JS genome head faces charges of conflict

- Watson expected to leave this summer
- Feud with Healy, Bourke led to showdown

Washington

NOBEL Laureate James Watson, the director of the US National Institutes of Health (NIH) genome project, is under investigation for alleged conflict of interest and is expected to resign his position rather than fight what his associates say is a concerted campaign to unseat him.

NIH officials say that Bernadine Healy, the NIH director, has raised concerns about stock that Watson owns in biotechnology and gene sequencing companies that she feels represents a possible conflict of interest. Healy reviewed Watson's files and told the agency's ethics officer, Jack Kress, about a number of such holdings. Kress, who met with Watson on 24 March, believes that Healy could resolve the conflicts by simply signing a waiver to allow Watson to keep the stocks. But Healy "has concerns about signing a waiver" and is reluctant to make such an exemption given the volatile nature of the issue, according to her spokeswoman, Joanna Schneider.

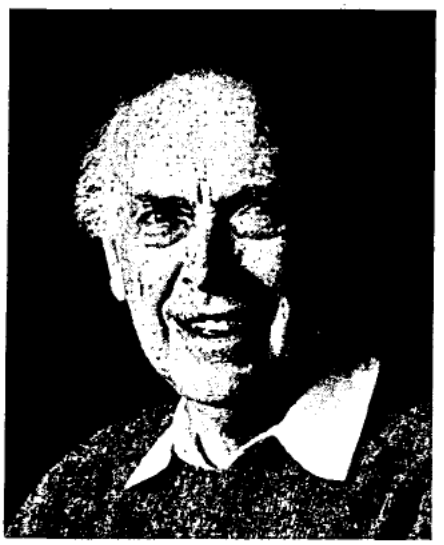
Although Watson could sell the stock in question and resolve the issue, he has told associates that he instead will resign, perhaps as early as 1 August. Contacted at home early this week, Watson said he had been forbidden to talk about the situation and would not comment further.

Watson's associates are concerned that the alleged conflict of interest is merely a smokescreen. They believe that last month's showdown marks the latest turn in a running feud between Watson and Healy that has been fanned by Watson's vocal opposition to Healy's decision to file a patent for DNA sequences last summer (*Nature* **353**, 485; 1991) and his attempts to derail a gene sequencing company proposed by Frederick Bourke, a wealthy entrepreneur (*Nature* **355**, 483; 1992).

Known for his outspoken and often acerbic leadership of the US genome project, Watson's three-year tenure at NIH has been controversial from the start. But in opposing Bourke, who is friendly with several prominent politicians in Washington, including Senate Majority leader George Mitchell, Watson appears to have made one enemy too many.

Bourke has been trying to sign up two prominent gene sequencing researchers — Robert Waterston of the Washington University in St. Louis and John Sulston of the UK Medical Research Council (MRC) Laboratory of Molecular Genetics at Cambridge — as the core of his new company. Watson feared that such a move might halt one of the most productive collaborations in the genome project and has tried hard to block it.

For example, in February Watson met with MRC officials in Britain to urge them to give Sulston more money to keep him in place. MRC apparently agreed. Sulston has not joined Bourke's company (which is not yet incorporated or named) and the MRC is planning to increase Sulston's funding significantly, although it has not released any details.



Watson may resign over charges.

While in Britain, Watson also met with officials at Glaxo, the British pharmaceutical company. Accounts of the meeting differ, but Bourke, in a letter last month to Healy and White House officials, alleged that Watson encouraged Glaxo to start its own gene sequencing company centred around Sulston. Such a step would have pre-empted Bourke's plans. In his letter, the details of which have been confirmed by several sources, Bourke also alleged that Watson owns some Glaxo stock and stands to profit should the new venture become a success.

Late last month, after receiving the Bourke letter, Healy passed the allegations on to Kress. "She has a concern about the appearance of, and actual, conflict of interest" in the charges, says NIH's Schneider. "The public deserves to know that there is no conflict of interest — that's Dr. Healy's responsibility."

But Kress disagrees, and says that he found "no substance" to Bourke's charges. The allegations "gave me pause", he says, "but after talking it over with Dr. Watson, I was satisfied that there was no conflict."

Because Watson continues to serves as director of the Cold Spring Harbor Laboratory, which receives NIH funding, he has already removed himself from the NIH grants process. Although Kress dismissed the allegations contained in the Bourke letter, he determined that some of Watson's other stock holdings might pose a conflict because of the impact of Watson's decisions on the entire biotechnology industry. He says he intended to recommend a waiver after a second meeting with Watson this week, despite Healy's resistance to such a resolution.

Kress confirmed that Watson told him he was planning to resign over the issue. But he emphasized that "there is no ethical reason for him to leave. I am in no way, shape or form recommending that he step down based on anything we discussed."

Watson is said to be treating Healy's ultimatum as a virtual sacking. Schneider says Watson has not been fired. "It's not as sinister as it seems," she says, "but there were some concerns expressed that need to be looked into. Some very difficult decisions are going to have to be made."

Although his associates say that Watson periodically has threatened to resign as a negotiating tactic, they say that this time is different. Norton Zinder, a Rockefeller University geneticist and former chairman of Watson's genome advisory panel, describes the clash as "a political in-fight that has unfortunately reached an impasse."

Earlier this year, NIH officials reviewed Watson's files and found that conflict-of-interest concerns had been raised several times over the past few years. But there is no record in the files of any waiver or other resolution of the issue, according to one official. Bourke's letter appears to have reinforced Healy's resolve to confront Watson on the issue. Watson's "relations with Healy have never been good," says Rich Roberts, Watson's deputy at Cold Spring Harbor, "but the letter from Bourke may have been the last straw."

Researchers are concerned that their feud may damage NIH and the genome project. Coming only days after congressional hearings on the agency's budget, and during a year in which funding is already squeezed by economic concerns, a battle between Watson and Healy could mean a leadership vacuum that costs both the agency and the genome project millions of dollars. Both Zinder and Robert Cook-Deegan, an analyst at the Institute of Medicine and a confidant of Watson, say they have urged Watson to remain on the job until the agency's funding is set, probably sometime in early autumn. But Kress says that Watson "is feeling the crush" and will probably resign sooner than he had planned.

Christopher Anderson

The Genome Project: Life After Watson

The Nobelist's abrupt departure from a project he has personified for 3 years leaves researchers wondering what kind of a leader the effort needs now

On 7 May 1991, James D. Watson stood in front of a hostile crowd at a packed auditorium in Dallas, Texas. The occasion was the annual meeting of the American Society of Microbiologists, and Watson had been invited to give a talk about the human genome program. Many of the microbiologists were skeptical about the effort: They saw it as an expensive boondoggle, soaking up research dollars at a time when resources were particularly scarce. Watson gave what had become his standard stump speech, explaining the importance of the project to the future of biomedical research. But he reassured the skeptics that the Human Genome Project would not be a blind, brute-force effort to sequence all 3 billion bases in the human genome, no matter what the cost. And he patiently answered questions about why the time was right to start such a large undertaking.

"He disarmed them," says Stanford geneticist David Botstein, who was at the meeting. Although Watson was delivering a message that many in the audience didn't want to hear, Botstein says they listened—and were persuaded largely because Watson is a hero to many of them. Afterward, as Botstein describes it, the microbiologists crowded around Watson "almost as if he were a rock star," anxious to have a word with the man who helped launch a new age of biology.

No, James Watson did not singlehandedly launch the human genome program, but, probably more than anyone else could, the 64-year-old Nobelist gave it instant credibility—both among scientists and the public. Not only was he the program's staunchest cheerleader, but Watson's fans say that, as head of the National Institutes of Health's National (NIH) Center for Human Genome Research, he played a critical role in holding together an often fractious amalgamation of researchers, bureaucrats, politicians, and foreign partners that made the project go.

But, famed for his blunt style, Watson has not always been the smoothest operator. He's had legendary run-ins with key researchers and government officials—including NIH Director Bernadine Healy, which led to his abrupt resignation last month. "He was intemperate from time to time in the way he spoke publicly about the project in relationship to his opponents and to the contributions of the Japanese," says one academic who has studied the genome program's origins.

Watson's abrasive management style has left the project with a clear direction, momentum, and a substantial budget. But the project's future is still far from assured.

A tough balancing act

Whoever follows Watson—and several names are already beginning to surface—will still have to contend with the project's influential critics. People like Harvard microbiologist Bernard Davis remain concerned about how useful a complete sequence of the human genome will be. They also worry that the effort has been oversold: Congress and the public may have been led to expect a cure for all genetic diseases once the sequence is known, an expectation researchers obviously will not be able to meet. And, with a budget now running at $164 million a year—split between NIH ($104.9 million) and the Department of Energy (DOE) ($59 million)—it has become highly visible on Capitol Hill. Unless Congress can be assured that the program is in good hands, friends of the program such as Norton Zinder of Rockefeller University worry that the political support the effort has enjoyed until now could dissipate in these tough fiscal times.

PETER MENZEL

Blunt operator. Watson shaped the project's public image and its scientific content.

If the critics outside the program can be satisfied—no small task—that still leaves the critics inside the program. Watson is widely credited with shaping the effort scientifically—sometimes over the opposition of researchers who want to see a different emphasis and others who argue that it should support far more investigator-initiated research.

The course of the project was formally charted at a joint meeting between DOE, NIH, and extramural scientists in 1989. By 1995, it was expected to accomplish several discrete goals:

- a high-resolution genetic map of the human genome;
- a complete physical map of certain model organisms and a start on physical maps of human chromosomes;
- the development of new technologies to increase the efficiency and accuracy of mapping and sequencing and to lower the costs.

Watson was a strong advocate of the need to create a physical map of the genome so that researchers could go directly to the appropriate spot on a chromosome when they found an interesting gene. "If you don't have a physical map, you're going to run up against a problem," says Watson. Initially, critics thought Watson was trying to commit enormous resources to what many thought would be a trivial task. "A lot of people in the nonmapping community thought that it was a no-brainer," says medical geneticist David Cox of the University of California at San Francisco (UCSF). But, says Cox, "people involved with mapping realized that this was a nontrivial exercise," and he says that without a strong commitment from Watson, physical mapping would have gone nowhere. Now Cox predicts it is about to take off.

Watson was also convinced that model organisms would play a crucial role in the genome project, another area that is currently paying significant dividends. A collaboration between John Sulston and Alan Coulson of the Medical Research Council's Laboratory of Molecular Biology in Cambridge, England, and Robert Waterston of Washington University in St. Louis has completed a physical map of the nematode *Caenorhabditis elegans*, and a sequencing effort is likely to be scaled up soon (see sidebar, p. 958).

Progress toward the third goal—the development of new sequencing technologies—has been more disappointing. Caltech's Leroy Hood argues that Watson did not devote adequate resources to new technology development in the genome centers he established. "I would argue that half the funds that a center gets should be put into technology

development," he says. Although there are some promising approaches, such as using mass spectrometry and a DNA "chip" (*Science*, 27 September 1991, p. 1489) to determine sequences, there have been no "breakthroughs" on the sequencing front that will speed things up (or lower the cost) in a way that would make starting a large-scale sequencing program practical.

But, Hood adds, even "if I gave you tomorrow a DNA sequencer that could do 50 times the throughput of sequencing, in many ways it wouldn't do you any good. The front end of producing the fragments for sequencing, and the back end of the computational tasks have to be matched," he says. "So there's this enormous task of systems integration which has largely been ignored."

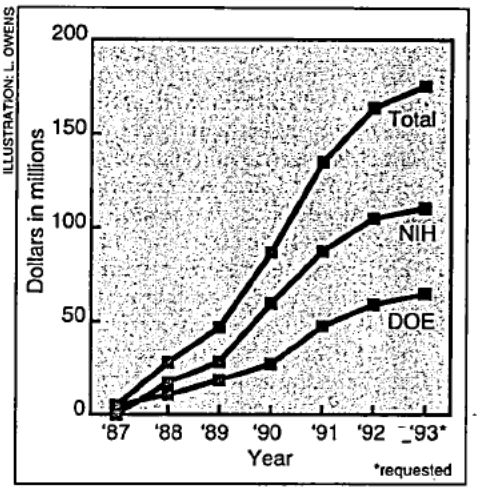
Big vs. small science

Hood's complaint lies at the core of the debate that the next director will have to resolve: how to balance small science that usually fosters innovation with the larger infrastructure needed to complete the genome project. The European Community has proceeded with a kind of "cottage industry" approach to the yeast genome (*Science*, 8 May, p. 730), but even proponents of that scheme admit it is not the most efficient way of getting the job done. So Watson, along with DOE, decided to establish larger centers.

There are now seven NIH-supported centers scattered around the country, and they account for about one-quarter of the NIH genome budget. Their share of the project is expected to grow, and that, says UCSF molecular biologist Bruce Alberts, is bound to cause political problems: "They are going to need more support than they have, and more support than the community would like, because it's the kind of support that most of us never get." Maynard Olson, a physical mapper at Washington University, agrees. Olson, who will leave St. Louis next fall to join a large genome effort being organized by Hood at the University of Washington in Seattle, says there is a reticence to move away from investigator-initiated projects: "There are many people in the American scientific community who will support small mediocrity before they will even consider the possibility that there can be some large excellence."

But in the minds of many, the move toward big genome centers is keeping people away from the genome project. Craig Venter, a sequencer at the National Institute of Neurological Disorders and Stroke, is a proponent of a distributed structure for the program. Venter, who caused a stir by applying for a patent on several thousand gene fragments without knowing the biological function of the proteins the genes coded for, says bigger isn't better: "People were told, 'If it isn't going to be large scale, don't apply here. If you're not going to sequence 2 million bases, don't send in an application because it will get turned down,'" says Venter. "As a result, nobody has sequenced 2 million of anything."

Stanford geneticist Paul Berg, who chairs the NIH Program Advisory Committee on the Human Genome, agrees that the next director should listen to what smaller labs say they can do for the genome project. Berg argues that more of the budget should be spent on pursuing the interesting biology that is discovered as scientists work on maps and sequences—a belief that put him at odds with Watson. "Clearly, Jim and I differ in that way. Jim says if you want to get the genome project done, you've got to keep people's nose to the grindstone, and not let them go off on tangents to satisfy their curiosity," he says. "I think that to maintain interest and excitement about the program, we have to link it to [gene] function in some way."



Reaching a plateau. Federal funding for the genome project, split between NIH and DOE, has begun to level off.

"Paul Berg has never really understood the point of the thing," says Watson, betraying the blunt style that some find off-putting. "He thinks we should be spending some of our money on gene function. I don't think so. We're there as a resource for other people. So if you want to study your gene, that part of the chromosome is already at hand, and you don't have to isolate it yourself."

