ploys the scientists.

The study by the General Accounting Office (GAO), Congress's investigative arm, reviewed DOE reports on nearly 5000 foreign excursions by scientists from four national laboratories: Sandia and Los Alamos in New Mexico; Livermore in California; and Oak Ridge in Tennessee. It found more than 75 incidents between 1995 and 1999 in which researchers reported the possibility of eavesdropping and luggage tampering or said they were offered sexual favors. The report does not identify specific researchers, laboratories, or the nations visited, and DOE officials say no secrets were revealed. Some of the travel involved the 25 nations on DOE's "sensitive" list, which includes Russia, China, and Ukraine.

The report makes for racy reading. In one case, a scientist visiting a sensitive nation was repeatedly propositioned by women who called his hotel room and knocked on his door. Another DOE researcher, in a post-trip debriefing with security officials, admitted to having sex with at least four women, including a prostitute, a waitress, and two employees of a laboratory he was visiting. Security officials were "particularly concerned about these activities because of the potential for blackmail," the report notes. There were also reports of tampering with personal equipment, including riffling through and then locking a previously unlocked briefcase, turning on a previously shut-down computer, and trying to pry open the back of a laptop.

Some of the incidents were almost comical. One researcher who telephoned his wife at home and chatted about her upcoming plans to play the game Bingo at a social gathering was later asked in the hotel bar about those plans. The next day another host asked him: "What is Bingo?" Some researchers even used the suspected eavesdropping to their advantage. After talking to their hotel walls about the desire for an extra roll of toilet paper or a television set, two scientists were pleasantly surprised to see the items appear within hours. Other episodes included "maids" interrupting a meeting to move potted plants closer to visiting U.S. scientists, and a technician who entered a conference room to change the tape in recorders previously hidden behind a wall. Dismayed U.S. officials hadn't been told the meeting was being recorded.

GAO investigators say the episodes highlight the need to brief researchers more carefully and to review all travel plans, because spies "can operate worldwide." They recommend that the weapons laboratories consult with counterintelligence agents and other scientists, who would be able to spot potentially sensitive information in planned presentations. Livermore and Oak Ridge currently conduct such reviews, which have prompted some scientists to alter or cancel travel plans.

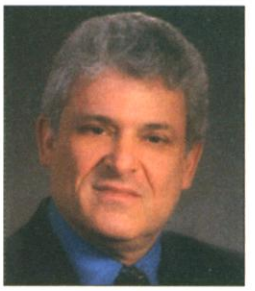
DOE officials agree with the findings and say they are expanding reviews and paying more attention to activities involving nonsensitive nations. But given limited funds, says one official, the agency "will probably continue to target the primary threat, and that is the sensitive nations."

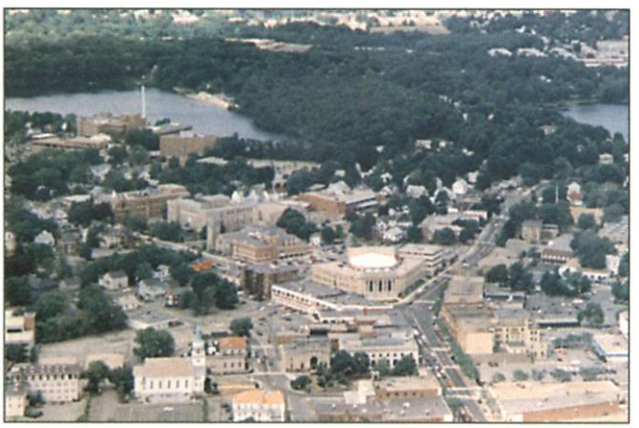
–DAVID MALAKOFF

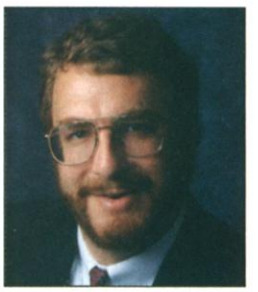
GENOMICS

University Company to Exploit Heart Data

BOSTON—As a boy growing up in the small town of Framingham, Massachusetts, medical ethicist Arthur Caplan remembers watching excitedly as distinguished scientists from nearby Boston visited his father's drugstore. They came to inspect the pharmacy's records of patients enrolled in the federally funded Framingham Heart Study, a massive government effort begun in 1948 to monitor the cardiovascular health of more than 10,000 townsfolk. "It was a great event," recalls Caplan, 50, who has long since left town for the University of Pennsylvania in Philadelphia. But the Framingham study, which helped establish a link between cigarette smoking and heart disease and between high blood pressure and stroke, continues to chart new territory—and Caplan is poised to play a role in its future development.







