The Importance of Proposed Changes in the "Common Rule" for Clinical and Translational Researchers

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In the July 25, 2011 Federal Register, the Department of Health and Human Services (HHS) released an Advanced Notice of Proposed Rule Making (ANPRM) changes in the "Common Rule," entitled, "Human Subjects Research Protections: enhancing protections for research subjects and reducing burden, delay, and ambiguity for investigators." The enhancements were proposed to "…ensure the highest standards of protections for human subjects involved in research, while enhancing effectiveness of oversight." Despite the seeming opacity of the announcement to many, and its arcane target, the procedures for protecting human research subjects, this represents a major event for clinical and translational researchers. The Society for Clinical and Translational Science, accordingly, will have weighed in on these changes before the deadline for comment, October 26, 2011. Once the rules have been revised, there will be another chance for comment, and all members of the translational science community should take the opportunity to weigh in on the changes if they have not already done so.

We all endorse vigorous protections of research participants. After a history of lack of reliable protections over the past several decades, research regulations and practices have improved significantly. In 1974, HHS human subject protection regulations were first issued based on statutory authority under the Code of Federal Regulations (CFR) as 45 CFR, part 46. In 1978, the National Commission for the Protection of Human Subjects of Biomedical and Behavioral Research published "Ethical Principles and Guidelines for the Protection of Human Subjects of Research," known as the Belmont Report. It identified the three fundamental ethical principles that are often cited as the basis for human subject research: respect for persons, beneficence, and justice. The current HHS regulations include five subparts, of which Subpart A (which specifies the basic set of protections for all human subjects of research conducted or supported by HHS) and Subpart E, (which requires registration of institutional review boards [IRBs] for human research studies) are most relevant to clinical research. In 1991, 15 federal departments and agencies together issued the "Federal Policy for the Protection of Human Research Subjects," known as the "Common Rule" based on the HHS 45 CFR part 46 Subpart A, providing identical language in the regulations of those departments and agencies, and technical amendments were made in 2005.

The changes now proposed by HHS are designed to strengthen protections for human research subjects. (The full ANPRM can be seen at http://www.hhs.gov/ohrp, and additional information can be found at http://www.hhs.gov/ohrp/humansubjects/anprm2011page.html. Particularly helpful is a table of comparison between the current rules and the changes being considered at http://www.hhs.gov/ohrp/humansubjects/anprmchangetable.html.) Some of the issues on which comments were invited included:

(1) Revising the existing risk-based framework to more accurately calibrate the level of review to the level of risk.
(2) Using a single IRB review for all domestic sites of multisite studies.
(3) Updating the forms and processes used for informed consent.
(4) Establishing mandatory data security and information protection standards for all studies involving identifiable or potentially identifiable data.
(5) Implementing a systematic approach to the collection and analysis of data on unanticipated problems and adverse events across all trials to harmonize the complicated array of definitions and reporting requirements, and to make the collection of data more efficient.
(6) Extending federal regulatory protections to apply to all research conducted at US institutions receiving funding from the Common Rule agencies.
(7) Providing uniform guidance on federal regulations.

There are several changes proposed in the ANPRM that are particularly attractive for streamlining clinical research. One of the most important is the clear stratification of research based on risk into three levels, and the implications for different types of research. The lowest risk level is research that is only for collection of information, which would be "excused" from IRB review. The next level is research in which there is an intervention that adds to that intrinsic to usual care, but the intervention itself is only of minimal risk, which is defined as not having higher risk than "…encountered in daily life or during the performance of routine physical or psychological examinations or tests." This could include additional testing due to the study, such as the performance of blood tests. Such research would receive a brief expedited review, by one person. Alternatively, the highest level of risk in research is designated if there are interventions and/or tests of more than minimal risk; for such studies, standard IRB review would be done.

Another important change is the proposal of standard simple one-time research consent for patients to sign upon initiating care at an institution or practice. From then on, all the patient's information (and biological specimens) can be used for research purposes—as long as reviews are done as mandated (as above) and rigorous standards of information protection are maintained. The standardization of this, and its intended wide promulgation, should greatly enhance clinical and translational research.

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It is worth noting that the combination of the proposed changes related to the three levels of research risk, especially the lowest risk category, with the use of the one-time consent for use of patient information, could have a major impact on the performance of clinical research. For example, were researchers to compare by random assignment, two alternative treatments that are part of usual accepted care and then collect medical information to compare the outcomes, this project would be "excused" from IRB review and would have no further need for consent other than the initial global permission. The reason this would not be considered to represent minimal risk is that there is no incremental risk added by the study—the only risk is that related to usual care. This clearly should facilitate clinical research, and especially comparative effectiveness research.

Another important change proposed is that, if multiple US institutions are used, a single IRB at one institution, presumably that of the principal investigator, would be able to approve the study for the entire consortium. This would lessen duplicative work and delays and should eliminate the confusion that can arise from different IRBs having different judgments on the same study—something commonly encountered at the present time. There have been many attempts to find ways to accomplish this, by use of federated IRBs and other approaches, all of which have taken years to develop; this change could resolve all this and greatly expedite multicenter investigation.

Additional changes that should lessen the burden on investigators and many needless reviews by institutional IRBs include the elimination of the need to have annual IRB reviews after the study intervention is completed and only follow-up data collection and/or analysis is being done as well as clarification of the exemption categories. The ANPRM has specifically asked for public commentary to identify areas of research that do not warrant the current degree of regulatory oversight so that review requirements are better calibrated to the level of risk.

In sum, we believe that the proposed changes in the Common Rule will have a very salutary impact on our ability to conduct translational research. Indeed, not only should they improve the efficiency of clinical research without diminishing important human subject protections by removing many delays from the research process, results will be available sooner, and the impact on health greater. The SCTS, representing member interests, has sent comments representing these views to HHS. These changes in the Common Rule will be a common good. **CTS**