
How Institutions Gain Research Opportunities from Partnering with Multiple Independent IRBs

DESCRIPTION

Academic Medical Centers (AMCs) across the U.S. are attempting to win more industry-sponsored research trials, and one strategy is to partner with the multiple external IRBs that sponsors and CROs designate as central IRBs. Three case studies illustrate how and why leading institutions have made the decision to switch from reliance on just one external IRB to partnering with multiple independent IRBs.

TOPICS

- **INSIGHTS FROM INSTITUTIONS**
- **DEVELOPING A SELECTION CRITERIA**
- **MANAGING MULTIPLE INDEPENDENT IRBS**
- **KEY ISSUES TO ADDRESS IN A MASTER SERVICES AGREEMENT**

Opportunities to Improve Ethical Review of Research

When the Food and Drug Administration (FDA) first authorized a framework for independent IRBs in 1981, it enabled the development of a central institutional review board (IRB) review model for multisite studies. Independent IRBs formed first to provide ethical and regulatory oversight of unaffiliated (aka community) investigators. But in the decades since 1981, the role of independent IRBs has expanded and industry sponsors and clinical research organizations (CROs) now urge research institutions to use a central IRB of record for multisite studies rather than an institution’s internal IRB. Industry sponsors have good reasons to use research institutions as investigative sites, and industry-funded research may present opportunities to an institution’s research programs, but longer timelines at institutions often discourage sponsors and CROs.

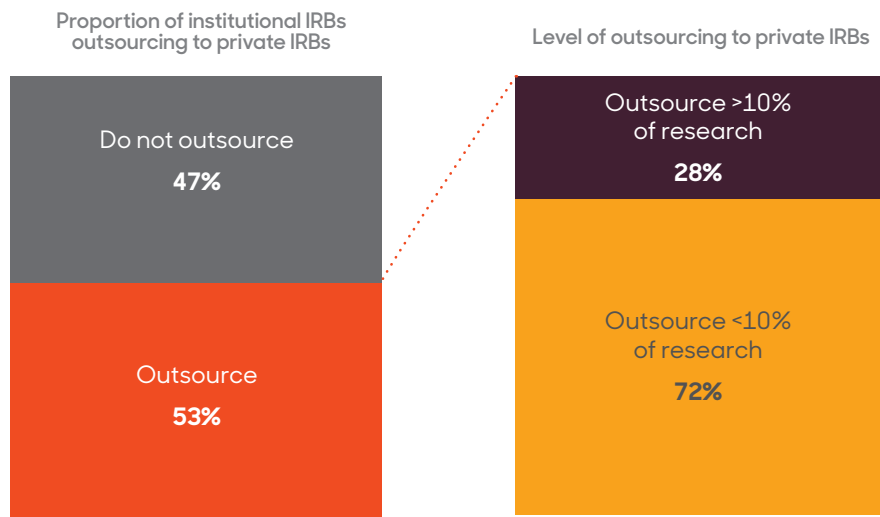
Academic Medical Centers (AMCs) across the U.S. are attempting to win more industry-sponsored research trials, and one strategy is to partner with the multiple external IRBs that sponsors and CROs designate as central IRBs. Three case studies illustrate how and why leading institutions have made the decision to switch from reliance on just one external IRB to partnering with multiple independent IRBs.

A representative from a CRO specializing in oncology research said that she values an AMC’s facilities and depth of knowledge for her trials. “For these first-in-human studies, we always want that expertise,” she says. But the CRO representative adds that these same AMCs can slow research down when they rely on their own IRBs, “even when alternatives exist.”

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While a slight majority of institutions outsource at least some IRB activities to independent IRBs, much of their research remains in-house. According to 2011 data, 53 percent of institutions used independent IRBs for some research but typically did not outsource more than 10 percent of their research. (See Chart 1).¹

Chart 1: Incidence and Level of Commercial IRB Use by Institutions



Source: CenterWatch, AAHRPP

The remaining 47 percent of institutions did not use independent IRBs for any reviews.

