small science, too. An analysis by the American Association for the Advancement of Science (which publishes *Science*), based on NASA's figures, calculates that the agency's 1995 request represents a 7.6% ($143 million) cut in basic research, a category made up mostly of grants to scientists for technology development and data analysis. (NASA's figures, which include mission operations and facilities, show an increase of 2.6% for space science.)

The cuts are likely to fall first on those analyzing data. For Jet Propulsion Laboratory space scientist David Crisp, the 1995 request means the loss of an already approved $140,000 grant to analyze data from Venus. Crisp's grant is a casualty of the cancellation of data analysis programs for Mars, the Voyager flyby of Neptune, and the Magellan and Pioneer missions to Venus. NASA saved $4.5 million by giving Venus the cold shoulder, but disrupted the lives of dozens of scientists. "I spent a month writing the proposal," says Crisp. "I hate to see these things fall by the wayside after they've been approved."

Individual programs have been killed before, but next year NASA will preview a new model that may be used to cut costs from any aging missions. For the first time, the agency will pay to operate spacecraft without funding scientists to analyze the data they produce. The initial round of spacecraft to go that route will be the International Ultraviolet Explorer (IUE) and the U.S. component of the international ROSAT mission. In a last-minute appeal to the White House, NASA won approval to request enough money to save the satellites but not enough to pay for data analysis.

NASA expects scientists somehow to find funding elsewhere to do the analysis, much as they now do for some ground-based observatories, such as Kitt Peak in Arizona. But researchers point out that the National Science Foundation, which supports work at Kitt Peak, is oriented toward ground-based astronomy and doesn't have the resources to pick up the tab for NASA programs.

Jeffrey Linsky, a University of Colorado astrophysicist who heads the IUE user group, says NASA asked the scientists to rank their needs before making the cuts. Keeping the spacecraft operating was at the top of the list, and data analysis grants were at the bottom. "We can't say they didn't follow our priorities," he says ruefully. But the $4-million cut will rob about 200 scientists of a significant part of their funding and eliminate slots for graduate students and post-docs.

And it gets worse. Linsky says NASA has warned scientists that it may adopt this strategy with other astrophysics missions that are already flying, including ASTRO-D, the Extreme Ultraviolet Explorer, and the Compton Gamma Ray Observatory. "This is going to mean an enormous amount of pain for university scientists," he predicts.

Guenter Riegler, head of the science operations branch of NASA's astrophysics division, confirms that the pay-your-own-way model may soon be extended to other missions, but he predicts it will work for only a few years. "After more and more missions get into this mold, the system will break," he says. "Then you have to trade new missions for old ones."

Many space scientists cringe at the thought of turning off productive missions, especially to make way for replacements that could fail. "It's foolhardy to pay to send up things and then turn them off to get money to start new things, which may not get up or work," says Harvey Tananbaum, an astrophysicist at the Harvard-Smithsonian Center for Astrophysics, who heads the AXAF science center. He also points out that the savings from shutting down any but the largest spacecraft would pay for only a fraction of the cost of a new mission.

Nevertheless, NASA officials don't see many other ways to accommodate new missions. "We want to make sure not to turn off missions prematurely," says Huntress. "On the other hand, we don't want to extend them so far—just for the sake of wringing every last drop out of them—such that we don't have enough money for new missions." The approach implies a tough choice: NASA must weigh the benefits of beginning a new program against what will be lost by terminating an existing mission. For the first time, says NASA chief scientist France Cordova, the agency plans to involve the science community in that decision, using interdisciplinary panels of researchers to analyze how much science would be generated by each spacecraft for each additional year aloft.

