Ohio CTSAs Implement a Reliant IRB Model for Investigator-Initiated Multicenter Clinical Trials

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Introduction

Effective clinical and translational research is an essential component of improving human health as delineated in the National Institutes of Health (NIH) roadmap, yet efficiently conducting that research remains problematic. Challenges include the high costs of conducting research, a shortage of qualified investigators, low subject enrollment rates, slow dissemination of results, reduced funding, lagging IT systems, and increased regulatory burden. A priority for the National Center for the Advancement of Translational Science (NCATS), and its Clinical Translational Science Award (CTSA) Consortium, is to address this last concern regarding regulatory burden. Specifically the focus is on the improvement of Institutional Review Board (IRB) processes, especially novel models for regulatory review of multicenter clinical and translational research studies. The three Ohio CTSA sites, housed at Case Western Reserve University (CWRU) in Cleveland, The Ohio State University (OSU) in Columbus, and the University of Cincinnati (UC), have collaborated to create a novel IRB review concept with the hopes of addressing this concern and achieving a more effective and efficient IRB review of multicentered clinical research studies.

Process Development

To date a number of different methods have been used to streamline IRB review of multisite studies. The central IRB model, where a “for-profit,” independent IRB (e.g., Western or Chesapeake) acts as the IRB of record for regulatory review processes, is commonly used for a large number of industry initiated and sponsored clinical trials. Federated IRBs are another type of review model in which one existing IRB within a network of sites serves as the IRB of Record for studies conducted within that network (e.g., Harvard Catalyst is the IRB of Record for all studies within the National Institute of Neurological Disorders and Stroke (NINDS) NeuroNext network). A simpler and less formalized model of reciprocal review involves the use of individual “Institutional IRB Authorizations” (IIA) between collaborating organizations whereby one organization can “authorize” a second organization’s IRB to act as the IRB of Record for one or more studies conducted at their organization. In an effort to create a “hybrid” model, the IRB Administration Offices within the Clinical Translational Science Collaborative (CTSC) based at CWRU and including University Hospitals Case Medical Center, MetroHealth Medical Center and the Cleveland Clinic Foundation, moved from a type of bilateral, inter-institutional agreement to a broader agreement amongst partners allowing the lead CTSC site to act as the IRB of Record for a multisite clinical research protocol conducted at any of the partner CTSC sites in late 2009. The CTSC named this process “facilitated review” as this model allowed for any participating IRB to serve as the IRB of Record for protocols conducted by any combination of participating sites while at the same time allowing each site to retain local context review and oversight. More importantly, to address the fact of disparate electronic IRB review systems, the CTSC IRB Advisory Group developed a centralized electronic IRB hub as the main point of interface for each application to further promotes efficiency in IRB review processes while facilitating document storage and communication across research sites amongst CTSC regulatory administrators and investigators alike.

In June 2011, 18 months after implementation of the initial facilitated review process and IRB electronic “hub,” reports of the CTSC facilitated review model, and information related to use and successes within the CWRU CTSC were presented at the annual Clinical Research Management Workshop sponsored by the CTSA consortium. Three months later, use of this type of model received significant support by the political leadership in the State of Ohio when the Governor of Ohio and the leader of “JobsOhio” (an economic growth engine for job creation) convened a meeting focused on leveraging healthcare and medical strengths in Ohio to catalyze industry interest and spur economic growth. One result of that meeting was a three-prong charge from the governor to the three Ohio CTSA sites to collaboratively develop Ohio as a recognized destination for clinical research, to foster more efficiencies within the translational research process, and to attract more pharmaceutical and device industries with the goal being improved human health.

The partner organizations that comprise the Ohio CTSA consortium (Table 1) discussed ways to collaborate shortly after initial discussions with the governor and conceptualized full IRB collaboration. The group immediately followed up with a face-to-face meeting (October 2011) where the CTSC “facilitated review” process and IRB electronic “hub” platform were demonstrated. Following that discussion, the CTSSAs across Ohio agreed to move towards the reliant model of IRB review. Members of the Ohio CTSA Consortium IRB Working Group agreed that each institution within the collaborative would participate and exercise authority of the proposed “reliant” IRB review model when investigator collaboration existed among one or more of the Ohio CTSA institutions (i.e., investigator synergy is the starting point). Using current partnerships within the group (the Cleveland CTSC, the IAA between Cincinnati Children’s Hospital Medical Center and the University of Cincinnati, and the IRB reciprocity agreement between The Ohio State University and Nationwide Children’s Hospital,) as well as other models of collaborative review (Harvard Catalyst Reciprocity Agreement) as a foundation
for legal agreement discussions, a decision was made to execute a single IIA signed by all eight participating institutions to clarify and solidify expectations. The total timeframe for the Ohio CTSA Consortium IRB Working Group to achieve a fully executed agreement was approximately 9 months. Much was accomplished in this timeframe without wavering from the ultimate goal of reduction of regulatory burden for investigators through reliant IRB review.

