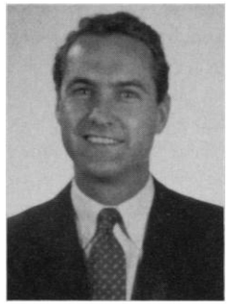
FDA Publishes Bovine Growth Hormone Data

In an attempt to quell a furor, the FDA is releasing safety data on a drug intended to boost milk production in cows

IN AN UNPRECEDENTED MOVE, the U.S. Food and Drug Administration is publishing data on the safety of a drug before it has been approved for use. The drug, recombinant bovine growth hormone (rbGH), has been the subject of a hot controversy over health effects. But in this issue of *Science* (see page 875), two FDA researchers publish a review of 30 years of studies on the hormone by its manufacturers and independent scientists and conclude that it presents "no increased health risk to consumers."

In spite of the fact that the FDA isn't expected to rule on use of rbGH for a year, the agency felt it couldn't wait to publicize the data. "There's this public concern about the safety and economics, and a lot of congressional interest," says Gerald Guest, director for the FDA's Center for Veterinary Medicine and the man who will decide whether to approve the drug for use in dairy cows. "We'd like to get our side of the story out, to show why we're comfortable with the safety. We'd like for people to know that it's a thoughtful process, and we want it to be open and credible."



Safe as milk. *Greg Guyer of the FDA.*

Both the congressional scrutiny and the consumer pressure are intense. The FDA is undergoing two congressionally mandated audits of the 10-year process by which it evaluated the health and safety effects of rbGH, which is intended to make cows produce more milk. At the same time, consumer groups are threatening to boycott milk from the cows that will be given the hormone if the drug is approved.

So it's understandable that the FDA wants to calm the waters. But the move may not get them what they want. Critics charge that publishing the article makes the agency a backer of the drug rather than a neutral evaluator. To Samuel S. Epstein, physician and professor of occupational and environmental medicine at the University of Illinois College of Medicine, what's "unprecedented" about the FDA action is that the agency is acting "as a booster or advocate for an animal drug that hasn't yet been approved."

Epstein, a vocal environmentalist, has joined ranks with genetic engineering critic Jeremy Rifkin in criticizing the FDA and the four companies that make rbGH: American Cyanamid, Elanco (a subsidiary of Eli Lilly), Monsanto, and Upjohn. Earlier this year Epstein published a paper in the little known (and non-peer-reviewed) *International Journal of Health Services* charging that the FDA had abdicated its regulatory responsibility by relying on research done by industry and industry's "indentured academics."

Epstein has done no experimental studies on rbGH, but reviewing studies by others convinced him, he says, that there are unresolved questions, including whether rbGH stimulates premature growth in infants and

Europe: Bovine Growth Hormone in a Political Maze

Although the U.S. Food and Drug Administration is touting the safety of recombinant bovine growth hormone (rbGH), in Europe the hormone faces a tough road. Here, nations are skeptical about the need for rbGH—partly in defense of small farmers, whose livelihood could be threatened by agribusiness' use of the expensive drug. And even if a European country approved rbGH, the hormone couldn't be licensed yet because the pan-European body that must approve all new drugs for veterinary use hasn't rendered a verdict.

The bureaucratic maze in which rbGH is trapped is best exemplified by what is now happening in Britain. Monsanto, maker of one version of rbGH, applied to the U.K. Veterinary Products Committee (VPC) for approval and was provisionally turned down late last month. The committee agreed that rbGH was effective and posed no risk to human health or the environment. But, the committee said, it "was not completely satisfied on the basis of the data with some pharmaceutical aspects of the product or with aspects of the safety of the treated animals." Neither the committee nor Monsanto would offer further details.

If all goes as scheduled, the VPC will confirm its decision not to grant a license on 13 September. When it does, Monsanto may appeal. But even if the VPC had decided in favor of rbGH, the hormone could not have been given a license in Britain—because the European Committee for Veterinary and Medical Products (CVMP) hasn't given an opinion. After the CVMP decides, countries may disagree, but until then no license can be granted.

And CVMP's verdict won't be coming for a while. Last year the European Parliament instructed the CVMP not to decide about rbGH before November 1991. That moratorium, the parliament said, was needed to give time for assessing the complex issues surrounding use of the hormone.

One issue is whether its use might have harmful social consequences. Under current European law, new medicines for people or animals must be safe, effective, and have no undue impact on the environment. Under pressure from small farmers, the European Commission last year debated amending a new veterinary products law to add another criterion: socio-economic effects. Though the amendment was dropped, agricultural experts in the EC are drafting a new version. If adopted, it would almost certainly block approval of products such as rbGH.

Francis Adriaens, a Monsanto product development specialist for the U.K., condemned these political moves for applying "subjective criteria" to scientific issues. Companies would be "uncertain and insecure" about developing products if the ultimate adoption of those products depended on political whims 15 years down the line. "A product should prove itself in the market," Adriaens said, "and not in theoretical considerations of need." But for the moment, Adriaens' argument—like the future of rbGH—is likely to remain trapped in the Alice-in-Wonderland maze of Europolitics. ■ JEREMY CHERFAS

breast cancer in women. He wants the FDA to require studies of the toxicological effects of milk hormones in large-scale tests on cows for several years to make sure there are no adverse effects on them or their offspring.

Another Epstein charge is that the rbGH manufacturers have manipulated published data on human health effects and failed to disclose data showing the drug causes ill effects in cows—including lesions and a higher incidence of infectious disease. Epstein is calling for a full-scale investigation of the FDA and the hormone's makers.