Wanted: working scientist

What kind of leader would be able to satisfy all the constituencies that make up the ge-

A Standing Ovation From the Troops

James Watson may have rubbed some researchers the wrong way with his blunt, abrasive style during his 3-year reign as head of the Human Genome Project at the National Institutes of Health. But, to judge by the reception he received last week from more than 450 scientists gathered at the Cold Spring Harbor Laboratory for the annual genome mapping and sequencing meeting, his leadership will be fondly remembered. In what was clearly a bittersweet moment for all concerned, Watson made a brief appearance before the overflowing crowd, which gave him a standing ovation.

"I had wanted to quit—but not necessarily the way I did," said Watson, in an obvious dig at NIH Director Bernadine Healy, who Watson says forced him out—a charge Healy roundly denies (*Science*, 17 April, p. 301).

Then Watson had a few words of advice for his successor: Whoever takes the job must be willing to fight for more money amid a chorus of demands for more support from other areas of biology, he said, adding in vintage Watson style: "All science isn't equally interesting. Getting the human genes and the other genomes is the most important thing in biology."

That kind of passion is just what the project will need in its new leader, says Maynard Olson, a physical mapper who will join the University of Washington this summer—and Olson should know: just last week he was appointed by Healy along with 13 other top scientists to act as a search committee (see accompanying story).

Watson, in any case, is convinced that he's handing the project over in good shape, a conclusion he said is evident from last week's meeting—with its 350 talks and posters. Even though large-scale sequencing still lags behind expectations, mapping is clearly going full tilt, and some notable advances were reported, including an all-but-complete map of the Y chromosome, done by David Page's group at the Whitehead Institute; the mega-YACS, or yeast artificial chromosomes, developed at the Centre d'Etude du Polymorphisme Humaine in Paris (without NIH funding), which promise to speed genome mapping worldwide; and the extensive maps of the mouse genome developed by Eric Lander's genome center at the Massachusetts Institute of Technology. "It has been an American success and an international success, and I am very pleased," said Watson.

—Leslie Roberts

Britain Plans Large-Scale Sequencing Center

LONDON—While U.S. researchers debate the future of the genome project without James Watson, the Wellcome Trust—Britain's largest medical research charity—is laying plans for a bold step into large-scale gene sequencing. Last week, the trust announced that it has asked geneticist John Sulston, a senior researcher at the Laboratory of Molecular Biology (LMB) in Cambridge, to submit a proposal for a new multimillion-dollar center for human gene sequencing. Why Sulston? He's been using the latest automated gene sequencing technology to tackle the genome of the nematode *Caenorhabditis elegans*. And now that the nematode project has shown the potential of this production-line approach, the Wellcome Trust sees the chance to turn Britain into a major player in human genome sequencing.

MRC

John Sulston

Sulston declines to discuss the details of the plan until he has completed his proposal, saying only that the center would be built around a team of about 30 people working on a scaled-up version of the *C. elegans* project. They would churn out about five megabases of completed nematode sequence a year—about five times the present output of Sulston's group at LMB. The center's human gene sequencing effort could start off at about the same level, says LMB director Aaron Klug, who has been involved in discussions with Wellcome Trust officials. Over time, this could be ramped up substantially, he adds, prognosticating that "this technology could be and should be applied to the human genome on a massive scale."

To broaden the center's outlook, Sulston hopes that he will pull in gene mapping groups, and he intends to expand his group's existing work on genome databases, making his proposed center one of "the largest [genome] facilities in the world." If all goes well, the center could open—initially in rented accommodations in Cambridge—by the end of the year.

Sulston's decision to concentrate on launching a genome center in Cambridge kills speculation that he and his collaborator on the nematode project—Robert Waterston, from Washington University in St. Louis—will join a commercial sequencing company in Seattle. Before resigning, Watson had gotten into a bitter tussle with entrepreneur Frederick Bourke, who planned to set up the company with advice from gene sequencing pioneer Leroy Hood, who moves to the University of Washington in Seattle later this year (*Science*, 7 February, p. 677). Watson violently opposed the idea of moving the nematode project—one of the few truly international collaborations in genome research—into the private sector. Now Waterston says that discussions with Bourke had broken down in any case: Bourke's interest was in commercial contract sequencing and applying the technology to medical diagnostics, rather than the "pure genomic sequencing" that he and Sulston want to pursue.

This should be welcome news to the wider genome community, which seems to agree that there is a demand for the type of center that Sulston is planning. Doug Higgs, from the Institute of Molecular Medicine in Oxford, for instance, wants to sequence the end of chromosome 16, which contains the alpha-globin gene cluster. "I'm not really interested in the technology and the handle turning," he says, so if Sulston's planned center could do the job, that would be ideal.

The proposal also comes just as Sulston's employer, the UK Medical Research Council (MRC), is due to launch a far-reaching review of the British genome project, which will be 3 years old this summer. The MRC hasn't yet funded large-scale human gene sequencing but views the *C. elegans* work as a pilot project to reduce costs and refine the technology. If the Wellcome Trust does decide to back Sulston with a multimillion-dollar budget for human gene sequencing, however, this is bound to color the MRC's plans. The MRC is already bidding for government funds to expand Sulston's *C. elegans* work and is now setting up a joint working party with the Wellcome Trust to discuss Sulston's proposal.

Whether Sulston's center will be among the leaders in the race toward production-scale human gene sequencing now lies in the hands of referees and the Wellcome Trustees, who will reach a decision later this summer. But, given that the trust has taken the unusual step of making a public announcement about the project even before receiving a formal proposal, the betting is that Sulston can trust he's about to get a warm welcome.

–Peter Aldhous

nome project? In addition to coping with the varying interests within the U.S. scientific community, the new director will have to be willing to play the role of diplomat. He or she will not only have to keep enthusiasm—and funding—for the project high, in this country and abroad, but will have to try to prevent any country, including the United States, from becoming excessively proprietary about the work its scientists are doing. "That's part of the reason why somebody like Watson is so essential, says Alberts. The new director should be "somebody with credibility who knows what's going on and can give people confidence that this is quality stuff."

Last week, three of the major players in the project flew to Washington for a private talk with NIH Director Healy—who will choose Watson's replacement—to discuss where the project is headed and who might lead it there. Healy doesn't want to second-guess her search committee, but, according to one of the scientists, everyone, including Healy, seemed to agree that rather than a senior statesman, the new head should be a practicing genome researcher who can command the respect of the scientific community. Moreover, the scientists said they wanted someone firmly grounded in medicine who can understand—and, more important, convey—just what this vast project means for human health. Some of the names being discussed at a meeting of genome researchers held last week at the Cold Spring Harbor Laboratory included UCSF's David Cox, Nancy Wexler of Columbia University, and, most frequently, Francis Collins of the University of Michigan.

Whether one of these three—or anyone else—would take the job, should NIH come calling, is another matter. But already, discussions are under way about setting up an intramural genome program that would allow the new director to continue his or her research, at least part time, at NIH.

NIH announced last week that Ruth Kirschstein, director, National Institute of General Medical Sciences, and George Vande Woude, director, Advanced Biosciences Laboratories Basic Research Program, will co-chair a search committee to find Watson's replacement. Acting director Michael Gottesman says Healy told him to be prepared to stay in that capacity for at least 6 months. The program's momentum should carry it along for that duration without difficulty, but if by the new year the interregnum has not ended, the babble of differing opinions about how to proceed may reach a deafening roar, and make leading the genome chorus a nearly impossible task.

–Joseph Palca

With reporting from Leslie Roberts at Cold Spring Harbor.

HGP

some of Brazil's overseas debt into obligations of restraint. Countries such as the Netherlands have already embarked along that route. The biodiversity treaty is a framework within which more comprehensive agreements might be reached, for the Amazon and elsewhere. But everything is a special case, requiring special study. That should be the cornerstone of the way in which the biodiversity treaty functions. Meanwhile, Mr John Major, the British prime minister, is surely right to advocate a programme of more vigorous taxonomic research in regions such as the Amazon (and it is needlessly mean, even by its own standards, for British Friends of the Earth to describe his Rio speech as "empty waffle").

None of this touches the poverty of the poor. Strong's fault is that he has encouraged, especially among the governments of the developing countries, the belief that compensation for custodianship will meet the capital costs of development. That is a gigantic and cruel mistake, especially with a Rio agenda innocent of the issue of population growth. But is not rapid population growth in the developing countries itself a consequence of their poverty? Nobody disputes that in the rich world, the benign demographic transition from high to low rates of birth and death has invariably followed rising prosperity and improved public health. Yet many governments of developing (and quickly growing) countries could be trying harder even as things are. Sooner rather than later, there will have to be a UN conference on that issue as well. □

Moratorium ending

The impending Washington summit has a daunting list of nuclear issues that must be tackled.

Now that the Cold War has ended, why does nuclear testing continue? That is an issue raised this week by the executive committee of the Pugwash Organization which, unlike other international pressure groups, is almost laconic in what it says in public. Specifically, Pugwash has taken fright that it will soon be a year since President Mikhail Gorbachev (remember him?) volunteered, on behalf of the Commonwealth of Independent States, a one-year moratorium on testing. Since then, President Boris Yeltsin had said that Russian tests will resume when the moratorium expires in September. Pugwash asks that the moratorium should be extended at the Washington summit this week, and that the United States should join in.

That, of course, would be an excellent development; there is more than an element of the bizarre in the continued and repeated testing of weapons whose purposes have been confused (or even made nugatory) by the events of the past few months. But, sadly, the summit planned for Washington has even more urgent nuclear business to attend to. Plans for a further bilaterally agreed reduction of strategic arms appear to have foundered on the issue of missiles carrying several warheads, while confusion persists about the role of Russia as the nuclear custodian of other ex-Soviet republics, the Ukraine conspicuously, but also Khazakstan. Will they eventually become members of the Nuclear Non-Proliferation Treaty (NPT), and if they do, will it be as nuclear or nonnuclear powers?

That question cannot be left unanswered for much longer. Three years from now, the NPT will lapse unless its members elect for its continuation (and for the restrictions it imposes on them). Already there are worrying signs of renewed hankering after independent facilities for making bombs — Iraq last year, reports of attempts illicitly to sell ex-Soviet fissile material by Vienna-based agents only last week. The big danger is that the nonproliferation regime will turn into a leaky sieve long before its sponsors (Russia, presumably, still among them) have worked out a way of selling its virtues to the nonnuclear members of the treaty. A moratorium on testing would help powerfully in that direction. □

Genome propaganda

Concealing the truth without lying is an old art, now spreading in the US human genome project.

By now there can hardly be a researcher who has not heard some account of the unfortunate circumstances behind the resignation in April of Dr James Watson as director of the US human genome project. But the account of the resignation in the current issue of *Human Genome News*, the project's official newsletter, recalls the old propaganda technique of reporting the facts without telling the truth. Nowhere does this account mention what most readers already know from other sources, that Watson resigned after Bernadine Healy, the director of the National Institutes of Health, launched an investigation into his financial holdings. Not even reading between the lines provides a hint of friction between the two.

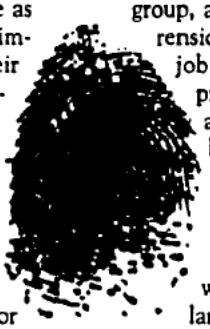
Instead, the newsletter treats Watson's departure as a routine transition. It quotes him to the effect that directing both the genome project (based in Bethesda, Maryland) and the Cold Spring Harbor Laboratory (in New York state) had become too burdensome for him and his family. It also notes that Watson had told his advisory committee as early as last January — before the controversy arose — that he was thinking of leaving. Although that is true, it is also true that the very press officer who wrote the newsletter account told reporters at the time not to take the comment too seriously; Watson often threatens to resign, she explained.

No one expects the genome project's official newsletter to wallow in gossip. But by pretending that there was no dispute at all — when even Healy was willing to discuss the situation openly — the newletters belittles its reseearcher-readers, who are grown-up people and who deserve an accurate and balanced report, and reflects badly on the credibility of the enterprise. Perhaps the lesson from this shabby episode is that the $7 million a year the United States is spending on the ethics of genome research is not enough. □

HGP

hilip Reilly, a lawyer and geneticist at the hriver Center for Mental Retardation in Waltham, Massachusetts, the Lander camp held sway, and early drafts of the statistics chapter were very conservative. In fact, two committee members were so disgruntled that they leaked an early draft of the statistics chapter to FBI scientist Bruce Budowle, prompting outraged letters from his boss, John Hicks, director of the FBI's crime laboratory. Having Lander coordinate that chapter is like having "the fox guarding the hen house," Budowle complained to *Science*.

The final product, committee members agree, is a more moderate one that they all could live with. The evolution came not from a change in politics or external pressure as sometimes alleged, the members say, but simply from new data that emerged during their deliberations. In the final version, the committee does assume that population substructure exists, as the cautious camp argues, but they devised a "practical and sound" approach for accounting for it: using the multiplication rule, but in combination with what they call the "ceiling principle." This, they say, will ensure that the frequency estimates are biased in favor of the suspect.



It would work this way. First crime labs must establish the ceiling, or upper bound, frequency for each allele at each site in 15 to 20 genetically homogeneous populations, such as English, German, Russian, Vietnamese, and Puerto Rican. This would be done by collecting blood samples and establishing cell lines from 100 individuals in each population. When it comes time to calculate the odds of a match, the lab would use the highest frequency found in any of the populations, or 5%, whichever is higher. Collecting the samples should take about a year and cost about $1 million, says McKusick. In the interim, the group recommends a shortcut—using the highest frequency found in any of three major population groups in the United States, or 10%, whichever is higher.

The end result, says study director Oscar Zaborsky, is that the most "extravagant" probability estimates will be replaced with numbers in the range of 1 in several hundred thousand or a million. "It tones down the hype but will still be useful." Lander agrees: "It is sufficiently conservative, yet sufficiently usable. I don't think anyone would fight it."

In a number of far less contentious recommendations, the committee came out strongly in favor of mandatory accreditation of DNA typing labs and mandatory proficiency testing. The problem, the committee says, is that this new technology burst on the scene so rapidly that there are essentially no standards and no regulation—a disturbing prospect since the largest potential source of error lies in poor laboratory practice. The group urges Congress to adopt legislation requiring accreditation of all DNA typing labs, and recommends that the courts allow DNA evidence to be admitted only if the laboratory has been accredited. They delegate the task of setting up the program to the Department of Health and Human Services, in consultation with the Department of Justice—but not to Justice directly, as one bill before Congress now suggests.

