely secretarial. The training materials we have seen are largely inadequate and often wrong—by omission or by implication. Accreditation seems not to have improved the situation; major human subjects protection scandals recur.

28. Public comment is sought regarding whether an investigator would be able to contrive his or her responses to the automated exemption determination produced by the decision tool where

investigators themselves input the data into the tool,

The kind of decision tool envisioned by the NPRM drafters is necessarily a coarse screen. In our experience, one new investigator met the IRB chair at a medical school social occasion and said he “just wanted to know how the game is played.” Any decision not to review a study requires situational awareness and careful judgment.

or whether there should be further administrative review in such circumstances.

For reasons stated above in our response to Question 27, administrative review will not suffice.

30. Public comment is sought regarding whether relying on the exemption determination produced by the decision tool where investigators themselves input the data into the tool as proposed would reduce public trust in research.

Yes, it would reduce public trust. Ultimately, something would be found amiss and would come to light. Does the agency want to answer the Congressional oversight hearing queries, “You have a legal obligation to protect human subjects but you let these researchers decide for themselves after keying in just enough information to pass your test?” “Tell us specifically what assumptions you fed into your screening program about which people would be at risk, how, in what circumstances.”

31. Public comment is sought regarding how likely it would be that institutions would rely on such a decision tool to provide a safe harbor for an investigator making a determination that the proposed research qualifies for an exemption,

A prudent institutional administration would not rely on such a tool; the tort liability potential is too great both in the regulatory arena and for privacy torts. The proposed regulatory “safe harbor” might be an excuse, but we doubt that a court would find it a complete defense. Federal agencies have no authority to grant a “safe harbor” against grantee and contractor liability for delicts in human subjects research.

or whether developing such a tool would not be worthwhile,

No, for reasons just stated it would not be worthwhile. To the contrary, it would encourage investigators to think in terms of generalities rather than specific people, plans, and circumstances.

and whether institutions would be able to adequately manage exemption determinations without the use of the decision tool.

So long as the rule provides for exemptions, the issues to which they give rise can be addressed best in agency guidance illustrated with specific examples.

32. Public comment is sought regarding what additional information should be required to be kept as a record other than the information submitted into the decision tool, for example, a study abstract, the privacy safeguards to be employed, or any notice or consent document that will be provided.

All the information that would normally go into a research proposal should be retained, with copies to the IRB as well as to sponsor agencies.

33. Public comment is sought regarding the value of adding an auditing requirement.

While institutional internal audits are important, we believe that the Federal Common Rule agencies need support, resources, and will to do the audits.

b. Exemptions Subject to the Documentation Requirements of Sec. __.104(c) and No Other Section of the Proposed Rule

i. Research Conducted in Established or Commonly Accepted Educational Settings (NPRM at Sec. __.104(d)(1); current Rule at Sec. __.101(b)(1))

(4) Questions for Public Comment

34. Public comment is sought on whether this exemption category should only apply to research activities in which notice that the information collected will be used for research purposes is given to prospective subjects or their legally authorized representatives as a regulatory requirement, when not already required under the Privacy Act of 1974.

This is insufficient. As we point out above, the Privacy Act, despite its name, affords none of the protections of the Common Rule.

Note also: As we point out in response to Question 65, below, who is a “legally authorized representative,” with what powers, is not necessarily clear and is not amenable to generalized definition.

If so, comment is sought on what kind of information should be included in the notice, such as the research purpose, privacy safeguards, contact information, etc.

The idea of “notice” does not substitute for full, individual informed consent in circumstances conducive to voluntariness.

Comment is also sought on how such a notice should be delivered, e.g., publication in a newspaper or posting in a public place such as the school where the research is taking place, or by individual email or postal delivery. Note that other requirements, such as those of the Family Educational Rights and Privacy Act (FERPA) or the Protection of Pupil Rights Amendment, may also apply.

Again, the idea of “notice” does not substitute for full, individual informed consent in circumstances conducive to voluntariness. As important as they are, neither FERPA nor the Protection of Pupil Rights Amendment provide the panoply of protections of the Common Rule even with its current weaknesses.

Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence?

Yet again, the idea of “notice,” perhaps posted or published somewhere or even mailed out, does not substitute for full, individual informed consent in circumstances conducive to voluntariness. This question poses a false dichotomy. The actual choice presented is between respect for persons and minimal or no regulatory protections for subjects. Beneficence might be a goal, but not necessarily for the direct benefit of these research subjects. Whether the outcome is beneficent cannot be assumed.

35. Public comment is sought on whether the privacy safeguards of Sec. __.105 should apply to the research included in Sec.

__.104(d)(1), given that such research may involve risk of disclosure of identifiable private information.

These proposed protections would be illusory; they are grossly inadequate. The technology is changing rapidly, data-acquisition, data-sharing, and data-mining are increasing, maintaining cyber security is a continuing challenge, and these putative protections call only for the Secretary to publish a list of desirable safeguards at least every 8 years.

ii. Research and Demonstration Projects Conducted or Supported by a Federal Department or Agency (NPRM at Sec. __.104(d)(2); Current Rule at Sec. __.101(b)(5))

(5) Questions for Public Comment

36. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement.

The projects contemplated in the current exemption are those involving evaluation and comparison in social welfare and benefit programs where legal entitlements will not be affected adversely. We believe that in appropriate circumstances the IRB can decide whether the proposed activity should come within the rule. Where personal data is obtained and retained, as in longitudinal projects, or where there is a research purpose rather than or alongside a demonstration purpose, the project should be subject to IRB oversight. “Notice” should be given in a way that actually reaches the persons affected by the activity. Longitudinal studies necessitate full IRB oversight.

Note again that the “legally authorized representative” must be legally authorized under local law.

If so, comment is sought on what kind of information should be included in the notice, e.g., the research purpose, privacy safeguards, or contact information.

This will depend on the project. See our response to Question 34.

Also comment on how such a notice should be delivered; e.g., publication in a newspaper or posting in a public place, or by individual email or postal delivery.

Actual notice should be required, and informed consent should be required for longitudinal studies and where personal data are obtained and retained.

Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence?

As we say above in response to Question 34: The idea of “notice,” perhaps posted or published somewhere or even mailed out, does not substitute for full, individual informed consent in circumstances conducive to voluntariness. This question poses a false dichotomy. The actual choice presented is between respect for persons and minimal or no regulatory protections for subjects. Beneficence might be a goal, but not necessarily for the direct benefit of these research subjects. Whether the outcome is beneficent cannot be assumed.

In many cases, it may be that individual notice or consent to all potentially affected persons before the research or demonstration commences is ordinarily impossible in the conduct of such studies. For example, if a research or demonstration project will affect all inhabitants of a large geographic area (e.g., a housing, a police patrol, a traffic control, or emergency response experiment), or all clients or employees of a particular program or organization or setting will be subject to a new procedure being tested (e.g. a new approach to improving student performance, a new anti-smoking or anti-obesity program, a new method for evaluating employee performance), would it be possible to make participation voluntary for all affected individuals, or even to identify and inform all affected individuals in advance?

That these activities pose differing levels of hazard to subjects necessitates case-by-case IRB determinations. They are not all comparable public-benefit programs. Several would make employees vulnerable, and some raise issues of unlawful discrimination in employment. Obesity interventions create risk of psychological and physical harm; obesity is a medical diagnosis, requiring history and physical examination of an individual by a licensed health care professional. How is it “ordinarily impossible” to obtain consent from persons if you access records documenting the diagnosis and intend to track changes in their weight?

37. Public comment is sought on whether this exemption category is appropriate based on the recognition that alternative processes are in place in which ethical issues raised by research in public benefit or service programs would be addressed by the officials who are familiar with the programs and responsible for their successful operation under state and federal laws, rather than meeting specific risk-based criteria,

The NPRM suggestion that the “ethical issues raised by research in public benefit or service programs . . . be addressed by the officials who are familiar with the programs and responsible for their successful operation under state and federal laws” assumes that these officials are disinterested parties who fully understand the rights and concerns of their research subjects. This proposal, like some current practice, would deny essential protections of human subjects.

or whether risk limitations should be included, and if so, what those limitations should be. Though long-standing, this exemption has never identified specific risk-based criteria, or risk limitations to bound the type of projects that may be covered. When originally promulgated, the exemption did stipulate that following the review of such projects, if the Secretary determines that the research or demonstration project presents a danger to the physical, mental, or emotional well-being of a participant or subject, then written informed consent would be required. Public comment is sought on whether to limit the risk that can be imposed on subjects while using this exemption,

The Secretary’s authority should not be limited in this regard. Requiring written informed consent may be insufficient. Agency guidance should consider circumstances under which the Secretary’s authority may be used to cancel or impose special conditions upon an agency-conducted or agency-sponsored project.

and if so, how to characterize those limits in a clear fashion.

This is a matter for guidance, because so many and varied possibilities arise.

If more than minimal risk interventions are included, public comment is sought on whether, for transparency, this should be made clear in the regulatory text.

If risks to subjects can be anticipated, then full Common Rule coverage, including arrangements for monitoring the welfare of subjects, is warranted.

