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Single-Minded Research Review: The Common Rule and Single IRB Policy

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It seemed straightforward on its surface: a minimal-risk study to look at financial incentives for evidence-based treatment of hypertension. In the end, however, it took 27 months and 115 submissions to get through the 17 institutional review boards (IRBs) involved in reviewing this multisite study (Petersen et al. 2012). More extreme cases have been detailed in reviews critical of current regulation of human subjects: 8 years of negotiations with multiple IRBs for approval of minimal risk health services research; delays to West Nile research in which investigators were forced to respond to questions that “ranged from grammatical and editorial requests to mandated inclusion of site specific language,” resulting in sites starting studies after peak viral season; and clinical trials delayed months as dozens of IRBs bicker over the details of consent forms (Schneider 2015). As Laura Stark, a sociologist from Vanderbilt University who studies IRB decision making, puts it, “It is a puzzle—and a persistent problem for investigators—that different IRBs never seem to agree on how research should be conducted. This causes a serious practical problem for many researchers who face competing and sometimes contradictory judgments from several boards about how a single study needs to be modified before it can be approved” (Stark 2011).

The final Common Rule aims to solve this problem by generally requiring a single IRB (sIRB) of record for review of research taking place in the United States at multiple sites. In the 2011 advance notice of proposed rulemaking (ANPRM), the Office of Human Research Protections (OHRP) stated, “There is very little evidence that having multiple IRBs review the same study, results in enhanced protections for subjects. By diffusing responsibility for that review, it might actually contribute to weakened protections” (OHRP 2016). Under the final Common Rule, United States-based institutions that receive federal funding and are engaged in cooperative research are required to use a single IRB for that portion of the research that

takes place within the United States if certain requirements are met (82 FR 7149–274 2017).

The National Institutes of Health (NIH) is at the forefront of streamlining multisite review. While the final Common Rule requirement for sIRB review of multisite research does not go into effect until January 20, 2020, NIH has issued a policy to establish the expectation that sIRB review will be used for all NIH-funded multisite clinical research studies, unless there is a requirement for local IRB review under federal, state, or tribal law or regulation. Effective for all NIH-funded multisite research studies submitted, issued, or received on or after January 25, 2018, this policy is one piece of our broader effort to enhance the quality and efficiency of clinical trials and research supported by NIH (Hudson, Lauer, and Collins 2016). The NIH sIRB policy is, by design, entirely complementary with the final Common Rule.

The concern about inefficiency of multiple IRB review and use of an sIRB to address this burden certainly did not originate with NIH. In fact, the value of sIRBs was actually recognized in the preamble of the 1979 regulation (44 FR 47699–700 1979). The organization Public Responsibility in Medicine and Research (PRIM&R) held a conference in 1998, bringing together more than 100 research representatives to discuss “Central IRB Review of Multi-site Research” (Levine and Lasagna 2000). In 2004, the Secretary’s Advisory Committee on Human Research Protections began a public discussion on the utility of sIRBs for multisite studies, leading to a stakeholder workshop to explore models for centralizing IRB review (Gordon, Culp, and Wolinetz 2017). In the interim decades, the potential of sIRB use to reduce burden and improve review has been proven in successful models. For example, while this policy met with resistance when it was set up in 2001, the National Cancer Institute’s Central IRB (“CIRB”), has rapidly developed into an exemplar of the efficiencies gained by use of an sIRB. In a 2005 survey of CIRB stakeholders, 80% of respondents described CIRB as saving them

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significant effort and time (Adler 2011), and a 2010 evaluation demonstrated the CIRB was associated with more rapid reviews, reduced IRB and research staff effort and time, and cost savings (Wagner et al. 2010).

In calls for reduction of research/regulatory burden, delays associated with review by multiple IRBs and calls for sIRB have been common themes across stakeholders, including the Presidential Commission for Bioethical Issues (U.S. Presidential Commission for the Study of Bioethical Issues 2011), the Federal Demonstration Partnership (Schneider et al. 2012), the Federation of American Societies on Experiment Biology (FASEB 2013), the National Science Board (NSB 2014), and—most recently—the National Academies (NAS 2016). Industry has also long been supportive of this approach (National Association of College and University Attorneys [NACUA] 2016). The Food and Drug Administration (FDA) issued guidance on use of a central IRB for multicenter trials in 2006 (FDA 2006), and its position was endorsed by OHRP's Correspondence (McDeavitt 2010).

