

University of Rochester Response to ANPRM (HHS-OPHS-2011-0005)
Executive Summary:

The Office of the Secretary of the Department of Health and Human Services (HHS) issued an advance notice of proposed rulemaking (ANPRM) to request public comment on how the current regulations for protecting human subjects who participate in research might be revised to be more effective. The ANPRM seeks comment on how to better protect human subjects, while facilitating valuable research and also reducing burden, delay, and ambiguity for investigators. Unfortunately, the time given for public input is incredibly short—comments are due to HHS no later than Wednesday, October 26, 2011.

The concerns about the current Common Rule were categorized in the ANPRM into seven areas:

1. Refinement of the existing risk-based regulatory framework;
2. Utilization of a single IRB review of record for domestic sites of multi-site studies;
3. Improvement of consent forms and the consent process;
4. Establishment of mandatory data security and information protection standards for all studies that involve or may potentially involve Personally Identifiable Information (PII);
5. Establishment of an improved, more systematic approach for the collection and analysis of data on unanticipated problems and adverse events;
6. Extension of federal regulatory protections to all human subject research, regardless of funding source, triggered by an institution receiving any federal funding from a Common Rule agency for research with human subjects; and
7. Improvement in harmonization of regulations and related agency guidance.

The Office for Human Subject Protection (OHSP) was charged with reviewing the ANPRM and developing a document to be sent to HHS commenting on the proposals and their impact here at the University of Rochester. A draft document containing responses to each of the 75 questions posed in the ANPRM was drafted and sent to approximately 30 University investigators, RSRB chairs/members, and legal counsel. Approximately 200 responses were collected and changes were made to the current draft (dated October 23, 2011).

While each of the seven areas garnered some comments, as expected, the most were in the areas that would affect the University community to the greatest extent:

1. Lessening of IRB burden by streamlining approval of expedited and minimal risk studies;
2. Mandated central/single IRB review;
3. Required written consent for research on existing data/specimens; and
4. Use of the HIPAA definitions and HIPAA information security standards for all research.

The University is pleased that our investigators, institutional officials, and Research Subjects Review Boards work hard to ensure that subjects who participate in research are protected and valued. Below is a summary of our some of our comments, which represent the synthesis of opinions that were shared with me. Attached to this summary is an additional document that provides a response to each of the questions posed in the ANPRM—each area below contains reference to the ANPRM questions. A cover letter and the document containing responses to each of the 75 questions posed in the ANPRM will be sent to HHS by October 26, 2011.

1. Refinement of the Existing Risk-Based Regulatory Framework (Q1 - Q29)

Changing the definition of *minimal risk*: The current definition of “minimal risk” is “the probability and magnitude of harm or discomfort anticipated in the research are not greater in and of themselves than those ordinarily encountered in daily life or during the performance of routine physical or psychological examinations or tests.” The University of Rochester believes that this is largely adequate, but the response offers two additional changes that would update the definition to be responsive to the current state of research. We believe that educational testing should be included in the definition and that it would be clearer to say “routine medical and dental examinations.” In addition, we suggest that risk mitigation mechanisms planned or in place should be considered when determining the risk level for a study.

Our suggested new minimal risk definition is: “*Minimal risk* means that the probability and magnitude of harm or discomfort, introduced solely by the research are not greater in and of themselves than those familiar and routine experiences ordinarily encountered in the daily life of the general population including the performance of routine psychological, educational, medical, or dental examinations or tests.”

Removing the requirement for annual continuing review: We agree with the elimination of routine continuing review for minimal risk studies. For greater than minimal risk studies, we suggest the IRB be allowed to set the time period when the remaining study activities only include those that could have been approved under expedited review, e.g., data analysis to eliminate continuing review.

Expanding expedited categories to include more types of research and procedures and regularly updating list to be current: Our response supports regularly updating and adding categories as needed to the list of expedited categories. We suggest allowing some exposure to radiation to be expedited (e.g., arm/leg x-ray, chest x-ray, DEXA, dental x-ray, CT with less than 3Rem).

Revising the exempt categories and changing the name to “Partially Excused” (Q14 - Q29): The University of Rochester does not support renaming the exempt categories to “Partially Excused.” Rather, we believe that it is best to retain the current exempt categories and expand them to provide more examples/categories, e.g., research tool/measurement development, psychometric research, cognition research, speech and childhood development research, word association, anonymous “internet research” (including web-based, email, tweeting, texting, etc.), and epidemiology. Also, we suggest adding a new exempt category for research that uses “activities of daily living” as the research procedures, e.g., walking, talking, viewing/seeing, listening, answering questions, filling out/in forms, etc.