Nearly everyone on both sides of the legal debate agrees that the current procedure for vetting new technologies—a string of interminable pretrial admissibility hearings—is not the way to go. To avoid these expensive courtroom fights in the future, the committee calls for the establishment of an ad hoc expert group, a National Committee on Forensic DNA Typing, whose primary job would be to evaluate new approaches. This committee should also oversee the collection of blood samples for the population studies, says the committee, and advise the courts on statistical questions as well. As they see it, the committee would be composed of molecular geneticists, population geneticists, ethicists, and lawyers, and would be housed in the National Institutes of Health or the National Institute of Standards and Technology, with support from the National Institute of Justice and the National Science Foundation.

The committee clearly hopes its new report will be the final word. And to McKusick, the fact that this disparate group was able to reach a consensus bodes well for the report's reception.

The committee's hard-earned compromise drew a tepid response from the FBI, the major practitioner of DNA typing and one of the report's sponsors. It's no secret that the FBI hated the November 1991 version that was leaked to them, which Budowle blasted as a "tainted document" that was skewed to the defense. But in another hastily called press conference on 14 April, Hicks said the bureau is "pleased with the report," although when pressed he wouldn't endorse it.

Nevertheless, the last-minute revisions of the report seem to have ameliorated most of the FBI's concerns. And that could be good news for everyone. Says committee member Reilly: "Tactically, it is unwise for them to oppose the report. It could cost them in court. If the FBI can live with it, this would close the door on much of the criticism from the defense side."

—Leslie Roberts

HUMAN GENOME

Why Watson Quit as Project Head

As predicted in last week's *Science*, James Watson has resigned as head of the genome effort at the National Institutes of Health (NIH). The resignation comes in the wake of a long-running feud with NIH director Bernadine Healy, punctuated by recent charges—and denials—of financial conflict of interest.

Watson resigned on 10 April, saying simply that, "Having accomplished this goal of launching the project, the time has come for me to step down." In a statement accepting his resignation, Healy replied: "Dr. Watson is an historic figure in the annals of molecular biology, and the National Institutes of Health has benefited from his leadership." Yet those carefully crafted words belie the tensions and animosity that led to Watson's departure. *Science* spoke with both Watson and Healy about the events leading up to the split. As will come as no surprise to their friends and colleagues, their versions are miles apart.

Rumors spread the first week in April that Healy had fired Watson over the alleged conflicts—his investments in several biotech firms including Amgen Inc. and DuPont-Merck Pharmaceuticals. Healy denies that, insisting that the two never discussed possible conflicts of interest until Watson resigned. But Watson, his friends, and his lawyer tell a different story. They maintain that Healy alleged conflict of interest to force Watson out because of his vehement criticism of her policies—specifically, NIH's attempt to seek patents on thousands of gene fragments (*Science*, 11 October 1991, p. 184). So while Healy's denial may be accurate, says Watson, she is splitting hairs: "She created conditions by which there was no way I could stay."

As Watson tells it, the patenting episode boded disaster right from the start. He was offended because Reid Adler, the director of technology transfer at NIH, filed the application—presumably with Healy's blessing—without bothering to inform him, even though it had major ramifications for the Genome Project. And Healy was clearly enraged when Watson began denouncing the plan as idiotic and destructive to the project, the biotech industry, and international relations. Faced with a groundswell of criticism here and abroad, Healy summoned Watson to her office last fall and told him to keep his criticisms "within the family." Since then, claims Watson, Craig Venter, the NIH researcher whose lab isolated the gene fragments, has become Healy's adviser on the Genome Project, while Healy made it very

clear she wanted Watson out. In fact, says Watson, the patent dispute underlies everything that happened since.

The current allegations revolve around two related events: a routine review of Watson's financial records, and complaints about Watson made by financier Frederick Bourke. Since Watson took the NIH post in 1989, he has openly declared all of his holdings each year, as required. And each year, NIH officials have signed off on them, declaring there is "no conflict noted," says one of his lawyers, Randy Moss of Wilmer, Cutler, and Pickering in Washington, D.C.

Holdings questioned. Last June, though, Jack Kress, the special counsel for ethics in the Department of Health and Human Services (HHS), called Watson in with some questions about his biotech holdings and how he recuses himself from decisions involving companies in which he owns shares, or Cold Spring Harbor Laboratory, where Watson is still the director. After a lengthy discussion, Kress told Watson he would get back to him if there was any problem. Watson says he heard nothing until Kress summoned him back for another chat on 24 March.

But then, Watson says, the writing on the wall became unmistakably clear. First they discussed one instance in which Watson had inadvertently failed to recuse himself from a decision involving a minor grant to a company in which he has an interest. Then, says Watson, Kress "raised the issue of whether my holding shares in biotech or pharmaceutical companies was compatible with having a policy on cDNA [gene fragment] patents."

And it was in Kress' office that Watson first saw a letter that financier Bourke had written complaining about him to Healy. Watson and Bourke had gotten into a shouting match a couple of months earlier when Watson learned that Bourke was trying to snare two stars of the genome project—Robert Waterston of Washington University and John Sulston of the Medical Research Council in England—for a sequencing company he was planning to start in Seattle. And in typical Watson fashion, he minced no words in denouncing the plan (*Science*, 7 February 1991, p. 677).

After their fight, an irate Bourke wrote to Healy, "saying damaging things about [Watson] and raising ethical concerns," Healy says. *Science* has not seen the letter, but sources say Bourke blasted Watson for interfering with his legitimate business activities. In addition, he specifically charged that Watson had approached Glaxo, the British pharmaceutical giant in which Watson's family owns some stock, and suggested that the company intervene in some way to keep Sulston in England. (Bourke did not return phone calls from *Science*.)

Bourke aside, Watson recalls that Kress said he saw no reason why he could not keep his job. In an interview with *Science*, Kress reiterated that Watson had done nothing unethical or improper. "I don't want people spuriously accused of unethical behavior when there is absolutely no truth to it."

But Watson told Kress he wanted out. "I realized I was in too hot of a position and I should just resign." To Watson, Healy's handling of the letter was the final insult. "The letter was written in February but I never saw it until last week [24 March] in Kress' office. I think Dr. Healy should have sent it to me. That led me to think that the sooner I left the employ of Dr. Healy, the better."

Watson's only question was when to leave, since NIH was just beginning its appropriations hearings. Kress said he would talk to James Mason, the assistant secretary for health. That night, Watson began telling his colleagues that "my position had become untenable." At the same time, Healy told *Science* that she had "serious concerns" about Watson's financial arrangements.

Watson got in to see Mason on 9 April and resigned the following day. He sees the entire episode as a blatant campaign to smear him. "I find it sordid, awful, and very depressing," he says. "The whole thing is sickening."

But Healy dismisses Watson's account as "totally incorrect." "He knew about the cDNA patent long before I did and never told me," says Healy, who maintains that she did not learn of the application until the fall. "The first thing I did was call him and say, 'What is this?' We had a good discussion." Watson's claims to the contrary, says Healy, their policy dispute over the patent application has "absolutely no bearing" on the current issue. "It is a matter of financial conflict of interest" that goes back well over a year, she says.

She says her concerns were triggered by phone calls from Bourke and molecular biologist Leroy Hood of the University of Washington, who is one of Bourke's advisers in the sequencing venture, and then by Bourke's subsequent letter, which she forwarded to the HHS ethics office. She did not show Watson the letter, she says, because Mason told her "the problem would be handled by them, not by me."

Faced with allegations of impolitic, if not unethical behavior, Healy did ask Kress to take another look at Watson's financial holdings to be sure everything was in order, says her spokeswoman, Johanna Schneider. To Healy, it didn't seem to be. "There may indeed be apparent if not real conflicts of interest," she says.

Now that Watson has resigned, the questions about his financial arrangements are largely moot. But that leaves the larger matter of what his departure portends, both for Healy and for the Genome Project.

Resignation a travesty. As to Healy's reputation, both with the scientific community and with Congress, where Watson has always been viewed with great respect, that will depend on which version of the story people believe—hers or his. Among the genome community, at least, it's clear which view will prevail. "The resignation of Jim Watson is a tragedy and the result of a travesty," says Norton Zinder of Rockefeller University. "It was his talents and will that led the Genome Project to an ongoing but still fragile reality."

As for the project, which has been under attack almost since its inception, it will need a leader, not just a bureaucrat, to chart its ambitious course and to defend it before Congress. Zinder and other genome experts think it will survive—provided Healy can attract someone of sufficient stature.

The looming question, then, is who will take Watson's place. Healy moved quickly to appoint Michael Gottesman of the National Cancer Institute as acting director, but he does not intend to stay. Johns Hopkins molecular biologist and Nobel laureate Dan Nathans is already being mentioned as a possibility, though he dismisses such talk as "nonsense." Watson, for one, is worried. "I don't know how to get someone to succeed me. I don't know anyone who doesn't have stocks. And I don't know anyone who would want to live with my boss."

–Leslie Roberts

© MARGOT BENNETT

He said, she said. Healy and Watson tell very different stories of the events leading up to his resignation.

Nobel prizewinner quits genome project

Phyllida Brown

JAMES Watson, the geneticist who shared a Nobel prize for discovering the structure of DNA, has resigned as head of the US government's programme of research on the human genome. His departure follows clashes with his director at the National Institutes of Health, whose decision last year to patent sequences of DNA he publicly opposed.

Watson met the director, Bernardine Healy, last Friday afternoon and handed her his resignation. His formal statement said he wanted to return to full-time work at his second job, directing Cold Spring Harbor Laboratory on Long Island. "My resignation at this time also provides Dr Healy . . . the opportunity to appoint her own director for the project," he said.

Cold Spring Harbour

Watson: conflict over patenting

There was confused speculation last week about why Watson intended to resign. Before his formal announcement, he had already told journalists in Washington that he had "strong and unassailable reasons" for thinking that Healy wanted him to leave. The two have publicly disagreed on several occasions.

However, Watson has also been under investigation by the NIH for possible conflicts of interest. He owns stocks in certain biotechnology companies, including Merck and Amgen, that are involved in gene sequencing. Last week, he told journalists he had been willing to sell his stock.

On the day before Watson resigned, Healy told journalists: "I have concerns that there may be apparent, if not real, conflicts of interest." She conceded that the two had had "differences of opinion" over the issue of DNA patenting, but denied that these were at issue. Watson, she said, had done "an excellent job". Privately, however, geneticists are convinced that Watson has resigned over the issue of patenting, not over his personal finances.

By Friday, a spokeswoman for the NIH appeared to support the view that Healy and Watson had clashed personally. There was "no wrongdoing" on Watson's part and "no conflict of interest", the spokeswoman said. Watson's lawyers have also issued a statement. It says the scientist had fully disclosed his holdings, had been "entirely candid" in his dealings with the government, and had "fully complied" with all the government's requests. The Special Counsel for Ethics "never reached a determination that Dr Watson's holdings created a conflict of interest," the statement adds.

Watson's successor has yet to be decided and researchers this week were hedging their bets about who would be chosen. Healy is expected "to think and wait awhile" before making a choice, according to a spokeswoman. In the short term, Watson will be replaced by Michael Gottesman, chief of the Laboratory of Cell Biology at the National Cancer Institute.

John Sulston, one of Britain's key genome researchers from the Medical Research Council, who was recently invited to join a private gene-sequencing company in the US, said he regretted Watson's decision. "We've found him extremely supportive and I am sorry that he won't be in office any more," said Sulston. □

Britain will drive Europe's transport

Mick Hamer

EUROPE's efforts to cajole members of the Community into adopting a sustainable transport policy depend in no small part on the new British government's attitude to green issues when it takes up the presidency of the Council of Ministers in July.

The Commission's green paper on the impact of transport on the environment, which was published in February, is currently the focus of a complex series of manoeuvres in Brussels.

The Green Paper advocates "encouraging more environmentally friendly modes" of transport and increasing investment in public transport. The paper was drawn up by the part of the transport directorate responsible for the "social and ecological impact" of transport.

However, these principles will find their way into Community transport policy only if the British government uses the power of its presidency to debate the issues among the Community's transport ministers. For another part of the transport directorate is also drawing up a White Paper on transport. This paper is currently in draft but it is understood to ignore or play down many of the more important principles in the Green Paper. Only after a debate among the transport ministers can the principles in the Green Paper now find their way into the White Paper.

The Green Paper argues for a more global approach to transport policy, which would take into account the impact of transport on the environment.

It forecasts an increase of 25 per cent in the number of cars on Europe's roads between 1990 and 2010 and a 42 per cent rise in heavy lorries over the same period. It says that if these trends continue the impact on the environment will "become more significant".

Existing research initiatives, such as DRIVE (Dedicated Road Infrastructure for Vehicle Safety in Europe) and STEP (Science and Technology for Environmental Protection) will "go some way towards resolving the areas of conflict between transport and the environment . . . however, on their own . . . they will not suffice", says the Green Paper.

It says that efforts to curb pollution and noise and to increase fuel efficiency will be easily offset by the forecast increases in traffic.

Instead it argues for a change in direction of transport investment away from roads and towards public transport. One of the main features of the draft white paper is thought to be a major programme of investment in new European highways. □

Skill shortages in US a 'myth'

CLAIMS made by the National Science Foundation during the 1980s that the US faced a shortage of scientists and engineers were based on a flawed scientific study, according to testimony at a congressional subcommittee last week.

Senior members of the NSF, including the former director Erich Bloch, quoted the study in important policy speeches and sometimes before congressional committees. The idea influenced decisions made by Congress.

"Until now no one has poked holes in the NSF, but people will look sceptically at what they say in future," said a source in Congress.

At the hearing, before Representative Howard Wolpe's subcommittee on investigations and oversight, witnesses said that the projected shortages have not materialised. In fact, the unemployment level among scientists and engineers is higher than average.

The study, undertaken by Peter House of the NSF's Policy and Research Analysis Division, predicted shortages beginning a few years ago, and said those shortfalls would reach 675 000 by the year 2010.

Congressional sources say they decided to investigate the issue when they heard criticism of House's study from other engineers and scientists. "Erich Bloch is not a statistician or economist, so he may not have known of problems with the data on which the study was based," said one official.

House's work did not go through peer review, nor did the NSF officially publish the report. The NSF told the subcommittee that procedures are now in place to prevent the same thing happening again. However, John Fluharty, a spokesman for the NSF, said that he did not know specifically what those procedures were. □

The Public's Share of Medical Research

By FAZLUR RAHMAN

N.Y. Times 4-26-92 p. 13 sect 3

A 42-YEAR-OLD woman with ovarian cancer has been in and out of the hospital for months. Her course is complicated by anemia, which requires frequent blood transfusions. But now she is experiencing debilitating side effects from the repeated use of blood.

