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Closing Loopholes in the Federal Research Regulations: Some Practical Problems

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Shamoo and Schwartz (2008) argue that to protect the dignity, rights, and welfare of people who participate in research, the U. S. should close existing loopholes in the federal regulations. Currently, federal regulations only apply to research conducted or funded by one of the 17 federal agencies that accept the Common Rule (45 C. F. R. 46), research that will be used to support an application for a new drug, biologic, and medical device regulated by the Food and Drug Administration, or research conducted to generate data to submit to the Environmental Protection Agency for regulatory purposes (Shamoo and Schwartz 2008, Resnik 2007). The Common Rule is the most influential of all of these regulations, because most academic institutions that receive federal funding have decided to apply the Common Rule to all human subjects research under their authority, regardless of the source of funding (Gunsalus 2006).

The idea of closing loopholes in the federal research regulations has been on the table at least since the mid-1990s. The Advisory Committee on Human Radiation Experiments (1995), the National Bioethics Advisory Commission (2001), advocacy groups (Citizens for Responsible Care and Research 2008), various writers (e.g. Shamoo 1999, Annas 1999), and even President William Clinton (1997) have endorsed the idea. Since 1997, six Congressional bills designed to close loopholes in the human subjects regulations have been drafted, though none have been approved by either house of Congress (Citizens for Responsible Care and Research 2008). The most recent version of this legislation, the Protection for Participants in Research Act of 2006 (H. R. 5578), would extend the Common Rule to all research conducted or supported by the federal government or subject to federal law (Protection for Participants in Research Act 2006).

Though strong moral arguments favor closing loopholes in the federal regulations, there are practical difficulties with implementing this proposal. The first problem is that there is not an accurate accounting of unregulated research with human subjects conducted in the U. S. There are no studies providing information on how many people in the U. S. are participating in unregulated research, what types of studies are being conducted, who is sponsoring the research, or who is conducting it (Gunsalus 2001). Shamoo and Schwartz (2008) claim that millions of research subjects may not be protected by the federal regulations, but this assertion is no more than an educated guess. Before undertaking the task of expanding the federal research regulations, it would be wise to gather more information about unregulated research with human subjects, in order to have a better understanding of the problem and how to deal with it. Enacting new laws without a good grasp of how they will impact society is a recipe for disaster.

Assuming that there is sufficient information about unregulated research to make reasonable decisions about it, policymakers will need to confront a second problem: how should society deal with unregulated research that poses very low risks to human subjects? Private companies and organizations currently perform some types of studies, such as marketing research and public opinion polls, which impose few risks on people. It is not obvious that society would

gain much by requiring an organization, such as Gallup or ABC News, to submit a proposal to an institutional review board (IRB) to conduct an anonymous survey each time that it decides to gauge public opinion on a particular issue. Social resources might be better spent overseeing riskier research, such as clinical trials (Gunsalus 2006).

The Common Rule exempts some types of low risk research from review by an IRB, such as some types of educational research, anonymous surveys, and studies involving existing data, records, or biological specimens (45 CFR 46.101b). If a proposed study falls into any of these categories, there is no need for an IRB to review it. Even though the Common Rule does not apply to exempt research, most academic institutions require an investigator to submit a brief application to the IRB describing the proposed research, so that the IRB, not the investigator, can determine whether the research should be granted an exemption (Gunsalus 2006).

Should the federal regulations be extended to cover all research with human subjects, it would be prudent to consider whether some types of research should be exempt from any new regulations, including research that falls into any of the Common Rule's exempt categories and other types of low risk research, such as marketing research, public opinion surveys, and consumer product testing. Private corporations, research organizations, and other groups would be interested in having their studies exempted from the new regulations, which could spawn ethical controversy and intense political lobbying.

A third practical problem with extending the federal regulations is that some definitions in the Common Rule, such as "research" and "minimal risk" are ambiguous (Gunsalus 2006, Borenstein 2008, Wendler et al 2005). The Common Rule defines research as "a systematic investigation, including research development, testing and evaluation, designed to develop or contribute to generalizable knowledge (45 CFR 46.102d)." This definition is based on one found in *The Belmont Report*, which serves as a conceptual foundation for the Common Rule and provides guidance to IRBs, investigators, and institutions (Jonsen 2005). *Belmont* distinguishes between research and professional practices, such as medicine, nursing, and psychotherapy. Professional practices are "interventions that are designed solely to enhance the well-being of an individual patient or client and that have a reasonable expectation of success," whereas research is "an activity designed to test an hypothesis, permit conclusions to be drawn, and thereby to develop or contribute to generalizable knowledge...(National Commission, 1979: 6)."

