IRB Appeals
By Norman M. Goldfarb

U.S. federal regulations give institutional review boards (IRBs) human subject protection oversight responsibility for a broad range of studies:

IRB review of research. (a) An IRB shall review and have authority to approve, require modifications in (to secure approval), or disapprove all research activities covered by this policy. (21 CFR 56.109, 5 CFR 46.109)

Review by institution. Research covered by these regulations [this policy] that has been approved by an IRB may be subject to further appropriate review and approval or disapproval by officials of the institution. However, those officials may not approve the research if it has not been approved by an IRB. (21 CFR 56.112, 5 CFR 46.112)

In most cases, the process works fairly smoothly. However, if an IRB does not approve a study or accepts it with conditions, the investigator (or study sponsor) might disagree with the decision.

It cannot be taken for granted that 100% of IRB decisions are correct. IRBs may require changes that are not justified by the regulatory criteria for approval, misunderstand the regulatory criteria for approval, make decisions without sufficient expertise, or review research that does not require IRB review. As a result, the conditions an IRB sets might have no effect — or a negative effect — on human subject protection, or unintended implications or consequences for future reviews. Even when the regulatory process is followed, reasonable people can disagree. Even if a decision is correct, the IRB might not clearly communicate its reasoning to the investigator.

When an IRB rejects a study or approves it with conditions, the investigator has four basic options:

- Accept the IRB’s decision.
- Modify and resubmit the application.
- Ask the IRB to reconsider the current application.
- Ask institutional officials to intervene.

The result might be that the investigator cannot conduct the study. Or, the investigator might be forced to conduct a study that he or she considers flawed. As side effects, the study might be significantly delayed, large amounts of time consumed in unpleasant interactions, and interpersonal relationships damaged or destroyed. In most cases, it is impractical for institutional officials to intervene without diminishing the IRB’s independence.

In theory, study sponsors and some investigators can apply to another IRB and hope for a different result. However, informing the new IRB of the previous rejection makes it difficult for that IRB to approve the study; if something goes wrong in the study, it will look very bad. Not informing the new IRB of previous IRB disapprovals is called “IRB shopping” and considered unethical. (Note, however, that when a sponsor asks 80 sites to each obtain local IRB approval for a study, it is, in essence, IRB shopping. This practice is considered ethical.)
If the investigator cannot persuade the IRB to approve a study as he or she wishes to conduct it, there is usually no recourse; that is, there is no higher official or body to which he or she can appeal.

**IRB Appeals**

Perhaps it is time for the clinical research enterprise to consider creating an appeals process to improve human subject protection, minimize delays, and reduce wrangling over IRB decisions. Just as appeals courts play an important role in the judicial system, appeals IRBs can play an important role in the human subject protection system.

Way back in 1981, when FDA published its final rule, “Protection of Human Subjects; Standards for Institutional Review Boards for Clinical Investigations,” it included supplementary information, including comment 94, which states: “The National Commission did not recommend that there be a mechanism for appeal from IRB determinations. However, there is nothing in §56.112 that would prevent an institution from formulating an appeals mechanism, so long as the final ruling body is an IRB that satisfies the requirements of Part 56. Appeal of an adverse IRB determination to other institutional bodies that do not meet the requirements of Part 56 is not allowed under the regulation.”

In 2006, FDA informally clarified its position: “The bottom line is whether the body to which decisions are appealed meets the requirements of the IRB regulations and whether the appeals mechanism is recognized by the institution. Therefore, it is possible to have such an ‘appeals IRB,’ but it would need to be a legally constituted IRB under the regulations and be sanctioned and recognized by the institution as well.” (http://firstclinical.com/fda-gcp)

In other words, institutions have the authority to establish an IRB appeals process that employs any legally constituted IRB that is acceptable to the institution. Further, FDA does not require the institution to have its own IRB, only that the appeals IRB be legally constituted and meet the institution’s standards. Independent IRBs could even establish their own appeals process and, if appropriate, a separate appeals IRB (an “Institutional Board of Appeals” (IBA)) established solely to hear appeals.

As in the court system, an appeal should state the grounds for the appeal, e.g., the first IRB did not comply with regulations, it did not have the necessary expertise to review the protocol, or it did not provide a sufficient reason for denial. The appeal might require approval by institutional officials and/or permission by the first IRB.

The IBA might require or advise the first IRB to revise its review process in certain ways. In this approach, the IBA might consider whether the first IRB appropriately applied the regulatory criteria, adequately justified its objections based on the regulatory criteria for approval, and accessed the necessary expertise to obtain and understand the facts. The IBA could then instruct the first IRB to reinterpret a particular regulatory criterion, reconsider specific objections in light of the regulatory criteria, validate certain assumptions, or obtain suitable expertise in a second review.

Or, the IBA might review the study for itself and render its own decision. In this case, it might instruct the first IRB to accept its decision and supervise the study accordingly, or it might supersede the first IRB and become the IRB of record.

Alternatively, the investigator could ask the first IRB to transfer its authority on the study to a second IRB. Because the transfer of authority must be approved by the first IRB, this approach does not constitute IRB shopping.

Or, the investigator could ask the first IRB to obtain a non-binding second opinion from a second IRB, which the first IRB would consider in reviewing its decision.
The Virginia Commonwealth University (VCU) has adopted a different approach. At VCU, the appeals board is called the “IRB Panel.” Its members include the chairs of VCU’s four IRBs, including that of the IRB whose decision is being appealed. The IRB Panel does not reverse an IRB’s decision. Instead, it has the authority to refer the study to one of the other VCU IRBs for a new review. For a study to qualify for a referral, the investigator has to demonstrate how another panel might have been better suited for the review because of more expertise or less bias (like an NIH study section appeal).

Another advantage of an appeals process would be better communication and interaction among IRBs, especially if IABs were to publish their decisions (within the bounds of confidentiality). IRBs often operate in a vacuum, so the opportunity to have greater communication about specific cases might improve IRB understanding of regulatory criteria, increase the consistency of decision-making among IRBs, and advance wide adoption of best practices. The possibility of an appeal might intimidate some IRBs into approving marginal studies, but government agencies and the plaintiff’s bar already provide intimidation in the reverse direction.

Should the public, e.g., potential study subjects, have a voice in appeal proceedings? Probably not, since federal regulations already address this issue by requiring IRBs to include a member from the community. However, if a study is especially controversial or uncertain, any IRB is free to invite community representatives to share their perspectives. Should members of the public be able to appeal an IRB decision that approved a study? Perhaps, but questions of standing, timing and other issues would need to be addressed.

Regardless of the approach, a proper IRB appeals process requires the following elements:

- Clear policies and procedures that are acceptable to all parties
- Participation by the investigator and first IRB
- Timely reviews
- Clear explanations of decisions

**Conclusion**

Court systems have appeal processes because they yield better results by ensuring that the judicial process is followed, preventing arbitrary decisions that cannot be justified by the law, and promoting consistency among lower court decisions. Perhaps it is time to implement appeal processes for our IRB system on an experimental basis to find the best approach.

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