She does not need to go through these ordeals. Erythropoietin (EPO), a product of genetic engineering, could treat her anemia. In the past, after taking the EPO for a few weeks, she improved. But then she had to stop. Her health insurer refused to cover her EPO treatment, and because of its high cost she could not afford it. As a school teacher, she has too much money to qualify for financial assistance but too little to pay for her therapy.

Like many other drugs created through genetic engineering, EPO is far too expensive. The manufacturers understandably claim they are entitled to a fair return on their research and investment. But their notion of what is fair is open to debate.

Basic biomedical research has long been heavily subsidized by United States taxpayers. The Federal Government spends billions for the National Institutes of Health and gives numerous grants to universities to further research. High-tech pharmaceuticals owe their origin largely to these investments and to Government scientists.

Dr. Fazlur Rahman is chief of hematology and oncology at West Texas Medical Associates and Angelo Community Hospital in San Angelo, Tex.

The public has earned the right to buy the products at a reasonable price. Already, about a dozen DNA-technology drugs are in the market; 21 other genetically engineered medicines are awaiting F.D.A. approval. More than 85 others — treatments for various ailments including cancer, AIDS, Alzheimer's disease, strokes and blood clots — are undergoing human trials.

Genetically engineered compounds are not the only ones that are high-priced. One monthly injection of carboplatinum, an anticancer agent, may cost $1,000; and a single capsule of VP-16, another antitumor medication, costs $40. And they have to be taken for months to achieve any benefit. Surely, the $36 billion pharmaceutical industry has room for easing prices on some products.

As a practicing physician, I wish I had better treatments for cancer patients. But what good is a superdrug if its cost is out of reach of our patients?

The Human Genome Project has embarked on an effort to map all human genes. At a cost of $3 billion over 15 years, this effort could exceed in scope the Apollo moon-landing program. Years from now, when it brings cures, we should remember that our citizens funded the project. ■

A New F.D.A.-Approved AIDS Test

To the Editor: N.Y. Times 4-26-92 p. 13 sect 3

In her roundup on AIDS testing ("All About H.I.V. Testing," April 12), Kathleen M. Berry failed to include the most recent AIDS test approved by the Food and Drug Administration. Fluorognost received approval on Feb. 5 as the first immunofluorescent AIDS test for both screening and confirmation. It takes only 90 minutes to process, can be used at small health care facilities, doctors offices and blood banks, and unlike the other confirmation test, it posts practically no indeterminate results. We soon intend to file an amendment to our existing license for Fluorognost to include a test for saliva.

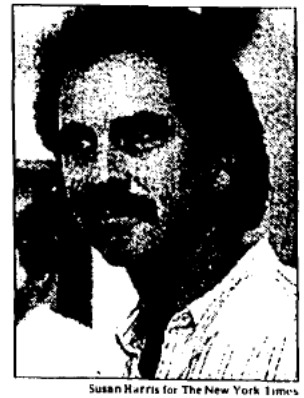
DETLEV BAURS-KREY
Southampton, N.Y., April 14

The writer is chairman and chief executive of Thermascan Inc.

No Admission

N.Y. Times 4-26-92 p. 7 sect 4

So what is it with the Greenwich Hospital in Connecticut? Dr. **Gary Blick**, who is a gay internist about one-third of whose 1,100 patients are H.I.V.-positive, says his admitting privileges were cut off at the hospital last year because of the nature of his practice. Hospital administrators are edgy about having too many homosexuals around, Dr. Blick contends, especially ones with AIDS. The administrators say the issue is not AIDS, but "quality of care," and that is about as specific as they will get. While Dr. Blick's suspension is being appealed — he'll sue if he loses, he said last week — there are rumblings in Hartford about a big expansion that the hospital is planning. A state legislator with a finger on the hospital licensing button has asked that the contretemps at Greenwich be "looked into" pending approval of the expansion. Dr. Blick thinks he knows what the problem is. "I'm gay and I'm Jewish and I'm treating AIDS patients," he said. "And that does not go well at Greenwich Hospital."



Susan Harris for The New York Times

Conflict of Interest?

Dr. Jim Watson's leadership of the Human Genome Project (HGP) is universally acknowledged. NIH's commitment to the HGP has been unwavering, as well.

Dr. Watson's resignation is a surprise to some, but he had said months ago that he intended to step down. It still is hard to believe that he actually did so because Dr. Watson and the HGP are so inextricably linked. However, Dr. Watson's influence on and commitment to the HGP are expected to continue, as is the support of the NIH.

The concern that no one can replace Dr. Watson is unfounded; Dr. Watson himself cannot be replaced, but the directorship should be assumable by an eminently qualified scientist. If that were not the case, the project itself would be flawed. Dr. Watson, like any leader, is vulnerable to life's vagaries, and every leader must think about a capable successor if his vision is to be fulfilled. I have faith in both Drs. Healy and Watson and do not expect the HGP to be impeded.

The question of conflict of interest relating to investment in biotechnology stocks poses a real and difficult dilemma. Questions abound and carry over to many professions. Should a physician hold stock in a company whose pharmaceuticals he often prescribes? Should academic researchers be prohibited from investing in companies that are supporting any research projects in their labs and/or institutions? Controversy currently exists about physician investments in private laboratories even if the laboratories are not in their geographic area of practice. Conflict-of-interest questions have been raised for years, and it is not unexpected that they will be applied to biotechnology investments as the field matures.

For some members of the biotechnology community, investing in biotechnology mutual funds is the ideal investment vehicle. Others feel that investing in individual companies is perfectly proper and in no way compromises scientific integrity. Clearly this issue is going to continue to grow, and we want to know your opinion. On page 24, you will find our first GEN FAXPOLL which asks questions relevant to this topic. Please fill it out and fax us your response. The results will be published in the June 1st issue of GEN.

Among the interesting articles in GEN this month is Stewart Rosenberg's "Point of View," discussing opportunities for biotechnology that exist in South Africa. Not enough attention has been given to South African biotechnology efforts to date, but opportunities for collaboration and investment exist and should be explored.

GEN takes to the air again this month, this time on United Airlines' flights, both domestic and international. If you're flying the "friendly skies" during May or June, please tune in to "Investing in Biotechnology III."

Thank you for your nice letters and calls about our expanded publication schedule. Now that we're doing it, we can't imagine how it was ever otherwise. Keep your comments coming, please—you see how responsive we are.

P.S. Don't forget to fill out our FAX poll on page 24 and fax it to us today.

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Republic of South Africa Has Much to Offer In Terms of Opportunities in Biotechnology

By Stewart Rosenberg

While biotechnology developments and opportunities around the world have been making news, one country yet to be covered with respect to biotech advances is the Republic of South Africa (RSA). However, now that many of the obstacles encountered in the late 1980s no longer exist, knowledgeable investors can find opportunities there.

Geographically, the Republic of South Africa lies at the southern tip of the African continent, and is divided into four provinces—Natal, Orange Free State, Cape Province and Transvaal. South Africa is, on the whole, a dry country, receiving rain only in the summer. The mean annual rainfall is approximately 500mm, compared with a world average of 850mm.

The total South African population is estimated at 31 million, of which six urban areas would be described as large by American standards. These areas, in which much of the biotechnology development has taken place, are Port Elizabeth-Uitewhage, Pretoria, the Cape Peninsula (including Cape Town), Johannesburg-Randburg-Soweto, the East Rand towns (including Benoni and Nigel) and Durban-Pinetown.

CSIR

The Council for Scientific and Industrial Research (CSIR), headquartered in the eastern suburbs of Pretoria, is the largest R&D organization in South Africa and sponsors the R&D training of top scientists. With an annual budget of approximately $150 million and staff of approximately 1,300 scientists, 1,100 technicians, and 2,000 support personnel, the CSIR has five major goals.

It wants to apply its expertise in science and technology to benefit industry and to provide the R&D necessary to position technologies where they can strengthen the economy. It also plans to support the training of engineers and scientists, offer a technology base of information services, and provide management and operations skills for technological and scientific research facilities.

The CSIR exerts a major economic and scientific influence throughout the country and overseas, with branch offices in other cities such as Durban, Johannesburg, Cape Town, and Stellenbosch, as well as science offices in Washington, London, Bonn and Paris.

The CSIR is divided into a number of groups, and biotechnology plays a key role in its food science and technology division. This division is pursuing a number of objectives:

- supporting the food, feed, fermentation and agricultural industries in South Africa through science and technology;
- developing cost-effective food-processing techniques and product formulation;
- transferring knowledge and offering collaboration with marketing boards and public sector agencies to ensure safe and nutritious food;
- evaluating food products by using specialized chemical, microbiological, and biochemical techniques;
- optimizing the utilization of South Africa's food resources;
- developing new and improved foods from agricultural produce;
- investigating and implementing innovative techniques in the food sciences; and
- implementing modern biochemical processes at South African industries.

Biotech Program

Within the Division of Food Science and Technology, the CSIR established the Biotechnological Products and Processes Program in 1979 to focus on R&D and applications of biotechnology. The program, currently active in immunotechnology as well as microbial and plant biotechnology, employs approximately 20 people. Areas of expertise include fermentation technology, the production of microbial-derived products, plant genetic engineering, and the development of immunoassays for use in agriculture and food industries.

CSIR biotechnologists and bioengineers carry out client projects to optimize processes for products relevant to industry. Lab-scale fermenters are available up to 20 liters, as is a pilot plant facility with a capacity of 150 liters.

Processes have been produced within the program for the manufacture of vitamins, single-cell proteins, amino acids, and industrial and diagnostic enzymes. The division has reported that through fermentation optimization, it has achieved 70g/L of extracellular cellulase enzyme produced in the fungus *Trichoderma reesei*.

The Biotechnological Products and Processes Program has used modern molecular biology techniques to improve microbial strains. Several industrial enzymes obtained from local isolates of *Bacillus* species have been successfully cloned and expressed; plans have been designed for plasmid maintenance during fermentation scale-up.

Agricultural Conditions

Conditions in South Africa are generally not optimal for agriculture. Less than 25% of the available 14

SEE POINT OF VIEW, p. 13

CSIR

Scientists at CSIR's division of food science and technology identify prepare and label culture specimens from a collection of more than 8,000 strains of yeasts, filamentous fungi and bacteria.

Index to Companies

HGP

Dr. Watson's Resignation Raises Questions On Future Commitment to HGP

By Bradie Metheny and Shirley Haley

The recent resignation of Dr. James Watson as director of the National Center for Human Genome Research (NCHGR) raises questions about the future shape and size of the nation's commitment to the Human Genome Project (HGP). It also contributes to a growing concern over the validity of conflict-of-interest definitions and rules.

How the National Institutes of Health (NIH), Congress and the scientific community respond will determine the future strength of the U.S. as a world leader in human genome research.

Dr. Watson resigned his position as the first director of the NCHGR after the question of a possible conflict of interest between his decisions as director of NCHGR and his biotechnology stockholdings was raised. He had, however, advised friends and associates several months ago of his intent to resign later this year for other reasons.

Two Questions

The HGP was launched largely due to Dr. Watson's influence and stature as codiscoverer of the structure of DNA, for which he won the Nobel Prize. His resignation brings to mind two immediate questions.

First, because of the nature of the HGP—its relationship to the progress and direction of biotechnology, and the potential for leveraging federal research funds with private money to support genome research—is it time and is it necessary to redefine conflict of interest laws relating to all officials at NIH?

And second, was the resignation prompted more, as some suggest, by NIH Director Dr. Bernadine Healy, who saw the possible conflict of interest as an opportunity to get rid of Dr. Watson, with whom she had strong disagreements over policy issues, than by any real conflict of interest threat?

Dr. Healy (who did not respond to our request for a statement on the issue) now is in the position to make pivotal decisions affecting the size and shape of the HGP. Some observers believe that if she maintains the project at or near its current high priority and visibility at NIH, the project will move forward, and the U.S. will continue to play a strong world role.

Their position, however, assumes that Dr. Healy can find a strong, scientifically respected and politically savvy director for NCHGR. Proponents of the HGP fear that without a strong NCHGR director the controversy around whether the project should be abandoned and the money used elsewhere in biology could well resurface, either stopping the project or tying it up in debate to such an extent that the U.S. effort won't be able to maintain its momentum. They say that this scenario would have a negative effect on the U.S. biotech industry, the nation's world leadership in genome research and biotechnology, and competitively, on the balance of trade in intellectual properties.

Not Science

Opponents of the HGP indicate that they believe the mapping and sequencing of genes is not "science" and that many of the results will ultimately not be productive. Much of DNA is "garbage," they say, and will not be found to be enlightening or to have purpose. Further, they assert that money to support genome research is being diverted from more important areas of biology. Their contention is that if it weren't for Dr. Watson the project could have been halted or at least scaled back long ago.

Dr. James Wyngaarden, who, as acting NIH director, appointed Dr. Watson, to the position of NCHGR director four years ago, believes that at the time, there was no one else inside or outside of NIH who could have led the project as successfully as Dr. Watson.

"Jim Watson had all the right assets: he was a well-respected scientist with a strong personal belief and commitment to the importance of the project, personal contacts in science nationally and internationally, courage to lead and the political savvy to attract congressional and administration support and funding," says Dr. Wyngaarden.

Officials at NIH and some members of the extramural community believe that since Dr. Watson's departure Dr. Healy has taken, at least initially, the right steps. They approve of her appointing Dr. Michael Gottesman as acting NCHGR director. Dr. Gottesman is "a very bright scientist," says Dr. Watson, adding that he will help the interim director in any way possible.

Dr. James Watson

Good Choice

An NIH official describes Dr. Gottesman as a good interim choice who can keep the project moving forward until a permanent director is found. The 46-year-old Gottesman is an M.D. biochemist who, until his appointment by Dr. Healy, was chief of the Laboratory of Cell Biology at the National Cancer Institute. Dr. Healy's announcement that she intends to actively search for a new director is viewed as a second positive step indicative of her commitment to the project.

However, while there is some concern among genome proponents that it will be difficult to find another leader of Dr. Watson's stature, and that his kind of leadership is needed to carry the HGP, others think his type of guidance is no longer as critical as it was two years ago when the project needed a substantial infusion of "second wave" money, particularly for the Centers Program.

The HGP's overall funding in FY '91 was $87.3 million; it increased to $104.8 million in FY '92. Now, they say, the program is an entity with momentum of its own.

