public hearing.'' is corrected to read ''Notice of proposed rulemaking by cross-reference to temporary regulations and notice of public hearing.''.

2. On page 236, column 3, in the preamble, under the paragraph heading ''Special Analyses'', last line of the column, the language ''sharing agreements. Few small entities'' is corrected to read ''sharing arrangements. Few small entities''.

3. On page 237, column 1, in the preamble, under the paragraph heading ''Special Analyses'', first paragraph of the column, line 2, the language ''agreements, as defined by these'' is corrected to read ''arrangements, as defined by these''.

4. On page 237, column 1, in the preamble, under the paragraph heading ''Comments and Public Hearing'', third paragraph, line 1, the language ''The rules of 26 CFR 601.601(a)(93)'' is corrected to read ''The rules of 26 CFR 601.601(a)(3)''.

§ 1.482–2 [Corrected]

5. On page 237, column 3, § 1.482–2(f)(2), the language ''Election to apply paragraph (b) of this section to earlier taxable years.'' is corrected to read ''Election to apply paragraph (b) to earlier taxable years.''.

LaNita Van Dyke,

Chief, Publications and Regulations Branch, Legal Processing Division, Associate Chief Counsel (Procedure and Administration).

[FR Doc. E9–4687 Filed 3–4–09; 8:45 am]

BILLING CODE 4830–01–P

DEPARTMENT OF HEALTH AND HUMAN SERVICES

45 CFR Part 46

Office for Human Research Protections; Institutional Review Boards

AGENCY: Department of Health and Human Services, Office of the Secretary, Office of Public Health and Science, Office for Human Research Protections.

ACTION: Advanced notice of proposed rulemaking; request for comments.

SUMMARY: The Office for Human Research Protections (OHRP), Office of Public Health and Science is seeking information and comments on whether OHRP should pursue a notice of proposed rulemaking (NPRM) to enable OHRP to hold institutional review boards (IRB) and the institutions or organizations operating the IRBs, hereafter referred to as the IRB organizations (IORG), directly accountable for meeting certain regulatory requirements of the Department of Health and Human Services (HHS) regulations for the protection of human subjects. OHRP is contemplating this regulatory change to encourage institutions to rely on IRBs that are operated by another institution or organization, when appropriate. Historically, OHRP has only enforced compliance with 45 CFR part 46 through the institutions that were engaged in human subjects research. This has been the case even in circumstances when a regulatory violation was directly related to the responsibilities of an external IRB that was designated on the engaged institution's assurance of compliance with OHRP. OHRP is considering whether to pursue a regulatory change that would enable the Department to hold IRBs and IORGs directly accountable for compliance with the provisions of 45 CFR part 46 that relate to an IRB's or IORG's responsibilities. OHRP believes that such a regulatory change in its enforcement authority may address one of the main disincentives institutions have cited as inhibiting them from exercising the regulatory flexibility that currently permits institutions to implement a variety of cooperative review arrangements and to rely on the review of an IRB operated by another institution or organization. If institutions become more willing to rely on cooperative review arrangements and on review of IRBs operated by other institutions or organizations, OHRP believes that this will reduce administrative burdens such as the time associated with IRB review for multi-site studies, the time devoted by IRB staff and investigators to duplicative IRB review, and the time and personnel costs associated with operating an IRB for those institutions that choose not to establish an internal IRB—without diminishing human subject protections. This request for information and comments stems from interest in this issue from the Secretary's Advisory Committee on Human Research Protections (SACHRP) and others, as well as two meetings on alternative IRB models that OHRP co-sponsored in November 2005 and November 2006 along with the National Institutes of Health (NIH), the Association of American Medical Colleges (AAMC), and the American Society of Clinical Oncology (ASCO).

DATES: Submit written or electronic information and comments by June 3, 2009.

ADDRESSES: You may submit comments by any of the following methods:

- *E-mail: IRBaccountability@hhs.gov.* Include ''IRB Accountability RFI'' in the subject line.
- *Fax:* 301–402–2071.
- *Mail/Hand Delivery/Courier [For paper, disk, or CD–ROM submissions]:* Julie Kaneshiro, OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852.