The comments in reaction to the NPRM and/or ANPRM on the Common Rule and NIH policy generally reflect support for this change. This includes a substantial number of commenters who noted concern for mandating such sIRB review, preferring it be strongly encouraged (82 FR 7149–274 2017; 81 FR 40325–331 2016). The Common Rule departments and agencies disagreed with this direction, noting in the preamble to the Common Rule, “We feel that this incentivized approach would ultimately fail to yield substantive positive change in the system. Rather, systematic efficiencies have the best chance of occurring if single IRB review is required for all review in domestic research involving more than one institution” (82 FR 7149–274 2017). This was echoed in the comments submitted on the NIH policy: “In spite of current guidance from OHRP on ceding to other IRBs, most local IRBs continue to refuse this approach and there is no apparent basis for this with respect to research subject rights and safety” (OSP 2015). Many supporters commented that use of an sIRB would likely reduce administrative burden and inefficiencies for investigators and research institutions. Individual investigators were particularly enthusiastic. As one commenter on the NIH sIRB draft policy stated, “This is long overdue. The approval of a multi-site protocol by the IRB of each site is redundant and wasteful of time and resources” (OSP 2015).

The final Common Rule requirement and NIH policy represent the culmination of a series of efforts originating within the agency and research community to move the clinical research enterprise toward sIRB review. For example, the National Center for Advancing Translational Sciences (NCATS) has recently unveiled the Streamlined, Multisite, Accelerated Resources for Trials (SMART) IRB Platform in conjunction with its Clinical and Translational Science Awards (CTSA) program. SMART IRB is intended to provide flexible resources that investigators can use to harmonize and streamline IRB review for their own multisite studies (NCATS 2016). Similarly, institutions have

been exploring innovative approaches to reliance agreements (Winkler, Witte, and Bierer 2015) and information technology (IT) platforms (Obeid et al. 2016) to facilitate multisite IRB review.

In recognition that catalyzing major changes, even in pursuit of long-term benefit, is not easy, NIH is working to smooth the implementation of our policy in ways that we hope will facilitate longer term implementation of the Common Rule requirement. The NIH sIRB policy applies to domestic sites of multisite studies conducting nonexempt human subjects research, which refers to all sites conducting the same protocol. This policy excludes foreign sites, career development awards, institutional training, and fellowship awards. In cases where federal, state, tribal, or local regulations require local review, exceptions will be granted. Exceptions may be requested and considered by a trans-NIH review committee when there is a compelling justification; however, exceptions are anticipated to be infrequent and rare. We are also considering ways to supplement support to cover direct costs for the development of costing models, business processes, system changes, and efficient procedures and tools needed to facilitate sIRB review for multisite research, as well as mechanisms for widely distributing those best practices.

At the end of the day, the final Common Rule requirement and NIH policy for sIRB review of multisite research exemplify why the department started down the path of updating the Common Rule. Fulfilling the promise of Common Rule reform is about safeguarding the people who agree to take certain risks involved in research, but freely give of their time to increase scientific knowledge and improve human health. As stewards of the public trust, it is our obligation to honor that contract by seeking to eliminate unnecessary burdens that delay research and frustrate researchers and participants alike. We believe that the shift toward requirement of single IRBs represents a common sense solution to a longstanding problem.

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Opportunities Missed and Created by the New Common Rule

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Like preparations for climbing the vertical face of El Capitan in Yosemite or the West Face of the Matterhorn, the daunting prospect of revising the 1991 Common Rule attained an almost mythical status as the years accumulated. Even as the revision process unfolded through the advance notice in 2011 and the

proposed rule in 2015, it seemed unlikely that a new final rule would appear in the final days of an outgoing administration. Changing directions on a complex rule that had been in place for so long, at so many institutions, and for so many agencies, was a monumental task to initiate. Adding to the pressure on the

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