With regard to the issue of risks encountered by participants in such research or demonstration projects, comments are also sought regarding the argument that any and every demonstration project involving changes in public benefit or service programs (e.g., water or sewage treatment programs or pollution control programs, programs involving educational procedures, or programs involving emergency procedures related to extreme weather events, etc.) exposes those affected to possible risks of some kind. In this regard, those risks are ordinarily and perhaps always no different in kind or magnitude than those involved in simply making the change in procedures without using research tools to evaluate them.

No. These activities should be evaluated case by case within a protective Common Rule framework. The formulation here leaves the door open for “study in nature” research akin to the Baltimore lead-paint study, pesticide exposure studies, and non-consensual testing of medical devices. The NPRM and the question conflate risks that people take for granted and hazards that are imposed or exacerbated and not taken for granted.

For example, health care providers could be required to perform certain sanitation reforms to prevent patient infections whether or not such reforms were first tested in practice through a research or demonstration project. It is common for all Federal departments and agencies that regulate private or public organizations to impose conditions of participation in public

programs providing for safety, program integrity, financial reporting, etc.

This paragraph raises the issue of purposeful denial of otherwise prudent precautions in order to determine whether someone might get hurt. The default position should be full Common Rule protection with special arrangements for data and safety monitoring.

Public comment is sought regarding whether there should be conditions (e.g., an individual notice or consent requirement) imposed on such research or demonstration projects involving public benefit or service programs which might lead to significant impediments or limitations on testing and evaluation before or after being imposed program-wide.

Whose risk for whose benefit? Common Rule protections are essential for research subjects who might be put at risk. It may be that proposed projects will have to be delayed or changed. That's not necessarily a loss.

Would the effect of imposing expensive or impracticable conditions on public benefits or services evaluations be to reduce the number of such evaluations and consequently to expose program participants to increased risk through exposure to untested reforms?

Not necessarily. This question assumes that the "untested reforms" necessarily would be improvements; if it is clear that they are improvements, then they don't need to be tested except in the public policy arena.

38. Public comment is sought on whether the existing privacy safeguards for such activities, including the Privacy Act, HIPAA rules, and other federal or state privacy safeguards provide sufficient independent controls, or whether other safeguards such as the privacy safeguards of Sec. __.105 should be applied.

Safeguards are needed, but neither the proposed Sec. __.105 nor existing law and practices suffice. As we point out in response to NPRM Questions 9, 14, and 34, the Privacy Act, and HIPAA records management statutes and regulations do not protect the rights of research subjects and do not even provide for

meaningful, voluntary consent, let alone adequate confidentiality. As we point out at Question 14, the Government Accountability Office and Congressional Research Service have found the U.S. Government and private entities unable to safeguard highly personal data adequately, and this lack of adequate safeguards has become a very serious national problem. The proposed Sec. __.105 contains so many exceptions and conditions that it is unclear and susceptible to misinterpretation. Even without exceptions, it appears toothless. The HITECH Act is a useful and important step toward better cyber security, but it does not apply in most research circumstances.

We are concerned not only about samples and gene sequences but also with their linking to other personal data, some in primary uses and some, perhaps in the gray and black markets or in law enforcement. In tort law these uses might amount to intrusion into seclusion (invasion of privacy) and non-consensual exploitation of someone's privacy or image for gain.

iii. Research Involving Benign Interventions in Conjunction With the Collection of Data from an Adult Subject (NPRM at Sec. __.104(d)(3))

(5) Questions for Public Comment

39. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement.

The law requires informed consent as a precondition to research on human beings.

See our response to Questions 64 and 65 concerning who may or may not be a legally authorized representative for what purpose.

If so, comment is sought on what kind of information should be included in the notice, such as the research purpose (if authorized deception is not utilized), privacy safeguards, contact information, etc.

We reiterate that the law requires informed consent as a precondition to research on human beings. Those very rare instances of scientifically justifiable and ethically sustainable deception research should have full IRB review and monitoring for subject safety and welfare. Project review should begin with the rebuttable presumption that deception is not justified.

Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence?

This question, like Questions 4, 35, and 36, presents a false dichotomy based on an unsupported assumption that the activity and outcome will be beneficent.

40. Public comment is sought regarding what improvements could be made to the language describing the type of interventions in this exemption category so as to make clear what interventions would or would not satisfy this exemption category.

Whether a project is benign depends on the project itself, the circumstances, and the study population. This necessitates IRB review. Sec. __.104(d)(3) is troubling. The NPRM drafters apparently meant that the project could proceed if subjects cannot be identified directly or if either unwanted disclosures would not “reasonably place the subjects at risk” or if both conditions apply. This proposal denies needed protections. Contamination of computers with spyware is commonplace, and identifiability of subjects, their computers, and perhaps computer-stored information is non-negligible. The risk provision appears to use a “reasonable person” standard to ascertain risk, when the possible risks anticipated are serious enough to warrant a subjective standard, candor, and fully informed consent in circumstances conducive to voluntariness. The consent process in these situations should include clear understanding of the risks and possible consequences of unwanted disclosures. Consequences could limit life choices—particularly with using neuroscience and genetic studies to ascertain susceptibility to disease and with increasing interest in prediction of behavior from neuroscience and from genetic studies.

The proposed conditions are a poor substitute for legally required protection of these human subjects.

41. Public comment is sought on whether it is reasonable, for purposes of this exemption, to rely on the exemption determination produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances.

Given (1) investigators’ conflicts of interest, and (2) pervasive problems in cyber security, it is not reasonable to rely on investigators to determine for themselves, with or without the proposed decision tool, whether individual

prospective subjects are vulnerable to unwanted disclosures that might “place the subjects at risk of criminal or civil liability or be damaging to the subjects’ financial standing, employability, educational advancement, or reputation.” Nor are IRB administrators to be relied upon for such analyses. Where this possibility exists, the project necessitates independent review.

iv. Taste and Food Quality Evaluation and Consumer Acceptance Studies (NPRM at Sec. __.104(d)(4); Current Rule at Sec. __.101(b)(6))

(1) Question for Public Comment

42. Public comment is sought on whether this exemption category should be narrowed to apply only to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement.

Yes, inasmuch as the subject’s medical circumstances (e.g., allergies; drug regimens) need to be taken into account. Cultural concerns also ought to be taken into account.

See our response to Questions 64 and 65 concerning designation and powers of supposedly legally authorized representatives.

If so, comment is sought on what kind of information should be included in the notice such as the research purpose, privacy safeguards, contact information, etc.

Testing in this category without warning and without consent might interfere with medication metabolism, might trigger allergic reactions, and might offend cultural sensitivities.

Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence?

This question, like Questions 4, 35, 36, and 39, presents a false dichotomy based on an unsupported assumption that the activity and outcome will be beneficent.

Should prospective subjects be given the explicit opportunity to opt out of such research?

The default position should be opportunity to opt in.

c. Exemptions Subject to the Documentation Requirements of Sec. ____104(c) and the Privacy Safeguards Described in Sec. ____105

i. Questions for Public Comment

43. Public comment is sought on the concept of requiring such minimum safeguards and limitations on disclosure,

Safeguards of subjects are essential, as recognized in the White House document, Precision Medicine Initiative: Privacy and Trust Principles (Nov. 9, 2015).

as well as whether the requirements of the proposed Sec. ____105 would constitute a broadening of IRB responsibilities rather than a streamlining of the implementation of responsibilities that many IRBs already adopted.

The proposed Sec. ____105(C) reliance on the Paperwork Reduction Act, Privacy Act, and other Federal records law provides no relevant protection; see our response to Questions 9, 14, 15, 34, and 38. Similarly, the White House statement, Precision Medicine Initiative: Privacy and Trust Principles, provides no protection. But that document offers no real protections. Its stated policy purposes are mostly unexceptionable but the document is nearly entirely aspirational, fails to provide for enforcement and vindication of rights, provides no remedies for violation, is unclear as to criteria for and authorization of data use, and is generally vague. These laws and policies do not substitute for adequate IRB review. IRBs would be burdened less by reviewing these projects as appropriate than by trying to parse this proposed rule. Be aware that highly qualified, conscientious review for adequacy of confidentiality safeguards could and should halt some proposed projects.

If an institution does view this as an inordinate broadening of responsibilities, does the institution currently have in place alternative mechanisms for ensuring data security and participant privacy in a research context?

IRBs are supposed to have the requisite mechanisms in place now. See their assurances.

Suggestions for alternative approaches

to meeting public expectation that federally sponsored research safeguard their data and protect privacy are sought during this public comment period.

The only way to foster “public expectation that federally sponsored research safeguard their data and protect privacy” is to actually protect data, actually protect privacy, to avoid surreptitious research, to avoid regulatory loopholes for secondary and subsequent data use, to respect the consent process, to provide a regulatory system intended to safeguard data and protect privacy, and, as we said in response to the ANPRM, foster a will to comply and a will to enforce. A rule that removes or weakens protections is bound to encourage distrust.

44. Public comment is sought regarding whether the proposed Rule's information security requirements for biological specimens and identifiable private information are highly technical and require a level of expertise not currently available to most IRBs.

It is not adequate, for the reasons stated above. Many institutions decline to provide their IRBs with necessary support.

