obvious areas of concern to his office, but he also expects OSTP to play a role in what he sees as one of the greatest crises of the next decade—life-extending technology. "We are rapidly approaching the time when we are going to have to withhold technology from some of the dying," Bromley told *Science*. "And we don't even have a fully developed value system for even beginning to figure out how to do that ethically." This, Bromley argues, is an area in which basic science and technology must "make common cause" with the "social sciences, with humanists, and with religion."

Before taking office Bromley recognized that if OSTP is going to be in a position to influence national policy, let alone take the lead, he would have to have staff and resources that surpassed those of his predecessors. In that he appears to be successful. Bromley has turned to senior hands to staff three of the four "associate director" positions he has created.

To fill the biomedical post—a long neglected area in OSTP—Bromley has recruited James B. Wyngaarden, former director of the National Institutes of Health. J. Thomas Ratchford, associate executive officer of the AAAS for the past dozen years, is slated to be Bromley's right-hand man for policy and international affairs. And the word around town is that Berkeley engineer Eugene Wong will be nominated as associate director for physical sciences and engineering.

That leaves just one top post vacant and Bromley acknowledges that he is having a tough time finding a seasoned researcher/administrator from industry to head activities related to industrial technology. "The problem is not comparatively low federal salaries," Bromley says. "People who want to perform government service can live with that. But the new financial disclosure and divestiture requirements make it very hard to attract the best people. It will just take time," he says.

Meanwhile, Bromley is busy going about his business of getting to know everyone he can in Washington and letting them know he wants to hear from them. A series of breakfast meetings with members of Congress has gotten under way, with help from the "science" members of the Senate—Al Gore, Jay Rockefeller, John Danforth, Jeff Bingaman, and others. Bromley has met with congressional staff members and he meets regularly with Richard Darman, director of the Office of Management and Budget, so that "OSTP is part of the budget process from the start of the cycle."

All in all, one of Bromley's main tasks right now is "building bridges," and he is going about it with a will.

■ **BARBARA J. CULLITON**

Plan for Genome Centers Sparks a Controversy

NIH is planning to set up targeted research centers to map and sequence the genome—a move that is setting off alarms among biologists

San Diego

IN JULY, the genome office at the National Institutes of Health took its first, halting step into the era of "big" biology. It announced that it would create special labs or centers, each with perhaps 25 investigators, to puruse the task of mapping and sequencing the human genome. What that means is that a good share of the genome project's budget—eventually half, predicts James Watson, the project's director—won't go to investigator-initiated science but to these new centers.

That's enough to send shivers throughout much of the biological community.

"Jim Watson is trying to change the social fabric of science. It's World War II and directed science all over again," grumbled one participant at a recent NIH workshop on centers.

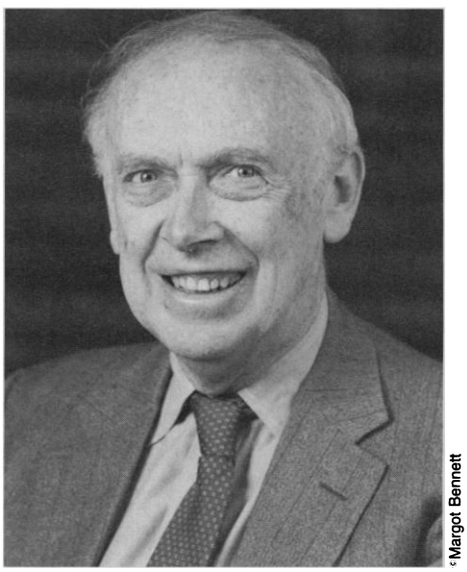
Not so, responds Watson, who says he is simply trying to get the job done. The "job" is to map the chromosomes within 5 years and to decipher the full nucleotide sequence, all 3 billion base pairs, within 15 years—and at a total cost of no more than $3 billion. "If we go along the way NIH usually does, it could easily take 100 years to get the sequence," said Watson, who outlined NIH's plans in San Diego last week at the Human Genome 1 meeting sponsored by *Science*. Moreover, the cost of doing business as usual would be prohibitive. "We really owe it to the scientific community to keep the cost down," he said.

"People want to do this with a cottage industry approach," Watson told *Science*, "but I don't think it will work. I'm not trying to take away RO1s [investigator-initiated grants] but to create something new."

Many scientists aren't impressed. Since NIH issued its request for applications, Watson and his staff have been inundated with complaints. Some investigators oppose centers outright. Others agree with Watson that something different is needed for the genome project, but don't believe that these centers, at least as originally proposed, are it. And there is lots of grumbling about whether it is wise to invest all that money in a few groups (especially if yours is not among them).

The complaints seem unlikely to deter institutions from lining up for a piece of the pie. Some 20 teams showed up at the recent NIH workshop for grant applicants, suggesting that competition for the first three grants for next year will be fierce.

Watson cites both Cold Spring Harbor Laboratory, where he remains as director, and MIT's Whitehead Institute as evidence that centers can work. But he acknowledges that some units set up to fight the war on cancer have poor reputations. With his characteristic bluntness, he told the workshop attendees: "We all know how fraudulent most centers are."



