JOHNS HOPKINS
UNIVERSITY

Center for Clinical Trials

Department of Biostatistics
Department of Epidemiology
Department of International Health

Department of Medicine
Department of Ophthalmology
Oncology Center

12 December 2014

Memorandum

To: Trialists

Fr: Curtis Meinert

Re: Comments on proposed NIH policy on use of a single institutional review board for multi-site research (http://grants.nih.gov/grants/guide/notice-files/NOT-OD-15-026.html; release date 3 December 2014; response date 29 January 2015)

The proposal is that NIH-funded institutions for multi-site studies use a single IRB. The proposed policy would apply to all domestic sites participating in NIH conducted or supported multi-site studies, whether supported through grants, contracts, or the NIH intramural program.

The policy change is driven by a desire of the NIH to achieve greater efficiencies and speed in the initiation of NIH-funded studies by reducing the administrative burden involved in duplicative reviews of the same protocol by multiple IRBs.

There is no doubt that the existing IRB system is cumbersome in multicenter studies, but it is a mistake to characterize individual IRB reviews as duplicative any more than it would be to characterize multiple peer reviews of a manuscript as duplicative. Every IRB is different and sees and responds to different things. No single IRB, no matter how comprised, can be expected to have the coverage and breadth of knowledge as with a collective body of IRBs.

The expectation is that the change will save money. Good luck on that.

The reality is that the change may actually increase costs given what IRBs of record have to do to acquire the necessary assurances and certifications. As one learns from Freakonomics (Levitt and Dubner; 2006; William Morrow publisher), things do not always turn out as expected.

The expectation is that the single IRB will shorten the time to start, but the reality is that times to start are driven largely by other factors like the time it takes for investigators to agree on a protocol, the time it takes to develop data forms and systems for data intake and, in the case of drug trials, the time it takes to get and package drugs for use in those trials.

Local IRBs under the proposal, of necessity, will retain responsibility for reviewing and approving consent forms and procedures at local sites. One assumes IRBs of record will have responsibility for approving consents used at local sites. Even if IRBs of record prepare prototype consents for local use, experience teaches that IRBs have predilections for wordsmithing. Hence, one can expect the most time consuming part of the approval process will be clearing consents for local use. The time can be considerable in network trials with, sometimes, as many protocols as there are clinics in a study.

The proposed change has downsides. An obvious one is what it does to local IRBs. There can be no question that the IRB system in place has been paramount in educating faculty and staff of academic institutions as to duties and ethical issues underlying the privilege of researching on human beings. Reducing the richness of exposure by siphoning away what is usually the most important and challenging research IRBs review will lessen their vitality and morale.

A likely unintended effect of the one IRB requirement is to further diminish the means and incentives for individual investigators to propose and initiate multicenter studies. As it is now, an ever increasing number of initiatives come from the NIH and fewer and fewer from investigators. A robust research environment needs balance between the two modes of initiation.

The argument by the proposers that there is no evidence that multiple IRB reviews enhance protections for human subjects is vacuous in the absence of detail. One can just as easily argue that there is no evidence of harm because of multiple reviews.

The proposers argue that the single IRB model may lead to enhanced protections by "minimizing institutional conflicts of interest". As a researcher I am more interested in balance of conflicts than in minimizing them. There is information in the different philosophies and points of views of individual IRBs that, in all likelihood, add to protections.

An effect of the policy will be to increase free-standing IRBs not affiliated with any institutions. Even some for profit, perhaps. It is hard to see this as a step forward or a direction we should be headed.

The current system of institution-affiliated IRBs is robust because of their autonomy. Shutdown of one IRB because of failure to obtain renewals or by action of the OHRP does not effect other centers under other IRBs in a study. Everything shuts down with the single IRB model if the IRB of record fails to renew in time or if it is shutdown by the OHRP.

Undertaking research on human beings is a high-risk activity. Trials, in particular, expose investigators to an array of risks. There is no doubt that I have had my share of disputes with my IRB, but I have also felt protected by my IRB if something bad were to happen on my watch. It is difficult to feel that same level of protection with a free-standing IRB comprised of members I do not know in some remote location that likely is more interested in protecting its own interests than mine.

Certainly, the fussy language in the proposal regarding consents is not reassuring if I was to find myself called to task by an angry participant in my center for something I did or said.

> *With regard to assuring that local perspectives are addressed, the assessment of a study's risks and benefits and the adequacy of the informed consent should not generally require the perspective of a local IRB. Local contextual issues relevant to most studies (e.g., investigator competence and site suitability) can be addressed through mechanisms other than local IRB review, such as the involvement of ad hoc members or consultants with the necessary specialized knowledge or expertise, or by submission of information by the individual site(s). Even when certain vulnerable populations are targeted for recruitment, such alternative approaches may be appropriate.*

If I was to offer advice to the NIH, I would suggest a more measured approach. We have had the current system in place for 40 plus years. We need time to assess the effect of changes and time to identify and understand unintended consequences of changes. The only allowable exceptions to the policy, as written, are if the designated single IRB is unable to meet the needs of specific populations or where local IRB review is required by federal, tribal, or state laws or regulations. The go for broke approach to implementation seems ill-advised especially when, all too often in government, something is implemented not even God can undo it.