Do these security requirements unrealistically expand IRB responsibilities beyond current competencies?

No. IRBs already have these responsibilities. But many are ill equipped or ill disposed to fulfill those responsibilities. The question for the IRB in these circumstances is not whether the particular, cited regulatory provisions exist but rather whether the subjects are protected in fact. The state of the technology at this point is likely that they are not protected in fact.

ii. Research Involving Educational Tests, Surveys, Interviews, or Observation of Public Behavior if the Information Is Recorded With Identifiers and Even if the Information Is Sensitive (NPRM at Sec. __.104(e)(1))

(5). Questions for Public Comment

45. Public comment is sought on whether the proposed exemption regarding the use of educational tests, survey procedures, interview procedures, or observation of public behavior (Sec. __.104(e)(1))

should be applied to research involving the use of educational tests with children

If the activity is not done for a research or research training purpose (including data acquisition and retention for future use) or with research funding and is not longitudinal, and does not violate any other law, including privacy torts, then the activity does not come within the rule. Otherwise it necessitates some degree of IRB review, the extent of which depends on the details—including selection of population, voluntariness, consent and good-faith determination of who is a legally authorized representative, and assessment of risks.

Because research oversight can be desultory, neither IRB administrators nor members are necessarily aware of relevant law other than the Common Rule—notwithstanding the Common Rule requirement that the project be consistent with local law.

School situations present special problems. Some involve study population selection and labeling and tracking of students, *contra* *Merriken v. Cressman*, *supra*. Some involve disclosure of information that could endanger the respondent or third parties. Some involve ordinary data security; in many schools some of the office work is done by students. In all but a few schools it implicates family and pupil privacy law. Some involve information technology, an emerging problem with commercial education and interview software that allows vendors to retrieve and sell data to third parties. Several states have tried to outlaw the practice. See, e.g., Natasha Singer, *Tools for Tailored Learning May Expose Students' Personal Details*, *New York Times*, Aug. 30, 2015.

Judgment of risk needs to be based on the situation, not on the technique. For example, eliciting political opinion can be innocuous in some settings, life-threatening in others—whether in some authoritarian country or in a gang-violence study.

As we point out above, some of these studies might pose significant hazard and thus necessitate independent review, not an automatic free pass. That many studies in this category might be low-risk does not support the conclusion that all are low-risk.

and whether it should also be applied to research involving the use of survey or interview procedures with children.

The exemption should not apply at all, let alone to studies of children.

If so, for research involving children, should the permissible survey or interview topics be limited in some way?

The question proves the need for case-by-case review. Even if the IRB intends that the family privacy and pupil rights law is followed faithfully, the study might be too risky.

46. Public comment is sought on whether this exemption category should only apply to research activities in which notice is given to prospective subjects or their legally authorized representatives as a regulatory requirement. If so, comment is sought on what kind of information should be included in the notice such as the research purpose, privacy safeguards, contact information, etc. Would requiring notice as a condition of this exempt research strike a good balance between autonomy and beneficence? Should prospective subjects be given the explicit opportunity to opt out of such research?

For the reasons we give in response to Question 10: Notice does not cure the problems; the privacy safeguards are inadequate; the opposing of autonomy to beneficence is unsupported and a false dichotomy, and the default position should be opt-in, not opt-out. The risk depends on the situation, and this in turns requires independent review. To do otherwise violates the legal mandate to protect the rights of subjects.

47. Public comment is sought on whether it is reasonable, for purposes of this exemption, to rely on the exemption determinations produced by the decision tool where investigators themselves input the data into the tool, or whether there should be further administrative review in such circumstances?

As we point out in response to Question 41: Given (1) investigators' conflicts of interest, and (2) pervasive problems in cyber security, it is not reasonable to rely on investigators to determine for themselves, with or without the proposed decision tool, whether individual prospective subjects are vulnerable to unwanted disclosures that might "place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, educational advancement, or reputation." Nor are IRB administrators to be relied upon for such analyses. Where this possibility exists, the project necessitates independent review.

48. Public comment is sought on whether this exemption category should be narrowed such that studies with the potential for psychological risk are not included. Are there certain topic areas of sensitive information that should not be covered by this exemption? If so, please provide exemplary language to characterize such topic areas in a manner that would provide clarity for implementing the Rule.

Our concern for this category as an exemption is the same as our concern for this category as an exclusion. Our response to Question 13 applies here too:

There should be no exceptions. See our response to Questions 10-12, above. This question shows that exclusions and exemptions can be dangerous. Even the possibility of psychological risk implies a danger from disclosure as well. Even intra-familial disclosures may be dangerous. Special scrutiny should be given to any project seeking any information for which unwanted disclosure would put the prospective or actual subject at risk in any way, ranging from physical danger to criminal or civil liability and including the consequences of unwanted disclosure of information pertaining to health, personal finance, employment history, personal relationships, educational and job performance, and lifestyle. The rule should require careful judgment in good faith, recognizing serious consequences of unwanted disclosures and recognizing individual vulnerability, as in this language in the current rule:

- (i) Information obtained is recorded in such a manner that human subjects can be identified, directly or through identifiers linked to the subjects; and
- (ii) any disclosure of the human subjects' responses outside the research could reasonably place the subjects at risk of criminal or civil liability or be damaging to the subjects' financial standing, employability, or reputation.

45 C.F.R. pt. 46 sec. 101(b)(2).

Selection of subjects is equitable. In making this assessment the IRB should take into account the purposes of the research and the setting in which the research will be conducted and should be particularly cognizant of the special problems of research involving vulnerable populations, such as children, prisoners, pregnant women, mentally disabled persons, or economically or educationally disadvantaged persons.

45 C.F.R. pt. 46 sec. 111(3).

iii. Secondary Research Use of Identifiable Private Information (NPRM at Sec. __.104(e)(2))

(5) Questions for Public Comment

49. Public comment is sought on the types of research that should fall under the proposed exemption.

This exemption should disallow such research except where (1) there is actual informed consent in circumstances conducive to voluntariness, (2) the subject has been informed that his or her data or biological materials may be used for research beyond original research purpose, (3) third parties will not be adversely affected, and (4) efforts will be made to maintain confidentiality but absolute confidentiality cannot be guaranteed.

The proposed Sec. ____104(e)(2) safeguards are illusory. “Notice” in the Sec. ____104(e)(2)(i) sense cannot substitute for actual consent. It allows consent to be presumed but more likely is akin to a contract of adhesion. Responding to several questions posed by this NPRM we show that law and policy cited in Sec. ____104(e)(2)(ii) are not protective of the rights of research subjects.

Should the proposed exemption be available to all types of research using identifiable data collected for non-research purposes

No, not without actual informed consent in circumstances conducive to voluntariness.

or should the exemption be available only to a more limited subset of research?

Only under the conditions that we specify above in our response to this question set.

For example, should the proposed exemption apply only for research using records and information already subject to comprehensive privacy and other protections in other Federal laws (e.g., records held by the Federal Government subject to the Federal Privacy Act, or records governed by HIPAA or FERPA)?

We reiterate that Responding to several questions posed by this NPRM we show that the law and policy cited in Sec. ____104(e)(2)(ii) are not protective of the rights of research subjects.

Depending upon the scope of the exemption, the relationship between this exemption and the exemption proposed at Sec. __.104(f)(2) would need to be clarified. Since a major justification for including this exemption is to reduce burden on IRBs, should the proposed exemption apply only to research for which IRBs typically waive informed consent, that is, where the research could not practicably be carried out without a waiver of informed consent, and the rights and welfare of subjects will not be adversely affected by the waiver?

We have no way to know why IRBs “typically waive informed consent.” The subject’s right to informed consent is a matter of human rights law.

If there is a possibility that “the research could not practicably be carried out without a waiver of informed consent,” then the matter obviously is serious enough to warrant full IRB and agency review to reverse an ill-advised approval, and the rebuttable presumption should be that the research proposal should be disapproved.

Finally, is there a sufficient need for this exemption at all given the other proposed exclusions and exemptions?

We find no ethical or legal justification for this exemption as proposed or for any similar exclusion.

50. Public comment is sought regarding whether the proposed exemption should be limited to research in which individuals had been informed of the potential future research use of their information, and given the opportunity to opt out of having their identifiable private information used for research. If the proposed exemption should be limited in this way, what information should be included in the opportunity to opt out?

Our response to Question 49 points out that “notice” is not a protection; it allows consent to be presumed but more likely is akin to a contract of adhesion. The default position should be to provide for opt-in with informed consent. This exemption should disallow such research except where (1) there is actual informed consent in circumstances conducive to voluntariness, (2) the subject has

been informed that his or her data or biological materials may be used for research beyond original research purpose, (3) third parties will not be adversely affected, and (4) efforts will be made to maintain confidentiality but absolute confidentiality cannot be guaranteed.

If the opportunity to opt out is made a condition of the exemption category how should it be structured (e.g., how long and under what circumstances should it remain in effect)

The subject should be enabled to withdraw permission at any time for the retention of data and materials not already used for research and to withdraw permission at any time for further uses of his or her data or biomaterials. Whether permission is attributed to a parent, guardian, or apparently legally authorized representative, the actual subject even though a minor should be informed periodically, at least every three years, of the existence of the data and biomaterials and directly or through a legal guardian should be empowered to withdraw use and retention permission at will. Many people without their knowledge have been the subjects of longitudinal studies.

