Fly on the Wall: My Visit to the Downstate IRB

By Deborah Hornstra

Have you ever wondered what goes on during a meeting of an Institutional Review Board? Are you even sure you know what an Institutional Review Board does? Though it is essentially concerned with ethics, the IRB has a more specific charge than a hospital's ethics committee. The IRB exists for one purpose only: to monitor and safeguard the rights and welfare of human subjects participating in clinical research. To this end the IRB regularly reviews research protocols to ensure compliance with all laws, regulations and institutional policies.

I was privileged to be permitted to attend a meeting of the IRB at the State University of New York/Downstate Medical Center in Brooklyn this spring. Downstate actually has two IRBs, known as Board A and Board B. They each meet monthly and divvy up the cases between them. I was there as the guest of Alice Herb, a lawyer by training who now teaches ethics to both aspiring health advocates at Sarah Lawrence and aspiring physicians at Downstate. Alice represents the Humanities in Medicine division of the hospital on the IRB. Mine was a rare opportunity to be the proverbial fly on the wall and see how an IRB functions behind normally closed doors.

The mix of people in the conference room was striking in its diversity and its uniformity. Federal regulations require that IRB members have a variety of backgrounds, education and experience. Like many hospitals, Downstate tries to include an expert in each medical discipline on each of its IRBs. So there's a pathologist, an endocrinologist, an emergency room doctor, a pediatrician, a psychiatrist, a neurologist, a surgeon, an ob/gyn, and a couple of internists. There is also one community member, who is typically a non-scientist with no current affiliation with the institution.

HAP graduate Donna Gentry serves as the IRB's Associate Administrator. As part of the three-person IRB staff, Donna manages the review of proposed research projects and ensures that all relevant information has been submitted to the IRB and forwarded to the appropriate reviewer (not every member reviews every case). The IRB administrators also serve as the liaisons between clinical researchers and the board, and help to train principal investigators in the rules and regulations applicable to research with human subjects.

"For example," says Donna, "a physician comes into the office wanting to do a study. First we have to make sure he's done the educational component required of the institution in order to do research on human subjects. We have an online course for investigators and all other individuals involved in research, and we have a database to track those who complete it and those who don't.

"If they've done their education," Donna continues, "we have to look through their paperwork and make sure it contains all the necessary documents and proper signatures. We then do a first review to decide if the request has to go to the full board or if it can go through an "expedited" procedure, which allows the chair to approve the study without board discussion. This decision is based on federal regulations that outline exactly what has to be reviewed by the full board and what doesn't."

Back in the stark, completely unadorned conference room, chairs are arranged in a square so everybody can see everybody else. There is a cheerful camaraderie as the meeting begins. Though it is still only mid-morning, almost everybody helps themselves to the thick New York-style sandwiches, potato chips and sodas available up front. (I am always amazed at the type of food available in health care institutions!)

Donna hands out the meeting agenda and related paperwork. Again I notice that the board is diverse in the sense that nearly all medical disciplines are represented. There are seven women and ten men. But still, 11 of the board's 17 members are medical doctors. Among the remaining six members, there are two lawyers (including the community representative), one nursing administrator, one pharmacist, and one person who holds a master's in public administration. Only two board members do not hold an advanced degree. Most members are in their fifties or older. The board is overwhelmingly white.

A few minutes are given over to small talk while members wait for a quorum, then the Board quickly reapproves a series of ongoing studies (all studies must be reapproved annually or more frequently). The only controversy among the ongoing studies concerned a study of melatonin in which the potential side effects were not clearly delineated in the consent form. The IRB members expressed collective disbelief that the study could have been ongoing for five years without this.

It is actually the IRB administrators who help investigators write their consent forms. "The consent forms have to be written at a sixth grade level," explains Donna, "and very often they need a lot of work before they're comprehensible by a lay person." By federal law, consent forms must give potential study participants enough information to make an "informed decision."

"We usually read the entire protocol, so we have to be comfortable with scientific language," says Donna. "We then try to help investigators condense the information into readable, understandable language. We try to use simple language, short sentences and the active voice. But no matter how much we try, it will often take months before a consent form is approved. Either the investigator doesn't make the changes promptly, or very often, the changes have to go back through the study sponsor who can object to all or part of what the IRB wants, typically for legal reasons. Usually we can work out a compromise, but it can take time."

Most of the new studies are quickly approved, but there are two controversial items on the day's agenda that provide a chance to see how the board operates in deliberative, collaborative fashion. The first concerns a new laser-type device for monitoring blood pressure in patients who have suffered traumatic brain injury. The study's principal investigator, a young physician who has apparently been waiting in the hallway, is about to answer some questions from the board about his study. The questions come from all over the room in an orderly fashion. First off, Will you be collecting clinical data? Yes, answers the P.I.

A board member asked the P.I. to explain exactly how the device is used, which he did. The researcher gave a few

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examples of how the new device was an advance over the existing technology for monitoring blood pressure.