Comments received within the comment period, including any personal information provided, will be made available to the public upon request.

FOR FURTHER INFORMATION CONTACT: Julie Kaneshiro, OHRP, 1101 Wootton Parkway, Suite 200, Rockville, MD 20852; 240–453–6900; e-mail *julie.kaneshiro@hhs.gov*.

SUPPLEMENTARY INFORMATION:

I. Background

HHS, through OHRP, regulates research involving human subjects conducted or supported by HHS in regulations codified at 45 CFR part 46. The HHS regulations at 45 CFR part 46 identify requirements that pertain to several different entities, including the IRB and the institution engaged in non-exempt human subjects research. The IRB is an administrative body that takes the form of a board, committee, or group, and is responsible for conducting initial and continuing review of research involving human subjects. The IRB must have authority to approve, require modification in (in order to secure approval), or disapprove all research activities covered by the HHS regulations (45 CFR 46.109(a)). An IRB's primary purpose in reviewing research is to ensure the protection of the rights and welfare of human research subjects.

Requirements for an Assurance of Compliance

The HHS regulations for the protection of human subjects require that each institution engaged in non-exempt human subjects research conducted or supported by HHS provide a written assurance satisfactory to the Secretary of Health and Human Services that it will comply with the requirements of the HHS regulations (45 CFR 46.103(a)). OHRP reviews and approves such assurances on behalf of HHS. The Federalwide Assurance (FWA) is now the only type of assurance accepted and approved by OHRP. An FWA commits the entire institution (including institutional officials, IRBs designated in the assurance, research investigators, and all other employees or agents) to compliance with the HHS regulations whenever the institution is engaged in HHS-conducted or

-supported human subjects research. In addition, domestic institutions may voluntarily extend their FWA to cover all human subjects research at their institution regardless of the source of support for the particular research activity.

Among other things, an institution's assurance of compliance must designate all of the IRBs that the institution will rely upon for the review of any research covered by its assurance (45 CFR 46.103(b)(2)). For each designated IRB, a list of IRB members identified by name, earned degrees, representative capacity, experience, and any employment or other relationship with the institution must be submitted to OHRP (45 CFR 46.103(b)(3)). The HHS regulations at 45 CFR part 46 provide an institution with significant flexibility in designating the IRBs that will review research under the institution's FWA. Options available to the institution include:

- Designating on its FWA one or more IRBs that are operated by the institution (sometimes referred to as ''local'' or ''internal'' IRBs; hereafter referred to as ''internal IRBs''); and
- Designating on its FWA one or more IRBs operated by other institutions or commercial or independent IRBs (hereafter referred to as ''external IRBs'').

As stated in the Terms of Assurance for the FWA (see *http://www.hhs.gov/ohrp/humansubjects/assurance/filasurt.htm*), for each external IRB designated on an institution's FWA, an IRB Authorization Agreement must be executed:

> Any designation under this Assurance of another Institution's IRB or an independent IRB must be documented by a written agreement between the Institution and the IRB organization outlining their relationship and include a commitment that the designated IRB will adhere to the requirements of this Assurance. OHRP's sample IRB Authorization Agreement may be used for such purpose or the two organizations may develop their own agreement. This agreement should be kept on file at both organizations and made available to OHRP upon request.

OHRP provides an example of an IRB Authorization Agreement at *http://www.hhs.gov/ohrp/humansubjects/assurance/iprotsup.rtf*. The agreement may be written to cover one research project, or to cover multiple research projects on a case-by-case basis, or to cover a class of research projects. This agreement will sometimes include a description of which regulatory requirements each party will be responsible for; *e.g.*, reporting unanticipated problems involving risks to subjects or others (45 CFR 46.103(b)(5)) or the maintenance of IRB records (45 CFR 46.115).

Requirements for IRB Registration

Before an IRB may be designated on an institution's FWA, the IRB must be registered with OHRP. For more information on IRB registration see *http://www.hhs.gov/ohrp/assurances/*.