We urge these precautions because there are questions of legitimacy of consent as well as long vulnerability to consequences of unwanted disclosures.

and what, if any, impact should the opt out have on other provisions of the rule, such as the ability of an IRB to waive informed consent for a subsequent research study using the individual's information?

There is no legal authority to waive an individual's refusal of consent in this process.

Are there other or alternative mechanisms that should be required to respect individuals' autonomy and other interests?

There is tort law, but for the purposes of the Common Rule there are no extant alternative institutional mechanisms.

51. Public comment is sought regarding what should constitute notice for purposes of this exemption category.

As we say in response to Questions 49 and 50, "notice" is not a protection; it allows consent to be presumed but more likely is akin to a contract of adhesion. The default position should be to provide for opt-in with informed consent. This exemption should disallow such research except where (1) there is actual

informed consent in circumstances conducive to voluntariness, (2) the subject has been informed that his or her data or biological materials may be used for research beyond original research purpose, (3) third parties will not be adversely affected, and (4) efforts will be made to maintain confidentiality but absolute confidentiality cannot be guaranteed.

Given the many different types of data that would be covered by this provision (e.g., data from private entities used for social or behavioral science research, government records for which laws already establish standards for notice, and data publicly available for harvesting from the internet), would it be possible to develop a uniform "notice" requirement?

No. Not a notice that would satisfy the legal mandate for protecting rights of research subjects. This provision allows unlimited, non-consensual data mining beyond the practical reach of regulation or protection of subjects' rights. The problem is the more serious because of behavioral, social, and genetic other biomedical data accumulated in short-term and longitudinal studies and subject to cross-linking far from legitimate research.

The problem is serious and large. Thousands of adults and children are enrolled in longitudinal behavioral, social, and biomedical studies. The Vanguard (Pilot) Study, in connection with the National Children's Study, began the tracking of genetic, biological, and behavioral characteristic of tens of thousands before conception or in utero. Department of Health and Human Services, National Institutes of Health, Notice: The National Children's Study, Vanguard (Pilot) Study Proposed Collection; 0925-0593, Expiration 8/31/2014—Revision; 60-day Comment Request, 78 Federal Register 52,548 (August 23, 2013). "The NCS Archive provides researchers with access to data and samples collected in the NCS Vanguard Study, which tested methods and procedures planned for use in a large epidemiological cohort study of environmental influences on child health and development." Eunice Kennedy Shriver Institute of Child Health and Human Development, National Children's Study (NCS) Vanguard Data and Sample Archive and Access System (NCS Archive), <<https://www.nichd.nih.gov/research/NCS/Pages/researchers.aspx>> (accessed Dec. 15, 2015).

What type of notice, in terms of its dissemination and scope, should be considered to meet this requirement of the proposed exemption?

The idea of notice as proposed here is ethically and legally inappropriate.

With regard to the dissemination of the notice, should the notice requirement be permitted to be fulfilled through a general public notice, not specifically directed to individuals who are potential research subjects, such as the notice allowable under the Privacy Act?

No. Privacy Act notices deal with where vaguely described systems of records are kept organizationally and are not directed to individuals. Nor does the Privacy Act address informed consent.

Would a prominent notice posted in all clinics or other relevant public places where information will be collected be acceptable?

No, for the reasons stated above.

Should each individual whose data could be used receive their own notice, such as is required of direct treatment providers covered by the HIPAA Privacy Rule?

The HIPAA rule requires the patient to ask; answering substantively is up to the health care entity; HIPAA gives no right of refusal. We say again that informed consent—in circumstances conducive to voluntariness—is essential.

With regard to the content of the notice required by this proposed exemption, what kind of information should be included in the notice, such as the types of research that might be conducted, privacy safeguards, contact information, etc.?

As we say in response to Questions 49, 50, and 51, “notice” is not a protection; it allows consent to be presumed but more likely is akin to a contract of adhesion. The default position should be to provide for opt-in with informed consent. This exemption should disallow such research except where (1) there is actual informed consent in circumstances conducive to voluntariness, (2) the subject has been informed that his or her data or biological materials may be used for research beyond original research purpose, (3) third parties will not be adversely affected, and (4) efforts will be made to maintain confidentiality but absolute confidentiality cannot be guaranteed.

52. Public comment is sought on whether, on the other hand, prior notice is necessary.

The law and ethics require informed consent, in advance.

Is the notice requirement proposed for this exemption a meaningful and important measure to respect individual autonomy, particularly if the notice requirement could be fulfilled through a general public posting?

It is not clear to us how a notice akin to an adhesion contract is respectful of research subject autonomy.

Current practices suggest that IRBs will frequently waive informed consent for studies involving the secondary use of identifiable private information collected for non-research purposes.

As we point out in response to Question 49, we have no way to know why IRBs “typically waive informed consent.” The subject’s right to informed consent is a matter of human rights law. If there is a possibility that “the research could not practicably be carried out without a waiver of informed consent,” then the matter obviously is serious enough to warrant full IRB and agency review to reverse an ill-advised approval, and the rebuttable presumption should be that the research proposal should be disapproved.

If the exemption were to exclude the notice requirement, but continue to require application of the data security and privacy safeguards of Sec. __.105 and restrict the use of identifiable private information to only purposes of the specific research for which the investigator obtained the information, would the exemption better strike a reasonable balance between respect for persons and beneficence, while eliminating the current requirement for IRB review?

No. The information is too sensitive, and proposed Sec. __.105 is not protective. It is appropriate that safeguards be established, but cyber security technologies and Federal and private entities are not yet adequate to the task, as the Government Accountability Office has recognized. That the safeguards to be established under Sec. __.105 would have to be evaluated “at least every 8 years” is indefensible as against the pace of technological change. Sec. __.105 would have the adequacy of safeguards determined by what the Secretary of HHS

deems adequate; but no standards of adequacy are given here. While the HITECH Act standards are a guide, that Act is limited in application. Sec. ___.105 assumes that the Privacy Act and Paperwork Reduction Act may substitute for safeguards, but they protect neither information nor research subjects.

53. Public comment is sought as to whether this exemption would provide appropriate protections for research conducted by clinical data registries, while enabling these research activities to proceed without delay, and what should be included in guidance regarding such activities.

The purpose of the law is to protect the rights of research subjects, not “protections for research.” As we note in response to Question 52, this exemption would not provide appropriate protections for research subjects.

Public comment is sought regarding the extent to which other exclusions or exemption categories would apply to research conducted by clinical data registries, such that the conditions of this exemption category would not apply.

Exclusions and exemptions should not apply to registries. Registries should be regulated under the Common Rule and under additional regulations that address criteria for access and protections against unauthorized use.

d. Exemptions Subject to the Documentation Requirements of Sec. ___.104(c), the Privacy Safeguards Described in Sec. ___.105, Limited IRB Review as Described in Sec. ___.111(a)(9), and Broad Consent in Accordance With Sec. ___.116(c)

(1) Exemption for the Storage or Maintenance of Biospecimens or Identifiable Private Information for Secondary Research Use (NPRM at Sec. ___.104(f)(1))

(2) Exemption for Secondary Research Use of Biospecimens or Identifiable Private Information Where Broad Consent Has Been Sought and Obtained (NPRM at Sec. ___.104(f)(2))

v. Questions for Public Comment

54. Public comment is sought on whether the NPRM's proposal of exemption Sec. __.104(f)(2) is the best option,

The concerns and provisions of Sec. __.104(f)(2) are important and show by their own terms that these activities should not be exempt. If they are subject to some kind of exemption, then the ostensibly provided protections are meaningless, inasmuch as there has been and will not be full Common Rule oversight. Note that a major purpose in storing these data is to sell access.

or whether there is a better way to balance respect for persons with facilitating research.

As a matter of law, rights are not to be balanced against facilitating research.

55. Public comment is sought on whether and how the provision regarding the return of research results in the proposed exemption Sec. __.104(f)(2) should be revised.

See our response to Question 54.

The concerns and provisions of Sec. __.104(f)(2)(ii), regarding return of research results to the subject should not be buried in a section dealing with exemptions. It should be a free-standing requirement. Its drafting is problematic in this respect also: Protections depend on whether the investigator anticipates; that's too loose.

56. Public comment is sought on whether there should be an additional exemption that would permit the collection of biospecimens through minimally invasive procedures (e.g., cheek swab, saliva).

No. This violates the rights of human subjects. Inclusion of such a provision would open the door to extensive gathering of materials and subsequent cross-linking studies without consent. The mere fact of seeking permission via this NPRM militates against public trust.

e. Applicability of Exemptions to the Subparts (NPRM at Sec. __.104(b); Current Rule at Footnote 1)

ii. Questions for Public Comment

57. Public comment is sought on whether research involving prisoners should be permitted to apply any or all of the exemption categories found at proposed Sec. __.104, either if the research consists mostly of non-prisoners and only incidentally includes some number of prisoners, as proposed in the NPRM, or if the research intends to involve prisoners as research subjects.