Both the FDA and the companies think they have good answers for all of Epstein's points. More than 130 studies have been done on rbGH by industry and independent scientists, and no definitive health effects have been found, industry and FDA spokesmen say. "Everyone in the whole science world except for Dr. Epstein would not think [rbGH] ever would be active in humans," says C. Greg Guyer, an FDA pharmacologist and one of the authors of the current review.

That review concludes that rbGH is very unlikely to be biologically active in human beings. For one thing, the hormone is known not to be active when injected intravenously into children suffering from dwarfism due to a lack of growth hormone. And in the review, Guyer and his colleague cite findings that even in rats—which are known to respond to intravenous doses—oral dosages don't produce biological effects.

As for safety effects on animals, Monsanto spokesman Larry O'Neill concedes that some cows given the hormone did develop mastitis, an inflammation of the udder, and other symptoms. But, O'Neill adds, those cows were given five times the normal dose of rbGH in toxicology studies that are now being reviewed by the FDA—not covered up, as Epstein has suggested.

Yet Epstein's report has had consequences. It caused four grocery chains and several food-processing companies to refuse milk from treated herds while the hormone remains under FDA review. And although the all-out blitz on the FDA he asked for hasn't happened, his criticisms did prompt the General Accounting Office and the Inspector General of the Department of Health and Human Services to begin audits of the agency's regulatory process for rbGH.

But those audits have begun to take on a routine character to the FDA, which has been looking into the health effects of rbGH since 1982. "You almost have to take a number to decide who's going to review our process next, but we feel comfortable about it," says Guest. "I suspect this will be the most extensively studied product we've ever handled." ■ **ANN GIBBONS**

Greens Make Physicists See Red

West Berlin

Last week, West Germany's Green Party notched up a victory over a nuclear reactor—and left many German researchers hopping mad. Michaele Schreyer, a Green member of West Berlin's elected council who has responsibility for the environment, refused to grant an operating license for a newly refurbished nuclear reactor at the Hahn-Meitner Institute (HMI). The decision, which will be difficult to reverse, could be the death warrant for the institute, the only West German national laboratory in West Berlin. And if HMI dies, it will be partly due to an action taken 5000 miles away in Washington, D.C., by the Sierra Club.

The Hahn-Meitner Institute is named after Otto Hahn and Lise Meitner, who (with Fritz Strassmann) discovered nuclear fission in Berlin in 1938. The small reactor, which cost $110 million to refurbish, was to have been the centerpiece of the institute's research. Scientists there planned to use it as a source of neutrons for biology, chemistry, medicine, and physics. If the reactor never starts up, fears HMI director Hans Stiller, the researchers will drift away.

Though the reactor would be operating in an urban area, Schreyer did not block it on safety grounds, but, instead, objected to HMI's plans to deal with the reactor's spent fuel. And that's where the Sierra Club comes in. Until 1988, operators of five existing German research reactors simply returned their fuel elements to their supplier—the United States—and HMI planned to do the same with the new Berlin II reactor. But a lawsuit filed by the Sierra Club in Washington, D.C., has forced the U.S. Department of Energy to suspend return of spent fuel rods while it prepares an environmental impact statement on the shipments. The other research reactors are storing spent fuel rods onsite until the issue is resolved, but HMI didn't have that option: The operators of new reactors must show they can dispose of spent fuel before they can get an operating license.

The institute did come up with an alternative. It proposed shipping the fuel rods to the United Kingdom Atomic Energy Authority's reprocessing plant at Dounreay in Scotland. Under an agreement already signed between Nukem, a subsidiary of Siemens that operates the reactor, and the UKAEA, the rods would be stored at Dounreay for 6 years and, if the U.S. route remained blocked, they would then be reprocessed there. The processed fuel rods would be returned to Berlin and Dounreay would hold the waste for a further 29 years. By then, Germany should have its own long-term waste repository.

Schreyer didn't buy it, pointing out that Germany's plans for waste storage are still uncertain. HMI director Stiller counters that Schreyer's demands for a final repository for the waste are "unrealizable and illegal," and says "we will challenge this decision in court." But Stiller estimates it could take several years for a legal appeal to run its course. Moreover, the courts can decide only whether Schreyer's ruling complies with the law; they cannot reverse it. If there is a legal flaw, the whole licensing procedure would have to start over.

Meanwhile, it is costing HMI $1.16 million a month to mothball the reactor. And, to make matters worse, the federal research minister, Christian Democrat Heinz Riesenhuber, has threatened to cut off Bonn's contribution to HMI's budget unless the license is granted; federal funds make up 90% of the $65 million total.

Berlin's senator for science and technology, Barbara Riedmüller, is angry about the delay and the final decision. The HMI is "like a steel mill without a blast furnace," she says. But at this point, there's little that the reactor's supporters can do. Schreyer's decision cannot be overturned by majority vote, since the nuclear licensing procedure, like all planning procedures, is specifically independent of political intervention.

A new government for a unified Berlin, to be elected on 2 December, could find ways to reverse Schreyer's decision, perhaps by rewriting the law. But that would take time, and the uncertainty is already clouding the HMI's future. Researchers have been leaving, and Stiller says the trickle will swell in the wake of last week's decision. Stiller himself had to be lured out of retirement 2 years ago to direct the HMI through these troubled waters. His term ends in December, and although the HMI has been searching for the past 4 years, no successor has been found. ■ **RICHARD SIETMANN**

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