Allowing investigators to self-determine review level and risk without any pre-review by IRB: Our response is that the University of Rochester does not agree that investigator self-determination of exemption is appropriate given investigators have difficulty judging the category of review and the risk level in our current system. Without the independent pre-review, we will lose the inherent system that allows for education of students and new researchers who are beginning their careers with exempt-level research.

Using a one-page registration form to allow investigators to self-determine exemption: The regulations should not dictate operational process; however, the University of Rochester may be supportive of a system that uses an internal institutional process. Any proposed form must be well thought out and provide specific criteria that the investigator must show to ensure the determination of exempt category is indeed justified.

Auditing the one-page registration form, rather than pre-reviewing protocols, to ensure appropriate investigator determination of exemption: We state that audits of the registration forms alone would only ensure that investigators are properly completing the form, but—without supporting documents—would do nothing to determine if the investigators are assigning the appropriate level of review for their research. We do not want such audits considered a “compliance audit” in the regulatory sense, which would require reporting to federal agencies. Post hoc monitoring could be implemented as an educational and operational activity by institutions with appropriate corrections, but with no federal penalties.

2. Utilization of a single IRB review of record for domestic sites of multi-site studies (Q30 - Q34)

Mandating use of a single IRB of record for a multi-site study: The response indicates that the University of Rochester is opposed to *federally mandated* review by a single IRB for all domestic, multi-site research. Our response agrees that efficiencies can be gained from central/single review and supports that concept of relying on a single IRB; however, it is the mandate to use a single IRB that is problematic. For an IRB to adequately conduct the review of multiple sites in a large multi-center study, it would need the resources to do this effectively, including extra IRB staff to manage the approval process, the continuing review—including collecting and assessing unanticipated problem reports and other required notices and potentially increased oversight/auditing function to ensure that the research is conducted appropriately. The University of Rochester response indicates that the proposed changes do not sufficiently address the concerns associated with assuming regulatory responsibility and liability for research conducted at another institution; we urge such impediments to be explored and removed.

3. Improvement of Informed Consent and the Consent Process (Q35 - Q53)

Creating standardized templates and providing greater specificity in the regulations about how consent forms should be written: The University of Rochester response acknowledges that the complexity of consent forms now is driven less by the need to provide useful information to subjects and more by institutional risk determinations, which are driven in large part by federal guidance. Concern about compliance creates the institutional tendency to be risk adverse. To solve the “complexity” of consent forms, the Common Rule must delink the regulations for obtaining informed consent from the requirements for signed documentation of consent; this would allow investigators to develop “Executive Summaries” for the consent form. The Executive Summary would be a short form containing just pertinent information and may include other attachments/appendices as needed to convey more detailed information, while the

consent process would include a discussion of all informed consent requirements. The form with its attachments/appendices would serve as reference materials for consideration of the initial decision at home or with advisors, as well as for ongoing reference as the study proceeds.

Requiring Consent Protections Related to Reuse of Existing Data and Biospecimens: The University of Rochester does not support the requirement for obtaining consent for de-identified biospecimens. Our response indicates that a requirement to obtain individual consent for each separate research study would create unmanageable logistical demands and impossible expectations for collecting choices and then tracking and complying with those stated options (yes/no/partial/specific), making valuable research in areas of public health, medical, behavioral, educational, and social concern impossible. We oppose requiring written consent for research on specimens and data collected for non-research purposes as long as the data or specimens cannot be identified. The costs associated with requiring written consent would greatly exceed any benefits to subject protection. We state that de-identified biospecimens from foreign sources should be considered de-identified when received in the U.S. and regulated as such.

Our response also indicates that in cases where consent for future research is not obtained at the time of collection, there should be a presumption that obtaining consent for the secondary analysis of existing biospecimens or identifiable data would be deemed impracticable and consent could be automatically waived. The University of Rochester may wish to set numerical and time parameters that would override the deemed impracticability and trigger an assessment, but that should be an institutional prerogative.

