



Office for Human Research Protections  
Rockville, Maryland 20852

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Dear Dr. Pronovost:

This is in response to your request for guidance regarding your plans for activities related to improving the rate of catheter-related bloodstream infections in hospitals and compliance with the Department of Health and Human Services regulations for the protection of human subjects in research (45 CFR part 46). We appreciate your interest in advancing the quality of healthcare across the country and beyond, and your proactive efforts to take steps to prevent needless delays which might arise due to possible confusion or uncertainty related to how the regulations for the protection of human subjects in research might apply to planned activities. We are happy to cooperate with you in those efforts.

Based on your letter of April 8, 2008 to Dr. Kristina Borrer and our follow-up communications, we present below our understanding of the planned Johns Hopkins University projects.

Johns Hopkins University is going to cooperate with various state hospital associations or other institutions to implement the same five part program for reducing catheter-related bloodstream infections that was implemented in Michigan hospitals and described in the New England Journal of Medicine (NEJM) article of 12/28/06. At this point, the participating hospitals wish to adopt the program in order to improve the quality of care in their hospitals, based on their belief that the program has been shown to be effective. Johns Hopkins University is willing to provide technical assistance to the state hospital associations and the participating hospitals to accomplish this objective.

At the same time, Johns Hopkins University also plans to carry out a study to improve the understanding of how hospitals implement this program on a wide-scale basis, what factors influence the effectiveness of those efforts, and whether

rates of infection reduction found in the Michigan study are replicated in other states and settings. The data collections included in this study are as follows:

1. The participating hospitals will provide aggregate data regarding the number of infections and the number of “catheter days” occurring at the hospital over identified periods of time. These data will be collected at the hospitals for the clinical purpose of monitoring the quality of care being provided and also will be shared with Johns Hopkins University for study purposes.
2. Staff at the participating hospitals will provide information about their perceptions of the culture of safety in the Intensive Care Units (ICUs) through surveys identified by institution but not by individual respondent, using either a survey instrument developed by the Agency for Healthcare Research and Quality or an instrument used in the Michigan study. Survey results will be provided to the participating hospitals to inform hospital staff/officials about the perceived quality of ICU operations at their own hospitals. The results also will be shared with Johns Hopkins University for the study purpose of comparing those perceptions with the rates of infection across the different hospitals.
3. Staff at the participating hospitals will provide information about their perceptions of the process of implementing the infection-reduction program in their hospitals’ ICUs through surveys identified by institution but not by individual respondent, using the Team Check-Up Survey instrument developed by Johns Hopkins University. Survey results will be provided to the participating hospitals for the purpose of informing hospital staff/officials about the process of implementing the program at their hospital. The results will also be shared with Johns Hopkins University for the study purpose of relating features of the implementation process with the rates of infections across the different hospitals.

Based on this description of the Johns Hopkins University projects, our analysis of how the regulations for the protection of human subjects in research (45 CFR part 46) apply to these projects is provided below.

First, we believe that the actual implementation of the five part catheter-related bloodstream infection reduction program in the participating hospitals is a quality improvement activity that does not meet the regulatory definition of *research*. This is because none of the parties involved are implementing the program as a research intervention in order to evaluate its effectiveness. Here, the program is being implemented solely for the purpose of improving the quality of care.

Second, we believe that the activity involving the analysis of the aggregate data about the rate of catheter related infections (Point 1 above) combined with the data drawn from the two surveys (Points 2 and 3 above) does not fall under the regulations, and therefore does not need to meet regulatory requirements, including the requirement for IRB review and approval. The planned activity does meet the regulatory definition of *research* (45 CFR 46.102(d)), because it is a systematic investigation that is designed to improve the scientific understanding of how to implement this quality improvement on a wide scale. However, obtaining and analyzing the aggregated data about the rate of infections at the participating hospitals does not meet the regulatory definition of *human subjects* (45 CFR 46.102(f)), because Johns Hopkins University is not obtaining identifiable private information about any living individuals, nor is anyone intervening or interacting with living individuals for research purposes. The two surveys represent *research* involving *human subjects* under the regulatory definitions, but since the survey information is being collected anonymously, this research activity, including the comparison with the aggregate data about the rates of infections, is exempt from the regulatory requirements under 45 CFR 46.101(b)(2).

Regarding these types of projects, where the implementation of a program is being studied, an important issue is whether the regulations apply to the program itself, or only to the information collection activities used to study the program. For each hospital where the program to be studied will be implemented, the question to ask is: "Is the program implemented for a research purpose, or altered or controlled in some way to answer a research question?" If the project leaders, quality and safety leaders, and physicians implementing the program at a particular hospital answer this question "no," then the program is separable from the research for that hospital, and only the various ways in which data will be collected and analyzed are part of the research activities that may potentially need to meet the regulatory requirements. If, on the other hand, a project leader, quality and safety leader, or physician answers "yes" with respect to the implementation of the program at a particular hospital, and the delivery of the program is initiated for a research purpose, or is altered or controlled in some way to answer a research question, then the program implementation at that hospital is not separable from the research. For the Johns Hopkins University projects described above, the implementation of the program is separable from the research at all of the hospitals involved.

We understand that Johns Hopkins University may be conducting additional information collection projects related to the planned activity, and that these additional projects will be reviewed by Johns Hopkins University to determine whether or not the regulations apply and if the regulatory requirements, including IRB review and approval, need to be satisfied.

I hope this analysis is helpful. We believe that the analysis offered here is consistent with our prior analysis of the research activity reported in the NEJM article. The difference between the two analyses is that for the planned projects the implementation of the program is separate from the research activity, and so the regulations at 45 CFR Part 46 do not apply to the program implementation. If at some point you find that it would be beneficial for us to communicate directly with some state hospital associations or other collaborating partners regarding these projects, we would be willing to do so. And if you have any questions about the relationship between the regulations and this or other future projects, please do not hesitate to contact us.

Sincerely,

/S/

Ivor A. Pritchard, Ph.D.  
Acting Director  
Office for Human Research Protections

cc: Dr. Daniel Ford, Vice Dean for Clinical Investigation  
John Hopkins School of Medicine  
Dr. Kristina Borrer