Germany's Gene Law Begins to Bite

Bureaucracy, regulation, and delay: Molecular biologists fear for their research as enforcement of the "gene technology law" begins in earnest and an unsympathetic public looks on

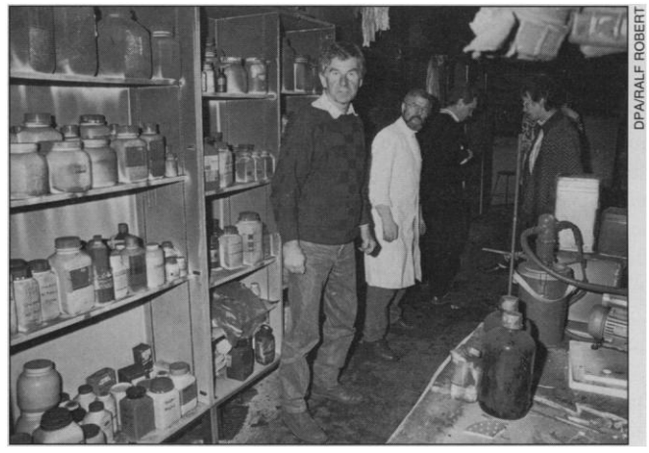
Heidelberg—HERMANN BUJARD, DIRECTOR of the prestigious Center for Molecular Biology (ZMBH) in Heidelberg, was getting angrier by the minute. Here he was, along with the heads of another 150 labs, being forced by local enforcement officials of the government's new "gene technology law" to sit through a 3-day course on the law and laboratory safety—despite having more than 30 years experience in the lab. Forty minutes into the first lecture, with the legal terms of genetic engineering still being defined, he decided he'd had enough and stormed out of the auditorium.

With that angry protest against a law that he says "makes no scientific sense," Bujard may have lost more than his temper: His failure to complete the course means that local enforcement officials now can deny him permission to lead new recombinant DNA projects in the institute of 140 researchers, which he heads. That may seem extreme, but for Germany's molecular biologists it is one of several ominous signs that a new era of government regulation has arrived in the laboratory.

Behind the change is one of the world's most comprehensive laws designed to regulate the use of recombinant organisms in laboratories and industry. Passed in the summer of 1990 after a long and bitter debate, its effects were at first barely felt. But in the past few months, local gene law enforcement offices have set to work and the law has finally begun to hit home. In the laboratories, scientists are now telling dispiriting stories of the enormous bureaucracy and long delays they face when they try to seek approval for new experiments—delays that could make it much harder for them to compete in fast-moving fields. Several researchers told *Science* that they had abandoned plans to pursue specific projects because of the law. And there is now evidence that recruitment of talented young scientists may also be at risk (see box).

If the strictness of the law seems hard to understand, the vehemence of the opposition to genetic engineering in Germany helps explain it. History is partly to blame: Just the words "genetic engineering" are enough to evoke fears that the technology could be misused for eugenic purposes, obviously a sensitive subject for Germans. And after Chernobyl, when fallout spread through most of Germany, many Germans felt that the "experts" had deceived them about the safety of nuclear power and resolved not to let the same thing happen again with other new technologies.

As opposition to gene technology in Germany grew in the late 1980s, scientists found themselves targets for terrorist attacks and threats. Hans Günter Gassen, director of the Institute of Biochemistry at the Technische Hochschule in Darmstadt, was one outspoken supporter of genetic engineering. In January 1989, a group calling itself the *zornige Viren* ["angry viruses"] set fire to his laboratory.



DPA/RALF ROBERT

Fire bombing. *For one outspoken supporter of genetic engineering the result was an attack by the* angry viruses *group.*

After the attack, Gassen was shocked to find how little public sympathy there was for his researchers. "We expected our fellow citizens to condemn the act of the *zornige Viren* as uniformly and emphatically as we did. But this was absolutely not so," a bitterly disappointed Gassen later wrote in *Bild der Wissenschaft*, a popular German science magazine.

The deeply rooted public mistrust of genetic engineering was reflected in the legislative battle over the gene technology law. Opposition parties called for a highly restrictive law, and the small Green party proposed a 5-year ban on all recombinant DNA research and the closure of all "gene technology" laboratories.