The definition of "research" can be difficult to interpret and apply because healthcare professionals often try new techniques, methods, and approaches and attempt to learn from their innovations. They may also collect data that could contribute to generalizable knowledge. For example, consider a surgeon who modifies a hernia repair technique and keeps records of his surgical outcomes, so that he can learn from them. Although his primary goal is to improve the health of his patients, he may also be able to develop generalizable knowledge from his clinical observations. Is he conducting research or just engaging in innovative surgery? IRBs and health professionals have struggled with questions like this one for quite some time. There is not always a definite boundary between innovative clinical practice and research (Brower 2003, Amdur and Speers 2002). Similar questions concerning the relationship between research and practice have arisen concerning healthcare quality improvement (QI) initiatives and new public health interventions (Gunsalus 2006, Amdur and Speers 2002).

Minimal risk is defined as "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 (45 CFR 46.102i)." Minimal risk plays a significant role in the Common Rule because studies that are classified as minimal risk do not need to be reviewed by the full IRB: they can be reviewed

by the IRB chair or designee on an expedited basis (45 CFR 46.110). Also, IRBs can approve pediatric research studies that offer the subjects no direct benefits, if those studies involve only minimal risks (45 CFR 46.404). Researchers have found that IRB members often disagree about how to interpret “minimal risk” (Wendler et al 2005). In one survey, 23% of IRB chairs classified allergy skin testing as minimal risk, 43% classified it as a minor increase over minimal risk, and 27% considered it to be more than a minor increase over minimal risk (Shah et al 2004). One reason why IRBs disagree about how to interpret “minimal risk” is that there has been considerable controversy and confusion concerning the meaning of risks “ordinarily encountered in daily life,” since people in different circumstances face different risks (Wendler et al 2005).

A recent controversy over a QI initiative conducted by Johns Hopkins University illustrates some of the problems that can arise when interpreting the definitions of “research,” “exempt research,” and “minimal risk” (Miller and Emanuel 2008). In September 2003, Johns Hopkins investigators submitted a request to their IRB to declare a QI project funded by the Agency for Healthcare Research and Quality exempt from the federal regulations (Miller and Emanuel 2008). On October 9, 2003, the IRB granted their request, and the investigators initiated the project. The initial results were published in December, 2006. The investigators demonstrated that adherence to a protocol they had developed and tested resulted in a dramatic decrease in catheter-related infections, potentially saving thousands of lives each year. On February 15, 2007, the Office of Human Research Protections (OHRP), which oversees IRBs that review research conducted or supported by the Department of Health and Human Services (DHHS) and other federal agencies, notified the Johns Hopkins IRB that it had some concerns with the QI project. In July of that year, OHRP sent a letter to Johns Hopkins declaring that the QI project did not qualify as exempt research but that it constituted human subjects research requiring full IRB review. Johns Hopkins then suspended the project (Miller and Emanuel 2008). On February 15, 2008, OHRP issued a statement saying that the Michigan hospitals could implement the QI protocol developed by the Johns Hopkins investigators, since the protocol was no longer being used for research purposes. However, OHRP also stated that during the research phase, the QI project would have constituted minimal risk human subjects research (Miller and Emanuel 2008).

To avoid repeating the predicaments like those that occurred in the Johns Hopkins QI initiative, important definitions in any new regulations, such as “research,” “exempt research,” and “minimal risk” should be clear and unambiguous. If the Common Rule is simply extended to cover all research in the U. S., then steps should be taken to clarify the meaning of important terms in the Common Rule. Currently, a committee that advises the DHHS Secretary is considering whether the Common Rule should be revised and whether agencies should issue additional guidance for investigators, institutions, and IRBs (Secretary’s Advisory Committee on Human Research Protections 2008). Since its inception, OHRP has issued some guidance concerning the interpretation of various definitions in the Common Rule, but more guidance may be needed.

To conclude, while I support the gist of Shamoo and Schwartz’s proposal, much more work still needs to be done to implement it. Policymakers, legislators, federal officials, researchers and scholars should think long and hard about the practical problems related to closing loopholes in the federal research regulations, and how to address them. Any proposal that is made into a law should include adequate provisions for exempting some low risk research and clarifying the definitions of important terms.

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