The copy machines in the IRB office get a daily workout. They hum and flash nonstop to keep up with the reams of paperwork that go through the hands of the Institutional Review Board staff and committee members.

“There are massive amounts of record-keeping,” said Dr. Gordon R. Bernard, professor of Medicine and medical director of the IRB. Since assuming his IRB role in the fall of 1999, Bernard has overseen a major overhaul of IRB operations.

The changes were prompted, he said, by clearer federal regulatory guidelines and by a need to improve investigator interactions with the IRB.

At Vanderbilt and other institutions, IRBs are responsible for reviewing proposed human subject research—any systematic investigations using human beings that are designed to create generalizable knowledge. In recent years, Bernard said, the entire arena of human subject research has come under much more intense scrutiny.

“The process of oversight has begun to mature,” he said. “As more precise standards and guidelines have been developed, the federal government has taken a much more aggressive stance in reviewing institutions.”

Reviews of major institutions around the country by the OHRP (Office for Human Research Protections) have clarified federal expectations for IRB practices. Clinical research at about ten institutions was halted for lack of documentation, not failure to protect human subjects, Bernard said. “If you take a business trip and don’t keep the records, it doesn’t matter how legitimately tax-deductible the trip was—you won’t be able to argue with the IRS.”

10 sets of eyes

In addition to poor record keeping, the OHRP found problems in some IRB practices. One was the handling of continuing reviews, formerly called annual reviews.

Continuing reviews are periodic (minimum annual) reviews of already-approved protocols. In the past—at Vanderbilt and elsewhere—these reviews were typically conducted by the chair of the IRB committee. Not anymore. Continuing reviews now come before a full IRB committee for consideration.

“Instead of one set of eyes, we now have ten to 15 sets of eyes looking at continuing reviews, making it more likely that issues will be raised that necessitate re-review,” Bernard said. “This change tremendously increased the workload of the IRB and slowed down the review process.”

It was a process that could not afford to be slowed down.

In short, here’s how the review process works. An investigator submits a protocol to the IRB, and the staff schedules the protocol for an IRB committee meeting. Currently, there are three IRB committees that meet weekly: two Health Sciences committees and one Behavioral Sciences committee. Each committee has 12 voting members, including at least one community member and one member with ethics or pastoral services expertise. Prior to the committee meetings, the IRB staff provides a meeting agenda and all protocols with informed consent documents to each member. IRB staff members

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attend the weekly meetings, take notes, and generate minutes and committee action letters, which inform the investigator of the IRB decision.

A year and a half ago, an IRB staff of six was struggling with this process. Turnaround times from protocol submission to committee action were not favorable.

“There were some horror stories out there,” Bernard said. “Clinical research was being severely hampered.”

the overhaul begins

Bernard’s appointment as medical director of the IRB gave the office a “coach-player kind of situation,” Bernard said. “I’m someone who knows the game and is committed to it being played well.”

Robin Ginn was hired in March 2000 as director of Research Informatics and Regulatory Affairs to oversee and reform IRB operations. New IRB staff members were hired, and the staff now numbers 22, with two still-vacant positions.

“It has taken this kind of increase in staff to make the required changes,” Bernard said.

“We’ve spent a lot of time and effort developing infrastructure,” Ginn said. “It takes six months to a year to fully orient and train new staff members.”

IRB protocol analysts now conduct thorough protocol pre-reviews and follow up with investigators to obtain additional information before the protocol goes to committee members, helping to avoid delays in committee action.

The IRB also has begun to reimburse committee members to combat past failures to meet quorum, which led to committee meeting cancellations, and “had a ripple effect through the system, slowing everything down,” Bernard said. While it may seem odd to pay faculty for serving on a committee-activity that is usually voluntary—the workload of IRB committees is unusual, he said. “IRB committees are in a class by themselves.”

On average, the two Health Sciences committees deal with 15-20 protocols per week, including adverse events, continuing reviews, amendments, and actions.

“We want to work together with investigators to protect human subjects.”

- Robin Ginn, IRB Director

new and improving

Under Ginn’s leadership, the IRB has expanded its educational offerings. IRB101, held monthly, teaches faculty, staff, and students about the IRB’s roles and responsibilities, federal regulations, and paperwork tips. The IRB also hosts a monthly brown bag lunch on a topic of special interest. Committee members will be trained quarterly instead of annually, and they are kept up to date with a “regulation of the week” at each meeting.

The IRB Web site (http://www.mc.vanderbilt.edu/irb/) also has seen vast improvement, Ginn said. It includes news, downloadable forms, educational opportunities, links to all of the regulatory agencies, contact information, and frequently asked questions.

All of the IRB forms have been–or are being–revised to fill previous “holes” in the application that slowed down the review process.

“We’re using what we’ve learned in the committee meetings to make the forms more complete and prevent additional requests going back to the investigator,” Ginn said. “We’re trying to be more proactive.”

Exciting changes to the IRB informatics infrastructure are on the horizon. A first phase revamping of the informatics systems, expected to be completed during the summer, will include a database that will allow investigators to view protocol status and capabilities for electronic filing of continuing reviews, adverse events, and reviewer’s comments.

In the next phase, electronic filing of the IRB application will be added. Bernard said the goal is to take a “Turbo Tax” type of approach—the program will first interview the investigator about the protocol, and based on the responses, it will prepare a customized list of applicable forms or parts of forms. The electronic application also will be designed to allow investigators to import standard template language where appropriate.