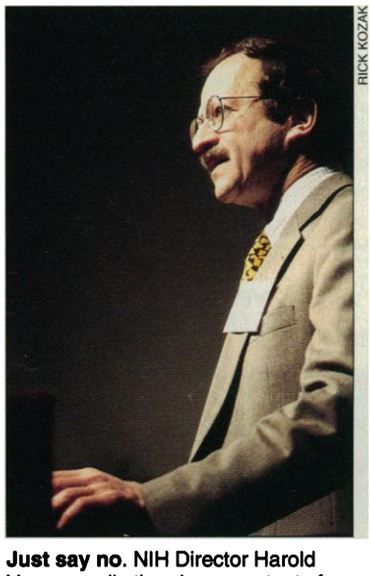
But whatever they do, space scientists cannot escape the fact that NASA has changed the way it does business. And over the next few years, those who observe the heavens for a living may find themselves wishing on a star for money to do their research.

–Christopher Anderson

BIOTECHNOLOGY

NIH Drops Bid for Gene Patents

In June 1991 the National Institutes of Health (NIH) stunned the biotech community by filing for patents on uncharacterized gene fragments sequenced by its scientists. The filings, which NIH officials said were designed to protect the government's rights in case the sequences had any commercial value, spawned a fierce debate about whether anyone could own such fragments, whose functions were not yet known, or whether the sequences should remain in the public domain.



RICK KOZAK

Just say no. NIH Director Harold Varmus pulls the plug on patents for gene sequences.

Last week NIH surprised the community again, announcing that it was withdrawing its patent applications for 6,869 sequences. Director Harold Varmus said patents on such partial sequences are "not in the best interests of the public or science." But the issue is far from dead, because NIH was not alone in trying to patent gene fragments. Several companies have said they are pursuing similar patents, and many others are thought to be doing so privately. These applications are not affected by NIH's about-turn.

NIH's decision leaves unresolved the question of whether uncharacterized gene fragments can, in fact, be patented. Early on, Officials from the Patent and Trademark Office (PTO) told NIH that they planned to reject the patents, which would force the matter to the patent appeals court, where a decision would have greater significance. But NIH dropped the application before the appeals court got the case. It will now be up to private companies to test the legal waters, but their dealings with the PTO are likely to be far more secretive. Indeed, if their patents are rejected, they may keep that information to themselves, on the assumption that acknowledging defeat could depress the price of their stock.

NIH started the ball rolling when geneticist Craig Venter, then at the National Institute of Neurological Disorders and Stroke, sequenced thousands of fragments of complementary DNA (cDNA), which represents expressed genes, as a quick way to get some genetic information without mapping and sequencing the entire genome. Then-NIH director Bernadine Healy, motivated by a congressional mandate to encourage the transfer of federal technology to industry, decided to file patents on Venter's sequences, with the idea of licensing them to

industry if they were found patentable. The move infuriated scientists, who feared that licensing battles over sequences with no known function would slow research for little or no benefit.

Once NIH made its move, others felt compelled to follow. In July 1992 the British Medical Research Council (MRC) filed applications on some 1,200 partial sequences, even as MRC officials argued that the applications should not be granted. MRC later decided not to file for any new patents, however, and last week it, too, withdrew its existing applications.

Although many patent attorneys believed the uncharacterized gene fragments would ultimately be found unpatentable on the grounds they were of little value by themselves, few companies in the gene sequencing business were willing to take the risk and forgo filing applications. For example, Human Genome Sciences of Gaithersburg, Maryland—the commercial arm of a nonprofit research institute launched by Venter when he left NIH in 1992—has filed for 9,900 sequences, according to a recent prospectus. And Incyte, a Palo Alto, California, biotech company, has filed for 40,000 more (*Science*, 15 January, 1993, p. 302). However, given the amount of time and money spent on pursuing the patents, most companies were happy to have NIH lead the way in trying to resolve the issue of patentability as quickly as possible.

Varmus says he and his advisers decided that playing such a role didn't justify pursuing the patents. "Although an appeals process by NIH would probably have provided some decision earlier than would have been possible if we had to wait for other applicants, it was unlikely to be a solid or definitive decision," he explains. He notes that the cDNAs underlying the application were not the best range of sequences on which to base a claim. In addition, he says, "if we had failed in the appeals process, it is unlikely that the decision would have been considered solid, because we might have been perceived as half-hearted in our attempts; certainly the motivation to succeed will be higher in the private sector."