"It was really crucial for the first four years to have Watson lead the [HGP]. It was during this period that the agenda, plan, style and funding level for the project were established," comments David Botstein, professor of genetics at Stanford University and a member of the NCHGR Advisory Council. "Dr. Watson left quite a legacy. NCHGR has momentum and direction, and it is distinctive at NIH. Now Dr. Watson's leadership is not as crucial. It (NCHGR) needs competent leadership, but most of the scientific

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Momoya Company Discovers Antineoplastic Protein in Matsutake Mushrooms

A research team at **Momoya Co.** (Fax: 81-3-3669-3087) and the **National Food Research Institute** (NFRI) discovered an antineoplastic protein in matsutake mushrooms (*Armillaria matsutake*). The scientists induced cancer in mice using the SV40 strain of virus, then gave the

mice feed containing the matsutke mushroom protein. Results showed that extremely low concentrations of the compound killed the cancer cells, leaving more than 70% of the healthy cells unaffected. According to the researchers, the protein is not effective when the mushroom is eaten due to enzymatic dissociation of the molecule in the GI tract. However, they say it has potential as an anticancer drug if it can be mass produced in genetically engineered microorganisms.

In related developments, Dr. Yoshiaki Takadani of the **Aomori Advanced Industrial Technology Center** and Dr. Jinichi Sasaki of the **School of Medicine at Hirosaki University** found an antineoplastic heteropolysaccharide in squid ink, and Tokyo-based **Koken Ltd.** (Fax: 81-3-3266-2673) isolated a novel antineoplastic substance from the culture fluid of cancer cells that exhibited a depressed rate of growth under high-density culture.

Dainabot Co. (Fax: 81-3-3437-9367) is marketing "Pepsinogen I-Riabead" and "Pepsinogen II-Riabead." RIA kits to detect diseases, such as atrophic gastritis, gastric polyps and stomach cancer . . . **Hitachi Chemical Co.** (Fax: 81-3-343-8488) of Tokyo has begun marketing "Hitazyme Chlamydia Ab," a reagent kit for in vitro diagnosis of Chlamydia infections . . . Osaka-based **Toyobo Co.** (Fax: 81-6-348-3192) is selling DNA probes for detecting infectious pathogens, such as the cholera bacillus . . . **Eiken Chemical Co.** (Fax: 81-3-3818-1207) launched "HCV Antibody IRMA Kit Eiken," an immunoradiometric assay test kit for detecting hepatitis C virus.

Tokyo-based **Meiji Milk Products Co.** (Fax: 81-3-3275-1050) isolated an immunostimulant from the cytoplasm of lactic acid bacteria . . . Studies at the **School of Medicine at Showa University** have demonstrated that green tea is effective against methicillin-resistant *Staphyloccus aureus*, a cause of opportunistic infections arising among immunocompromised hospital patients . . . **Kissei Pharmaceutical Co.** (Fax: 81-263-25-7899) has begun marketing noodles prepared specifically for chronic kidney disease and hemodialysis patients. The noodles have one-third the usual content of protein, calcium and phosphorus, thereby reducing the dialysis load on the kidney.

Kyowa Medix Co. (Fax: 81-3-5566-1734) expects to begin marketing a clinical test reagent for the diagnosis of adult T-cell leukemia . . . **Dainippon Pharmaceutical Co.** in Osaka (Fax: 81-6-203-6581) developed a technique for diagnosis of hypertriglyceridemia. The method uses monoclonal antibodies to measure epitopes of lipoprotein lipase (LPL) and hepatic triglyceride lipase (HTGL), enzymes involved in the catabolic metabolism of blood triglycerides . . . Tokyo-based **Kirin Brewery Co.** (Fax: 81-3-3499-6190) employed recombinant DNA technology to develop a mini Turkish bellflower (*Eustoma grandiflorum*).

Mitsui Toatsu Chemicals in Tokyo (Fax: 81-3-3592-4267) developed a microbe-based paddy field herbicide that is effective against barnyard grass (*Panicum crusgalli*). The herbicide consists of spores of a filamentous fungus . . . Researchers from the **Agency of Industrial Science and Technology's Fermentation Research Institute** (Fax: 81-298-54-6005), the **University of Tsukuba**, and **Nippon Mining Co.** discovered bacteria which can break down dibenzothiophene (DBT) and alkyl dibenzothiophene, aromatic sulfate compounds found in crude oil.

A survey by the **Environment Agency** (EA) has found that most environmentally-aware Japanese people are concerned about the possible effects of recombinant DNA technology on the environment. The agency sent questionnaires to 1,500 people participating in an EA environmental monitoring program. Three out of four of the 1,363 who responded expressed concern about potential adverse effects of genetic engineering on the environment and public health. About 66% believe that biotechnology will contribute to the development of new pharmaceuticals and improved organisms. But roughly 49% want to see tighter measures to protect the environment and ensure safety; 32% said they would oppose plans to establish a biotechnology research center in their neighborhood.

The agency is preparing guidelines for local authorities to prevent potentially hazardous effects of genetic engineering on the environment.

A research team at the **Central Research Laboratories of Ajinomoto Co.** (Fax: 81-3-5250-8314) and the Faculty of Agriculture at Kyoto University has developed a technique for producing useful proteins in cultured transformed human cancer cells. The method, which uses the MDR gene that encodes multiple drug resistance, entails the production of a construct consisting of the MDR gene linked to a gene encoding the desired protein. The construct is then introduced into cultured human cancer cells which are then subcultured through a series of media containing a chemical to induce amplification of the MDR-containing construct. The result is a chemical-resistant cancer cell line containing many copies of the MDR and target protein genes. ■

Observer

from page three

community agrees that the [genome project's] five-year plan is what it should be."

Dr. Watson told *GEN* that he remains firmly committed to the success and vitality of the genome program. Friends and colleagues say that because he is no longer an employee of NIH, he may well be in a better position to be an advocate and protector of the project.

Some on Congressional Hill believe that the implications of Dr. Watson's resignation should not be overstated. "I never felt he [Dr. Watson] was critical to the funding. Once the importance of the [HGP] became evident, it didn't need Dr. Watson," offers one staff member.

Others believe, however, that without Dr. Watson, more effort will have to go into maintaining the funding level required to make the project a success and enable it to meet its five-year goals.

On the Hill, people are questioning whether Dr. Watson's resignation is not an opportunity to get a full-time director on board for the increasingly demanding job of NCHGR director. They foresee that the project is soon going to require more time and effort than Dr. Watson would be able to provide as a part-time director of the NCHGR and the full-time leader of Cold Springs Harbor Laboratory on Long Island.

"The real question at this moment is whether or not Dr. Healy and the NIH can get anyone to take the job as director," says a non-staff member of the National Academy of Science (NAS). Because other first-rate people have conflict-of-interest concerns, they question the process by which Dr. Watson was essentially forced to resign.

Disagreed Over Decision

Dr. Watson disagreed with Dr. Healy over her decision for NIH to apply for patents on thousands of gene fragments identified by an NIH scientist, calling the patent idea "sheer lunacy." His position is one that any pharmaceutical, biopharmaceutical or biotechnology company could be expected to hold. In fact, Dr. Watson's position would be the position of most of the industrial firms involved with genome research, and is certainly not relevant solely to companies in which he or his family had holdings, says the NAS scientist.

Further, Dr. Healy was distressed by a letter she received from Frederick Bourke, a Connecticut businessman who is attempting to start a DNA sequencing company. Dr. Watson, upset about Bourke's effort to hire away from government service two leading scientists and to take over the genome mapping of a certain worm, reportedly felt that Bourke's move threatened a cooperative project with the United Kingdom's equivalent of NIH and attempted to use his influence to stop Bourke's efforts. It was Bourke's letter to Dr. Healy that reportedly raised the question of possible conflict of interest on Dr. Watson's part.

Once Dr. Healy got the letter, she asked the ethics officer of the Department of Health and Human Services (HHS) to take over the matter. Reportedly, the HHS ethics office suggested to Dr. Healy that she allow Dr. Watson to have a waiver in this case. Dr. Healy supposedly didn't want to follow that path of action.

Defensible Decisions

Dr. Watson's decisions and activities were defensible on a number of levels, says the NAS scientist. First of all, he was part-time at NIH and performing, really, a public service to the government.

"This is a clear case of Dr. Healy wanting to get rid of Dr. Watson because of personality clashes, and taking advantage of circumstances. Not many people will want to be in the position of that kind of personal vulnerability," says the scientist.

In addition, the NAS scientist maintains that the rules on conflict of interest essentially keep "people who have accomplished anything and are capable" from becoming involved with government in general, and, with the HGP in particular. He points out a recently completed NAS study, "Science & Technology Leadership in American Government," that shows the increasing difficulty of getting the best people to assume leadership roles in government because of the cloud of rules around ethics and conflict-of-interest laws.

Based on the results of the study, which advocates that federal ethics laws should be streamlined at once and contained in a single comprehensive section of the U.S. Code, he foresees the recruiting of a permanent NCHGR director as being a difficult task. ■

Bradie Metheny and Shirley Haley write and publish Washington FAX.

Genomyx

from page fifteen

prototype will be put to work sequencing fragments for Genentech, which is the largest single shareholder in Genomyx. If the trial works, Genomyx may open a sequencing service which could generate $5 to $7 million a year.

Contract Service

If that sounds like a reprise of early days at ABI and other instrument makers, it is. Almost every company that made DNA synthesizers tested and refined their early prototypes in the price-conscious world of contract service.

"It's an early way to test our instrument," Ruderman explains. "It will generate some income and help us understand the demands of a high-volume user."

Whether contract sequencing ever gets beyond Genentech is an open question. There are plenty of small-volume labs out there with a need but without their own expertise. That's a formula for a service.

But the marketplace can be parochial. People don't like to let their sequences out of their grasp. There's a real hesitation, particularly in the industrial segment, to let go of clones.

If the contract DNA sequencing business does not become a reality, the Genentech connection takes on even more importance in providing credibility for this technology.

Genomyx also expects to benefit from the proprietary reagents associated with the instrument. Not only will these reagents assure a regular, year-round income stream independent of instrument sales, but they give Genomyx a potential marketing edge. If a customer can't swing the capital expenditure to buy an instrument, Genomyx could establish an instrument rental program, and still enjoy reagent revenue. ■

tility and pregnancy. After studying the effects of PAF in rodents, the researchers believe that it must be present for the fertilized egg to implant in the uterine wall. Johnston and other researchers have shown that PAF cannot be detected in the amniotic fluid from women at term who are not in labor, but that PAF appears during labor. It also causes uterine muscle contractions in vitro in studies that use rodent and human tissue. However, researchers still poorly understand which types of cells produce or respond to PAF in reproduction, or what other factors are involved.

Even more intriguing, researchers suspect that PAF may be used as an intracellular regulator because cells that are activated by PAF store it as a phospholipid precusor rather than degrade it, but no one has found the precise evidence to confirm its function within cells, if it has any.

Despite the uncertainties about PAF, researchers are gradually assembling the PAF puzzle. Last year, for example, Takao Shimizu, Zen-Ichiro Honda, and their colleagues at the University of Tokyo cloned a receptor for PAF (see April 1991 issue, page 78), although some evidence indicates that PAF may bind to more than one receptor.

Donald Hanahan, professor of biochemistry at the University of Texas Health Sciences Center in San Antonio, another co-discoverer of PAF, says that researchers have been able to observe PAF's effects in diseases such as asthma and emphysema only because it is overproduced where an inflammatory response occurs, such as in lung tissue. Basic researchers face a challenge in determining PAF's normal physiologic actions because it acts in exceptionally small concentrations and across short distances. Indeed, research by Hanahan and Merle Olson, chairman of the biochemistry department at the same university, indicates that many cells that bind PAF, including platelets, neutrophils, and liver cells, are exquisitely sensitive to it—so much so that PAF can activate cells with high-affinity binding sites, such as human platelets, at concentrations as low as 10^{-9} M.

For those reasons, the compound from cigarette smoke—or any chemical that regulates PAF-AH activity—will help basic researchers to unravel PAF's role in normal physiology, says Snyder. PAF's ability to lower blood pressure has already captured the attention of pharmaceutical companies, although the mechanism has barely been studied.

Compounds that inactivate PAF-AH, and thus increase PAF in the blood, could be tested on the Goldblatt strain of spontaneously hypertensive rats. These rats have greatly increased concentrations of PAF-AH in their blood, says Snyder, and the resulting depletion of PAF contributes to their high blood pressure. Snyder and his colleagues have found the same defect in some humans. But at the moment, people with hypertension could not safely benefit by increasing the PAF in their blood. Although PAF may lower blood pressure in such people, it would also increase the risk of blood clotting and thrombotic injury such as stroke or heart attack. Snyder says that biochemists hope to create analogs of PAF that will minimize its inflammatory effects while capitalizing on its ability to lower blood pressure, but so far, no such drug exists.

Researchers from around the world will have the opportunity to discuss their latest discoveries about PAF this fall at the Fourth International Congress on PAF and Related Lipid Mediators, to be held Sept. 22–26, in Snowbird, Utah.

—JEFF JOHNSTON

Can The Genome Project Flourish Without Watson?

Ironically, Nobel Prize–winner James Watson was planning to step down soon anyway as head of the human genome project. He told friends—and strongly hinted to the advisory council of NIH's National Center for Human Genome Research (NCHGR)—that he thought the genome-mapping program was safely on track and that he would probably resign as director by Oct. 1, after helping to choose a successor.

MARGOT BENNETT, COLD SPRING HARBOR LABORATORY

Conflict of interest, and personalities, led to James Watson's resignation.

But instead of the smooth transition he had hoped for, Watson got a bumpy exit. Within just a few days in early April, conflict-of-interest questions about his financial holdings and his dual role as head of the genome project and the Cold Spring Harbor Laboratory in Cold Spring Harbor, N.Y., escalated into a battle of wills with NIH Director Bernadine Healy and climaxed with Watson's abrupt resignation on Friday afternoon, April 10.

To many observers, the falling-out between Watson and Healy seemed inevitable. They had only recently clashed publicly over NIH's effort to patent more than 2,000 complementary DNA (cDNA) sequences whose function, in most cases, is unknown (see December 1991 issue, page 25)—a patent application that Healy embraced and Watson attacked scathingly. "No one here is surprised there was a personality conflict," says one congressional staff official.

The genome project itself seems likely to ride out the storm. Its prospects have brightened since 1990, when the administration wanted to nearly double genome funding just as biomedical researchers were protesting the lowest number of new and competing research grants in a decade. Watson, who had been recruited to head the project in 1988 by then–NIH Director James Wyngaarden, at one point threatened to resign unless Congress gave him the budget increase he was asking. (He got about half, and stayed.)