The IRB’s continuing improvements should ease some of the frustrations felt by investigators applying and waiting for IRB review. To do their part, investigators should know the regulations and submit high quality applications, Bernard said. Ginn hopes that the process will become increasingly collaborative between the IRB and investigators.

“We all want to efficiently protect human subjects,” she said. “I hope that investigators will let me know when there’s an issue, a problem. Only by communicating with us can we work together towards a solution.”
New center boosts mouse studies

The ability to assess genetically modified mice for physiological defects has taken a giant leap forward at Vanderbilt with the establishment of the Mouse Metabolic Physiology Center (MMPC).

The Center recently received funding from the NIH as one of three national centers for studying mouse models potentially useful for understanding diabetes and its complications. The national centers—the others are at the University of Cincinnati and Yale University—will work together to analyze mouse models from across the country.

“This new mouse physiology center was designed to dovetail with other efforts in the Vanderbilt Diabetes Center,” said David H. Wasserman, Ph.D., professor of Molecular Physiology & Biophysics and director of the MMPC. “We will now have an even more comprehensive program for studying diabetes and related disorders.”

Three core MMPC laboratories will analyze metabolism, energy balance, physical activity, vascular physiology, and other physiologic alterations associated with diabetes. Vanderbilt’s strength, Wasserman said, is in the ability of its cores to perform physiological tests in “conscious unstressed mice.”

A good example of this, he said, is the insulin clamp, a test commonly used to assess insulin sensitivity. To perform an insulin clamp in conscious mice requires the surgical introduction of catheters for infusing insulin and glucose, a technically demanding procedure. Wasserman credits Masakazu Shiota, Ph.D., research assistant professor of Molecular Physiology & Biophysics, with adapting the technique for conscious mice and securing Vanderbilt’s unique ability to perform such tests.

“Our tests are demonstrably more sensitive because our approach does not require the use of anesthetics or excessive handling of the mouse during the measurement period,” Wasserman said.

Vanderbilt investigators also have miniaturized standard analytical tests for hormones and metabolites and have adapted echocardiography, EKG, and blood pressure recording for conscious mice.

“Our strengths in mouse testing in vivo were recognized by the funding of this new mouse physiology center,” Wasserman said. “The center grant brings resources to Vanderbilt that will allow us to lead the international community in describing and studying the gene defects that may be involved in diabetes, and in identifying potential sites of action for correcting diabetes and its complications.”

Network changes speed data movement

The 1999 launch of the Center for Structural Biology, one of Vanderbilt’s cross-campus research initiatives, presented challenges to the network infrastructure that was in place at the time. Structural biology researchers need to move hundreds of megabytes to gigabytes of data at a time between facilities in the Stevenson Center and workstations in the Medical Center, said Jarrod A. Smith, Ph.D., assistant director of the Center. A year ago they couldn’t.

Now, improvements to the network infrastructure have made such data movement possible, and coming changes promise to make the situation even better. Improvements started last fall, said Jeff Kimble, director of Network Computing Services, when his division and Information Technology Services increased bandwidth between the two sides of campus. Both sides are currently in the process of converting to a Cisco gigabit network, and they expect to begin linking the university and medical center networks in the summer.

“The infrastructure changes so far are really just the tip of the iceberg,” Kimble said. “The continuing network improvements will facilitate more efficient movement of data.”

Network Computing Services also is participating in research informatics meetings—listening sessions with groups of researchers to learn about informatics-related research needs. The meetings are part of efforts aimed at making the Informatics Center more researcher-friendly.

“There has been a realization that there are research groups on campus with special computing needs,” Smith said, “and a real willingness and effort to work with us to solve these challenges.”

For more information about the Informatics Center and NCS, see http://www.mc.vanderbilt.edu/infocntr/ and http://ncs.mc.vanderbilt.edu/.
Join the Community of Science

Anyone surfing the VUMC Web site looking for a researcher with specific expertise is directed to the Community of Science—a global network of scientists and scholars. Vanderbilt is a COS subscriber, and many faculty members are included in the database of COS Expertise profiles (http://expertise.cos.com/).

The COS Expertise database includes professional information for nearly 460,000 scientists and scholars across all disciplines in the sciences, social sciences, and humanities. The database is searchable by researcher name, institution, geographic location, and key words.

COS members also have access to COS Funding Opportunities, a database of more than 20,000 grants updated daily. And members can opt to receive weekly email funding alerts, tailored to individual research interests.

Some VUMC faculty members have been frustrated with the COS funding alerts, finding them too general, said Barbara O. Meyrick, Ph.D., professor of Pathology and director of Program Development in the Office of Research.

But, noted Lee E. Limbird, Ph.D., associate vice chancellor for Research, “the funding updates are only as good as your definition of who you are and the science you’re interested in.” To make the alerts useful, she said, scientists need to be more deliberate in refining their search queries.

Even if faculty members opt not to use the funding alert or other features of COS, Meyrick encouraged all investigators to enter profiles that at least include areas of expertise, research interests, and key words. That way, any faculty member searching for a potential collaborator, for example, will have the best possibility of finding a match.

For questions about COS or how to refine your search, contact Paula Seibert in the Office of Research (2-4303 or paula.seibert@mcmail.vanderbilt.edu).