Heart of the matter. The longitudinal heart study in Framingham (*above*) has great commercial value, says Fred Ledley (*right*), but must be done properly, says medical ethicist Arthur Caplan (*top*).

This month, Boston University (BU), which directs the study and maintains the records, announced plans to form a bioinformatics company that will mine the data. The university will own 20% of Framingham Genomic Medicine Inc., which hopes to raise $21 million to begin modernizing the immense database and packaging it in a format that will be valuable to the pharmaceutical industry. The plan raises a host of difficult ethical issues, including patient privacy, academic conflicts of interest, and reciprocal value to the Framingham residents whose medical data will form the basis for the new enterprise. "These are all choppy waters," says Caplan, who may become a paid ombudsman for the community in its dealings with the company and the university. But he thinks it's a voyage that may be worth taking: "We're talking about the gold standard of epidemiology."

Fred Ledley, chief scientist for the new company and its only full-time employee to date, also sees a golden opportunity to use what is now largely gathering dust in warehouses. "There's an enormous amount of data that's never been pulled out of boxes," he says, "and I don't think the government has the money to do it." However, the university's actions touch on issues similar to those raised by a controversial decision by the government of Iceland to provide a private company with health records on all its residents in return for an upgraded record-keeping system and free access to any new drugs the company develops (*Science*, 30 October 1998, p. 859). The University of Utah, Salt Lake City, also has provided private companies with genealogical data from Mormon church records, says Richard Koehn, Utah's vice president of research, after taking steps to ensure confidentiality and requiring involvement by faculty members.

The Framingham company's first move will be to build a comprehensive electronic database over the next several months. Its second, more ambitious, step will be to correlate clinical records with DNA analyses from blood samples on file, with the goal of

CREDITS: (CLOCKWISE FROM LEFT) PHOTO COURTESY FRAMINGHAM.COM; R. CLINK; WORK OF ART STUDIO

identifying some 50,000 genetic markers in individuals that are linked to specific abnormalities or diseases. Now that the human genome has been nearly sequenced (see p. 2294), Ledley and BU are betting that biotech firms also will find the Framingham data a valuable tool.

Before Ledley can realize that dream, however, the company must win the support of residents, other universities involved in the study, and the National Heart, Lung, and Blood Institute (NHLBI) in Bethesda, Maryland, which has put up $34 million over the years. NHLBI director Claude Lenfant could not be reached for comment, but his staff says he plans to visit BU soon to discuss the new company and the institute's concerns about privacy, data access, and conflict of interest. NHLBI officials and researchers outside BU want continued access to the data, whereas residents—who for the past decade have signed consent forms for genetic analyses of their blood and tissue—want to safeguard their health records, which include psychosocial data. The relationship of BU researchers to the new company must also be resolved. "This is a difficult dance," says Caplan.

But Ledley and BU managers say they know the moves. The revamped database will remain available to researchers at no cost. "We're not taking any data out of the public domain, and we're not selling patient data," Ledley says. "We're selling tools to analyze that data." In addition, BU researchers involved in the study will be precluded from owning company stock, although they will be able to serve as consultants. "We want to preserve the integrity of the study," says BU associate vice president David Lampe.

A 25 April letter to the 1000 or so surviving study participants spoke about "entering an important new era of medical research" and promised to maintain "exemplary ethical standards." It also proposed an ethical review group, to be based in Framingham, and said "a portion of its resources"—perhaps a chunk of stock—would be put in a trust controlled by a community board. "You can never pay people back, but you can show social responsibility," Ledley says.

Jay Lander, a Framingham attorney and vice chair of an organization called Friends of Framingham Heart Study which represents participants, says so far the community feels "surprised and somewhat apprehensive" about the new company. Pending a clearer idea of how the venture might affect the study, he says, "this thing isn't going anywhere." But some ethicists are intrigued by the plan and see its potential value to society. "I would caution against a knee-jerk reaction about this. It's not a bad thing," says Norman Fost, director of the medical ethics program at the University of Wisconsin, Madison.

