1979 after spending 10 years at Rockefeller University and Yale University in the United States. They applied up-to-date Western research techniques in their laboratories and as a result were able to win grants from the U.S. National Institutes of Health.

But for many Romanian scientists, a second job is a necessity, and some institutes earn extra funds working for private companies. For example, scientists help bolster the organic chemistry institute's meager budget by using a spectrometer to analyze water samples for Pepsi Cola bottling plants. Says Marius Peculea, a nuclear engineer who is secretary-general of the Romanian Academy: "There is very little money available now to truly invest in science. And without such investment, we cannot do much more than persevere."

In Romania, as in the rest of Eastern Europe, international cooperation and grants sometimes provide a welcome lifeline. "We would all like to see more substantial funds dedicated to improving the obsolete equipment in our labs, but the only hope is from external funding," says chemist Alexandru T. Balaban of Bucharest's Polytechnic University. Aurel Sandulescu, a theoretical physicist who is also a member of Parliament, agrees that "we badly need international cooperation. The best Romanian scientists have good contacts abroad, and those contacts can benefit our research."

As a vice president of the Romanian Academy, Sandulescu helped introduce a system of competitive grants at its research institutes in 1994, and he strongly backs the government's new plans to award grants to other research centers on a competitive basis. "The doors are opening here in Romania," says Sandulescu, who has conducted research at the Institute of Atomic Physics since 1956. "But we are still in a transition period." Ene, a fluid-mechanics specialist who became Romania's research minister earlier this year, told *Science* that the new open grants process soon will apply to all institutes that his ministry supervises. "We are serious about stimulating competition," he says. "I want to finance research, not chairs" in institutes.

One trend that has worried some researchers is the government's enthusiasm for applied research. In all, Ene expects to spend 20% of the science budget on basic research and the rest on fields such as materials research, biotechnology, and communications. "My hope is that the high quality of our individual scientists will help us revitalize Romania's research program and restore science to its proper role," Ene says.

Many Romanian scientists, however, feel that the government needs to do more in support of basic research. That sentiment is echoed by the only Romanian-born scientist to win a Nobel Prize, George E. Palade (medicine, 1974), now dean of scientific affairs at the medical school of the University of California, San Diego. Even though he left Romania for the United States a half-century ago, Palade has assisted many Romanian biologists over the years—including the Simionescus—and has kept up with scientific developments there. Romania, he says, should try to foster both basic and applied research and focus resources on the best institutes. Romania "shouldn't phase out basic research," he warns, "because, once disassembled, it may take many years to start again when economic conditions improve."

–Robert Koenig

Robert Koenig is a writer in Bern, Switzerland.

HUMAN EXPERIMENTATION

Review Boards: A System 'in Jeopardy'?

An ad in a Philadelphia subway asks: "Is addiction a problem for you or someone you care about?" It continues: "Free help is available in exchange for research participation at The Treatment Research Center." Subway riders are invited to call the clinic to set up an appointment for screening. It is one of several ads cited in a report to Congress last week illustrating what the authors see as a worrisome trend in clinical research—an increasing reliance on slick marketing techniques to recruit subjects for drug trials.

Marketing techniques are not the only problem the report, by the Inspector General (IG) of the U.S. Department of Health and Human Services (HHS), turned up. The study concludes that the growth of commercially sponsored clinical trials, coupled with an expected boom in government-funded clinical research, is outpacing the ability of a 25-year-old federal system to oversee volunteer recruitment, fee payment, and other issues. The chief author, Mark Yessian of the IG's Boston office, said during a hearing on 11 June in the House government reform subcommittee on human resources: "We are offering a loud warning signal" that the system to monitor such practices "is in jeopardy." Deputy HHS Inspector General George Grob added that "we are not talking about tweaking the system at the edges" but about the need for "a major overhaul." (The report is available on the Web at www.hhs.gov/progorg/oig)

Aggressive recruitment. Growth in clinical trials is stressing the system to protect volunteers, says HHS report.

The system they targeted for analysis is a collection of more than 3000 locally managed "Institutional Review Boards" (IRBs) empowered by HHS and 16 other federal agencies to protect volunteers in studies at U.S. hospitals and clinics. Each IRB—made up of at least five unpaid members, one of them a nonscientist—is responsible for checking out the ethical aspects of projects within its purview.

The small group of IRBs sampled by HHS reported experiencing on average a 42% increase over 5 years in the number of primary reviews they've been asked to do. Some are now overseeing more than 2000 active protocols. Because many academic medical centers depend on clinical research funds for income, the HHS authors also expressed concern that IRBs might trim their sails to "accommodate institutional financial interests." They also said they feared that such pressures may be particularly intense at the 16 or so privately owned IRBs that do reviews for profit-making research organizations. The report urged the federal government to certify all IRBs, reform the system to give members less paperwork but more substantive assignments, establish a new education program for IRB members, seek to reduce potential conflicts of interest, and institute stronger federal oversight.

The warnings from HHS drew emphatic declarations of concern from House subcommittee members, particularly from the chair, Christopher Shays (R–CT), and ranking Democrat Ed Towns (D–NY). Citing a 1995 New York study of serotonin and aggression in which minority children were given the drug fenfluramine (now withdrawn from the market), Shays said, "The current system of bioethical review failed miserably." Towns said it would be best to "tear the system down and rebuild it. ... I don't like

this word 'reform.'" The full committee chair, Dan Burton (R–IN), said there were "very serious and ... growing problems" in clinical trials, and that "conflicts of interest among members of IRBs" may explain lax reviews.