THIS WHITEPAPER EXAMINES HOW OTHER INSTITUTIONS HAVE IMPLEMENTED ONE OF THOSE ALTERNATIVES: ESTABLISHING SERVICE AGREEMENTS WITH MULTIPLE INDEPENDENT IRBs.

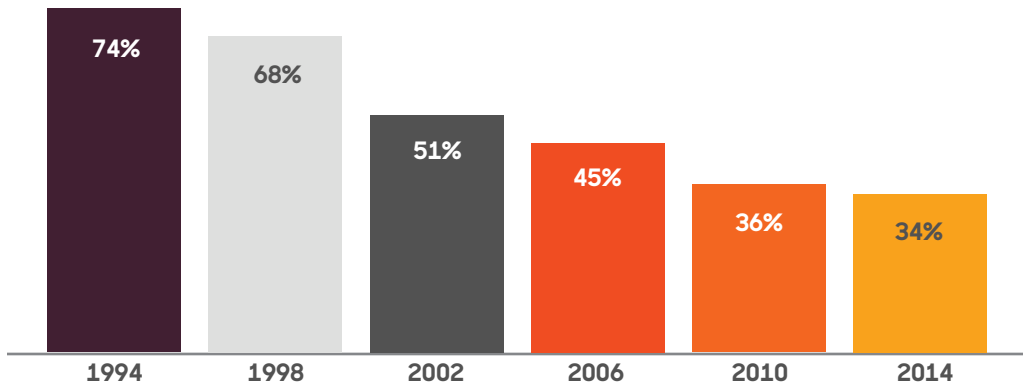
Multiple service agreements with well-vetted independent IRBs enable a research institution to join in multisite trials quickly by accepting the oversight of the central IRB of record. This paper examines how three institutions accomplished this and what lessons they learned.

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Why Change Now?

Although sponsors and CROs support bringing research institutions into their studies, recent statistics suggest that the institutions' share of industry research is falling. As the table below shows, AMCs participated in 74 percent of industry-funded trials in 1994, but that number has steadily diminished to just more than 34 percent. By 2014, AMCs were participating in just over a third of privately-funded research.²

Chart 2: AMC share of phase I-III industry-funded clinical trials

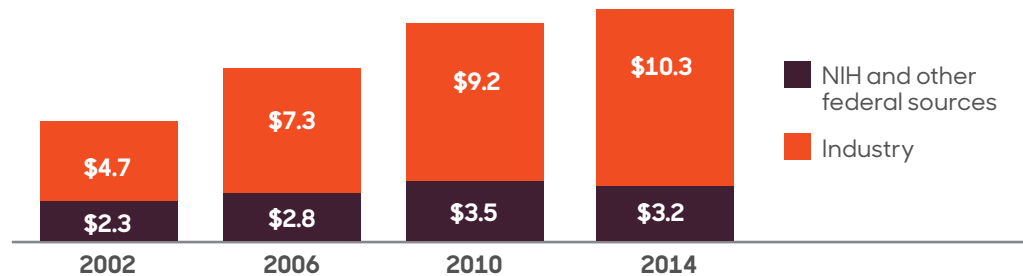


Source: CenterWatch

While the AMCs' share of industry-funded research dropped, that sector's overall contribution to research grants rose. In 2010, industry-funded research worldwide was \$9.2 billion, and federally funded research totaled \$3.5 billion. Even then, private industry was providing twice as much for research as that of federal sources (72 percent of the total and 28 percent of the total clinical trial spending); but by 2014, that gap had widened further. From 2010 to 2014, federal research funding dropped to \$3.2 billion (an 8.5 percent decrease), while private industry spending increased 11 percent to \$10.3 billion.³

Chart 3: Global clinical study grant spending

\$U.S. billions



Source: CenterWatch, NIH

Taken together, these dual trends—the decreasing role of AMCs in industry research and the increasing presence of private industry funding—suggest AMCs are missing research opportunities.