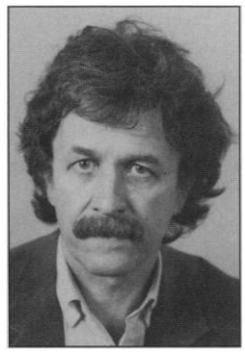
In the end, the Bundestag passed a law that appears relatively benign (although the penalties for breaking it—from 1 to 5 years imprisonment and fines of up to $60,000—clearly are severe). Just like the familiar guidelines of the National Institutes of Health, it divides experiments into four categories, from S1 to S4, based on the known or predicted pathogenicity of the organisms in the experiment. But turning from the letter of the law to its enforcement, the parallels with the United States end.

In the United States, S1 experiments (those using nonpathogenic organisms) require no documentation, and all except a few controversial types of experiments—such as gene therapy and deliberate release of genetically modified organisms—are dealt with by in-house safety committees, which generally favor an unbureaucratic approach. But under Germany's new law, decisions are enforced by officials who, although generally trained scientists, operate in a tense atmosphere that makes them nervous and over cautious.

The process of getting approval for a gene technology lab is now a "bureaucratic nightmare" as one scientist put it. Take the case of Achim Leutz, a junior group leader at ZMBH who plans to continue earlier S1 and S2 experiments on retroviruses and oncogenes, particularly sensitive areas under the new law. His last laboratory's pre-law application was just eight pages long. This time around, it weighs in at almost 4 lbs—and that is just one of the six required copies. At the Gene Center in Munich, Professor Ernst-Ludwig Winnacker's application for S2 work was 92 pages, times 10 copies. "We almost needed a truck to send it," he told *Science*. "Most of the questions were completely irrelevant or repetitive." Scientists registering S1 labs must provide the same detailed information about lab installations—for example, positive air-pressure systems—as those working in S3.

But while documentation can be frustrating, the bureaucratic delays that follow are

far worse. Researchers must wait for their applications to be processed before beginning their experiments, which, in theory, means a maximum of 3 months for first applications and 2 months for follow-up experiments (required for S2 and above). But the law provides many ways to stop the clock—for instance, if officials request additional information—and first signs are that the process is taking much longer than planned. "The time for processing an application can vary from 2 to 6 months," admits one gene law enforcement official who did not want to be named.



Hermann Bujard

"The delays are a big problem," says Leutz. "Creativity suffers because you want to do an experiment, today, or...you just got an idea while speaking to someone and you want to work on it together....[The law] kills spontaneity, which is one of the fun things about molecular biology." Not only fun, but also international competitiveness is threatened: A 6-month-old idea in molecular biology is often obsolete.

Faced with these problems, some scientists are choosing to forgo certain areas of research rather than face the bureaucracy. "I'm sure that people begin to do experiments not...for scientific reasons but rather on the basis of how difficult the bureaucracy will be to get the experiment approved... like change to other organisms," said Winnacker. Peter Gruss, a director at the Max Planck Institute for Biophysical Chemistry in Göttingen, provides an example. He has given up the idea of doing any projects that would generate transgenic mice classified as S2 or above; the law would require him to restructure his entire animal house as an S2 or S3 facility, an effort he says would simply be too great.

Even worse, he fears, is another aspect of the law that could cripple international collaboration—the lifeblood of molecular biology. Exchange of recombinant organisms with researchers in the United States requires official approval—in other words, more bureaucracy and delays. Says Gruss: "This is to me the most striking shortcoming of the law...and seriously threatens our [Germany's] international competitiveness."

Some researchers protest that regional differences in enforcement constitute another serious problem, and that the differences are not scientifically based but represent officials' own interpretations of the law, fear of making mistakes, or, worst of all, local political attitudes. According to Winnacker, "Some authorities look at the last sentence they can find that restricts any movements of scientific work. Others try to look at it in a very open way and try to support science as much as possible....This results in... a gradient of how permits are issued and how long it takes."

The 3-day course requirement provides another example: Although enforcement officials from all states agreed that all principal investigators must attend a course, scientists in Baden-Württemburg received threatening letters requiring them to take the course right away, while researchers in certain other states have yet to hear anything about it.

Although regional differences mean that few scientists have an overall picture of the impact of the law, the immediate question for all of Germany's molecular biologists is whether they should fight back or accept the situation and try to live with it. Many researchers are afraid to take on the system: They fear reigniting public opposition to genetic engineering and attracting closer scrutiny of their labs from the gene law enforcement officials. "Everything is relatively quiet now, which we're very happy about, and we want it to stay that way," one prominent researcher told *Science*. It would be "dangerous" to criticize publicly certain sensitive aspects of the law, he said.