These comments provoked strong responses from defenders of the system. Gary Ellis, director of the Office for the Protection From Research Risks, who oversees the national network of IRBs from an office within the National Institutes of Health (NIH), said that the "system is not in jeopardy." He observed that "when you set aside the language of danger and menace," the HHS report offers no evidence that patients have been harmed or are at risk. Noting that every clinical trial goes through many layers of ethical review, Ellis said he considered the likelihood of a "catastrophic failure" to be "slight." And children in the fenfluramine study, according to a psychiatrist who chaired the IRB that approved the research, reported side effects no more serious than a headache or fatigue. He insisted that the study had included no white children because almost all the candidate subjects were black and Hispanic.

Robert Levine, an ethicist at Yale University, head of Yale's IRB, and spokesperson for the Association of American Medical Colleges, also rose to the defense. "I reject the mischaracterization" in the HHS report of the IRB network as "a system in crisis," Levine said. He warned against loading down IRBs with new tasks and limitations, noting that funding is inadequate as things stand and that getting qualified reviewers to serve for IRB duty "is not easy." Levine did not think it made sense to impose demanding new conflict-of-interest rules to prevent institutional employees from reviewing studies done within the institution. Speaking as Yale's IRB chair and a Yale employee, he said, there is "no real conflict" in these roles, as "what we really want [as an institution] is rigorous review."

Ellis and Levine both agreed, however, that the IRB system needs improvement. For example, Ellis suggested that federal protections be expanded to cover all private research, some of which is now exempt. Both Ellis and Levine supported the HHS's recommendation that IRBs' workload be reduced. Both agreed that the IRBs and their federal overseers could do a better job of monitoring research, but they said this could require more money to pay for staff.

Neither Shays nor Burton expressed interest in tightening controls on private research—or in boosting appropriations to the IRB system. Shays did say, however, that he intends to bring leaders of the NIH and Food and Drug Administration in for more questioning.

–Eliot Marshall

BREAST CANCER

Australia Takes Two-Step Approach on Genetic Studies

MELBOURNE—With its modest research budget, remoteness, and sparse population, Australia may seem an unlikely place for a model study of the epidemiology of breast cancer. But in the last few months, Australian researchers have been adding the finishing touches to an integrated national program that has won international plaudits for its design and its ability to answer the most compelling questions about breast cancer. The effort combines a nationwide study of high-risk families to track down genes associated with increased breast cancer risk and a population-based study to determine the prevalence and actual risk that such genes confer. "I have nothing but praise and envy [for the work]," says British geneticist Ian Tomlinson of the Imperial Cancer Research Fund. "They will get the sample sizes needed to study the genetic profile of predisposition and genetic changes in [breast] cancer."

On the team. Leaders of Australia's Consortium for Familial Breast Cancer Study are Joe Sambrook, second row, fourth from left, and John Hopper, seated on right.

The need for such comprehensive epidemiological information arises from the Pandora's box opened by the cloning in 1994 of the first breast cancer predisposition gene, *BRCA1*, followed 15 months later by *BRCA2*. Those discoveries quickly led to tests for mutations in the genes, but there was insufficient data to tell women who tested positive how great a cancer risk they faced. The goal of the Australian program is to assess the risks associated with breast cancer genes as quickly as possible, as well as other factors that could help carriers lower their risk.

Such combination studies are now seen as the model for the genetic epidemiology of cancer. "Almost all sites in a newly funded colorectal cancer registry have adopted this model, with both a high-risk and a population-based component," says Daniella Seminara, who coordinates an international registry on familial breast cancer maintained by the U.S. National Institutes of Health. The Australian data will make up a large proportion of the registry.

Australia's effort owes much to the work of two men: University of Melbourne epidemiologist John Hopper and molecular biologist Joe Sambrook, director of Melbourne's Peter MacCallum Institute for Cancer Research. Although the joint study now appears seamless, its components were formed separately and continue to have a life apart from one another.

A step ahead. John Hopper and colleagues Margaret McCreadie, director of the New South Wales Cancer Council, and Graham Giles, director of the Anti-Cancer Council of Victoria, began their population-based study of breast cancer in 1992, even before *BRCA1* was identified. They had the good fortune to work in Australia, where every breast cancer case in the country must be listed in registries compiled by each state. Individuals are also relatively easy to track down. With a population of only 19 million, Australia is highly urbanized and its families tend to stay together in one city—and those who do move can be located via electoral rolls made complete by the country's compulsory voting registration laws.

At the same time, researchers who want to use the data must comply with stringent international guidelines. Hopper adds that Australians, although demographically similar to the U.S. population, have yet to develop a heightened awareness of medical privacy.

Hopper also guessed that developing a population-based database would be useful for a relatively small player on the world scene: "While others were trying to find cancer genes, we were looking one step ahead at what [that knowledge] might mean for the population." Toward that end, Hopper interviewed and took blood samples not only from a selected sample of women who agreed to participate in the study but also from every