OHRP has been operating a system of IRB registration since December 2000, which was initiated in response to a 1998 HHS Office of Inspector General recommendation that all IRBs register with the Federal government on a regular basis as part of an effort to develop a more streamlined, coordinated, and probing means of assessing IRB performance and to enhance the Federal government's ability to identify and respond to emerging problems.

The OHRP IRB registration system was designed to collect information required under the HHS human subjects protection regulations at 45 CFR 46.103, as well as additional information that is provided voluntarily by institutions or IRBs regarding the accreditation status of the institution or IRB organization, the total numbers of active research protocols reviewed by the IRB (including protocols supported by other Federal departments or agencies) and the nature of those protocols, and IRB staffing.

On July 6, 2004, OHRP published in the **Federal Register** a Notice of Proposed Rulemaking (NPRM) seeking public comment on changes to the current IRB registration system administered by OHRP (69 FR 40584). OHRP proposed to amend the HHS human subjects protection regulations at 45 CFR part 46 by adding an additional subpart, entitled ''Registration of Institutional Review Boards.'' Under the proposed new subpart, for any IRB designated under an FWA that reviews human subjects research conducted or supported by HHS, most of the information, including the information that previously was provided on a voluntary basis, listed on the current OHRP IRB registration form would have to be submitted to OHRP. By requiring such information to be provided for all IRBs being registered, OHRP's IRB registration requirements would become substantially consistent with requirements for IRB registration that were simultaneously proposed by FDA (69 FR 40556).

After taking into consideration the comments received during the public comment period, OHRP and FDA issued separate final IRB registration rules on January 15, 2009, that will become effective on July 14, 2009 (74 FR 2399; 74 FR 2358). OHRP's and FDA's IRB registration rules are compatible and largely consistent with one another. Under these final rules there will be a single registration system, accessible on the OHRP Web site, in which all IRBs that review research conducted or supported by HHS or clinical investigations regulated by FDA will need to be registered.

Enforcement Authority

Section 289 of the Public Health Service Act authorizes OHRP to, on behalf of HHS, establish a compliance oversight process regarding violations of the rights of human subjects of research conducted or supported by HHS. Pursuant to this authority, OHRP may receive reports of such violations and take appropriate action.

OHRP also derives compliance oversight authority from the previously discussed provisions of the HHS regulations at 45 CFR 46.103(a) and its implementation of the FWA.

Unlike the FDA regulations pertaining to IRBs, which explicitly include compliance oversight provisions at subpart E of 21 CFR part 56, the HHS regulations at 45 CFR part 46 do not include provisions specifically addressing IRB or IORG compliance with the regulatory requirements.

II. History of OHRP Compliance Oversight and the Changing Research Environment

Historically, OHRP (and its predecessor office, the Office for Protection from Research Risks) has only enforced compliance with 45 CFR part 46 through the institutions that were engaged in human subjects research. This has been the case even in circumstances when the regulatory violation was directly related to the responsibilities of an external IRB that was designated on the engaged institution's assurance of compliance with OHRP. Therefore, when OHRP received an allegation or indication of a regulatory violation on the part of an external IRB related to research to which the HHS regulations apply, OHRP has directed its compliance oversight evaluations and enforcement actions to the relevant FWA-holding institutions, not the external IRB or IORG at issue. When the HHS regulations related to IRB review last underwent a substantive revision on June 18, 1991 (56 FR 28003), few institutions were designating external IRBs to review research conducted under their assurances of compliance, in part because single site studies were more common than they are today, and it was more common for HHS-supported

research to be conducted by large academic medical centers that had their own internal IRBs. Therefore, there was no perceived need to hold IRBs or IORGs directly accountable for meeting any of the requirements of the HHS regulations at 45 CFR part 46. However, as HHS support for multi-site studies has increased, and previously non-traditional research settings, such as community hospitals and medical clinics, have become frequent research sites, the research community has looked for ways to make IRB review more effective and efficient.