Now, times have changed. "I think we are just about on track," Watson told the House Appropriations Subcommittee on Labor, Health and Human Services, and Education on March 25. Fears that the project "was going to divert resources away from more important areas have for the most part vanished," he said. In an interview after his resignation, he added, "We have a much better feeling [now] of what should be done and how to do it." But he declined other comment, except to offer any assistance his successor might ask—"and that's genuine."

David Botstein of Stanford University School of Medicine in Stanford, Calif., a member of NCHGR's National Advisory Council, agrees that the project now has staying power. "It has a program everyone can understand, has goals nearly everybody can agree to, has good people, and has momentum and direction," he says.

The genome project has something else

that is important in Washington: a constituency. About 60 percent of its $104.8 million budget this year and its $110.4 million request for fiscal year 1993, which starts Oct. 1, is targeted for research project grants—181 individual grants this year and 201 next. Seven research centers have been funded, and five more may be added this year. As for human-health benefits, NCHGR funding already has helped identify some genes that predispose a person to disease, including the gene linked with fragile X syndrome, Watson told the subcommittee (see December 1991 issue, page 41).

Even so, Wyngaarden, now foreign secretary for the National Academy of Sciences and the Institute of Medicine in Washington, D.C., warns that budget-driven attacks could reemerge. "If you don't have someone of Jim's stature to run it, it could suffer. The critics may resurface," he says. "Jim was able to handle them. And not simply by shouting them down, but by arguing substance."

Whether Healy will be able to recruit such a high-profile scientist is uncertain. Wyngaarden predicts that a scientist of Watson's stature would almost certainly want to take on the genome project only on a part-time basis, to retain ties with his or her own institution. But Healy, in a meeting with reporters the day before Watson resigned, said that his dual responsibilities, to the genome project and to Cold Spring Harbor Laboratory, troubled her.

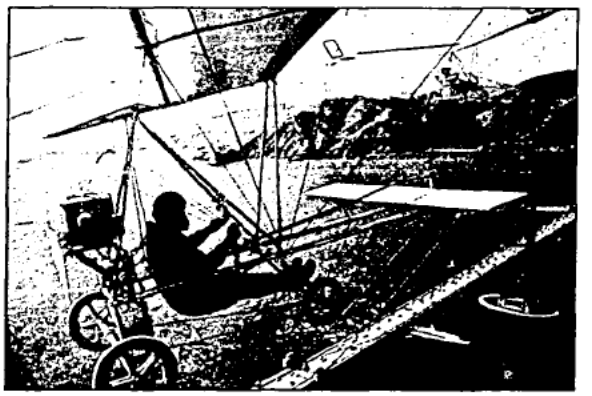
Between the lines of their terse public statements on April 10, it was apparent that Watson and Healy each thought the other was being unreasonable. In a statement after his resignation, Watson pointedly omitted Healy from the list of present and former officials whom he thanked for supporting the genome project. Healy immediately named an acting director for the genome center—Michael Gottesman, chief of the Laboratory of Cell Biology at the National Cancer Institute, a well-regarded intramural scientist and, incidentally, a classmate of Healy's at the Harvard Medical School in 1966–1970.

Perhaps the most disturbing aspect of the fracas is that it could have been avoided. It's hard to believe that there was no face-saving way out of a difference of opinion over conflict-of-interest regulations—particularly at a moment when Watson was planning to step down anyway in a few months. Neither Healy nor Watson has much to gain from his sudden—Watson's friends would say, forced—departure from the NIH campus.

—BRUCE AGNEW

Powerful Forces Propel Rehabilitation Research At NIH

Today, one in seven Americans has a physical or mental disability. In 1991, people with disabilities cost the nation an estimated $374 billion for services, medical costs, and lost productivity. Until last year, NIH had never made a coordinated and comprehensive commitment of research dollars to address the needs and improve the capabilities of people with disabilities.



A disability does not mean the end of sports activities. Pilot Jack McCornack flies a modified ultralight aircraft near the Golden Gate Bridge (top). Peter Axelson, who is paraplegic, designs sports equipment. His Arroya monoski (bottom) combines an alpine ski with a suspension system. Arm-held outrigger skis provide balance. [Courtesy Peter Axelson, Beneficial Designs Inc., Santa Cruz, Calif.]

Then, last May, NIH inaugurated the National Center for Medical Rehabilitation Research (NCMRR). The center is unique because, rather than take a disease-oriented approach to research, it is addressing the much broader issues of how to improve the function and quality of life for the nation's 35–43 million people with one or more disabilities.

Perhaps the primary reason for the center's unusually broad approach is its national advisory board, which sets NCMRR's research goals. The high-powered, high-profile group includes attorneys, physicians, researchers, and rehabilitation health-care professionals, many of whom have disabilities. The board met at NIH March 19–20 to discuss an overarching research plan that ranges from basic research on halting the progression of disability to developing new prosthetic and orthotic devices.

Now, the advisory board and groups of people with disabilities who are shaping the new center face one of their biggest challenges—trying to lure extramural investigators to the field. Physicians and scientists have shown little interest in rehabilitation research, says Theodore Cole, a physician who serves on the center's advisory board and is professor of physical medicine and rehabilitation at the University of Michigan at Ann Arbor. "Rehabilitation has been a big black hole," says Cole. "A lot of people haven't understood it, to say nothing about being attracted to it." But, he adds, "that has turned around as NIH has focused on rehabilitation and increased credibility in the field."

According to *Disability in America*, a 1991 report from the Institute of Medicine, almost 4 percent of all Americans have disabilities so severe that they cannot perform the major activities of their age group, such as playing, attending school, working, or caring for themselves. An additional 6 percent of the U.S. population faces restrictions in performing such activities. A 1986 Louis Harris survey commissioned by the National Council on Disability in Washington, D.C., revealed that 68 percent of all people with disabilities who can work and want to work are unemployed. This represents the largest group of unemployed people in the nation. "I think that's a national disgrace," said Leonard Suchanek. Suchanek, a judge who is chairman of the General Services Administration's Board of Contract Appeals, is blind.

The new rehabilitation research center is a part of the National Institute of

HGP

THE SCIENTIST®

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RODENT OR REMEDY?

Some People Just See a Rat. We See a Cure for Cancer.

MEDIA BLITZ: This full-page ad, which recently ran in the *New York Times, Wall Street Journal,* and other widely read U.S. publications, is the work of a new group, called Americans for Medical Progress, that supports animal research. Because of the organization's grandiose public relations efforts, the emotional battle over animal welfare is heating up—with many researchers finding themselves caught in the middle. See story on page 8.

Academic Researchers Pursue Survival As States Slash Budget Support For Science

With recession taking its toll on campuses throughout the U.S., scientists seek ways to cope with hard times

BY RENEE TWOMBLY

Sizable cutbacks in state funding to public and private academic institutions are taking an increasingly heavy toll on campus research, say university scientists and administrators throughout the United States.

The debilitating impact, they claim, is being felt as the 1991-92 school year draws to a close. While summers past may have carried the promise to university researchers of a fall term spiced with pay raises, new equipment, and refurbished labs, for many scientists the coming autumn looms like a bad storm on the horizon.

The problem—and the pressing question of how to cope with it—are evident nationwide. Some 30 states have reduced their 1992 higher education appropriations: In California, Maryland, Massachusetts, and Oregon, the cutbacks will be at least 10 percent; Connecticut is being hit with an 18 percent reduction; Virginia is reducing its higher education allocation by 17 percent.

What some observers consider to be an imminent crisis has been building for several years, they say, and few predict a reversal in the discouraging trend. Robert Rosenzweig, president of the Association of American Universities (AAU), all of whose 58 members are major research institutions, says: "No one sees relief in the future. I have talked to administrators who have had to make six successive budget cuts, some in midyear, each of which is more difficult than the last. They solve the easier problems first, and then it gets hard."

For many scientists, the hard part already is upon them as they struggle to develop stratagems for maintaining an acceptable level of instruction and lab productivity, despite the tightened purse strings: Administrators are asking science faculty to take early retirement; instructors are picking up teaching loads from assistants who have been laid off; principal researchers are scrambling more animatedly to find federal grant support; and the folks in the lab are sharing equipment, shopping for used equipment, or just learning to make do with their old equipment until better days come along.

PENNYWISE: U. Maryland's Richard Herman must ease impact of a 10 percent cut.

At the University of Maryland, zoology department chairman Arthur Popper says he is using the "bubble gum" approach to keep his four old bacteria-killing autoclaves up and running. The department does not have money from the state

(Continued on Page 6)

Hanging On To A Research Grant For Decades: What's The Secret?

BY SCOTT HULER

Scan the lists of grants awarded by the National Institutes of Health or the National Science Foundation, and you'll find that there are several hundred scientists who seem to have the knack of finding a funding source and keeping it—not for the one or two renewals that most scientists consider the answer to a prayer, but for two or three decades. How do they manage this?

Scientists whose research has earned them decades-long stretches of government funding deny that there is anything special about their work—and some funding-agency officials agree.

Wisconsin geneticist Oliver Nelson: "Stick with the real problems. Stay flexible and learn new techniques."

"I'm not sure there's a formula except doing good science," says Anne Dieffenbach of the

(Continued on Page 20)

INSIDE

A GLOBAL BIOETHIC 10

Watson Departure Vexes Genome Experts

They fear that funding support for their vast gene-mapping project could erode now that the Nobelist is leaving

BY SCOTT VEGGEBERG

While the head of the nation's premier health agency may not be losing sleep over the resignation of James Watson as head of the Human Genome Project (HGP), many genetic researchers are distressed to see him go.

Genome scientists interviewed for this article say it will be difficult for the National Institutes of Health, via its search committee, to find someone with the same drive, vision, and scientific stature—which, they generally agree, translates into an ongoing ability to obtain high-priority funding from Congress.

Preceding the resignation was well-publicized friction between the Nobel Prize-winning Watson—noted both for his achievement in identifying the double helix structure of DNA and for his outspokenness—and NIH director Bernadine Healy.

Recently Watson lashed out at Healy over her support of NIH's pursuit of patents on partial DNA sequences, known as expressed sequence tags. Watson and many other genome scientists feel these patent applications will inhibit international collaborations and could stimulate a gene patent race (*The Scientist*, April 27, 1992, page 1).

Photo: Margot Bennett

INDISPENSABLE?: James Watson has lent significant luster to the HGP.

Watson, who was not available for comment at press time, said in an April 10 statement that he feels the ambitious genome project is mature enough to continue without him. And in an apparent reference to strained relations with the NIH director, he said, "My resignation at this time provides Dr. Healy, the current director of NIH, the opportunity to appoint her own director for the project." Watson had been director of the project since its official launch in October 1989; Healy became NIH director in April 1991.

Paul Berg, a Stanford University molecular biologist who chairs the NIH advisory committee on the HGP, says the reasons for Watson's departure are not mysterious or complicated. He suffered under the stress of being overextended, Berg says, given his simultaneous directorship of Cold Spring Harbor Laboratory, on Long Island, N.Y. (a position he will continue to hold), and of his being in conflict with Healy. "It's clear there was not a good rapport between them," says Berg, and Watson's undiplomatic public statement that the gene patents filing was "sheer lunacy" did little to bridge the gap between them.

According to Berg, Watson's departure in April was not unexpected.

(Continued on Page 4)

LABEL

NEWSPAPER: Time-Sensitive Material

Notebook

❑ **Pugwash For The Pros** Young scientists and other professionals who as students were active in Student Pugwash USA now have a means to stay involved with the Pugwash movement after they graduate. The Student Pugwash office has announced the birth of Professional Pugwash, a new arm of the movement that explores the relationship of science to society (*The Scientist*, April 2, 1990, page 7). While Student Pugwash is itself a spin-off of the 33-year-old Pugwash society of senior scientists and diplomats, "in senior Pugwash, you have to be asked to join; it's only for eminent scientists," says Mike Smith, Student Pugwash USA's management director. Professional Pugwash, by contrast, "is open to any nonstudent," Smith says. "You don't have to have been active in the Student Pugwash group; you don't even have to have graduated." The Student Pugwash office is now collecting names of those interested in forming Professional Pugwash chapters. "The first step is to get interested people in touch with one another," Smith says. For information, contact the Student Pugwash USA office, 1638 R St., N.W., Suite 32, Washington, D.C. 20009-6446; (202) 328-6555.

❑ **Keeping Current—Sort Of** *Science and Technical Writing: A Manual of Style* (New York, Henry Holt and Co. Inc.) will be hitting bookstores in August. The book's general editor, Philip Rubens, a professor of technical and visual communication in the graduate program at Rensselaer Polytechnic Institute, says that "people doing research who are not [native-born] Americans" are among the intended audience. "Successful communication . . . requires the author to develop an accurate profile of an audience and then write for that audience," proclaims the preface of the book, uncorrected galley proofs of which were recently sent to potential reviewers. Maybe the contributors ought to take a closer look at women doing science today. In a section on "Personal Names," the text states that "North American civil practice encourages women to adopt their husband's [sic] surname on marriage," without mentioning the practices of hyphenating a maiden name and a married name or keeping one's maiden name after marriage. "We talk about naming in many different cultures, [and] gender-based conventions throughout the world," says Rubens. "All we're doing is presenting them." So why not mention the nontraditional but now-common practices? "I guess that's something we'll have to do at a different time," says Rubens.

❑ **Olympic Trials** Before the start of the 1992 Winter Olympics, female athletes were genetically tested to determine the extent of their "femaleness." Olympic officials screened women athletes for the presence of the Y chromosome, normally only found in males. Under normal circumstances, females carry two X chromosomes and males carry one of each. However, in rare instances a female may have acquired a Y, yet retain the physical characteristics of a woman. Two geneticists at Johns Hopkins University, Claude Migeon and Gary Berkovitz, say the test is discriminatory, since a woman who possesses a Y chromosome but still has female physical characteristics probably does not have the Y gene, which produces the hormones responsible for male strength. Although no one was disqualified in the Albertville games, the testing will be performed at the Summer Olympics as well.

MIGEON BERKOVITZ

❑ **Peak Conditions** A six-member team of Indiana University researchers started up the slopes of Alaska's 20,320-foot Mount McKinley early this month to study calorie intake, energy expenditure, and weight loss at high altitudes. The team, under Joel Stager, acting research director of the university's Human Performance Laboratory, also is researching acute mountain sickness (AMS), especially the common use of the drug acetazolamide to counter symptoms of the disease. Stager's previous research shows the drug may reduce the ability to do exercise by 30 percent. This is the second team Stager has taken up Mount McKinley—the first was turned back by injury, illness, and severe weather without reaching the summit. "It's no piece of cake," says Jayne H. Spencer, a university spokeswoman. "But high-altitude studies have long been a focus at Indiana—which is in the middle of a corn field."