No. Any research on prisoners or other persons whose liberty interests are restricted or under threat should be given special scrutiny under the Common Rule. To do otherwise violates U.S. and international law. We reiterate our response to Question 25.

No. Guidance should make clear: Anyone whose liberty interests are impeded or at risk should not be denied Constitutional rights or Common Rule protection of his or her rights in research. The term “prisoner” is insufficient. The same consideration should apply to detainees, to persons held without charge, to probationers, to persons who are parties at interest in law enforcement cases, to parolees, to persons under arrest, defendants, suspects, and others under or facing a legal disability under criminal law.

Prisoners, including those awaiting trial, are Constitutionally protected against forced medication except in rare circumstances. *United States v. Sell*, 539 U.S. 166 (2003) (6-3, forced medication of prisoner Constitutionally impermissible except in rare cases combining medical necessity, absence of less intrusive alternatives, and important state interest). That is for medication. Non-consensual research does not begin to satisfy that kind of Constitutional standard.

Note also that the Geneva Conventions and Additional Protocols prohibit research on individuals caught up in war, whether or not they have prisoner status.

58. Would it be preferable for language at Sec. __.104(b)(2) to resemble the 2002 epidemiologic waiver criteria and state that the exemptions apply except for research where prisoners are a particular focus of the research?

No, for the reasons stated in our response to Question 57.

59. Is the proposed application of the exemptions to subparts B and D appropriate?

No, for the reasons stated in our response to Question 57.

f. Question for Public Comment

60. What topics should be addressed in future guidance on improving the understandability of informed consent?

2. Broad Consent to the Storage, Maintenance and Secondary Research Use of Biospecimens and Identifiable Private Information (NPRM at Sec. __.116(c), (d)).

f. Questions for Public Comment

61. Public comment is sought on whether broad consent to secondary research use of information and biospecimens collected for non-research purposes should be permissible without a boundary, or whether there should be a time limitation or some other type of limitation on information and biospecimens collected in the future that could be included in the broad consent as proposed in the NPRM.

We discuss some of the relevant considerations in response to Question 49. Question 61 poses broader issues. The Question 61 proposal may be ethically and legally sustainable with appropriate protections, including: (1) Actual (not passive or opt-out) informed consent in circumstances conducive to voluntariness; (2) the subject has been informed that his or her data or biological materials may be used for research beyond original research purpose and perhaps for non-research uses; (3) third parties will not be adversely affected; (4) efforts will be made to maintain confidentiality but absolute confidentiality cannot be guaranteed; (5) consent must be by the actual subject, not by the subject's parent or legally authorized representative; (6) ownership issues are made clear; (7) the subject must be empowered and enabled to withdraw consent to further use; (8) the right of withdrawal of consent to further use can be exercised at any time; (9) the subject will be reminded periodically, at intervals no longer than every two years, of the fact that the data has been and may still be collected and of the right to withdraw consent; and (10) the subject will be notified as soon as possible of any failure or lapse of confidentiality or security relating to the subject's data.

Agency guidance should emphasize the importance of candor and good faith in the informed decision process.

If a time limit should be required, is the NPRM proposal of up to 10 years a reasonable limitation?

A time limit should be required. In no event should uses of the materials and data be allowed past the subject's 18th birthday without positive, first-person consent and under the conditions that we state above.

Would a limitation related to an identified clinical encounter better inform individuals of the clinical information and biospecimens that would be covered by a broad consent document?

Yes, but subject nevertheless to the conditions that we state above.

62. Public comment is sought on whether all of the elements of consent proposed at Sec. __.116(c) should be required for the secondary use of biospecimens or identifiable private information originally collected as part of a research study that was conducted without consent because either the original research study met an exclusion or exempt category of research, or a waiver of consent was approved by an IRB.

Yes, but not unless the Sec. __.116 language, "Except as provided elsewhere in this Policy . . . " is eliminated and the language of the entire section is simplified so that it can be read and interpreted as a single, comprehensive statement.

We point out in response to the rationale that fully informed, fully voluntary consent is essential for the protection of the subject's rights and for the protection of primary and subsequent users as well, because one patient's tissues and related data may be claimed by multiple institutions.

63. Public comment is sought on whether oral consent should be permissible in limited circumstances as proposed under exemption Sec. __.104(f)(1).

No. Such circumstances are unlikely to be fully informed or fully voluntary, and as we say in response to the regulatory rationale and Question 62, short-cutting full consent can impede the use of biomaterials and related data.

64. Would research subjects continue to be appropriately protected if the definition of "legally authorized representative" were broadened to include individuals authorized by accepted common practice to consent on behalf of another individual to participation in clinical procedures?

No. Such a change would tempt investigators into violation of local law, while the Common Rule requires a good-faith inquiry into who is qualified as a "legally authorized representative." These questions are not overly difficult but they require advice of qualified local counsel. Definitions and powers differ; for example:

Guardian . . . Person assigned by a court to act for and protect the ward for the purposes delineated in the order of guardianship. Must act in ward's best interests. Guardian's authority usually includes power to make medical decisions. In the District of Columbia, unless expressly authorized by the court in the guardianship order, it excludes authority to consent to the ward's being a research subject, and if such authority is granted the research must be in the best interests of this individual ward.

Conservator . . . Sometimes a guardian; usually a financial guardian.

Attorney . . . Usually a lawyer; advises, represents a client within agreed scope of representation.

Attorney in fact . . . Person designated by a principal to represent the principal in the event of the principal's incapacity.

Attorney and guardian ad litem . . . Person assigned by a court to act for and represent another in a specific court case and related activities.

Custodian or caretaker . . . Person who normally cares for someone who lacks legal capacity. Not necessarily designated by the court. May be a custodial parent. In some circumstances a court may limit a parent's power of decision.

Foster parent . . . Person assigned by a government social service agency, subject to court supervision, to care for someone else's child in the foster parent's own home; normally responsible for medical care decisions for the foster child.

Spokesperson or representative . . . Informal term for a person designated by family to speak for an incapacitated patient; has no legal authority except as specified in law or as ordered by a court.

Surrogate . . . In this context, person who speaks for someone else; may have legal powers, may not, depending on the jurisdiction and terms of appointment.

If the definition of "legally authorized representative" was broadened in this way, public comment is sought on the

interpretation of ``accepted" and ``common" as these terms would be used in the revised definition.

For the reasons just stated, institutions and researchers relying on such a provision would do so at their legal peril while likely depriving subjects of protection

B. Proposed Changes To Obtaining, Waiving, and Documenting Informed Consent (Sec. Sec. __.116 and __.117)

1. Required Elements of Informed Consent (NPRM at Sec. __.116(a), (b))

f. Question for Public Comment

65. Public comment is sought on how the waiver criterion regarding ``practicably" at Sec. __.116(d)(3) could be explicitly defined or otherwise clarified (e.g., what term should replace ``practicably"?).

This path around Common Rule is anomalous and contrary to law in the extant rule and ought not to be incorporated in any revision of the rule. It has been cited to justify research activities that because of violation of subjects' right of consent or because of risk never should have been conducted. If the concern behind the rule is medically necessary for these particular patients with still experimental interventions in emergent circumstances, then this provision is unnecessary; such interventions are already legally permissible as medical practice.

66. Public comment is sought on the proposed differences between the criteria for waiving informed consent for the research use of biospecimens versus identifiable information.

As we point out in response to Question 65, waiving the requirement for informed consent is contrary to U.S. and international law. The waiver language in the extant rule should be stricken and should not be incorporated in any revision.

67. Public comment is sought on whether the proposal to permit an IRB to waive consent for research involving the use of biospecimens should be included in the regulations.

No. IRBs have no authority to waive a subject's legal rights.

68. Public comment is sought on the proposal to permit an IRB to waive consent for the secondary use of biospecimens or information originally collected for research purposes, even if the original research study required subjects' informed consent.

No. IRBs have no authority to waive a subject's legal rights.

69. Public comment is sought regarding how likely investigators are to seek broad consent for the use of identifiable private information (as contrasted with biospecimens), given that there are provisions within the NPRM that would make it easier to do such research without consent (such as the new exemption at Sec. __.104(e)(2)).

We reiterate that research on human beings without their consent is unlawful. We have no way to know the likelihood of investigators' following the apparently easier procedure. Many will. They and their IRBs are advised routinely by some prominent IRB consultants not to follow any regulatory procedure if there is wiggle room. We know also that there are many conscientious investigators and IRBs who are diligent in their respect for and protection of research subjects.

In this regard, note that the NPRM proposal to prohibit waiver of consent by an IRB if a person has been asked for broad consent and refused to provide it might create a disincentive on the part of investigators from choosing to seek broad consent for research involving secondary use of identifiable private information. Given the costs and time and effort involved in implementing the system for obtaining broad consent for the use of identifiable private information and tracking when people provide consent or refuse to do so, are the benefits to the system likely to outweigh the costs,

As we point out, waivers of consent are unlawful. Allowing IRBs and investigators any way to get around a refusal of consent is contrary to law.

This weighing of “costs and time and effort” and “benefits to the system” against the right of consent or refusal is contrary to law and ethically deplorable.

and if so, should the broad consent provisions be limited to obtaining broad consent for research use of biospecimens?

