Benefits of Working with a Central IRB

Improved Efficiencies and Enhanced Human Subject Protections

As timelines and budgets continue to shrink, while the pressure to generate meaningful clinical data continues to grow, the clinical research enterprise increasingly turns to experienced central institutional review boards (IRBs) with expert reviewers to perform knowledgeable IRB reviews in a timely manner. This article examines how using a central IRB creates significant efficiencies throughout the IRB review process and improves the safety of human subjects participating in research.

Consistent Reviews and Streamlined Processes

The current regulations governing clinical research were established when most research studies took place at a single institution overseen by that institution’s IRB. Today, industry-funded and federally funded studies alike are often conducted at many sites, making the use of multiple local IRBs an increasingly cumbersome and inefficient practice. It has even been suggested that the use of multiple IRBs is among the factors that push the cost of research and healthcare higher.

Within the U.S. Department of Health and Human Services, the Office for Human Research Protections (OHRP) is considering a change to the Common Rule that strongly encourages the increased use of central IRBs in research. Meanwhile, the Food and Drug Administration has already indicated its support of central IRBs via a 2006 guidance document.

These developments suggest the central IRB model has gained quite a bit of traction throughout the industry and regulatory world. Indeed, central IRB review would already seem to be recognized widely for helping to simplify the IRB review process while maintaining high-quality ethical review throughout the life of a study.

Having multiple local IRBs reviewing a multisite protocol can lead to duplicative review activities and disproportionate resource use. All sites must use the same protocol for a given study, so that procedures and the resulting data are consistent and appropriate. With multiple IRBs reviewing a given protocol, however, it’s possible that each IRB will request changes to the protocol, resulting in significant delays as the sponsor works to revise the protocol in a way that satisfies all of these requests.

On the other hand, because review is distributed among several entities, it’s also possible that multiple reviews may result in a dissolution of responsibility, potentially leading to fewer recommendations for applicable protocol changes.

In addition to protocol-level changes, each IRB will likely require changes to the informed consent, as it pertains to local considerations and institutional...
policies. These individual informed consent documents could vary significantly in how they present study information to the subjects, and could potentially create real differences in the way subjects are enrolled at each site.4

Additionally, study sponsors must manage all informed consent documents as they are revised throughout the study, creating additional administrative burden and increasing the potential for errors.

Using a single central IRB for a multisite study dramatically simplifies the review process; for every event reportable to the IRB, materials are submitted to, and reviewed by, a single entity. The protocol is reviewed once on behalf of all sites, and the sponsor responds to one board’s feedback. In such a scenario, study timelines can be planned more accurately, as only one IRB’s meeting calendar is considered.

When a central IRB reviews on behalf of all sites, one informed consent is developed between the IRB and sponsor and approved for use by all sites, ensuring that subjects are receiving consistent information throughout the study. This consent can be modified on a site-by-site basis to manage the inclusion of site-specific informed consent text, ensuring that local considerations are addressed.

Often, the revisions recommended by local IRBs reflect nonsubstantive changes related to institutional policies, rather than human subject protections (for example, subject injury language).5 A central IRB will help to ensure individual sites’ requirements are appropriately addressed, while mitigating potential administrative complications for sites and sponsors. Also, working with a central IRB ensures consistency across all sites and removes the complication of multiple IRBs’ requirements, so that sponsors and sites focus more on overall study management and safety.

Although IRB review is only a small consideration in an overall study budget, multiple local reviews increase the overall cost of conducting a trial.5 As illustrated in Figure 1, significant cost savings can be realized by using a central IRB, especially in multicenter studies.

Additionally, it seems that, especially for smaller research institutions, it is difficult to completely and accurately quantify the costs associated with managing a local IRB office. This can lead to the actual institutional cost of conducting an IRB review being significantly higher than the associated cost that is passed on to sponsor organizations, representing a real financial disadvantage for the institution.2

If IRB review is outsourced to a central IRB, the costs become à la carte, which are incurred only as applicable, making it much easier for all involved to understand the cost of IRB review for a given study.

