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Dockets Management Branch

May 10, 2002

Re: Docket No. 01N-0322

To Whom It May Concern:

The investigators and coordinators of the Public Access Defibrillation (PAD) Trial support and encourage the ethical conduct of research. IRB review is the cornerstone of the oversight that assures this ethical imperative. The practice of "IRB shopping" threatens to compromise the integrity of this process. Thus, the PAD investigators concur that IRBs should have full knowledge of any prior unfavorable IRB reviews when asked to review the same or an essentially similar protocol.

However, we are concerned about the practical implications of the proposed rule as it would apply to multicenter trials like ours. The PAD trial was initially reviewed and approved by the University of Washington IRB (Seattle, WA) and then by the applicable IRB at each of the 24 participating sites. Approval was then sought from hospitals that might receive enrolled subjects. This has involved protocol submission to date to 101 IRBs and has resulted in at least 50 requests for revisions. We believe that requiring all IRBs to be notified of all the decisions of all other IRBs involved in a multicenter trial would impose a tremendous, if not impossible, burden without adding significant protection to subjects.

We do, however, propose a process for multicenter trials that should achieve the desired goal. We suggest that negative final decisions (or investigator withdrawal because of likely denial) be reported in hierarchical fashion. Denial by a site or secondary IRB would be reported to the primary IRB for the multicenter trial. (Figure) Denial by, for example, a community hospital IRB (a tertiary IRB) would be reported to the site IRB, and so on. The IRB receiving such notification would then review the reporting IRB's rationale and concerns, review the approved protocol and determine if the issues raised by the denying IRB required action, such as protocol modification and/or notification of other IRBs involved in the trial. Importantly, simultaneous (or near simultaneous) submission to multiple hospital IRBs at a particular site after approval by the primary (coordinating center) and the site (secondary) IRBs should not be considered "IRB shopping."

As the request for comments states, some process issues will need to be addressed as well, including who makes the report, what should be reported, and when to report. It seems reasonable that investigators should be obliged to report, but also requiring the denying IRB to report to the appropriate hierarchical IRB as described above would help to promote compliance. We believe only final negative decisions and protocol withdrawals should be required to be reported, although it would seem advantageous for investigators to report prior approval. The report should indicate the reason for the denial so that the IRB can determine the need for any further action. For ongoing trials, a negative review at a secondary or tertiary site would be reportable immediately to the appropriate IRB as described above.

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Public Access Defibrillation

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For the initial submission of a multicenter trial to a primary IRB, that submission and any action should be treated like a single site study, with full disclosure of any denial to any other IRBs if the study is resubmitted elsewhere for primary IRB approval.

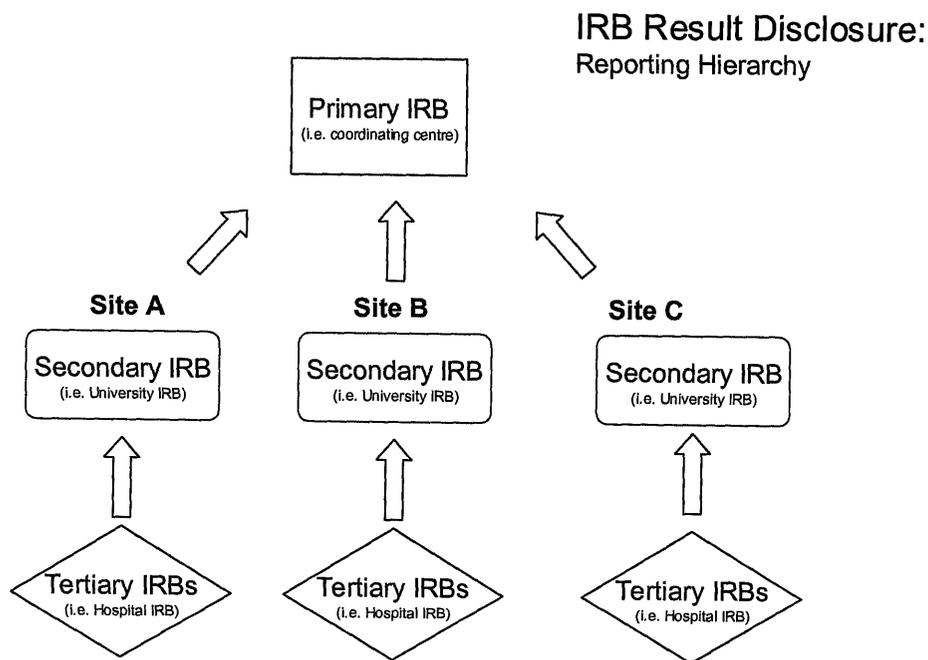
In summary, based on our experience with a large multicenter trial, we feel strongly that safeguards against the potentially unethical practice of “IRB shopping” may be warranted but must be carefully crafted to avoid being unreasonably burdensome or even untenable in the setting of a multicenter trial involving a large number of IRBs often simultaneously reviewing and seeking revisions of the same protocol. We have proposed a process that we believe would provide appropriate reporting and review of negative decisions without excessive burden.

Sincerely,



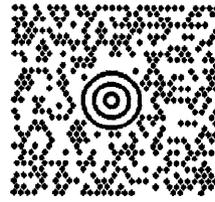
Joseph P. Ornato, M.D.  
PAD Executive Committee Chair

Figure.



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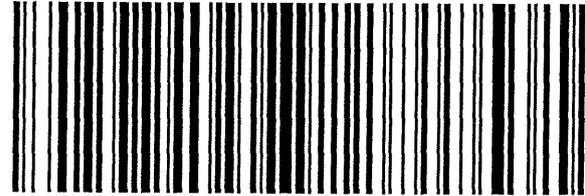


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