The issues are far more complex. We address these issues at Question 61.

70. Public comment is sought on the proposed prohibition on waiving consent when an individual has been asked to provide broad consent under Sec. __.116(c) and refused.

To waive the requirement of consent as a precondition violates the protective legal mandate. No means no.

In particular, how would this prohibition on waiving consent affect the secondary research use of identifiable private information?

It should mean that a refusal of secondary research use of identifiable private information actually bars the secondary use of that information.

If an individual was asked to provide such consent, should the absence of a signed secondary use consent be considered a refusal?

No credible evidence of valid consent? Then no consent.

Does this prohibition on waiving consent for the secondary use of identifiable private information create a disincentive for institutions to seek broad secondary use consent and instead seek a waiver of consent from an IRB?

No IRB waiver of consent is legally permissible.

Under what circumstances, if any, would

it be justified to permit an IRB to waive consent even if an individual declined or refused to consent?

None. Any investigator or institution would do so at legal peril.

C. Proposed Changes To Protect Information and Biospecimens (NPRM at Sec. __.105)

6. Questions for Public Comment

71. Public comment is sought regarding whether particular information security measures should be required for certain types of information or research activities

Security measures and security audits of the kind contemplated in the HITECH Act are needed, because of current security gaps, increased hacking, and advances in data mining and cross-linkage.

and, if so, what measures and for what types of information or research. Specifically, should the safeguards be calibrated to the sensitivity of the information to be collected?

No. The loss or hacking or misuse of seemingly innocuous data has become highly consequential.

72. Are the proposed limitations on re-disclosure more or less restrictive than necessary? Are there additional purposes for which re-disclosure of biospecimens or identifiable private information should be permitted?

Current and proposed limitations on re-disclosure are insufficiently protective. There are no legally enforceable standards of access, and there are no meaningful sanctions for violation.

D. Harmonization of Agency Guidance (NPRM at Sec. __.101(j))

6. Question for Public Comment

73. Will the proposed language at Sec. __.101(j) be effective in achieving greater

harmonization of agency guidance, and if not, how should it be modified?

Harmonization of agency guidance properly belongs in the agencies' rules of procedure although the Common Rule may reference those rules. Some agencies operate under law more specific than the Department of Health and Human Services. For reasons of transparency and public trust, and consistent with the purposes of the Administrative Procedure Act, Common Rule harmonization activities should be public. Ex parte contacts in the generation, drafting, and consideration of Common Rule guidance should be barred under agency rules of procedure. The bar on ex parte contacts should extend to meetings of agency officials with private and mixed Federal-private entities where the topic is Common Rule change or promulgation or amendment of guidance, except when such meetings, including advisory services, are conducted as if covered by the Federal Advisory Committee Act and Government in the Sunshine Act.

The proposed Sec. ___.101(j) language makes harmonization optional. Complete harmonization is not possible. But consultation is desirable, especially because IRB's and their advisers are not generally aware of legal requirements other than those of the Food and Drug Administration and the Department of Health and Human Services.

E. Cooperative Research (NPRM and Current Rule at Sec. ___.114) and Proposal To Cover Unaffiliated IRBs Not Operated by an Institution Holding a Federalwide Assurance (NPRM at Sec. ___.101(a))

6. Questions for Public Comment

74. Is mandated single IRB review for all cooperative research a realistic option at this time?

No. Single, IRB-like central review is appropriate for technical, safety aspects of these studies. But the research institutions retain liability for what is done in their name. To exercise their own responsibilities and to ascertain whether to empower their agents to conduct research, they need to retain their own IRBs, which, unlike central IRBs, have local knowledge, are less likely to be swayed by appointees from among advocacy organizations, are more likely to be credible within their own research communities, and are more likely to have requisite local knowledge.

That IRBs may differ on the same project may be inconvenient but is likely to reveal problems in the protocol. Example: A study approved by several IRBs but had to be modified when one IRB observed that the protocol sought incriminating admissions from subjects.

As serious or more so is the changing nature of the IRB industry, which has experienced numerous mergers and consolidations recently. Now there are a relatively few commercial IRB providers. They tend to secrecy, process thousands of protocols, and promise rapid turnover and customer satisfaction. Because of high volume, IRB meetings often take place by telephone, or because IRB business may be conducted on-line, there is likely insufficient face-to-face deliberation. This easily becomes processing rather than critical scrutiny. There is no way to tell from their public disclosures how they handle their corporate conflicts of interest, pressures to perform, local knowledge, and the need for neutrality. Among the largest such entities is the Western-Copernicus Group, which advertises: “WIRB is the leading provider of independent IRB, biosafety and other human protection services to research institutions, CROs and major sponsors. The company has offices in the U.S. and Canada and provides review services in all 50 states and in more than 60 countries around the world.” Western-Copernicus Group is one of several properties “in the portfolio” of Arsenal Capital Partners, whose portfolio includes service companies in the hospital and medical device industry.

The scandals at some institutions that have been accredited give us no faith in accreditation of IRBs.

Reliance on commercial IRBs as central IRBs does not promise better review. Reliance on university IRBs may work if they are staffed up and well supported. Reliance on government IRBs is vulnerable to personnel and budget uncertainty, to agency project momentum (and what the military terms “command influence”), and to over-representation from advocacy organizations.

Please provide information about the likely costs and benefits to institutions.

For non-government institutions, likely costs include:

- Increased liability exposure from:
 - Loss of control over activities for which they are responsible.
 - Loss of researcher involvement in Common Rule oversight.
 - Loss of apprenticeship in Common Rule oversight.
 - Lower overhead reimbursement despite the need to maintain IRB capabilities for oversight of research nevertheless, for research not sent to central IRB review.
 - Uncertain indemnification for central IRB delicts.

- Reliance on central IRBs driven by agency momentum or by need for high volume, rapid turnover, and customer satisfaction.
- Legal costs of negotiation and contracting.
- Charges by central IRB.
- Loss of researcher involvement in Common Rule oversight.
- Loss of training in Common Rule compliance.
- Reputational costs in event of adverse news and adverse events.

For non-government institutions, likely benefits include:

- Fewer large protocols for in-house review.

Will additional resources be necessary to meet this requirement in the short term?

Not likely; government and university budgets are too tight and uncertain.

Should savings be anticipated in the long run?

There is no way to know.

75. What areas of guidance would be needed for institutions to comply with this requirement?

Requirement of reliance on central IRBs changes the system from one of investigator involvement, institutional involvement, and buy-in by the regulated community; no longer audited self-regulation, it would become high volume protocol processing, with loss of what little transparency there is. No such move should be made in that direction until enforceable standards are in place to ensure review quality, to insist on deliberation, and to establish accountability.

Is there something that OHRP could do to address concerns about institutional liability, such as the development of model written agreements?

No. Institutional liability has elements in common but is largely a matter of state common law. For OHRP to develop model agreements would put OHRP in the position of practicing law with neither a license nor competence, and the

institutions would rely on such documents at their legal and financial peril. These are decisions to be made by institutions on the advice of their legal counsel.

There a tendency among IRB administrators and chairs to ask each other for legal advice but not to consult their institutional counsel. The existence of model documents exacerbates the problem.

76. Would it be useful for this requirement to include criteria that Federal departments or agencies would need to apply in determining whether to make exceptions to the use of a single IRB requirement? If so, what should these criteria be?

If there is such a requirement, it should not go into effect until the requisite integrity standards and quality-of-review are established in regulation and the agencies are willing to monitor, inspect, and enforce.

77. Are the exceptions proposed appropriate and sufficient, or should there be additional exceptions to this mandate for single IRB review than those proposed in the NPRM? If additional exceptions should be included, please provide a justification for each additional exception recommended.

See our response to Question 76.

78. Is three years appropriate timing to establish compliance with this provision?

No, for reasons stated in our response to Question 76.

F. Changes To Promote Effectiveness and Efficiency in IRB Operations

1. Continuing Review of Research (NPRM at Sec. __.109(f); Current Rule at Sec. __.109(e))

Exemptions from continuing review are hazardous and inadvisable in any event. They foster continuing use of these human subjects although the scientific warrant the research may have been obviated by events. They remove research activities that were cleared at one time from Common Rule oversight and thus eliminate legally mandated protections even though some of the exemptions appear to permit non-consensual research. They assume that additional, material information bearing on research protections is of no importance. They impede the IRB's fulfilling its responsibilities. And they assume that the go-ahead was a right decision in the first place and now beyond question.

I . . . said I was sorry to create annoyance and disappointment, but that upon reflection it really seemed best Their disapproval was prompt and loud; their language mutinous. Their main argument was one which has always been the first to come to the surface, in such cases, since the beginning of time: "But you decided and AGREED . . ."; as if, having determined to do an unwise thing, one is thereby bound to go ahead and make TWO unwise things of it, by carrying out that determination.

Mark Twain, A Dying Man's Confession, Life on the Mississippi (1883).

