IRB ADVISOR

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IRBs and IBCs: Critical Partners in Gene Research

Common Rule changes could create disconnect

In addition to IRB oversight, the National Institutes of Health (NIH) requires that research using "recombinant or synthetic nucleic acid molecules" for gene transfer into human research subjects be approved by institutional biosafety committees (IBCs).

A primary concern is the transfer of genetic material via a virus, for example, that can then replicate in a living cell. Thus, the need for biosafety to protect workers and the public as researchers seek ways to use gene therapy to fight disease.

"Over time, many institutions have chosen to assign their IBCs the responsibility of reviewing a variety of experimentation that involves biological materials (e.g., infectious agents) and other potentially hazardous agents (e.g., carcinogens)," the NIH states. "This additional responsibility is assigned entirely at the discretion of the institution."[1]

An institution must follow the NIH guidelines if it receives any funding from the NIH for research. Institutions at the local level must ensure that the IBC has adequate expertise and training. In addition, the IBC must file an annual report with the NIH clearly indicating the chair and the human gene transfer expert.

While clear communication and synergy between IRBs and IBCs is needed for timely and safe review of research, the two panels look at gene research through separate lenses.

While the primary role of the IRB is to protect research subjects from safety and ethical compromise, the primary role of the IBC in clinical trials is to protect study staff and the general public from risk associated with gene transfer agents, explains **Currien MacDonald**, MD, CIP, IRB chair at WIRB-Copernicus Group. *IRB Advisor* asked MacDonald about the overlapping missions of these two important review groups.

IRB Advisor: Can you comment on what some of these risks are and, specifically, how an IBC can mitigate them?

MacDonald: The majority of concerns that an IBC is looking at are the potential unintentional spread of the gene transfer agent. For example, viruses infect cells, which is not a good thing in most cases. But scientists can transfer genes into that virus to only infect cancer cells. So it is infecting a cell, and making more virus that contains a gene to turn a disease into a cure. That also makes that agent that they are working with infectious, so it could spread. And just like in every other medical intervention, there could be risk from that spread, and risks from even the intended and intentional outcome of the gene transfer agent.

We never want to expose people to risks. To prevent them, the IBC is looking very closely at gene transfer agents, their ability to infect, and what measures there are to limit the chances of that happening. They are very attentive to all of the details, including to the level of going to the site and inspecting the equipment that protects the clinic staff from exposures, such as the cabinet where the agent is readied. The IBC looks at all of those details, both for the clinical staff and the general public. They look at the

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procedures and make sure that the waste from the agent is disposed of properly and does not go somewhere else.

IRB Advisor: With the expanding array of procedures, are the odds of these kinds of risk increasing?

MacDonald: No, current agents and several that are approved are not really infectious in any way. So, the gene transfer review is really focused on what the intended outcome is from the agent itself, and it's much less a concern of the agent spreading. The field is still growing, and it is now getting into some of the [research] going into cells and producing those kinds of effects. But the fear about the spread of the agents has largely been without any evidence of it happening.

IRB Advisor: Are there instances where IBCs and IRBs can be at cross-purposes due to their different respective goals of protecting staff and public vs. research subjects?

MacDonald: It's really not common at all for that to happen. The missions are parallel, so cross-purposes are exceedingly rare. The one that [is possible] is the IBC wanting to stop use of the agent while it improves their environmental protections for staff, while the IRB may be concerned that a subject receives a treatment that is controlling a disease. I've never seen that happen, but the resolution to that is the same as the resolution for common issues; for example, a disagreement about the way something is worded in a consent form. All that needs to happen is a discussion to make sure their two perspectives align. In most cases, they can very quickly come to a mutually agreeable solution.

IRB Advisor: The revised Common Rule emphasizes single IRB rule of multisite studies, but you note that is not currently allowed for IBCs. Do you see a possible growing disconnect between IRBs and IBCs if the rule is finalized as-is?

MacDonald: That is a very real concern. There is some contention that to the extent that the local IRB and the local IBC currently communicate well, that is mitigated by the fact that local IRBs never communicate with one another. As we just discussed, the reasons for local IBC review — for example, being able to know the site well enough, knowing what masks they wear, who removes the medical waste, quality sorts of things — kind of make sense, while the concern for multisite IRBs does not really make sense. The protocol or consent form being different between sites leads to so much duplication of effort and delay, it really is a burden and a waste. So, any local IBC that worked with a local IRB could be at a disadvantage if they then lose that relationship they had when a central IRB review is mandated.

But not necessarily. If they already have in place procedures and infrastructure to have timely and clear communications, then there is no reason they couldn't adapt that to work with an IRB that is open to that kind of communication. Of course, each of those would have to have the components to ensure that the communication was done well.

For example, if the local IRB just defers to the local IBC all the time, then a central IRB is going to be much less likely to be open to that kind of mandated communication. The local IBC would then have to come up with a new communication style or strategy to ensure their communication is being received well.

IRB Advisor: Expediency and speed are understandably overshadowed by safety in these discussions, but why is it important to have better logistics between these two types of committees?

MacDonald: Expediency of review is important. A lot of people say cutting through red tape might sacrifice safety, but I see them as hand in glove. For example, if there is a concern from one of the two committees that is not well communicated, then you can have a delay in a study that could have some benefit to subjects.

For example, if one committee says, "Stop the study — something terrible has happened," then the other committee can say, "If we do this, we can maintain the benefits to the subjects." There may not be anything available like that [intervention] in the community and this research is very valuable [to continue] while mitigating the risk. It's kind of like the baby with the bathwater. Communication and timely review of the process can [ensure] the safety of the subjects and the overall research benefit to the community. ■

REFERENCE

1. HHS. NIH Guidelines for Research Involving Recombinant or Synthetic Nucleic Acid Molecules. April 2016. Available at: https://bit.ly/2yOg0ud.

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