But isn't the device also more intrusive? he was asked. The device is exactly the same as the old device except for a 5 mm fiber extension, and the way the old device is inserted, you get practically the same result with this one. The researcher reminded the board that this device is typically used during an emergency, life-saving procedure. It may sound like we're violating informed consent but these are very acute situations. Alice pointed out that there are emergency exemptions from informed consent requirements and that these situations either do or they do not fall under those emergency exemptions.

Clearly the board had issues with this study: the collection of clinical data (for what purpose?), the invasive nature of the procedure performed with the device, and the inability of most potential study participants (or even their family members, in many cases) to give informed consent to the use of the experimental device due to the emergency nature of its indications for use. The doctor was thanked and asked to leave the room. After some discussion, the Board agreed the study was not necessary as the indications for use of the experimental device fell under the emergency exemptions.

The other controversial study on the agenda involved a new medication for children with hypertension. Of course research with children as subjects always presents additional ethical (and legal) considerations. Most researchers do not want to do research on children for these reasons and there is a serious shortage of medical research on children.

As an IRB member pointed out, almost all medications are therefore not officially approved for children, and almost all medications (including psychiatric medications) prescribed to children are prescribed "off-label." It's "standard practice," this doctor said, and no one there disagreed with him.

The federal government recently enacted a law meant to motivate pharmaceutical companies to sponsor research on children. Companies are now allowed a potentially lucrative six-month patent extension if they will perform the research. This study involved a researcher who wanted to take a group of hypertensive kids off the medication they were currently on (which was controlling their condition) and put them on either a new medication he was testing or a placebo.

The P.I. was brought out of the "soundproof booth" (the hallway), greeted politely and immediately asked, Why take people off their meds if they're doing well on those meds? He replied it was standard practice to take people off these meds periodically anyway to see if they still needed them. An IRB member said that does not address our concerns about taking people off their meds, it just tells us that other people are doing it as well.

This study had been turned down once before. A board member noted that it is rare they turn something down, so it's an indication they are "unusually concerned." The P.I. said the participants' parents would monitor their blood pressure once a week using kits provided by the drug manufacturer. If it spiked above a certain level, the child would be brought in for immediate treatment. The P.I. reiterated that the study involved patients with only mild hypertension and no endocrine damage. He added that many doctors would not even medicate patients with this level of hypertension; instead they would treat it by prescribing exercise and change of diet.

Asked the purpose of the study, the P.I. said We're trying to figure out what the starting dose is for a child. We don't know so we're starting with a very small dose, a baby dose. And yes, the drug's manufacturer was sponsoring the study because they want the six-month patent extension. The P.I. said nobody will pay for a study of the proper dose of the medication currently being prescribed because it is already off patent and available in generic form.

The board wanted to know whether the FDA required a placebo in this type of research. Clearly their concern was with the stopping of the medication for up to 24 days in the case of participants receiving the placebo. The researcher explained that doing it without a placebo would require a much larger sample which would increase the general risk. Additionally, he noted that there is a lot of "white coat hypertension" in kids, and that hypertension is a totally different disease in kids and we have virtually no data. He also mentioned that the FDA has issued a general directive encouraging research in kids.

Another member raised an issue everyone on the board agreed was problematic: a proposal to pay a $50 payment per needlestick to each participant. This was readily seen by most (but not all) board members as far too attractive to a child and therefore coercive. The board also raised concerns about the monitoring process. What will make the mother do the monitoring, they wanted to know. What will make the child cooperate? How do we know the mother knows how to do this? Many studies call for monitoring at home, responded the P.I. If we doubt this can be done we doubt all such studies.

Again, the board members had had their chance to ask questions and the researcher was thanked and politely shown the door. One member proposed some changes to the study, including monitoring three times a week by staff, not parents, education for the parents, and a modest payment to participants of $10 per needlestick. A vote was taken which ended in a tie, defeating the motion to approve the study. But a second vote to establish a committee comprised of pediatricians and cardiologists, to be chaired by Alice and charged with studying these issues further, passed easily.

The meeting went an hour over its scheduled length and concluded with people either rushing out of the room or falling into small groups to talk. The meeting demonstrated to me the strength of the idea of Institutional Review Boards and the importance of their mission. The members took their responsibilities very seriously and were in no sense pushovers. That said, I do believe more diversity must be encouraged, if not mandated. We need not only a diversity of medical viewpoints, but a diversity of viewpoints in general, including those from outside the medical community.

Perhaps IRBs should be mandated to include at least one patient advocate. Donna says that advocates should argue for more oversight and monitoring of the process, especially with the growing awareness of clinical research among the general public. "By protecting human subjects in a particular research study in a particular place, we are practicing a type of advocacy," Donna suggests. "We try and look at each study and each consent form with the eye of a potential participant, asking, Would I understand what this means? Are these people being coerced in some way to do something unsafe? Is this a feasible thing to ask people to do?" ■