III. Current Regulatory Flexibilities for IRB Review Arrangements

The regulations offer institutions significant flexibility to implement a variety of cooperative review arrangements as permitted under 45 CFR 46.114. In addition, this flexibility is facilitated by the ability of institutions to designate external IRBs on their FWAs that will be responsible for the review of one or more research studies in which the institution will be engaged. These regulatory flexibilities are intended to reduce administrative burden without diminishing human subject protections. For example, two or more institutions engaged in the same multi-center research project can designate the same IRB (*e.g.*, an IRB operated by one of the institutions engaged in the project) on their FWAs to review that research project. Similarly, institutions that do not have an internal IRB (for example, because they conduct little human subjects research) may designate an external IRB on their FWAs to review one or more research studies. Another IRB review model permitted under 45 CFR part 46 is for an institution to designate more than one IRB on its FWA to share authority and responsibility for the review of certain research studies. For example, the facilitated review model developed by the National Cancer Institute utilizes a central IRB, as well as review by another IRB—typically an internal IRB operated by the institution engaged in the research—that is responsible for considering issues related to the local context in which the research will be conducted. These regulatory flexibilities under 45 CFR part 46, that permit institutions to implement a variety of IRB review arrangements, are intended to reduce administrative burdens such as the time associated with IRB review for multi-site studies, the time devoted by IRB staff and investigators to duplicative IRB review, and the time and personnel costs associated with operating an IRB for those institutions that choose not to establish an internal IRB.

Despite the regulatory flexibility to implement a wide range of IRB review arrangements, OHRP has become aware that some institutions remain reluctant to designate external IRBs on their FWAs and/or rely upon cooperative IRB review arrangements.

IV. OHRP Co-Sponsored Meetings on Alternative IRB Models

OHRP's practice of holding an institution engaged in a human subjects research study accountable for noncompliance on the part of an external IRB that was designated on the institution's FWA and was responsible for reviewing the research was identified as one of the key factors influencing institutions' decisions about this issue by participants in two meetings on alternative IRB models that OHRP co-sponsored in November 2005 and November 2006. OHRP co-sponsored these meetings along with NIH, AAMC, and ASCO, in response to a suggestion made by SACHRP in the fall of 2004 that OHRP further explore issues associated with the use of alternatives to local IRBs. Reports summarizing the findings of these two meetings can be found at *http://www.dhhs.gov/ohrp/sachrp/documents/AltModIRB.pdf* and *http://www.aamc.org/research/irbreview/irbconf06rpt.pdf*. Participants in the 2005 and 2006 meetings included individuals from a variety of perspectives, including IRB chairs, academic investigators, community-based researchers, attorneys, patients, ethicists, industry officials and senior university and medical school research administrators. While other factors were also identified as contributing to institutions' reluctance to adopt alternatives to the internal IRB review model, it is OHRP's understanding from participants in this meeting, as well as others in the community, that concerns related to regulatory liability are a significant consideration. Namely, one of the main factors identified as contributing to institutions' reluctance to rely on an external IRB is OHRP's current practice of enforcing compliance with 45 CFR part 46 through the institutions that were engaged in human subjects research, even in circumstances when the regulatory violation is directly related to the responsibilities of an external IRB. Given this, OHRP believes that expanding its enforcement authority to include IRBs and IORGs directly may make institutions more likely to designate external IRBs on their FWAs and/or enter into cooperative IRB review arrangements.

V. Possible Administrative Actions for Noncompliance by IRBs or IORGs

If HHS were to implement a regulation that would enable OHRP to hold IRBs and IORGs directly accountable for meeting certain regulatory requirements of 45 CFR part 46, OHRP envisions that it would generally only exercise this regulatory option when the IRB at issue was external to the institution engaged in the human subjects research, and was designated on the institution's FWA to review the research. In circumstances when the IRB at issue was internal to the institution engaged in the human subjects research, OHRP expects that it would continue to enforce compliance with 45 CFR part 46 through the engaged institution.