**Dedicated IRB Members and Staff**

Professional organizations like the American College of Surgeons have charged their member institutions with increasing clinical trial accrual rates, in order to provide better research data, which in turn can result in great improvements to patient care.

Teaching institutions require attend-ees to conduct research, and many oncology departments also have research requirements. Additionally, institutional leadership may push for more research in order to increase revenues, as well as bolster the institution’s reputation.

These initiatives put significant pressure on already shorthanded local IRB offices, and often little can be done in the way of additional institutional support to help the local IRB manage this increased influx of research.3 In addition, researchers might not be properly aware of their ethical responsibilities in conducting research, which can lead to serious problems for institutions that do not have adequate research support.

Furthermore, although some local IRBs may have knowledgeable IRB staff available to assist in these situations, the members of these boards often have other responsibilities at the institution that keep them from providing assistance in a timely manner. In these instances, working with a central IRB can make local workloads much more

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**Figure 1 Average Cost of IRB Initial Review: 10-Site, Industry-Sponsored Study**

- Local IRBs: average $2,000 per initial review; each includes protocol and site review
- Central IRBs: average $1,000 for initial protocol review and $700 for each site review

Source: Internet survey of average costs for 12 research institutions and six of the largest independent central IRBs (Western IRB, Schulman Associates IRB, Quorum Review, Copernicus Group IRB, Chesapeake Research Review, and Sterling IRB)
manageable, and can provide local staff with the assistance they need to ensure that research activities across the institution are being conducted as the regulations and institutional policies require.

Local IRBs are often composed of volunteers for whom the IRB is one of many responsibilities, so meeting schedules vary dramatically depending on member availability for quorum. This leads to local IRBs convening, on average, once or twice a month, at most. Figure 2 presents a comparison of the average amount of time from submission to board review for local IRBs and central IRBs.

Additionally, if an IRB quorum is not met at a given meeting, review cannot take place, and reviews must be postponed until the quorum can be met. Hence, a local IRB’s infrequent meeting schedule can significantly delay an investigator’s study startup. This becomes an issue when sponsors encourage competitive enrollment among sites—a not uncommon practice. By the time the local IRB provides approval documentation, competitive enrollment may be completed, and investigators relying on local IRBs may already be locked out from ever participating in the study.

Being able to work with a central IRB can make a research site more appealing to sponsors, and thus more likely to be selected to participate in industry-funded studies. Some sponsors will even inform their potential sites that, if IRB approval is not granted by a certain date, the investigator will not be invited to the investigator meeting.

For one matter, having a central IRB review on behalf of all sites for a given study reduces duplicative work for the sponsor or contract research organization (CRO) and allows the sponsor to conduct a much more efficient study overall.

Another consideration is that, since so much time and resources are spent during study startup, rapid enrollment is vital to a study’s success. Recruitment delays can create significant costs for a sponsor; the efficient review processes a central IRB offers can mitigate these delays considerably.

In addition to the benefits central IRBs offer sponsors and CROs, sites benefit from a central IRB’s experience in regularly working with many different sponsors and CROs. Central IRBs have unique perspectives into how these various organizations operate, and can assist sites in navigating these entities’ processes and requirements.

Particularly at smaller research institutions, local IRB offices can face resource limitations that make it more challenging for them to adequately support IRB operations and monitor research activities at the institution. Working with a central IRB can help to mitigate these challenges, as the central IRB can provide resources that reduce local workload and improve the quality of IRB review.

Dedicated board members at the central IRB are available to review studies much more frequently—once or twice a week, at a minimum. This allows central IRBs to deliver timely review services while also spending more time in thoroughly reviewing each study.

Because of their limited meeting schedule, local IRBs can find an agenda packed with a dozen or more studies, sometimes leaving the board with as little as 15 minutes to discuss each study. With more frequent meetings, central IRBs can have fewer studies on each agenda and more time to discuss each study appropriately and thoroughly.

Additionally, in comparison to some local IRBs, a central IRB may be better informed of contemporary issues in human subject protections, and thus perform reviews with the most up-to-date information and guidance in mind. Smaller institutions can be particularly constrained by limited availability of expertise at the institution, making it more challenging to conduct a thorough, knowledgeable review.