One way a research institution can position itself to take advantage of those opportunities is to develop a system to receive, initiate, and conduct industry trials faster and more efficiently, but without compromising the quality of research. A number of institutions are seeking to do this by agreeing to rely on the central IRB of record—*independent IRBs*—for a sponsor’s multisite trials.

The same oncology CRO referenced earlier in this paper has observed that institutions can start studies faster when they turn to a central IRB for oversight. In one trial, the CRO approached an AMC that preferred to use its local IRB. The time requirements of the study, however, were too short for the local IRB to meet. The AMC subsequently agreed to try an independent IRB, and the more streamlined process enabled the AMC to join the study faster and help it meet participant recruitment targets on time.

Here are observations and insights from three institutions that have expanded, or are in the process of expanding, beyond reliance on their local IRB to engage with multiple independent IRBs.

The University of North Carolina Chapel Hill: Testing a Hypothesis

DO INDEPENDENT IRBS DELIVER AS PROMISED?

In 2012, Professor Daniel Nelson and his colleagues at the University of North Carolina (UNC) Chapel Hill had questions about central IRB review. As director of the university’s Office of Human Research Ethics, Nelson wondered whether working with multiple independent IRBs offered any tangible advantages. Could external IRBs ensure that all regulatory requirements were met? Would transferring oversight to independent IRBs review save any staff time or university resources? Would an external board consider the same ethical and procedural issues as a local board?

Nelson and his colleagues launched a six-month pilot to compare reviews by external independent IRBs with the university’s own IRBs. True to the rigors of clinical research, the pilot established eligibility criteria, randomized the selection of studies, and blinded the participants. The pilot demonstrated that the answer to all of Nelson’s questions was, yes.

Under the pilot⁴, the university allowed the transfer of jurisdiction to qualifying independent IRBs that:

1. Were the central IRB of record on a multisite study in which UNC Chapel Hill was participating
2. Held active accreditation with AAHRPP
3. Were in good standing with FDA and OHRP
4. Were willing to establish a master services agreement with the university

Over those six months, 48 qualifying studies came to UNC Chapel Hill. They came from 32 sponsors and utilized eight independent IRBs. (The studies amounted to about one-third of the university's overall IRB workload.) After referring the studies to the respective independent IRBs, Nelson's study team asked the local IRB to review them without sharing any results. The researchers then compared review outcomes, performance timelines, and investigator satisfaction between the external and internal systems.

According to Nelson's 2012 presentation, the IRB determinations were essentially the same between the external and internal reviews, but **the independent IRB reviews saved up to 20 days during site initiation**. In a survey of investigators and study teams, 85 percent of respondents said that the use of independent IRBs was advantageous.



THE IRB OFFICE STARTS A NEW POLICY

After assessing these results, UNC Chapel Hill decided to change its policy regarding independent IRBs. Now, research teams may work with a UNC Chapel Hill-approved independent IRB whenever that IRB is the central IRB of record in an industry-sponsored multisite study. Professor Nelson **emphasized the importance of working with multiple IRBs rather than remaining exclusive to one**. An exclusive arrangement, he said, would be like "trading one IRB for another," and it would not deliver the same improvements in performance for every industry study.

Benaroya Research Institute: Diversifying the IRB Pool

The Benaroya Research Institute at Virginia Mason (BRI) had been working with one independent IRB for many years, but the IRB office and Clinical Research Program (CRP) faced growing requests from investigators to expand, as they noticed that an increasing number of studies were using other independent IRBs.

As a first step, BRI established a services agreement with one other IRB. According to Chris Weir, the head of BRI's IRB office, one reason for this change was to take advantage of central IRB efficiencies in more trials; diversification was another. Chris said it seemed a safe move to "not have all of our eggs in one basket."

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The expansion has worked well, according to Weir. The two IRBs have different management styles, each with different advantages, and Weir says that **reviews happen more quickly when BRI can use the IRB of record in their multisite studies**. BRI is now considering a further expansion of its program to include more independent IRBs.