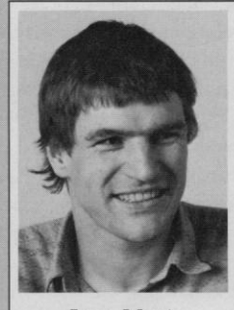
Many of Germany's department and institute heads, who presumably have the most clout with the government, are afraid to speak out because they fear their actions may adversely affect not only themselves but also their younger colleagues. Junior people cite pressure from peers and lab directors not to criticize the law publicly; one outspoken young scientist was told by his boss not to be a ***Bildersturmer*** ["iconoclast"].

Institutions are taking steps to help scientists cut through some of the red tape. Biological safety officers are being hired (as the law requires) to help scientists manage applications and compliance with safety regulations, and labs are computerizing information about building specifications and

No Place for Nonconformists

Heidelberg—If the decision made by Jean-Marie Buerstedde, a German immunologist currently working in Switzerland, is a sign of the times, then the German molecular biology community had better start worrying. Like several hundred other young, German molecular biologists, Buerstedde was eager to bring his skills back home. Last fall, an offer came up—as a junior group leader in a prestigious research institute in Germany. Buerstedde was ready to accept—but he had not reckoned with the atmosphere surrounding the new gene technology law.

In November 1991 Buerstedde, in preparation for his new job, attended the 3-day course required of project leaders under the law, along with other scientists from the institute. "Undiplomatically," as he now puts it, during the course he vigorously stated his opinion that the previous recombinant DNA guidelines had worked perfectly well and that the new law was unnecessary and overly restrictive.



Jean-Marie Buerstedde

The next day, Buerstedde heard that the enforcement officials present at the course were upset about his statements. They were also concerned about the safety and ethical aspects of his proposed research involving the use of oncogene-transformed B-cell lines to clone the genes for enzymes involved in homologous recombination. As a result, the institute's safety officer told him, he could expect the officials to monitor his future laboratory very closely, for example, by making unannounced visits to check whether his lab complied with the law's safety requirements.

Some of the institute's scientists were also upset, Buerstedde says. They felt that he had been unnecessarily provocative and had risked damaging the good relationship between the institute and the local officials, perhaps even leading to closer monitoring of all labs. Their attitude was, as Buerstedde describes it: "Look, if you want to come back to Germany you have to be very careful....There could have been a journalist in the audience and he could hurt the reputation of [the institute]." The experience was enough for Buerstedde. He turned down the job and has decided to remain abroad for the foreseeable future. "I think the law will make it harder to recruit young scientists to Germany," he says, "Especially people like me, who are not very diplomatic. The system selects for conformity." ■ P.K.

safety procedures to help fill in forms quickly. One enforcement official says he believes things will get better as researchers and officials gain experience with the law and with each other. "Right now, understanding between scientists and officials isn't what it could be," he says. "Some acceptance, and a collegial atmosphere, needs to be developed."

Ernst-Ludwig Winnacker

For Winnacker, who advised parliament while the law was being drafted, such measures are necessary but not nearly enough. He is collecting stories of the problems faced by scientists and will present them at a parliamentary hearing next month in an attempt to have the law amended. He also hopes to persuade enforcement officials to reduce the paperwork required for S1 applications down to a page or so. But Gerd Hobom, chairman of the Central Commission for Biological Safety (which administered the old guidelines) and professor of molecular biology and microbiology at the University of Giessen, is skeptical of Winnacker's chances: "The bureaucrats live from administering this thing," he says pessimistically.

That leaves the more radical group of scientists who are convinced that drastic measures are necessary. One possibility under discussion is a challenge to the law's constitutionality. Bujard, one of the supporters of this approach, argues that the right to teach and to carry out research without interference is guaranteed in the German constitution, and that the new law and the way it is being enforced violate this right.