NIH Establishes Search Committee To Seek New Genome Project Head

(Continued from Page 1)

Berg says that at the January meeting of the genome advisory board, Watson made it clear that he would be stepping down as director within the year.

In the wake of the departure, Healy called a May 4 news conference to reassure the scientific community of her continued support for the Human Genome Project.

"This is one of the jewels in the crown of the NIH," she said. The goal of the project is to sequence all of the genes contained in human chromosomes by the beginning of the next century.

Glen Evans: "[Watson's] leaving is tragic. Without his support, the project wouldn't be going today."

Healy also said at the news conference that Watson's departure had not engendered much "angst" at NIH, and she announced that a search committee of distinguished scientists had been empaneled to find and recommend a new director for the HGP.

Photo: Scott Veggeberg

NO ANGST: NIH director Bernadine Healy, left, told reporters at a recent news conference that Watson's departure doesn't trouble her.

While Healy may be angst-free over the Watson departure, many genome researchers are not. "I think his leaving is tragic, to say the least," says Glen Evans, a molecular geneticist involved in mapping of chromosome 11 at the Salk Institute in San Diego. "Without his support and vision, the project wouldn't be going today."

Helen Donis-Keller, a geneticist at Washington University in St. Louis, says, "My concern is: Who will NIH find to replace James Watson, who was such a unique individual and very effective in the job? He was the kind of person who always had his finger on the pulse of what makes sense in science."

Biotech Group Set To Push Its Agenda With Candidates

(Continued from Page 3)

recast regulations according to the new "risk-based" criteria of the scope document.

"There's been a receptivity to biotechnology in Washington concerning reform of the patent and regulatory processes," says Stephen A. Duzan, CEO of Immunex Corp. of Seattle and chairman of IBA's board of directors. "It's important not to have excessive hoops for the industry to jump through. There's plenty that still needs to be done—getting more resources for the relevant agencies, for instance—but the FDA and USDA [U.S. Department of Agriculture] have improved their processes, and the patent office has hired new examiners.

"But one of the most important issues to the biotechnology industry is the taxation of capital. Biotechnology is a very capital-intensive, high-risk industry."

Several recently proposed changes to the capital gains tax structure have had IBA's approval in the past and are included in the agenda. The group endorsed a provision, part of an economic package sponsored by the Democrats, that would have lowered the maximum tax rate on qualified capital gains to 14 percent from the current 28 percent. The package was approved by Congress, but President Bush vetoed it on March 20. The veto came—despite the fact that the rate was lower than the president's proposed rate of 15.4 percent—because Bush objected to other aspects of the package.

Currently, IBA is working with lawmakers to achieve changes in the laws governing capital gains that would encourage investors by allowing them to realize more gain after taxes.

IBA's Eric Christensen: "The highest visibility issues for this election surround health care reform and patents."

IBA opposes a bill proposed by Sen. Carl Levin (D-Mich.) and Rep. John Bryant (D-Texas) that the association says would require all companies to calculate the value of unexercised employee stock options and to show that value as a liability on their books. This is "unreasonable," according to IBA's Christensen, because there is no way to assign value to an unexercised option that is not necessarily artificial.

IBA claims the law would depress earnings—or increase losses—making it more difficult for smaller biotechnology companies to compete with larger ones for scientific talent. Three-quarters of independent biotechnology companies would be negatively affected by this law, says IBA.

"Options are worthless until exercised," Christensen says. "The law is aimed at cutting CEO compensation, but it unfairly affects the biotechnology industry."

"Stock options have been an extremely important tool for us," says Duzan. "Every employee at Immunex gets stock options—it provides incentive to work hard."

Duzan adds: "Larger, older companies are the target of this law, not the biotechnology companies. We don't want to throw the baby out with the bath water."

The Republican National Committee has scheduled hearings for June 15 in Washington, D.C., where testimony on technology issues will be considered for inclusion in the party platform. The Democratic National Committee held hearings in Cleveland May 18. IBA has submitted its agenda for consideration by both committees. Spokespersons for both parties say that platform language will not be finalized until after the conventions this summer.

"Biotechnology may not be one of the burning issues of this election," says Duzan. "But, as an emerging industry, it is important to the future economic health of the United States. For now, we're preeminent in this industry, but there's plenty that needs to be done to ensure that continues in the future. We would like both parties to adopt these ideas." ❑

Donis-Keller describes Watson as "brilliant and eccentric" and says that, despite his opinionated manner, he listens to the ideas of other scientists and is willing to modify his viewpoint based on this listening. "I don't know who's going to defend and support genome research now," she says.

Leonard Lerman, a molecular biologist at the Massachusetts Institute of Technology, says, "The change in leadership is unfortunate. Watson brought a lot to the project."

In the interim, Healy has appointed Michael Gottesman, chief of the Laboratory of Cell Biology at the National Cancer Institute, as acting director of the HGP, with the Watson-appointed staff remaining on the job.

Evans says Gottesman is an appropriate choice for the transition, since he is well regarded in his field. Moreover, because he is an outsider to the genome project, his appointment won't be perceived as setting a new agenda for the project.

Michael Gottesman: NCI cell biology chief will direct genome project during search for Watson successor.

The search committee, which NIH says will have up to six months to identify a replacement for Watson, is, for the most part, a "five-star" list of scientists, according to both Evans and Berg. Included are Phillip Sharp, director of the MIT's Center for Cancer Research; Maxine Singer, president of the Carnegie Institution in Washington, D.C.; geneticist Maynard Olson of the Washington University School of Medicine in St. Louis; Nancy Wexler, president of the Hereditary Disease Foundation in New York; and Princeton University biologist Shirley Tilghman. The remainder of the 14 positions on the committee are occupied by ranking NIH division directors.

Healy believes the search committee should have no trouble attracting top players as candidates for the director's position. "This is a great job," she said at the news conference.

But Donis-Keller, for one, does not paint a rosy picture of the genome project director's job: "The pay's lousy, everybody hates you, and it's hard work."

Berg, who has been widely mentioned as a possible successor to Watson, says, "I'm not a live candidate." The problem faced, he says, is finding someone of "impeccable scientific standards," who can also be a forceful advocate of the project.

There are two other difficulties, he notes, that prevent him and will prevent other qualified candidates from considering the job—the new director would have to drop all research activities and would probably have to move to Washington, D.C.

The stakes are high in the search for a Watson successor. If NIH is unable to find the ideal director with all the requisite qualities that Watson seems to embody, the Human Genome Project could suffer in future funding battles, says Berg: "If we get a weak sister who nobody respects enough, [the HGP] will have a hard time." ❑

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HGP

some of Brazil's overseas debt into obligations of restraint. Countries such as the Netherlands have already embarked along that route. The biodiversity treaty is a framework within which more comprehensive agreements might be reached, for the Amazon and elsewhere. But everything is a special case, requiring special study. That should be the cornerstone of the way in which the biodiversity treaty functions. Meanwhile, Mr John Major, the British prime minister, is surely right to advocate a programme of more vigorous taxonomic research in regions such as the Amazon (and it is needlessly mean, even by its own standards, for British Friends of the Earth to describe his Rio speech as "empty waffle").

None of this touches the poverty of the poor. Strong's fault is that he has encouraged, especially among the governments of the developing countries, the belief that compensation for custodianship will meet the capital costs of development. That is a gigantic and cruel mistake, especially with a Rio agenda innocent of the issue of population growth. But is not rapid population growth in the developing countries itself a consequence of their poverty? Nobody disputes that in the rich world, the benign demographic transition from high to low rates of birth and death has invariably followed rising prosperity and improved public health. Yet many governments of developing (and quickly growing) countries could be trying harder even as things are. Sooner rather than later, there will have to be a UN conference on that issue as well. □

Moratorium ending

The impending Washington summit has a daunting list of nuclear issues that must be tackled.

Now that the Cold War has ended, why does nuclear testing continue? That is an issue raised this week by the executive committee of the Pugwash Organization which, unlike other international pressure groups, is almost laconic in what it says in public. Specifically, Pugwash has taken fright that it will soon be a year since President Mikhail Gorbachev (remember him?) volunteered, on behalf of the Commonwealth of Independent States, a one-year moratorium on testing. Since then, President Boris Yeltsin had said that Russian tests will resume when the moratorium expires in September. Pugwash asks that the moratorium should be extended at the Washington summit this week, and that the United States should join in.

That, of course, would be an excellent development; there is more than an element of the bizarre in the continued and repeated testing of weapons whose purposes have been confused (or even made nugatory) by the events of the past few months. But, sadly, the summit planned for Washington has even more urgent nuclear business to attend to. Plans for a further bilaterally agreed reduction of strategic arms appear to have foundered on the issue of missiles carrying several warheads, while confusion persists about the role of Russia as the nuclear custodian of other ex-Soviet republics, the Ukraine conspicuously, but also Khazakstan. Will they eventually become members of the Nuclear Non-Proliferation Treaty (NPT), and if they do, will it be as nuclear or nonnuclear powers?

That question cannot be left unanswered for much longer. Three years from now, the NPT will lapse unless its members elect for its continuation (and for the restrictions it imposes on them). Already there are worrying signs of renewed hankering after independent facilities for making bombs — Iraq last year, reports of attempts illicitly to sell ex-Soviet fissile material by Vienna-based agents only last week. The big danger is that the nonproliferation regime will turn into a leaky sieve long before its sponsors (Russia, presumably, still among them) have worked out a way of selling its virtues to the nonnuclear members of the treaty. A moratorium on testing would help powerfully in that direction. □

Genome propaganda

Concealing the truth without lying is an old art, now spreading in the US human genome project.

By now there can hardly be a researcher who has not heard some account of the unfortunate circumstances behind the resignation in April of Dr James Watson as director of the US human genome project. But the account of the resignation in the current issue of *Human Genome News*, the project's official newsletter, recalls the old propaganda technique of reporting the facts without telling the truth. Nowhere does this account mention what most readers already know from other sources, that Watson resigned after Bernadine Healy, the director of the National Institutes of Health, launched an investigation into his financial holdings. Not even reading between the lines provides a hint of friction between the two.

Instead, the newsletter treats Watson's departure as a routine transition. It quotes him to the effect that directing both the genome project (based in Bethesda, Maryland) and the Cold Spring Harbor Laboratory (in New York state) had become too burdensome for him and his family. It also notes that Watson had told his advisory committee as early as last January — before the controversy arose — that he was thinking of leaving. Although that is true, it is also true that the very press officer who wrote the newsletter account told reporters at the time not to take the comment too seriously; Watson often threatens to resign, she explained.

No one expects the genome project's official newsletter to wallow in gossip. But by pretending that there was no dispute at all — when even Healy was willing to discuss the situation openly — the newletters belittles its reseearcher-readers, who are grown-up people and who deserve an accurate and balanced report, and reflects badly on the credibility of the enterprise. Perhaps the lesson from this shabby episode is that the $7 million a year the United States is spending on the ethics of genome research is not enough. □

nature

NATURE · VOL 356 16 APRIL 1992

New government, old problems

The surprise re-election of the Conservative British government may not be as bad for British science as the past decade would suggest. Much will depend on new people's willingness to listen to the truth.

AGAINST the bookmakers' odds and the confident predictions of the commercial polling organizations, the British government was re-elected last week. Although its majority is small, it is enough to keep it in office for a full five years. On the face of things, that is bad news for the British research enterprise. Why should a government convinced that it has done as well by science as anybody could have expected now change its view, especially after an electoral upset?

Luckily, there is some hope. The Prime Minister, Mr John Major, has been speaking of a government "of all the people"; the hope must be that even researchers and academics are counted among them. Then, as is customary, there is a change of faces at the two ministries with an important influence on research. Mainland-minded Mr Michael Heseltine, with hankerings after industrial policy (or public support for chosen innovation), will run the Department of Trade and Industry (DTI). And Mr John Patten, previously at the Home Office, becomes the sixth Secretary of State for Education and Science in twelve years; the hope is that, with a Cambridge PhD and a spell as an Oxford academic, he will at least acknowledge that there is a problem to be tackled. If he plays his cards well, he may yet collect the honorary degree Oxford's academics denied to Mrs Margaret Thatcher a decade ago. Certainly, neither of the new men needs feel bound by the complacency of his predecessor.

The diagnosis is now well-known: British researchers are mostly demoralized, underpaid and inadequately supported in research, while the institutions in which they work (universities and public research organizations) are so much in flux that opportunities for long-term programmes of research have dwindled. Demoralization, being a state of mind, cannot confidently be measured objectively, although there are putative proxies — emigrant inclinations, for example. But Patten (for it is his responsibility) should be readier than his predecessors to listen to what researchers say. As the whole world knows, people are most easily further demoralized by being told that their assessment of their own states of mind must be imagined.

It also falls to Patten to promise a measure of stability for the British system of research support. Three important changes are now under way [em] the transfer of a chunk of the collective recurrent budget of the universities to the research councils (which will then accompany research grants with overhead payments), the designation of polytechnics as universities and the balkanization of the system of university support (with separate funding councils for Scottish and Welsh higher education). It remains to be seen what scope there will be for institutional self-improvement under the new overhead arrangements, the redesignation of polytechnics is welcome but precipitate and the balkanization of funding arrangements a needless concession to regional ambitions that oddly conflicts with Major's passionate defence of the integrity of the Union (of the United Kingdom) during the election campaign. Patten could do worse than promise that this will be an end to structural change for the time being.

At some stage, he will also have to find more money, and be content that most of it should be spent on salaries. It is absurd that the chief avenue of recruitment into British research should require PhD students to subsist on less than half the income of a stenographer, but at present there is no choice; students might otherwise be earning more than those who teach them. The research community could help Patten (and itself) by hammering out a tolerable mechanism for deciding researchers' pay. But that will not pay for more research, which is where Heseltine has a role to play. DTI is traditionally responsible for British representation at Brussels, which has more money than good ideas. If Heseltine were to push for a European Community research programme functioning as a grant-making agency, he would win many friends and do a lot of good. □

Healy in a hurry

Dr Bernadette Healy has rid the Human Genome Project of Dr J. D. Watson in a distasteful way.

DR James D. Watson, co-discoverer (with F. H. C. Crick) of the structure of DNA, director of the Cold Spring Harbor Laboratory and of the US Human Genome Project, can be an awkward customer. Unsurprisingly. He has strong opinions. He usually knows what he wants. He is often right. Dr Bernadette Healy, director of the US National Institutes of Health (NIH) for the past year, also has strong opinions and seems to know what she wants. It has been plain for some time that she has wanted

Watson out of the Human Genome Project. Now she seems to have had her way; Watson resigned last week (see page 549). But Healy will find that she has damaged herself more than she has hurt Watson. The Human Genome Project itself will be the chief victim of her impatience.