However, when the possible regulatory noncompliance at issue was the responsibility of an IRB external to the institution engaged in the human subjects research, and the external IRB was designated on the institution's FWA to review the research, OHRP generally would expect to enforce compliance with 45 CFR part 46 directly with the external IRB, and not the FWA-holding institution. OHRP contemplates a number of administrative actions that HHS could take in response to a finding of noncompliance with 45 CFR part 46 by an external IRB designated on an institution's FWA. Depending on the nature and scope of the IRB's or IORG's noncompliance, OHRP could, for example, require that the IRB or IORG implement certain corrective actions, restrict or impose conditions on the IRB's registration with OHRP, or suspend the IRB's registration with OHRP which would prohibit the IRB from being designated on any institution's FWA.

VI. Identifying Responsibilities of the IRB/IORG and FWA-Holding Institution

In considering how HHS would implement a regulation that would enable OHRP to hold IRBs and IORGs directly accountable for meeting certain regulatory requirements of 45 CFR part 46, OHRP has begun the process of identifying which entities might be responsible for fulfilling the various regulatory requirements. Some of the regulatory requirements seem to fall uniquely to either the IRB/IORG or the FWA-holding institution, and others seem to be requirements that could be carried out by either the IRB/IORG or the FWA-holding institution. OHRP envisions that some form of agreement between the IRB/IORG and the FWA-holding institution would determine which entity would be responsible for

fulfilling the regulatory requirements that could be carried out by either the IRB/IORG or the FWA-holding institution. In an attempt to facilitate public comment on this request for information regarding IRB accountability, OHRP has made a preliminary attempt to group the regulatory requirements into the following three categories: (1) Responsibilities that may be unique to IRBs and IORGs; (2) responsibilities that may be unique to institutions engaged in human subjects research; and (3) responsibilities that may be fulfilled by either IRBs/IORGs or institutions engaged in human subjects research.

OHRP considered whether there are any regulatory requirements that are inherently shared by both the IRB/IORG and the FWA-holding institution, but did not identify any requirements that seemed to fall into this category. Section VII of this notice includes a question that specifically seeks public comment on this issue.

The categorization below is in no way intended to be definitive or complete, but rather a basis for public comment.

Responsibilities That May Be Unique to IRBs and IORGs

- The provisions regarding IRB membership and qualifications necessary to promote complete and adequate review of the human subjects research conducted by the institution for which the IRB was designated on an institution's assurance of compliance with OHRP (§ 46.107).
- The provision that the IRB follow written procedures in the same detail as described in 45 CFR 46.103(b)(4) and to the extent required by 45 CFR 46.103(b)(5) (§ 108(a)).
- The provision that except when an expedited review procedure is used (see § 46.110), the IRB review proposed research at convened meetings at which a majority of the members of the IRB are present, including at least one member whose primary concerns are in nonscientific areas. In order for the research to be approved, it shall receive the approval of a majority of those members present at the meeting (§ 46.108(b)).
- The provision that an IRB shall review and approve, require modifications in (to secure approval), or disapprove all research activities covered by 45 CFR part 46, for which the IRB was designated on an institution's assurance of compliance with OHRP (§ 46.109(a)).
- The provision that an IRB shall require that information given to subjects as part of informed consent is in accordance with § 46.116. The IRB may require that information, in addition to that specifically mentioned in § 46.116, be given to the subjects when in the IRB's judgment the information would meaningfully add to the protection of the rights and welfare of subjects (§ 46.109(b)).
- The provision that an IRB shall require documentation of informed consent or may waive documentation in accordance with § 46.117 (§ 46.109(c)).
- The provision that an IRB shall notify investigators and the institution in writing of its decision to approve or disapprove the proposed research activity, or of modifications required to secure IRB approval of the research activity. If the IRB decides to disapprove a research activity, it shall include in its written notification a statement of the reasons for its decision and give the investigator an opportunity to respond in person or in writing (§ 46.109(d)).
- The provision that an IRB shall conduct continuing review of research covered by 45 CFR part 46, at intervals appropriate to the degree of risk, but not less than once per year (§ 46.109(e)).
- The provision related to expedited review procedures for certain kinds of research involving no more than minimal risk, and for minor changes in approved research (§ 46.110).
- The provision that identifies the criteria for IRB approval of research (§ 46.111).
- The provisions that permit an IRB to approve a consent procedure which does not include, or which alters some or all of the elements of informed consent set forth in § 46.116, or waive the requirements to obtain informed consent provided the IRB finds and documents that specified criteria have been met (§ 46.116(c) and (d)).
- The provisions that require informed consent to be documented by use of a written consent form approved by the IRB and signed by the subject or the subject's legally authorized representative, unless the IRB finds that specified criteria permitting the waiver of documentation of informed consent have been met (§ 46.117).