In fact, central IRBs often have access to a broader range of therapeutic expertise than smaller institutions and, by partnering with a central IRB, the institution gains access to additional expert insight on issues, further strengthening overall subject protections. In turn, a research site may provide the central IRB with additional information about the community surrounding the site, local subject populations, and the investigators themselves. This sharing of information and perspectives can lead to valuable exchanges with an end result of further improving subject protections.

**Concerns About Central IRBs**

Some research organizations may balk at the notion of shifting from local to external IRB oversight because of potential liability issues.

Conducting clinical research certainly brings with it liability, and a research site should always carefully consider the research it conducts and the investigators who will conduct it. However, outsourcing the IRB review actually reduces liability for the site, as any issues resulting from the external IRB’s negligence are reflected solely on that IRB, not on the institution relying upon it.

By establishing an agreement between the research site and the central IRB that clearly outlines oversight responsibilities, liability concerns can effectively be managed and mollified. Additionally, should OHRP enact the changes...
proposed in its recent Advanced Notice of Proposed Rule Making, this will provide local offices with extra assurances regarding how liability is assigned.\(^2\)

Another concern particular to for-profit central IRBs has to do with the independence of the board’s review. Local IRB members volunteer their participation and thus, it can be argued, are less likely to be swayed by how a given study will affect the organization’s finances. Thanks to external accrediting organizations like the Association for the Accreditation of Human Research Protection Programs (AAHRPP), however, this perceived conflict of interest is just that.

An AAHRPP-accredited central IRB must adhere to very high standards, which are reflected in the board’s policies and the way the board does and does not interact with business operations. Appropriate management of potential board conflict of interest is a key responsibility for any AAHRPP-accredited IRB.\(^7\)

Additionally, a central IRB may very well be more objective in its review than a local IRB, as it is removed from any bureaucracy and institutional politics that might be experienced by a local IRB.\(^5\)

Although central IRBs are not physically present at each site, working every day with local patient populations and getting to know the personal particulars of each investigator, these boards do, however, have the advantage of being able to review all safety information for the entire study.

When a local IRB reviews unanticipated problems that take place at that site, it only has that local information with which to work. In contrast, central IRBs review each unanticipated problem in the context of the entire study, and are more likely to realize and address study trends that could affect subject safety; and, with dedicated board members and staff, central IRBs can implement changes very quickly across a study, thereby preventing further potential harm to subjects.

It is important to note that choosing to work with a central IRB is not an “all or nothing” proposition. There are a variety of ways in which a site or research institution can work with a central IRB (see Table 1).

Central IRBs provide numerous efficiencies and added subject protection capabilities, but each site should determine how it will interact with a central IRB and whether it should keep a local IRB operational. Each site still retains responsibilities related to the ethical conduct of research, but by outsourcing some or all IRB review to a central IRB, an institution free up resources to focus on other pressing issues related to human subject protection.\(^8\)

Site staff will continue to play important roles in supporting the central IRB and local investigators, and in monitoring study activities at their site. Experts who may have served on the local board will continue to be valuable resources for the organization, and may even collaborate with the central IRB to ensure appropriate expertise during reviews. Thus, in working with a central IRB, staff at research sites often find that they are able to focus more on local concerns and significantly strengthen their research programs overall.\(^2\)

### Table 1 Options for Working with Central IRB

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<thead>
<tr>
<th>Central IRB Reviews All Research</th>
<th>No local IRB review; local research staff manage local responsibilities</th>
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<tr>
<td>Central IRB Reviews Certain Research</td>
<td>Local IRB reviews certain research, sends other research to central IRB as appropriate</td>
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<tr>
<td>Facilitated Review</td>
<td>Central IRB reviews protocol, local IRBs review local context matters</td>
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<tr>
<td>Consortium-Based Central IRB</td>
<td>IRB is composed of representatives from each consortium member organization</td>
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#### Conclusion

With dedicated staff and board members and streamlined operational processes, central IRBs are equipped to provide consistent, high-quality, and efficient IRB review. By working with a central IRB, sponsors and research sites significantly enhance human subject protections and improve the overall quality of clinical research.

#### References


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