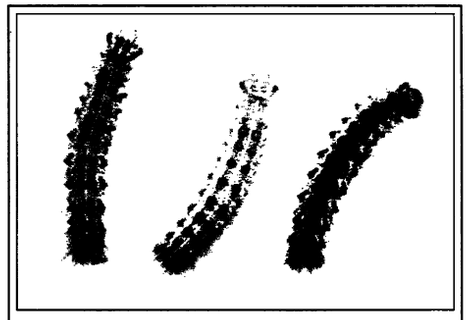
Whether or not the constitutional challenge is successful, Bujard is convinced that the situation can improve only if scientists take a strong public stand. His recent experiences on a committee that evaluated East German science have strengthened his conviction. "I see a parallel with other periods in history where scientists didn't show enough *Rückgrat* ['spine']," Bujard says. "We scientists cannot go along with every irrational demand of a politicized bureaucracy." ■ PATRICIA KAHN

Patricia Kahn is a freelance science writer based in Heidelburg.

Asian Gypsy Moth Jumps Ship to United States

Since the first European gypsy moth landed on Massachusetts soil in 1869, this pest has munched its way through the forests of New England—devouring oak, birch, poplar, willow, and other hardwoods. How did it get here? Unfortunately, science was to blame. The first moths were hand-carried from France by a scientist, Leopold Truvelot, who planned to breed them with silkworms to make a hardier silk-spinning hybrid. But in mid-experiment, a windstorm knocked over a cage, freeing the moths. Today the descendants of those original immigrants have gone as far south as West Virginia and as far west as Ohio and Michigan, where they have become a horror story for gardeners and the timber industry.

Now comes the sequel, as U.S. Forest Service scientists brace for the arrival of a relative, the gypsy moth of Eastern Asia. Eggs from the Asian strain of *Lymantria dispar* apparently came to the West Coast last year as unwelcome cargo on board grain ships from ports in the Asian part of Russia, a region where the moths are common, and a severe outbreak is under way.



WILLIAM WALLNER/USFS

No two alike. *Genetic variability of the Asian gypsy moth is shown by these three distinctly colored larvae.*

The special threat of the Asian moths stems from the fact that, unlike their female North American counterparts, females of the Asian strain can fly long distances. U.S. Forest Service research entomologist William Wallner, who has traveled to the Soviet Union six times in the past decade to study ways to control the pernicious pest, explains the problem this way: The Asian female "zips right along with a payload of 600 to 700 eggs and will fly in to lay its eggs just like a stealth bomber."

Indeed, they've been dropping their payload in Seattle, Portland, and Vancouver, British Columbia, ever since they first took shore leave last May—apparently in Vancouver. In that port, Agriculture Canada inspectors found several thousand eggs on board the *Angara*, a Soviet ship out of Nahodka. And the really bad news was that by the time the inspectors found the eggs, many already were hatching—and larvae were blowing toward shore. So far, 20 males of the Asian strain have been trapped in seven locations and identified by Cornell University geneticist Richard Harrison using mitochondrial DNA sequencing. (Only males have been detected because the traps are baited with the female's sex pheromones).

The problem isn't just that the Asian females travel so far—it's also that their larvae devour a broad range of trees in Asia: At last count, they had an appetite for more than 500 species of plants, including conifers, such as larch. And that's an ill omen for the Northwest's timber industry, based primarily on conifers, such as Douglas fir, larch, and spruce. When the moths turn to birch, alder, willow, and poplar, they could imperil endangered species being protected from the threatened timber industry—those trees form an important part of stream and riverbank habitats that are home to several endangered species.

Denver Burns, station director of the Forest Service's Northeastern Forest Experiment Station, says: "The U.S. Department of Agriculture has plans to go forward with pest control efforts, but the Forest Service is not sure that normal pest control strategies will work." Although the relatively slow-spreading North American strain can be controlled with a biopesticide, *Bacillus thuringiensis* (Bt), or a virus that homes in on the species, the Asian strain is more diverse genetically and may have better defenses. Next month, Forest Service entomologists will begin testing Bt on Asian gypsy moths held in quarantine in Massachusetts.

But even if the pesticide strategy works, it won't be easy to find the flighty Asian females. By the time a male population is detected, the stealthy female moths will have moved to new sites to lay their eggs. Says Wallner: "My concern with the new species is that we could see a faster spread." That means far larger areas would have to be sprayed. And that's not the only concern. In the native strain, the males are mobile—and entomologists fear that newcomers will mate with the moths that are already here to produce a horde of hybrids in which both males and females can get around. ■ ANN GIBBONS