2. Expedited Review Procedures and the Definition of "Minimal Risk" (NPRM at Sec. Sec. __.110 and __.102(j))

f. Questions for Public Comment

79. How often should the Secretary's list of minimal risk activities be updated?

As we point out in our response to the regulatory rationale, promulgating broad categories of research as a priori minimal risk or not worth review but re-examining the list every eight years do not substitute for weighing the ethical merits and drawbacks of individual research projects involving circumstances, subjects, and research activities that may differ significantly. But the NPRM rationale does not consider these issues.

The proposed Sec. __.102 amendment does not solve the problem. We have observed from IRB members' and administrators' discussions that IRB compliance may be desultory, and IRBs have been advised to do only the minimum absolutely required, and one result is an erroneous belief subjects are vulnerable only if in a group identified in the Common Rule subparts. The NPRB amendment provides for review of the minimal-risk list at intervals of no more than eight years. The NPRB says the the default position is that anything on the list is in fact minimal risk and that IRBs may consider other categories as minimal risk if they see fit to do so. That is not protective.

The kinds of issues that give rise to the idea of a list of minimal-risk categories are better dealt with by guidance, with examples. If a list is published in the rule or if the list refers to a promulgated list, then the list is subject to challenge at any time under the Administrative Procedure Act. Technologies are changing so quickly that if such a list is promulgated then it should be reviewed and revised at intervals of no more than two years and sooner if events warrant. An event that would warrant review would be a major cyber security failure involving a public or private entity and involving data that were supposed to be confidential.

Should advice be solicited from outside parties when updating the list?

Yes. This should follow a notice-and-public-comment procedure, with any ex parte participation made public; this would be conducive to public trust. (For a procedural model, note that Federal Energy Regulatory Commission ex parte staff contacts are reported routinely in the Federal Register.)

80. Is this Secretarial list of minimal research activities a useful tool for the research community, or does it represent a loss of IRB flexibility in risk determination?

It is unlikely to be useful if the measurement of utility is fulfillment of ethical and legal responsibility. The default positions in the proposed amendment and explanation appear to reduce IRB authority to provide more protection where warranted. Institutional counsel should address this question.

G. Proposed Changes to IRB Operational Requirements

1. Proposed Criteria for IRB Approval of Research (NPRM at Sec. __.111)

f. Questions for Public Comment

81. What should IRBs consider when reviewing the plans for returning research results, for example, what ethical, scientific, or clinical concerns?

All information to which the subject is entitled as a matter of law, and all personal medical findings, including those that are medically actionable and those that are not medically actionable.

82. Is the Sec. __.111(a)(3) and (b) focus on issues related to coercion or undue influence in research with vulnerable populations, and not other considerations related to vulnerability, appropriate? Note that this focus also appears in proposed Sec. __.107(a).

We address these issues also in response to Questions 25, 26, 36, 41, 47, 57, and 79.

Issues related to coercion and undue influence are important, but this provision should make clear its applicability to any subject or group of subjects

whose freedom of choice is limited, whether by vulnerability to coercion or undue influence or by lack of an accessible avenue of legal redress, or by physical condition or mental impairment, or by limited education, or by legal disability, or by socioeconomic factors, or by local circumstances, by threatened or restricted liberty, or by any other factor that limits voluntariness. Such factors should be taken into account whether or not the subjects are covered by a subpart of the Common Rule. Here again, special attention should be paid to the problem of the current, narrow interpretations of “prisoner.” We reiterate:

Anyone whose liberty interests are impeded or at risk should not be denied Constitutional rights or Common Rule protection of his or her rights in research. The term “prisoner” is insufficient. The same consideration should apply to detainees, to persons held without charge, to probationers, to persons who are parties at interest in law enforcement cases, to parolees, to persons under arrest, defendants, suspects, and others under or facing a legal disability under criminal law.

Prisoners, including those awaiting trial, are Constitutionally protected against forced medication except in rare circumstances. *United States v. Sell*, 539 U.S. 166 (2003) (6-3, forced medication of prisoner Constitutionally impermissible except in rare cases combining medical necessity, absence of less intrusive alternatives, and important state interest). That is for medication. Non-consensual research does not begin to satisfy that kind of Constitutional standard.

Note also that the Geneva Conventions and Additional Protocols prohibit research on individuals caught up in war, whether or not they have prisoner status.

83. Should pregnant women and those with physical disabilities be included in the category of subpopulations that may be vulnerable to coercion or undue influence?

See our response to Question 82.

2. Proposed Revisions To IRB Operations, Functions, and Membership Requirements

e. Question for Public Comment

84. Should populations be considered vulnerable for reasons other than vulnerability to coercion or undue influence?

Yes. See our response to Question 82.

Are the proposed categories appropriate?

The regulatory problem is to foster good-faith judgment. The subpart categories are important but do not describe the range of vulnerabilities to undue influence and coercion.

H. Other Proposed Changes

1. Proposal To Extend the Common Rule to All Clinical Trials (With Exceptions) (NPRM at Sec. __.101(a)(1))

Although the NPRM does not ask a question here, we must point out that this section is far too permissive in its provision, “except that each department or agency head may adopt such procedural modifications as may be appropriate from an administrative standpoint.” Without language clarifying that procedural conveniences shall not relieve the agency or research institutions and researchers from the substantive, protective obligations of the Common Rule.

f. Questions for Public Comment

85. Public comment is sought on whether there might be unintended consequences from the clinical trials expansion proposed in the NPRM in Sec. __.101(a)(2)(i). Unintended consequences may include an increase in burden or costs, or an inappropriate redistribution of costs.

The burdens most important to consider would be burdens borne by research subjects where full Common Rule oversight and protections do not apply. In this regard, neither the current rule nor the NPRM deal with the respective duties of IRB and data and safety monitoring entities.

It is not clear why sponsor departments and agencies would not, sensibly, direct institutions that feel themselves “burdened” to expand their review capacity to meet demand. Federal grants, with overhead, are paid to the institution.

86. Public comment is sought as to whether the criterion that the policy extends to all clinical trials conducted at an institution that receives federal support (see the NPRM at Sec. __.101(a)(2)(i)) should be further clarified in some way.

Yes, inasmuch as the definition of clinical trial is confusing; see our response to Question 87, below.

For example, should it specify a timeframe for support (e.g., within the past number of years), or a minimum monetary threshold value?

No. If an activity must be regulated in order to protect human subjects of research, then it must be regulated.

87. Public comment is sought on whether the definition of clinical trial (NPRM at Sec. __.102(b)) should include additional explanation of what is encompassed by the term behavioral health-related outcomes.

The proposed definition raises problems. The definition appropriately includes n-of-1 studies that otherwise qualify in that they involve health-related interventions. But the definition also is so broad as to cover large population-based epidemiologic studies. At the same time, the question is open as to whether it applies to preclinical studies, pharmacokinetic studies, and some Phase Zero and Phase One studies, because they are not medical interventions with therapeutic intent. The definition given will require a great deal of careful parsing. Here the rule should defer to the Food and Drug Administration.

2. Changes to the Assurance Process (NPRM at Sec. Sec. __.103 and __.108; Current Rule at Sec. __.103)

e. Question for Public Comment

88. Would protection to human subjects in research be enhanced if OHRP conducted routine periodic inspections to ensure that the membership of IRBs designated under FWAs satisfy the requirements of Sec. __.107?

The NPRM proposes deletion of the requirement that changes in IRB membership be reported to the department or agency head, or to OHRP when the existence of an HHS-approved assurance is accepted. The deletion is not conducive to public trust. The IRB system is an example of what administrative and regulatory law scholars term audited self-regulation. It depends on law and public trust for its societal legitimacy. IRB membership is an essential part of the public record and should be treated and accessible as such. The NPRM itself suggests why: Often enough to merit comment from the drafters, persons not formally appointed to the IRB appear as alternates and vote. We have seen alternates who viewed their task as representing their departments rather than as vetting protocols and protective measures under the Common Rule.

For the same reason, IRB minutes should be public records—although redacted to eliminate disclosure of trade secrets and to protect confidentiality of research subjects identified from or identifiable in the minutes.

Routine periodic inspections of IRBs to verify compliance with assurances are essential even when IRB rosters are filed with OHRP or other Common Rule agency.

3. Department or Agency Discretion About Applicability of the Policy (NPRM at Sec. __.101(c), (d), (i)) and Discretion Regarding Additional Requirements Imposed by the Conducting or Supporting Department or Agency (NPRM and Current Rule at Sec. __.124)

4. Research Covered by This Policy Conducted in Foreign Countries (NPRM at Sec. __.101(h))

Although the NPRM does not request specific comment on this provision, we express our dismay at the proposed removal of reference to the Declaration of Helsinki, the research ethics statement so widely used that it is incorporated by reference in a great deal of foreign law, including law of the European Union. In the current regulation, the Helsinki document is referenced as an example of an ethical norm consistent with our Common Rule. From the NPRM language, this amendment, and the proposed rule, we fear that the Common Rule will no longer be consistent with the ethical norm expressed in Helsinki.