Responsibilities That May Be Unique to Institutions Engaged in Human Subjects Research

- The provision that institutions engaged in HHS-supported human subjects research must submit an FWA to OHRP for approval and comply with the requirements imposed as part of the FWA, including among other things, the designation of one or more IRBs on the institution's FWA that have been registered with OHRP (§ 46.103).
- The requirement that before implementing a change to an IRB-approved research study, an investigator must obtain IRB approval for the change, unless the change is designed to eliminate an apparent immediate hazard to subjects (§ 46.103(b)(4)).
- The requirement that an investigator must obtain continuing IRB review of ongoing non-exempt human subjects research prior to the expiration date of the current IRB approval (§ 46.103(b)(4)).
- The requirement for the prompt reporting to the IRB of any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB (§ 46.103(b)(5)).
- The requirement that an investigator must obtain IRB review and approval before beginning any non-exempt human subjects research (§ 46.109(a)).
- The provision that the IRB must have authority to approve, require modifications in (to secure approval), or disapprove all research activities for which the IRB was designated on an institution's assurance of compliance with OHRP (§ 46.109(a)).
- The provision that the IRB must have authority to observe or have a third party observe the consent process and the research for all research activities for which the IRB was designated on an institution's assurance of compliance with OHRP (§ 46.109(e)).
- The provision that research covered by 45 CFR part 46 that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, these officials may not approve the research if it has not been approved by an IRB (§ 46.112).
- The provision that the IRB must have authority to suspend or terminate approval of research that is not being conducted in accordance with the IRB's requirements or that has been associated with unexpected serious harm to subjects for all research activities for which the IRB was designated on an institution's assurance of compliance with OHRP (§ 46.113).
- The requirement that except as provided elsewhere in 45 CFR part 46 no investigator may involve a human being as a subject in research covered by 45 CFR part 46 unless the investigator has obtained and documented the legally effective informed consent of the subject or the subject's legally authorized representative (§ 46.116 and § 46.117).
- The requirement that investigators give a copy of the informed consent document to each research subject or

the subject's legally authorized representative, and keep the signed original or a copy of it for their records, unless the IRB finds that specified criteria permitting the waiver of documentation of informed consent have been met (§ 46.117; § 46.115(b)).

Responsibilities That May Be Fulfilled by Either IRBs/IORGs or Institutions Engaged in Human Subjects Research

- Determining the applicability of the HHS regulations at 45 CFR part 46 (*e.g.*, the exemptions at 46.101(b)).
- Developing written IRB procedures which the IRB will follow:

(1) For conducting its initial and continuing review of research and for reporting its findings and actions to the investigator and the institution;

(2) For determining which projects require review more often than annually and which projects need verification from sources other than the investigators that no material changes have occurred since previous IRB review; and

(3) For ensuring prompt reporting to the IRB of proposed changes in a research activity, and for ensuring that such changes in approved research, during the period for which IRB approval has already been given, may not be initiated without IRB review and approval except when necessary to eliminate apparent immediate hazards to the subject (§ 46.103(b)(4)).

- Developing written IRB procedures for ensuring the prompt reporting to the IRB, appropriate institutional officials, and the Department or Agency head of:

(1) Any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and

(2) Any suspension or termination of IRB approval (§ 46.103(b)(5).

- Promptly reporting to the appropriate institutional officials and the Department or Agency head:

(1) Any unanticipated problems involving risks to subjects or others or any serious or continuing noncompliance with 45 CFR part 46 or the requirements or determinations of the IRB; and

(2) Any suspension or termination of IRB approval, including a statement of the reasons for the IRB's actions (§ 46.103(b)(5); § 46.113).