University of Rochester: Moving out of the Comfort Zone

The University of Rochester has relied on one independent IRB to manage industry studies for nearly 20 years. Kelley O'Donoghue, the Associate Vice President for Human Subject Protection and the Director of the Office for Human Subject Protection (OHSP), said comfort was a primary obstacle to expanding its roster. The decades-long relationship with one IRB meant that the university, its IRB office, and its investigators had a degree of familiarity with the IRB and that fostered a resistance to change.

O'Donoghue estimates that the school has about 250 industry studies active at any point in time, about 15% of its overall research portfolio. But over the years, **the investigators have indicated to the OHSP that they'd like to try working with other independent IRBs**. Only recently has the OHSP pursued expansion. "We saw the writing on the wall," O'Donoghue said; the office is now developing agreements with two other independent IRBs.

Best Practices and What These Institutions Learned

The experiences of these institutions can provide useful guidance for any institution considering a similar expansion. Common threads run through all three experiences:

- The need for clear and consistent selection criteria
- The importance of following a consistent procedure with each of the independent IRBs
- The critical first step of establishing master services agreements with the selected independent IRBs, and
- The need to ensure that the institution's human subject protection program can monitor all of the institution's research activity

HAVE CLEAR, CONSISTENT SELECTION CRITERIA

It is crucial that everyone in the institution has confidence in the independent IRBs that are selected. Investigators should feel comfortable reporting to the independent IRB; directors must have trust that an independent IRB is credible, solvent, and reliable; and **those at the institution who work in human subject protection must have confidence that the independent IRBs will meet all regulatory requirements**, honor the institution's own requirements, and ensure participant protections. A credible selection process will help convince those stakeholders.

After its pilot program, UNC Chapel Hill decided to expand its use of independent IRBs. In qualifying IRBs for consideration, it largely followed the same criteria as the pilot. Under the expanded program, investigators at UNC Chapel Hill may submit to an independent IRB for review if:

1. The IRB is the IRB of record for a selected industry study
2. The IRB is in good standing with OHRP and the FDA
3. The IRB has or is willing to establish a master services agreement (as opposed to a one-off, study-specific agreement) with UNC Chapel Hill
4. The IRB has accreditation from a recognized agency

Quorum has participated in the full spectrum of qualification processes with institutions, from formal requests for proposals to less formal presentations and conversations.

To date, BRI has followed a less formal selection process, but Chris Weir emphasized the importance of getting it right. "This is a huge deal," he said. "When you are at an institution you have to wonder who has your back. Who is watching out for the institution?" Weir said that, like UNC Chapel Hill, accreditation is a key factor. BRI did have a trial period with the additional IRB before permanently changing the policy.

Each of these institutions required that independent IRBs carry accreditation. Accreditation demonstrates that a knowledgeable outside authority has confirmed that an IRB meets specific requirements and follows established procedures. And, as any organization that has gone through an accreditation process can attest, receiving and maintaining that certification demonstrates a commitment to rigorous standards of compliance.

The selection process for the University of Rochester was also less formal, and Kelley O'Donoghue said that was in large part because of accreditation. "Accreditation has to be there for an independent IRB to be considered," she said. "(It), absolutely, is important. That allows us to avoid a more formal due diligence process. It is sort of our own mandate. Without it, we won't even start the discussion. We just can't take that risk." The University of Rochester is looking at expanding to include two additional independent IRBs, and for O'Donoghue, overall capacity is important too. The IRBs they select must have the capabilities to support the university's busy research portfolio. Another benefit for O'Donoghue is the training resources that independent IRBs offer. "The nice thing is that they are willing to provide training and conduct webinars on process and software so we don't have to do it."

The selection process for independent IRBs is crucial for getting off to the right start. The Clinical Trials Transformation Initiative (CTTI) offers a set of materials that can help an institution determine selection criteria. As part of its Central IRB project, CTTI created the "Evaluation of a Central IRB" checklist.