Reliant IRB Review Model
Specific requirements of the reliance model include that “each institution agrees to maintain a registered IRB and an OHRP approved Federalwide Assurance (FWA) for human subject research.” In order to serve as the “designated IRB of Record” for State of Ohio consortium-wide projects, the designated IRB of Record’s institution must have achieved AAHRPP or other accepted accreditation.” That IRB will then perform the “initial and continuing review and review of amendments; unanticipated problems that may involve risks to subjects or others; and other documents/information related to the approval and continuing oversight of the research (as applicable).” The quotations emanate from the executed IIA.

The relying institutions within the Ohio CTSC accept the IRB of Record’s review, approval, and continuing oversight of research covered by the IIA, but retain primary and ultimate responsibility for the protection of human subjects with respect to the conduct of the research covered by this agreement and agree to comply with applicable federal, state and local laws and applicable FWA requirements; as well as to review and manage appropriate education and conflict of interest requirements and any resolutions thereof, and to communicate any events or actions affecting that institution’s compliance to the designated IRB of Record.

A “reliant IRB” workflow, initially adopted from the CTSC’s “facilitated review model” initiative has now been extensively modified and access expanded for more broadly to the Ohio CTSA Consortium (Figure 1). Each participating institution in this model is part of an Academic Medical Center (AMC) and a key driver of such organizations is investigator-initiated clinical research resulting in the focus on executing that part of the institutional mission for each entity in this model. The agreements and the process flow can also be used when and where applicable for industry, foundation, and other sponsored project research activity in order to reduce redundant reviews or improve efficiencies.

Discussion
The strength of the agreement is in its simplicity, as it is strictly focused on IRB activities and responsibilities as defined by Human Subject Protection Regulations and promulgated by the Department of Health and Human Services and the US Food and Drug Administration described in 45 CFR 46 and 45 CFR 50 and 56. It does not extend into additional institutional specific human research protection plan requirements beyond those required for FWA and/or AAHRPP accreditation, it does not address grants administration, nor does it delve into HIPAA requirements and conflicts of interest. The purpose of focusing on only IRB related matters was to ensure that other institutional processes were not altered by IRB collaboration. Each institution is also responsible for managing budgets and contracts as such differs between public and private institutions.

Institutions Participating in Ohio Collaborative IRB Review Model*

(1) Case Western Reserve University
(2) Cleveland Clinic
(3) Cincinnati Children’s Hospital
(4) MetroHealth Medical Center
(5) Nationwide Children’s Hospital
(6) The Ohio State University
(7) University Hospitals Case Medical Center
(8) University of Cincinnati

*Eight legally separate institutions that constitute three separate CTSA funded entities.

Table 1. Participating Institutions
The process flow of this model is being refined, but this is an encouraging example that each of these AMCs has been able to agree on basic principles and simplified legal approaches to solve long standing regulatory challenges for conducting multisite clinical research. The model will continue to be refined and tested throughout Ohio. With the continued input and collaboration of its originators, our goal is to expand across the national CTSA consortium, and to also include non-CTSA sites.

Conclusion

We anticipate that the economic impact of this regulatory initiative will be positive, accelerating the initiation of clinical and translational research at participating institutions. Metrics are currently being gathered that will quantify protocol review and approval times; and whether use of this approach and electronic system has shortened study timelines. These improvements will likely result in ancillary successes including increased study revenues, increased job opportunities for research coordinators, study nurses and other allied research professionals in regions where institutions participate, increased subject enrollment as patients travel to regulatory efficient sites for access to innovative trials not open for enrollment (or not available) elsewhere; increased clinical volumes due to stimulated clinical trial activity, and finally the reduction of IRB regulatory burden will move innovative treatments more efficiently to the practice of medicine.

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