4. Establishment of mandatory data security and information protection standards for all studies that involve identifiable or potentially identifiable data (Q54 - Q66)

Strengthening Data Protections to Minimize Information Risks: The University of Rochester response indicates that using the HIPAA security standards will put a huge burden on institutions to construct a separate research IT infrastructure that will be prohibitively costly to implement. The response states that the HIPAA definitions for “individually identifiable health information,” “de-identified information,” “limited data set,” and “data use agreement” should not be used.

The University of Rochester does not support the adoption of the HIPAA security and notification standards as a model for the proposed mandatory data security and information standards. The HIPAA Privacy and Security Rules include complex standards with extensive enforcement rules and penalties that are not appropriate to minimal risk research and non-healthcare, non-clinical research.

Considering all biospecimens as identifiable: - The University of Rochester response indicates that the federal regulations should not require biospecimens to be considered as identifiable. The impact on basic and clinical science would be staggering. Biospecimens that include DNA do not identify individuals without other linked information or a large database that contains the individual’s specific DNA sequences. Our response indicates that the type of genomic test should not make a difference to how identifiable the biospecimen is because genomic data should not be considered identifiable for research.

The University of Rochester believes that including biospecimens without identifiers within the human subject research provisions related to information risk would inappropriately expand the meaning of “human subject” and add unintended burden to the system of human subject research oversight. We state that neither de-identified data nor biospecimens without identifiers should be considered research involving a “human subject.”

Establishing Standards for Data Security and Information Protection: The University of Rochester response acknowledges that data security is an important step in minimizing information risks, but IRBs should have the expertise to address security issues. The response indicates that standards for how data should be managed (encryption, firewalls, etc.), such as those contained in the Federal Information Security Management Act, may not be appropriate for research involving little informational risk. We state that the institution can enforce a prohibition against re-identifying data and do not support including this requirement in federal regulations.

5. Establishing an improved, more systematic approach for the collection and analysis of data on unanticipated problems and adverse events (Q67 - Q70)

The University of Rochester response indicates that the current reporting system (i.e., individual letters to the regulatory agency/sponsor/institution) and required reports to federal offices are burdensome and offer little benefit. It is also difficult to see any benefit from reporting unanticipated problems to federal regulatory authorities that justifies the burden. We only support the collection of data when there is a clear reason to do so and resources to analyze and act upon the analysis in a timely manner. This is absent in the ANPRM proposal to collect adverse event data, and it would seem that the central reporting system would create not only an unmanageable burden and cost but also a huge agency liability.

6. Extension of Federal regulatory protections to all research, regardless of funding source, conducted at institutions in the U.S. that receive some Federal funding from a Common Rule agency for research with human subjects (Q71)

The University of Rochester response indicates that extending the applicability of the Common Rule to all research—including that which is not federally funded—is an attractive goal; however, extending the Common Rule based on federal funding may not effectively fill the current gap in protections.

7. Improvement in harmonization of regulations and related agency guidance (Q72 - Q74)

Our response states that it would be a major step forward in terms of both protecting human subjects and relieving burden if the differences and complexities that exist just within the HHS offices can be removed or harmonized. The response suggests that HHS can harmonize guidance from the Office for Human Research Protections (OHRP), the Food and Drug Administration (FDA), and the Office of Civil Rights (OCR), even if the other Common Rule

agencies require separate guidance. One issue that the University of Rochester notes must be addressed is that “guidance” should be guidance, i.e., clarification and instruction in the application of the regulations; it should not be used to extend the regulations, i.e., to add new requirements that must be accomplished to comply with agency goals, which have not been vetted through the formal rule-making process.

Additional points suggested in the University of Rochester Response (Q75)

1. The University of Rochester response indicates that when proposing federal regulations, the least complex rules are preferred, as long as those measures address important problems and are effective in resolving those concerns. The response indicates that institutions should have the flexibility to determine how to accomplish oversight responsibility.
2. To be effective and efficient, responsibility should be placed on the investigators who initiate and conduct research and are in the best position to protect human subjects. Therefore, the University of Rochester response suggests that the Common Rule regulations should be amended to include investigator responsibilities.
3. The response suggests that a financial conflict of interest disclosure regulation for investigators could be added to the Common Rule, but it must be consistent with the other financial conflict of interest regulations (NSF, NIH, and FDA).
4. The University of Rochester response suggests that the role of the Data Monitoring Committee (DMC) be codified in the Common Rule.