Some U.S. researchers harbor the belief that there is no relevant foreign or international law. Our Common Rule should alert U.S. researchers, research institutions, and their foreign collaborators of their obligation to observe relevant international law referenced by periodic publication by the Office for Human Research Protections. The relevant international law applies at home and abroad and are civilian as well as military obligations, as we point out above. We call special attention to this law here because of expanding U.S. research involvement in places of war, unrest, and inability to vindicate human rights—including that of informed consent. Among requirements to be kept in mind:

- 1949 Geneva Conventions, common articles:
 - Wounded, sick military at sea or in field: No biological experiments.
- Prisoners of war:
 - no medical or scientific experiments not justified by individual POW's medical need and conducted in this POW's interests
- 1977 Geneva Convention Protocols: Victims of armed conflicts:

- Wounded, sick, or shipwrecked : No medical or scientific experiments even with consent.
- Interned, detained, or otherwise held persons: No medical procedure not indicated by the individual's medical status; no medical procedure inconsistent with medical standards for free persons.
- International Covenant on Civil and Political Rights:
 - “In particular, no one shall be subjected without his free consent to medical or scientific experimentation.” This right is non-derogable (absolute) even in time of public emergency.

Refugees and other internationally displaced persons are especially vulnerable—some to others traveling alongside them, and some to discrimination and persecution. Accordingly, they are supposed to be protected under international law. Because of research on these people, guidance should alert researchers to relevant law and policy and ethical concerns. See James G. Hathaway, *The Rights of the Refugee in International Law* (Cambridge 2005) at 380 (on Ugandan discrimination against refugees).

. . . [R]esearcher and the sponsoring organization have a duty to make a safety assessment: Are the research subjects still vulnerable to coercion or retribution? . . . [C]onfidentiality and security of the original research records cannot be ensured, despite . . . good intentions. . . .

. . . There are many reasons to collect data in an emergency setting (administrative data collection, physician interviews, surveillance, to name a few), but not all of these are . . . research. However, they may still involve potential risks and benefits for research subjects, depending on the future use of such data.

The dangerous and extreme circumstances that accompany conflict and forced migration can make it very difficult to conduct ethical research. For example, . . . public health workers crossed . . . accompanied by armed insurgents as security guards . . . to conduct public health surveys. Can one ethically make use of the data they collected? Many nongovernmental organizations (NGOs) collect program data that are meant to be internal, but are later used by researchers; is it ethical to use these found data? If they are individual case notes, is the answer different than if they are macro-level data? Also, it may not be known whether or not the data were collected in an ethical manner. All of these issues are real dilemmas in the field when data are precious but may be fraught with ethical concerns.

National Research Council, Roundtable on the Demography of Forced Migration, in *Research Ethics in Complex Humanitarian Emergencies* (2002) at 2-3.

The effort of response poses an inescapable burden in the potential for opening or re-opening of emotional wounds despite ethical obligations. Nicholas Howen, Fundamental Protection Function of the Human Rights Field Operation, in *Human Rights Field Operation: Law, Theory and Practice*, supra (Michael O’Flaherty ed., 2007) at 43.

The United States has relevant international legal obligations under the International Covenant on Civil and Political Rights, under customary international law, see Restatement (Third) of the Foreign Relations Law of the United States sec. 702 (1986), and as a state party to the 1967 Protocol Relating to the Status of Refugees, 19 U.S.T. 6223, T.I.A.S. No. 6577, 606 U.N.T.S. 267.

The Protocol obligates the United States is obligated to cooperate with the U.N. High Commissioner for Refugees in conduct of the UNHCR’s mission. The UNHCR’s protective mission in turn requires deference to UNHCR administrative interpretations, including the paramount principle of personal security. “The personal security of refugees is an essential element of international protection. Unless the fundamental rights of refugees as human beings . . . are safeguarded, other rights . . . are of little use. Ensuring the safety of refugees and asylum seekers . . . has consequently been a major preoccupation of UNHCR and an important component of the Office’s field activities.” UNHCR, *The Personal Security of Refugees*, EC/1993/SCP/CRP.3, <http://www.refworld.org/docid/3ae68cd10.html> (5 May 5, 1993).

UNHCR thus cautions: “In the context of standard programming in refugee settings it is not recommended to do research on prevalence figures of mental disorders because this is methodologically complicated, requires specific resources and, most importantly, the research outcomes are not essential to design services.” UNHCR, *Operational Guidance: Mental Health & Psychological Support Programming for Refugee Operations*, <http://www.refworld.org/docid/53a3ebfb4.html> (2013).

Accordingly, we recommend that the agencies adopt appropriate guidance and reference that guidance in the Common Rule.

I. Effective and Compliance Dates of New Rule (NPRM at Sec. __.101(k))

1. Effective Dates

2. Transition Provisions

a. Research Initiated Prior to the Effective Date of This Subpart (NPRM at Sec. __.101(k)(1))

b. Use of Prior Collections of Biospecimens (NPRM at Sec. __.101(k)(2))

Although the NPRM asks no specific question about rule-change transition, we point out that it leaves research institutions with discretion to remove studies from Common Rule oversight but sets no protective standards for doing so.

D. ADDITIONAL COMMENTS.

We recommend that the Common Rule agencies withdraw the rule proposed in the NPRM and reconsider whether major revisions of the existing Common Rule are warranted instead of guidance on issues addressable within the existing rule. The changes proposed in the NPRM would alter relationships between research institutions and the agencies, between researchers and their institutions, and between research subjects and researchers, between physicians and patients, and between regulatory agencies and industry at home and abroad. The proposed changes would further reduce transparency and would reduce public trust.

The NPRM, as we pointed out concerning the ANPRM, relies mainly on highly questionable assumptions and a biased, largely one-sided selection of relevant literature and reflects inadequate consideration of how the proposed changes would play out in practice. It is telling that critics of the existing rule address not workaday problems under the rule but theoretical issues—over-regulation, for example, and, like the NPRM drafters, seeking to balance personal rights against supposed ultimate societal benefit. The NPRM drafters attempted to justify the changes largely on theoretical grounds rather than on the actual operation of the existing rule. The existing rule has been the core of an imperfect but generally successful, widely emulated, generally protective, predictable, stable, relatively simple, easily understood system for maintaining trust and protecting the rights of research subjects.

Problems arising under the current rule can be addressed in agency guidance, with notice and opportunity for public comment.

Whether a destabilizing change of the kind proposed in the instant NPRM is warranted requires more thought—especially as to its legality and ethicality. If the agencies still believe that extensive changes in the Common Rule are legal, ethical, prudent, and needed, then after considering responses to this NPRM they can undertake another cycle of notice and comment. Authorities in administrative and regulatory law advise that, as the Administrative Conference of the United States has recommended and as courts have favored, agencies will find it useful to go through another round of notice and comment where previous cycles have raised substantive and legal issues that warrant more attention. Jeffrey S. Lubbers (American Bar Association, Government and Public Sector Lawyers Division & Section of Administrative Law and Practice, 3d ed. 1998) at 193 (annotations omitted).

Such problems in this NPRM include:

- Failure to recognize the breadth and reach of the legal mandate for protection of the rights of human subjects of behavioral, social, and biomedical research, including the requirement for fully voluntary, informed consent.
- Failure to address problems these changes would introduce for industry and research institutions by disrupting harmonization of U.S. and foreign regulation of clinical trials and by conflicts of personal privacy law.
- Assumption that current law and policy on information privacy are adequately effective and may substitute for the protections intended in the current Common Rule.
- Failure to take account of recent major Federal agency and private entity cyber security vulnerabilities and failures involving unwanted disclosures of high-value, highly personal data on millions of identified Americans.
- Failure to take account of recent rapid growth of unregulated data acquisition, data mining, cross-linkage, and analytics involving identified personal data.
- Failure to take into account the increasing research quest for predictive power of behavioral, social, neuroscience, and genetic studies with regard to behavior and susceptibility to disease, and the consequent exacerbation of possible personal consequences of unwanted disclosures.
- Failure to take account of recent consolidations and conflicts of interest in the commercial IRB industry.
- Failure to account for how short-cutting consent would give rise to disputed ownership of biomaterials and related data.
- Failure to take into account any of the major problems identified in the news and in Inspector General reports dating back for the last 15 years.
- Proposed changes inconsistent with relevant international harmonization in drug regulation and failure to account for incompatibility of the proposed rule with foreign law, including that of the European Union, that is more protective of privacy and other rights of research subjects.

The NPRM rationale and proposed rule would replace a well established, workable regulation with an attempt through rulemaking to legitimize turning millions of people into subjects of studies overseen secretly if at all and to gather highly personal data without adequate safeguards. Much of this would be without even a pretense of seeking legally required, fully voluntary, fully informed consent. This is not conducive to public trust.

The NPRM rationale should be rejected and the rule proposal withdrawn.

Sincerely,

For Citizens for Responsible Care and Research:

[Electronic filing]

Elizabeth Woeckner, M.A.
President, CIRCARE

[Electronic filing]

Gerald S. Schatz, J.D.
(Of the Bars of the District of Columbia and Pennsylvania)
Past Vice President, CIRCARE

Reply to: Elizabeth Woeckner, M.A.
President, CIRCARE
1024 N. 5th S.
Philadelphia, PA 19123-1404
E-mail: lizwoeckner@mac.com
Telephone: 267.671.8212

Or: Gerald S. Schatz, J.D.
10788 Brewer House Rd.
Rockville, MD 20852
E-mail: geraldschatz@att.net
Telephone: 301.984.6142