<http://bit.ly/evaluationofacentralirb>

HAVE A CONSISTENT PROCESS FOR MANAGING INDEPENDENT IRBS

At BRI, the IRB office serves as a key coordinator between the BRI investigators and independent IRBs. The IRB office receives the investigator's study submission, ensures that the investigator has met all other institutional reporting requirements, and then passes the submission on to the independent IRB (this is an administrative check, not an IRB review). As part of the agreement, independent IRBs only accept BRI submissions that come from the IRB office.

The University of Rochester has a less centralized system, but the university's Office for Human Subject Protection (OHSP) must authorize the submission before it goes to the independent IRB. Within 24 hours of receiving a potential submission OHSP confirms whether all institutional requirements—such as conflict of interest, compensation for injury, investigator education requirements, and electronic health record issues—are met. "We ensure those aspects are addressed before IRB review and not added as an afterthought," O'Donoghue says. "It is very important to us that this information is considered as part of the review, not afterwards." One employee in the university's OHSP is responsible for tracking and coordinating all independent IRB activities.

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ESTABLISH A MASTER SERVICES AGREEMENT WITH EACH INDEPENDENT IRB

One conclusion of the UNC Chapel Hill pilot project was that a master services agreement with an independent IRB serves an institution better than a one-off, study-specific agreement. Part of the lesson from the pilot was performance; negotiations over service agreements can be lengthy, and to complete one for only one study could erase any time savings that the external review would otherwise produce.

Another reason for a master services agreement is to establish expectations on both sides. A comprehensive services agreement acknowledges both the importance and the potential complexity of jurisdiction transfers between IRBs. The agreement should define clearly who is responsible for what, and it becomes the institution's opportunity to codify the institutional requirements it expects the independent IRB to honor. Research institutions commonly have concerns about procedures for conflict of interest, compensation and injury, HIPAA, and specific information or language to include in consent forms.

Here are some key issues that services agreements typically address:

- 1. Liabilities:** Questions of liability are a common concern when institutions consider deferring ethical and regulatory oversight to an external IRB. The language of a master services agreement should define terms to the satisfaction of all parties.
- 2. Reporting Responsibilities:** Inadequate procedures for safety reporting are one of the most common findings from federal auditors against IRBs. Federal regulations establish clear expectations regarding which offices should receive copies of safety reports and reports of non-compliance. The services agreement should remain consistent with those reporting duties, and state clearly to which offices the independent IRB should send its correspondence.
- 3. Institutional Requirements:** An agreement can state specific institutional requirements that the independent IRB should consider during submissions or reviews. A common example is a conflict of interest policy that differs from the policy of the independent IRB. (BRI, for example, expects independent IRBs to hold BRI investigators to thresholds for reporting financial conflicts of interest that are more stringent than federal regulation.)
- 4. Unique Consent Form Language:** Research institutions have language that they prefer in consent forms. This can complicate a central IRB review when the IRB of record and sponsor already have agreed on standard language. A services agreement with an independent IRB can confirm what language the independent IRB will add or revise for the institution. (Continuing the conflict of interest example, an institution may have specific language to use in those cases.) We have found that delays are avoided if the independent IRB and the institution negotiate the language as part of the services agreement.
- 5. Authority to Submit:** The research institution should expect that an independent IRB will not process a submission if it does not have the correct authorizations from the institution. Stating who from the institution can submit to the independent IRB confirms channels of communication. The policies can differ—at BRI, the IRB office submits for the investigator, while at the University of Rochester, the investigator can submit but must demonstrate that the OHSP has agreed to it—even if the goals are the same.

A number of resources are available to help an institution understand what to include in a master services agreement. The Office of Human Research Protections (OHRP) has samples of jurisdiction transfer agreements, and CTTI includes a thorough list of topics in the "Considerations Document" in the Central IRB Toolkit as well as a sample authorization agreement.

<http://bit.ly/considerationsdocument>





“Research institutions should expect that their representatives can access records detailing what studies are underway with any particular independent IRB.”