To signal its good intentions, the company intends to give the proposed board $150,000 to hire an ethicist. Ledley has suggested native son Caplan, noting that "he would be accountable to the community, not to us." Caplan says the unusual arrangement would be workable if the company's contribution doesn't come with any strings attached. And he thinks that BU officials realize they are under close scrutiny. "This is a monumental study," he adds. "Doing it right is crucial."

—ANDREW LAWLER

PATENT DISPUTES

Biotech Giants Butt Heads Over Cancer Drug

Mountain sheep settle disputes by knocking their heads together until one of them gives up and walks away; biotech companies do much the same, except they enlist patent lawyers to do the head-butting. The most recent display of this kind centers on an important new breast cancer drug, Herceptin. Developed by Genentech Inc. of South San Francisco in the 1990s, Herceptin has been generally available only since November 1998. Already, though, it has won acceptance as an adjunct to other therapy and is earning big revenues for the company—$68.7 million in this year's first quarter alone, according to Genentech. But success breeds competition. On 8 June, Chiron Inc. of Emeryville, California, challenged Genentech's patent claims and sued for a share of the profits.

Chiron accuses Genentech of "willful, wanton, and deliberate" patent infringement.

Chiron's 4-page complaint, filed in the federal district court in Sacramento, California, accuses Genentech of "willful, wanton, and deliberate" infringement of one of its patents. It seeks an unspecified amount of money for damages, including a trebling of normal penalties "due to the willful nature of Genentech's infringement." Sean Johnston, vice president for intellectual property at Genentech, says Chiron's patent is "invalid"; the company plans to say so in an answer to be filed with the court in August. The case is being closely watched in the biotech industry not just because of the money at stake but also because it involves one of the first therapies to emerge from the burgeoning field of cancer genetics.

Chiron launched its attack after winning what some observers call a "submarine patent"—one that had been quietly wending its way through the U.S. Patent and Trademark Office (PTO) for the past 16 years. On 25 April, PTO awarded Chiron U.S. Patent 6,054,561, which traces its lineage back to an application filed at the PTO in February 1984 by scientists from another California biotech firm, the Cetus Corp. Cetus was merged into Chiron in 1991. Among the patent's 31 claims is the invention of a monoclonal antibody that binds to a cell surface receptor called c-erbB-2, also known as HER2—the very target that Herceptin binds.

For its part, Genentech owns six or seven patents in the area, according to a spokesperson, including one (U.S. Patent 5,677,171) that claims "a monoclonal antibody which specifically binds to the extracellular domain of the HER2 receptor and inhibits growth of SK-BR-3 breast tumor cells. ..." Genentech filed for its patent in 1988 and received it in 1997.

It's "not uncommon at all" to have patents appear to overlap, says Robert Blackburn, Chiron's chief patent counsel. He suggests that the Cetus-Chiron patent is broader and, more important, was filed earlier. Blackburn claims Genentech talked about getting a license from Chiron several years ago, but "they seemed to lose interest and go away."

"If [Chiron is] saying they offered reasonable royalty terms, I would disagree," says Johnston, who acknowledges that the two companies did discuss a license. Johnston argues that in this case Chiron owes its success at the PTO more to clever management of a fragmentary legal claim than to diligent investigation of the clinical uses of HER2. "We're confident that we can demonstrate that the Cetus-Chiron scientists were not the first to make antibodies [to the c-erbB-2 receptor]," Johnston adds. For example, he notes that Robert Weinberg of the Whitehead Institute in Cambridge, Massachusetts, identified the key protein in 1982. This and other early research, Johnston claims, can be used to disprove Chiron's claim of priority in 1984. Blackburn, without going into details, dismisses these arguments as "a red herring."

Why is it taking so long for these disputes to surface? "Unlike chip technology," says Rachel Krevans, lead outside counsel for Genentech at the firm of Morrison & Foerster in San Francisco, "biotech products take a long time to mature." Questions about who profits from them take even longer to answer, "and that's why we're litigating the science of the early 1980s in the year 2000."

—ELIOT MARSHALL