David Galas, the former head of the Department of Energy's share of the human genome project and now scientific director of Darwin Molecular in Seattle, Washington, agrees with those arguments. "If [NIH officials] didn't think that the granting of the patents was in the public interest, then they were put in the position of pursuing with public funds something they hoped they'd lose," he says.

Academic scientists also appear pleased with NIH's decision. James Sikela, a University of Colorado geneticist, says his team has obtained some 3,000 cDNA sequences but has not pursued patents because he believes such sequences should be available to all researchers. "There's a sense of relief that NIH is not pursuing these partial sequences," he says. "It makes things a little less complex."

Varmus says his decision was heavily influenced by Rebecca Eisenberg, a University of Michigan law professor who was part of a panel Varmus convened on 20 December to advise him. Varmus intends to flesh out last week's statement in the next several weeks with a legal brief written by outside patent experts. He says NIH may participate in a forum on the issue under the auspices of the PTO, as well as convening a meeting to discuss the international aspects of the subject. "We do not believe we have settled any questions," he says, "but a brief can serve as a point of reference" for others.

–Christopher Anderson

CANCER PREVENTION

Restating the Risks of Tamoxifen

A much-debated trial of the anticancer drug tamoxifen is heading into stormy seas once again. Prescribed for more than a decade to treat women with breast cancer, the drug is to be given to 8,000 healthy women who have a high risk of breast cancer to see if it can prevent the disease. Some critics fought this trial before it began in April 1992, arguing that this experimental use is too risky because tamoxifen appears to increase the odds of getting other diseases, such as endometrial cancer and deep vein thrombosis. But proponents countered that the endometrial cancer risk is acceptable, partly because tamoxifen appears to reduce breast cancer risk dramatically and partly because uterine cancers can be remedied with surgery if detected early. Now, new data on endometrial cancer mortality among breast cancer patients in one tamoxifen study may rekindle this controversy.

The information has already prompted the National Cancer Institute (NCI) to instruct clinics conducting research on tamoxifen to rewrite consent forms and ask participants to sign again. NCI has also started an "ancillary study" to monitor 800 healthy women in the preventive tamoxifen trial. Researchers will be looking for signs of endometrial cancer, and NCI will pay the costs of following these women closely and giving them yearly biopsies. This is "an encouraging sign," says Trudy Bush, an epidemiologist at the Johns Hopkins University who's concerned about tamoxifen risks. To her, it looks as though NCI is becoming more "responsive."

"We have conducted risk-benefit analyses, and we still find that there is a benefit of going ahead with the trial."

—Bernard Fisher

The complete data on which these actions are based haven't been made public, however, because they are awaiting publication in the scientific literature. Leslie Ford, NCI's project coordinator for the prevention trial, told *Science* she couldn't release the information because it belongs to Bernard Fisher, a surgeon at the University of Pittsburgh and one of NCI's senior extramural researchers. Fisher declined to release the data because he has sent a paper to NCI, which is still in the peer-review process for potential publication in the *Journal of the National Cancer Institute*. Fisher would only say that the new data don't undermine the rationale for the prevention study: "We have conducted risk-benefit analyses," he says, "and we still find that there is a benefit of going ahead with the trial."

Fisher oversees a study of tamoxifen therapy for cancer patients that began in 1981 (the B14 trial), and he serves as principal investigator on the prevention study, known as the Breast Cancer Prevention Trial (BCPT). In December, Fisher's group sent out an alert to all participating BCPT clinics, noting in general terms that "updated information regarding the risk of uterine cancer" from the B14 trial would require a revision of consent forms. The recommended new wording went out on 14 January. Two days earlier, NCI had sent out a more detailed advisory to doctors using tamoxifen in treatment trials.

Both the letter from Fisher's group and the NCI's letter, written by Jeffrey Abrams, senior investigator at the Clinical Trials Evaluation Program, indicate that patients in the B14 trial appear to have a risk "approximately three times greater than that of a similar group of women in the general population" of contracting endometrial cancer. This is at the high end of the range researchers had predicted. But there were more deaths than expected: Abrams' letter says four of the 23 women with uterine can-