ENSURE THE HUMAN SUBJECT PROTECTION OFFICE CAN MONITOR RESEARCH

IRB offices within institutions do not like surprises. This is why a standard expectation for institutions is that representatives of the institution remain aware of all of the current, ongoing research that is happening, regardless of the IRB involved.

To this end, institutions and independent IRBs can establish standard processes for submission, as was discussed above; but active research is another matter. Research institutions should expect that their representatives can access records detailing what studies are underway with any particular independent IRB. Typically, these records are available electronically, so an institutional representative can view online what research the institution has with an independent IRB. Kelley O’Donoghue said that her University of Rochester office wants to “see everything.” The realization that more than one independent IRB has this capacity reassured her when it was time to expand.

A Final Note: A Shift in IRB Review Represents a Shift in Thinking

A research institution can look forward to the successful conduct of industry studies with a robust system of reliance on multiple independent IRBs. A satisfactory vetting process, which includes clear requirements and a master services agreement with explicit delineation of responsibilities, can overcome many of the barriers to fully utilizing the advantages of central IRB review in multisite studies.

Accepting external IRB review, however, inevitably requires some adjustment. Professor Dan Nelson at UNC Chapel Hill observed that changing to central IRB review for multisite studies means a change in perspective. Rather than submitting a new protocol and a study plan to a local board, he said, institution staff now provides site-specific information to a central board that already understands the protocol. Nelson characterized this as changing from a “protocol submission process” to a “site registration process.”

Chris Weir of BRI described a similar shift in thinking. Local IRBs are already familiar with their facilities and investigators, so their review of an industry-sponsored study emphasizes what is new: the protocol. For a central IRB review, however, the IRB of record has already reviewed the protocol. Similarly, the IRB of record has already made any necessary determinations and set out any specific requirements for the investigators, which the institution/investigator must, in turn, demonstrate.

In a sense, the two review committees approach research questions for a multisite study from opposite ends: one wants to see how the study procedures will fit within its facility and with its investigator; the other aims to determine how an additional facility and investigator will fit within the existing protocol. With adequate preparation and a clear definition of responsibilities, a research institution can have the confidence that the latter approach—the central IRB’s view—will continue to protect the people who enroll in studies and move research forward.

References

- [1.] CenterWatch & AAHRPP
- [2.] Growing Role for AMC clinical trial offices,” CenterWatch Monthly, October 6, 2016; page 14
- [3.] Ibid, page 15
- [4.] For more information about the UNC Pilot Program and its results, please see the CTTI Presentation

The Quorum Commitment to Institutions

In 1991, the founders of Quorum saw a need for an IRB that protected human subjects while providing high-touch customer service. That's exactly what Quorum delivers. Each member of our team brings a wealth of experience in clinical research human subject protection—plus exceptional service, streamlined study start-up time, and efficient study processes that put you in control. **The Quorum difference is dependable dedication to your research.**

ONE TOUCH COLLABORATION

One-Touch Collaboration™ is why Quorum is the most preferred central IRB among institutions—it is our goal to build a collaborative community, proactively facilitate your study experience, and deliver unmatched support. You'll gain:

- One dedicated institutions team working with sponsors on your behalf
- One study contact who knows your policies
- One stream of clear, coordinated communications
- One form and IRB submission process for researchers—we accept your institution's forms

About Quorum

Quorum Review IRB is the first name in streamlined, service-centered independent ethics and regulatory review. Our service offerings include full study review in the U.S. and Canada, international ethics review, a specialized Phase I early engagement team, and unique processes to accelerate minimal risk research. Quorum works closely with institutions and researchers on studies from all over the world. Kinetiq, a new consulting and technology division of Quorum, provides services that enhance and optimize the clinical research process.

Quorum has been fully accredited by the Association for the Accreditation of Human Research Protection Programs (AAHRPP) since 2006. AAHRPP's "Full Accreditation" emblem signifies that Quorum Review consistently demonstrates excellence in comprehensive protections for research subjects while facilitating the highest quality research processes.

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