- Promptly reporting to the investigator any suspension or termination of approval by the IRB, including a statement of the reasons for the IRB's actions (§ 46.113).
- Fulfilling the documentation and recordkeeping requirements associated with IRB activities (§ 46.115).

VII. Request for Information and Comments

OHRP is seeking information and comments from the public about whether OHRP should pursue an NPRM to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain regulatory requirements of the HHS regulations for the protection of human subjects at 45 CFR part 46. OHRP specifically seeks information and comments on the following issues; comments should also include a reference to the specific numbered question being addressed:

1. Is there sufficient need for HHS to pursue a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46? Please explain your response.

2. Would the proposed regulatory change reduce concerns about regulatory liability as a barrier to the use of external IRBs and contribute to an increase in collaborative IRB review arrangements?

3. Are there other approaches and strategies that would decrease concern about regulatory liability and increase collaborative IRB review arrangements?

4. If HHS were to issue a regulation that would enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46, would this have the unintended effect of making institutions or IORGs less willing to have their IRBs designated as external IRBs on other institutions' FWAs? If so, would there still be sufficient benefit for HHS to pursue a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations? Are there other possible unintended effects of the proposed regulatory change? Please explain your responses.

5. If HHS pursues a regulatory change to enable OHRP to hold IRBs and IORGs directly accountable for meeting certain requirements of the HHS regulations at 45 CFR part 46, what kinds of administrative actions would be appropriate for OHRP to take against IRBs that are found to be out of compliance with 45 CFR part 46? For a description of some of the corrective actions that OHRP has required when it has been determined that an institution was not in compliance with 45 CFR part 46, see OHRP's guidance document entitled, ''OHRP's Compliance Oversight Procedures for Evaluating Institutions'' at *http://www.dhhs.gov/ohrp/compliance/ohrpcomp.pdf*.

6. As described in Section VI of this notice, in order to facilitate public comment, OHRP has made a preliminary attempt to group some of the regulatory requirements under 45 CFR part 46 into the following three categories: (1) Responsibilities that may be unique to IRBs and IORGs; (2) responsibilities that may be unique to institutions engaged in human subjects research; and (3) responsibilities that may be fulfilled by either IRBs/IORGs or institutions engaged in human subjects research.

6a. Are these categories appropriate? If not, what other categories should there be?

6b. Is there a fourth category of responsibilities that are inherently shared by both the IRB/IORG and the FWA-holding institution? If so, please provide examples of such shared responsibilities.

6c. Are the regulatory provisions identified under each of the categories appropriate? If not, which regulatory provisions should be re-categorized, removed, or added?

6d. For institutions that have relied upon joint IRB review arrangements in the past, how have the regulatory requirements been divided or shared by the IRB/IORG and the institution engaged in the human subjects research? We would welcome examples or descriptions of such agreements between IRBs/IORGs and institutions engaged in human subjects research that describe their respective responsibilities.

7. With regard to the responsibilities that may be fulfilled by either IRBs or institutions, the IRB Authorization Agreement between an external IRB and an FWA-holding institution is often used to clarify which entity will be responsible for carrying out these regulatory requirements.

7a. If a regulatory change to 45 CFR part 46 is pursued, should OHRP use the IRB Authorization Agreement or other forms of agreement, if they exist (*e.g.*, contract or memorandum of understanding) to inform its compliance oversight evaluations about which entity should be held responsible for fulfilling regulatory requirements that could be met by either an external IRB or the FWA-holding institution?

7b. If a regulatory change to 45 CFR part 46 is pursued, should there be new provisions that require specific content for IRB Authorization Agreements or for other forms of agreements between external IRBs and FWA-holding

institutions? If so, what types of content should be required?

7c. If a regulatory change to 45 CFR part 46 is pursued, should the regulation describe which regulatory requirements would need to be met by external IRBs and which regulatory requirements would need to be met by institutions engaged in the research?

Dated: February 27, 2009.

Jerry Menikoff,

Director, Office for Human Research Protections.

[FR Doc. E9–4628 Filed 3–4–09; 8:45 am]

BILLING CODE 4150–36–P