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James Watson: *"We all know how fraudulent most centers are."*

Norton Zinder of Rockefeller University, who chairs the NIH genome advisory board, matched Watson's outspokenness: The issue, he told *Science*, is how to avoid creating a monster—and how to kill it if you do. "In the past, centers were like werewolves—you couldn't kill them. And a lot of them go bad."

That makes decisions on how to structure these centers and ensure accountability ex-

tremely important. But the proper directions are not entirely clear even to NIH, which is, by necessity, making up the rules as it goes along. "This is a way biology has never been done before in the United States," says Shirley Tilghman, a mouse geneticist at Princeton who served on the National Research Council committee on the genome project.

What Watson envisions is a group of perhaps 25 or 50 people working toward a sharply focused objective—say the sequence of the nematode *C. elegans* or yeast, to start with. The goal is not so much getting the sequence per se, he says, as it is to demonstrate that it can be done cheaply. As Watson described it at the San Diego meeting, what he is looking for are strategies that will drop the cost of sequencing from its current $5 to $10 a base to 50 cents or so, which is what it will take to complete the human genome for $3 billion.

Watson also wants centers dedicated to completing physical maps of various human chromosomes. But it is sequencing that needs the biggest push. "The mapping is going to get done," he says, citing the remarkable progress in just the past year in developing new mapping strategies (*Science*, 29 September, p. 1439).

In terms of funding, NIH expects to get $8 million, out of a budget of $62 million, for centers in 1990—enough to get three or so off the ground. Over the next 5 years, Watson expects to establish 20 such units—not just at universities but in companies as well.

If these centers are to work, says Watson, they will need strong leaders—not an administrator but a top scientist "with a track recording of getting things done." He adds: "If you don't have someone with slight monomania, you can go sour."

Peer review, too, will have to be unflinching. Each of the research projects proposed in a center application will be reviewed separately, says Elke Jordan, deputy director of the NIH genome center. "You don't have to carry along research that is not that strong; you don't have to fund a project because it has been submitted as part of a center grant."

Then comes the hard part: ensuring quality may ultimately come down to being hard-nosed enough to kill those centers that aren't working. Quips Zinder: "We have to have the courage to 'just say no.' " That would represent a break from past practice. As Jordan readily admits, reviewers have often been reluctant to pull the plug when a center is no longer performing cutting-edge work. To help avoid this, the genome office plans to review the centers 3 years into a 5-year grant, which would leave investigators 2 years in which to find additional support if necessary.

Princeton University

Shirley Tilghman: *"The actual work . . . will be done in a way we have never done biological research before."*

Amidst all this brave talk, no one is quite clear on exactly how the centers themselves will be structured. Indeed, NIH was put in the somewhat embarrassing position of issuing a request for applications and then essentially recalling it.

"The best posture you could put on it is that the announcement was a first pass," concedes Mark Guyer of the NIH genome center. "The worst is that we don't know what we are doing."

At first, the genome office, assisted by its program advisory committee, came up with a model known as a core center, based loosely on the structure of existing cancer centers. The way this would work is that NIH would provide money for core facilities—say a sequencing or cytogenetics lab and shared equipment—but investigators would obtain their own grants. It would essentially be a collection of independent investigators who are pursuing a similar goal.

Several of the people who advise NIH on these matters hated the idea. In fact, it was trounced at a retreat at Cold Spring Harbor in late August, where NIH and DOE officials, along with 25 prominent biologists, met to plan the next 5 years of the genome project. The problem, the critics said, is that such a structure would be too loose to achieve the specific goals of the genome project.

One of the more vocal critics was David Botstein of Genentech. "The genome project has a series of real goals, real requirements, and real work to get there," he said in an interview. "The cancer model didn't work that way. We really need a different structure in which the funds are tied to the goal."

To Princeton's Shirley Tilghman, the model didn't pass the acid test of accountabilty. "My major concern is peer review and accountability. There has to be a way of deciding at regular intervals that the center is heading toward its goal at good speed."

Another problem with the cancer center model is that, at most institutions, there simply aren't enough people with genome-related grants already in place to constitute a center.

Heeding the complaints, the genome office has crafted another request for applications describing a new type of center, in addition to the first. This second model is known as a specialized center, or a P50 in the grants vernacular, and in it, research as well as core facilities are funded directly by the center.

But even these troublesome questions about the initial organization of centers pale before the management problems that may have to be faced when the nitty-gritty work of the genome project actually begins.

Right now, as investigators are devising new strategies for mapping and sequencing, the work is exciting and creative. But, says Tilghman, "in the fairly near future, the work needed to generate a physical map won't be creative or ground-breaking science funded through an RO1. Once the community settles on what is an effective way of generating a physical map, there will be a huge amount of extremely excruciating data gathering that no self-respecting post doc or graduate student will participate in."

"The actual work," Tilghman adds, "as opposed to technology development to make it possible, will be done in a way we have never done biological research before: technician-oriented, hard-slogging, and not much fun."

And that means, Tilghman says, that the project will have to be organized in a different way. "What it comes down to is a single person has to be accountable for progress toward the map." The difficulty of that managerial task—of riding herd over technicians and keeping them motivated—she says, should not be underestimated.

"I still don't know," she opines, "who will want to take on this job and do it, not just accurately, but with a little flair and creativity." ■ LESLIE ROBERTS