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May 1, 2011

Public Commentary

The Presidential Commission for the Study of Bioethical Issues  
1425 New York Ave. NW, Suite C-100  
Washington, DC 20005

Dear Commissioners,

On behalf of the University of North Carolina at Chapel Hill, please accept this in response to your “Request for Comments on Human Subjects Protections in Scientific Studies” (Federal Register Notice 3/2/2011). Our university is a broad-based research institution, with over 4000 active studies involving human subjects and a long-standing commitment to human subjects protections; we have been active participants in many of the initiatives undertaken in recent years to examine and enhance this system. Our comments draw on this experience and commitment.

In fairness, we must preface the criticisms that follow with the observation that there do not appear to be widespread or systemic abuses of research subjects. Relative to the number of research studies and the number of subjects involved, there are thankfully few problems that can be traced directly to a failure of the oversight system. To that extent, the system can be said to be working. Nevertheless, there are areas of concern, areas where improvement is needed, and areas where maintaining the status quo will eventually erode the system in ways that may expose subjects to harm. These areas form the basis for the comments that follow.

- The current system of protections is based on a “patchwork quilt” of regulations, with applicability dependent on the funding and/or purpose of the research. For example, NIH funding will trigger the requirements found under 45 CFR 46 (the “Common Rule”) while studying an FDA-regulated drug or device will trigger requirements found under 21 CFR 50, 56, 312, 812 and others. In addition, multiple federal agencies have their own regulations that superimpose on these basic requirements. Each of these regulations stems from a different point of authority, enforced by a different agency. This patchwork quilt is confusing and difficult to apply, for investigators and Institutional Review Boards (IRBs) seeking to comply. At the same time, the patchwork creates gaps in coverage, such that many areas or sources of research are unregulated. True systemic reform would demand a critical look at integrating and harmonizing this regulatory structure.

- Along these same lines, the implementation of the HIPAA Privacy Rule in 2003 imposed additional requirements on a considerable subset of research studies that involve Protected Health Information. These requirements overlap, but are not entirely consistent, with the research-based regulations that also apply (per above). This has added one more piece to the patchwork quilt, resulting in additional confusion and complexity, for questionable benefit. Subjects would not be protected any less if research was exempted from the provisions of HIPAA, as was originally proposed and is now again under consideration.
- The complexities described above have forced institutions conducting research to focus increasingly on nuances and esoterica, to the detriment of the research itself, and most importantly, the very subjects we strive to protect. There is justifiable concern that so much time and effort are being devoted to bureaucratic issues that we may be in danger of “missing the forest for the trees,” at a systemic level.
- One concrete example of this phenomenon is the regulatory requirements for informed consent, as they have come to be understood and practiced. Obtaining truly informed consent from subjects is a cornerstone protection, but this ethical aspiration is increasingly burdened... and weakened... by the use of consent forms that are overly long and complicated. It is arguable that consent documents are drafted and reviewed in ways that serve the interests and concerns of institutions and sponsors, rather than the needs of subjects. While lip service is given to the “process” of consent, as involving more than just the document, the reality is a collective focus on the written, signed consent form. This will not change meaningfully without federal-level intervention.
- The system of protections was largely established in the 1970s and early 1980s, when the research environment was much different than it is today. This system is predicated on local review by IRBs at individual institutions, failing to anticipate the way multi-center research is conducted in the modern setting. Redundant review by dozens or hundreds of local IRBs is of doubtful benefit in scenarios where the protocol in question is essentially a “take-it-or-leave-it” proposition, because it must be conducted identically across all sites. Simply put, the oversight system has failed to evolve to keep pace with the volume, complexity and nature of the research it oversees. Alternative models exist, and should be explored and encouraged.
- The problems noted above are, if anything, exacerbated in the international context. The U.S. regulations travel along with U.S. investigators and U.S. funding, with their attendant idiosyncrasies and confusion. While the underlying concepts may translate to research settings in other countries, there are both ethical and practical challenges to applying these regulations overseas in culturally appropriate ways. Investigators and IRBs are uncertain how to obtain local input to the review process, how to meaningfully obtain informed consent, and how to balance the risks and benefits of research in resource-poor settings.
- It is often argued that the current system was designed for oversight of biomedical research, and that research in the social sciences and humanities suffers from being forced into this biomedical model. If we accept that ALL research carries the potential for risks or discomforts, which must be balanced against the potential benefits, there is relatively little in the regulations that applies solely to biomedical research. Having said,

there are clearly examples where the regulations have been over-applied to social, behavioral and educational research, in ways that add little value or protection. Some of this is self-inflicted by well-intentioned IRBs that presume worst case scenarios, in the absence of any evidence that these hypothetical harms have occurred. Clarification and education are needed to bring a proportional level of review to these and other low-risk areas of research. Expanded and appropriate use of the categories for exemption would also help in this regard.

- Finally, it must be acknowledged that the IRB process relies heavily on subjective human judgment. The regulations provide a flexible framework for decision-making, but rarely provide the “one right answer” to a given scenario or dilemma. This is both a blessing and a curse. We can be thankful that those who established the structure did NOT attempt to anticipate every scenario that would present itself in the future and proscribe answers in advance, as they surely would have failed. The flexibility to apply the regulations to each new scenario is a strength of the current system. On the other hand, the reality is that the answer often depends on the single person or small group conducting that review. This inevitably results in variability and inconsistency between (and even within) IRBs, which is frustrating for researchers and does little to enhance protection of subjects. One of the many challenges in considering systemic changes is how to preserve the desirable flexibility, while minimizing the variability inherent in human judgment calls.

Thank you for the opportunity to comment.

Respectfully Submitted,

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cc: Barbara Entwisle, Vice Chancellor for Research