The way in which Watson has been forced out is discreditable, and is a worry for all who may in future be asked to help out at NIH. That Healy and Watson did not get on has been an open secret for some time. Healy seems to like decisions to be clear-cut, Watson tends to reflective procrastination. For example, he openly disagreed with Healy's support for the NIH plan to seek patent protection for the nucleotide sequences of human genes when nothing was known of their function, chiefly on the grounds that this activity may make a monkey of the Human Genome Project (which it will). That is an issue that NIH should have been willing to talk out with the research community. Instead, Healy has got rid of Watson by fussing about the supposed conflict of interest arising from his ownership of shares in various pharmaceutical and biotechnology companies, potential beneficiaries of the Human Genome Project.

Ends do not justify all means. The means chosen in this case, those of casting a slur on a distinguished helper, even if one chosen before her time, are likely to rebound on Healy. People will wisely think twice before acceding to future requests for help. And what if Congressman John Dingell and his eager committee aides get wind of this whiff of scandal? Neither Healy nor NIH would benefit from the full rigours of congressional control of appointments to the army of advisory committees without which its external functions would collapse. Yet much the same has already happened as a result of Healy's precipitate intervention last year in the affairs of NIH's Office of Scientific Integrity (OSI); she may have had good cause to demand that OSI's procedures should be more formally judicial, but the manner of her removal of Dr Suzanne Hadley has had the effect of transferring control of OSI to the Department of Health and Human Services — and of unjustly delaying several important decisions. Everybody will sympathize with Healy's wish to get things done, but will hope that she learns the benefits of circumspection. Quickly. □

Lost numbers game

The US National Science Foundation (NSF) should apply to its own studies the rigour it expects of grant-applicants.

NSF MADE a sorry mess of its defence last week of a poorly done forecast that the United States will be short of 675,000 scientists two decades hence (see page 553). The chief author of NSF's study, policy analyst Peter House, was obliged to admit to a congressional subcommittee that it was a theoretical exercise without bearing on reality.

To be fair, NSF's fuzzy thinking on manpower is encouraged by the inclination of elders in the research community always to advance bullish estimates of future demand, apparently indifferent to the hundreds of PhDs competing for each academic vacancy and the thousands of lay-offs of skilled people by companies in high technology. Sadly, these arguments stem more from the heart than from the head. The elders are dismayed that the brightest students no longer automatically specialize in science, mathematics and engineering. They fail to recognize their own love of learning in those who choose law or business studies and are saddened that a starting salary of $80,000 a year on Wall Street should often seem so much more desirable than a post-doctoral fellowship worth, say, $18,000. They say publicly that the United States needs talented youngsters in science to compete with economic powers such as Japan and Germany, but cannot back up their assertion with evidence.

Of course, there is no accepted yardstick for telling how many scientists a country needs, but even the simple concept of supply is fraught with danger. One reason why the NSF study ran aground was its assumption that the supply of 22-year-olds is a proxy for overall supply when, in truth, there is an untapped pool of millions of scientists in the labour force not at present working in their chosen fields. Moreover, the preferences of 22-year-olds are shaped by crises, real or imagined. For example, the rate of participation in science rose after the Soviet Union put the first satellite (Sputnik) into space in 1957; only a few years earlier, it had fallen precipitously as a result of the glut of talent generated when returning soldiers resumed college education and flowed into technical fields. If women and minorities begin to enter science in numbers closer to their representation in society, supply will rise on its own.

The other half of the labour equation, the demand for scientists, is shrouded in similar uncertainty. The health of the economy, rather than a preference or distaste for scientific talent as such, determines how many technical jobs there are. In the United States just now, less spending on defence has significantly shrunk the technical work-force, for example.

The NSF study disregarded such factors in its search for a single number that might rally support for its cause. Inevitably, it backed into an indefensible position. In doing so, it has given comfort to those who doubt NSF's capacity to carry out analyses of complicated problems.

But there will be lasting and more serious consequences. This fiasco muddies the waters for the next attempt. It also chips away at NSF's credibility when its small but growing budget is under attack from those whose causes, from education to housing, have not been similarly blessed. None of this implies that there are no problems in the recruitment of able technical people, but merely that NSF has missed a chance to find solutions of them. □

Department Sets Gauntlet for NIH Strategic Plan

The NIH Strategic Plan, centerpiece of the year-old regime of Director Bernadine Healy at the National Institutes of Health, continues to be viewed with deep suspicion as a budget-busting ploy in the Department of Health and Human Services, according to documents obtained by SGR.

In preparation almost since Healy arrived at NIH last April, a 500-page draft of the Plan—setting an ambitious growth course for NIH well into the next century—was scheduled for unveiling in February in San Antonio, with George Bush in attendance. But three weeks prior to the event, a red flag was hoisted by Martin H. Gerry, HHS Assistant Secretary for Planning and Evaluation, who warned that the "President and the Secretary [of HHS] would be seriously embarrassed by the plan's unveiling in Texas."

Stressing that the NIH Plan implied heavy additional spending, Gerry observed that the President's proposed budget for NIH allowed for only modest increases next year, and that the rate of growth was not likely to change soon. The implication was that Bush's presence at the meeting could be interpreted as a repudiation of his own insistence on spending restraints—a welcome gift for Democrats accusing the President of domestic neglect.

With the Presidential presence scrubbed from the San Antonio program, the NIH Administration withdrew the draft document, substituting a 14-page Framework for Discussion that has since been discussed at a series of regional meetings around the country.

But even the skimpy Framework is considered suspect in the upper reaches of HHS, where a formidable gauntlet of review has been prescribed for any further editions of the Strategic Plan that may come out of NIH.

In a memo dated March 31, Carol Wigglesworth, of the Executive Secretariat in the Office of the Assistant Secretary of Health, advised senior HHS officials that "the Secretary's office has indicated that they must have the revised draft of the NIH plan at least two weeks prior to the NIH publication date, which will be determined based on when OS [Office of the Secretary] receives the plan.

"Similarly," the memo continues, "Dr. Mason [Assistant Secretary of Health] and his staff offices will require at least two weeks to complete their review prior to forwarding the plan to the Office of the Secretary."

Attached to the memo are critical analyses of the Strategic Plan produced by the HHS Assistant Secretary for Planning and Evaluation and the HHS Assistant Secretary for Management and Budget

Dated March 6, the analysis from Planning and Evaluation states: "To avoid creating any false expectations in the science community, NIH should indicate that large-scale expansions are not likely, given the current budget resources." Attached is an earlier memo from the same office stating that NIH should make it clear that "implementation of the proposed science initiatives would require reductions in existing programs. Omission of such a statement would create false expectations in the science community."

The March 6 analysis from HHS Management and Budget states that in the Framework for Discussion, "The cost management section is historical in nature. The section does not specifically identify a cost control strategy for future biomedical research programs. A framework to develop a plan for controlling future costs should be incorporated. In addition, NIH should acknowledge its role as manager of both direct and indirect costs."

The memo continues: "The Framework needs to identify and examine the existing relationship between the extramural and intramural programs to ensure more effective future interactions. In addition, those policies that NIH views as detrimental to the intramural program should be subject to an intra-Departmental review before legislative action or public forum discussions occur."

The San Antonio meeting brought demands from NIH's extramural clients for participation in the planning process. Healy welcomed them to join in. The reshaping of the draft continues, but when it will surface, if ever, is not clear.

Behind Watson's Exit

James Watson's encouraged resignation last week from the Directorship of the National Center for Human Genome Research at NIH has been most directly linked to concerns about his pharmaceutical drug holdings and the possibility of conflict of interest with his government responsibilities.

But other factors may have been involved, too, namely: Watson's unusual, if not unique, position as a government official and director of the private Cold Spring Harbor Laboratory, Long Island, NY, and a miscalculation about the clout of NIH Director Bernadine Healy.

At a meeting of the DC Science Writers Association on April 9, the day after Watson quit, Healy was asked whether his twin-hatted status had caused her any concern. She replied that Watson's employment at NIH, which long preceded Healy's arrival there, had been reviewed and approved. She added, however, "that doesn't mean that there aren't some added burdens and difficulties about such a perhaps ambiguous situation, and I think some of that may be what's coming forward at the present time."

Two years ago, in a Q&A with SGR [March 15, 1990], Watson was asked whether the genome project was affected by the long delay in finding a new Director for NIH. No, he replied, explaining:

"When I say it hasn't affected us, it reflects how little power the NIH Director has. The institute directors are pretty much masters in this ... The Director [of NIH] can't do anything—I think that's probably the chief reason people don't want the job."

Nobel Prize Biologist Watson Plans to Resign U.S. Position

By David Brown and Malcolm Gladwell
Washington Post Staff Writers

Nobel Prize-winner James D. Watson, head of the U.S. office of human genome research, said yesterday he will resign his position "as soon as possible" over what he calls a professional insult and what federal officials say could be a potentially serious conflict of interest over his financial holdings.

The precipitating event came in the context of a routine review of Watson's personal finances two weeks ago. But the famed biologist's decision, he said, derives chiefly from his belief that Bernadine P. Healy, director of the National Institutes of Health, "does not want me."

"I generally like to be at a place where I'm wanted. I have very strong and unassailable reasons for thinking she wants me to leave," Watson said yesterday.

A co-discoverer of the double-helix structure of DNA, Watson has served as the part-time director of the National Center for Human Genome Research—which is part of NIH—since its inception in 1989. He has also retained his job as head of Cold Spring Harbor Laboratory in Long Island.

Watson and Healy have disagreed publicly on science policy, most recently on the issue whether the federal government should attempt to patent DNA sequences its researchers discover.

Speaking through a spokesman, Healy said that although she had nothing but the "highest regard" for Watson's "scientific capabilities and his leadership," she had no choice but to confront Watson over his stock holdings in biotechnology companies.

The Healy-Watson dispute hinges on two unrelated incidents—one involving his financial holdings, the other a written allegation of inappropriate conduct—both of which are interpreted in dramatically different ways by each party.

According to Watson's version, he went to the ethics office of the Department of Health and Human Services in late March for an annual discussion of his personal investments, which include stock in several biotechnology companies. Such annual reviews are standard practice for federally appointed officials in similar positions.

NIH and HHS officials had previously expressed some concern that Watson's holdings might constitute a real or apparent conflict of interest, since his job involves overseeing a multimillion-dollar federal effort to decode human genes. This information will ultimately be of great commercial value to drug and biotech companies.

Watson said yesterday that he had been willing to sell his stock.

But during the course of the March interview with an HHS attorney, Watson said, he was shown a two-page letter written to Healy by Connecticut financier Frederic A. Bourke Jr., alleging that Watson had threatened "all-out war" if Bourke tried to lure two prominent genome researchers out of strictly research positions into a commercial venture that Bourke was considering setting up.

Bourke's letter complained that Watson had tried to exert inappropriate pressure against Bourke's project and also accused the biologist of being "excessively profane and vulgar."

Watson would not comment specifically on the allegations in Bourke's letter, saying that he looked at it only briefly during the March meeting.

Watson was angered because he believes that Healy should have brought the letter to his attention personally rather than forwarding it to the ethics office.

"I did not think that was the way I should receive a letter like that," Watson said yesterday. "After I saw the letter, I decided I was out."

Healy's version of events is quite different. She says that the reason she did not give him the letter is that she was instructed not to by senior HHS officials who advised that government protocol required that it be given to Watson through a neutral intermediary, as was done at the March meeting.

"Dr. Healy doesn't have the luxury of ignoring ethical questions, even for a Nobel Prize winner," said Johanna Schneider, the director's spokesman. "Healy inherited a questionable situation," she said. "It was her responsibility to take some action."

The stocks in question included holdings in the Merck pharmaceutical company, Amgen, a drug company that uses recombinant DNA technology, and at least one other firm. Watson yesterday said these were not recent purchases.

"They knew exactly what I had a year ago, and nothing has changed. Nothing has happened, except that I think Dr. Healy wishes me to leave. I could divest most of them, but it would be pointless now because she doesn't want me."

Watson did not set a date for his departure. "I have a fine reputation, and they are trying to soil it when I've worked very hard for 3½ years on behalf of the country," he said yesterday. "I would say this is the lowest moment of my life—to work so hard and to be treated so badly."

Watson, who is 64, had from the beginning said he would stay only about four years in the post of genome director. In January, he told his panel of scientific advisers that he would leave in about six months.

WASHINGTON POST - THURSDAY, APRIL 9, 1992 P. A3

Watson resigns, genome project open to change

■ Will leave immediately, acting head named
■ Smaller centres, more research anticipated

Washington

JAMES Watson, who officially resigned last week as director of the $3,000 million US human genome project, was probably the only person who could have brought the effort so far in its first three years. But now that the once-controversial project is on its feet, many researchers are hoping for a change of pace.

Advocates of cDNA sequencing, small genome centres and more research on the way genes function — all of whom struggled for funding under Watson's vision of a high-technology genome effort with an emphasis on mapping large stretches of DNA in the human genome and other model species — are likely to see their fortunes brighten under new leadership. And other researchers are hoping that a change at the top may mean an end to the 'old boys' genome network' that they believe has kept the Center for Human Genome Research at the National Institutes of Health (NIH), which Watson directed, from evolving as quickly as similar efforts in other countries and even within the US Department of Energy (DOE), which shares responsibility for the project.

Watson departed in the wake of concern over possible conflict of interest in his holdings of various biotechnology stocks and an increasingly visible dispute with Bernadine Healy, the NIH director. His stepping down is seen as the loss of an able genome advocate and a harbinger of difficult political times. Genome researchers have expressed nearly uniform sadness over the circumstances and haste of his departure. They also credited Watson for giving the project shape in its early years, and leading it through initial congressional opposition.

But it was the timing of Watson's decision that concerns researchers most. He had been expected to leave soon anyway, says Norton Zinder, a Rockefeller University geneticist and former chair of Watson's genome advisory panel. But Zinder and other associates had recommended a graceful departure towards the end of the year, after seeing through this year's congressional budget process. Almost any arrangement, in fact, would have been better than what actually happened: a tumultuous resignation coming just days after the first congressional hearing on the project's proposed 1993 budget.

If the project can survive this year's budget cycle, however, it may emerge reinvigorated. Watson formed a working enterprise out of what was only an idea four years ago, but "he never planned to stick around to micromanage the genome project," says Zinder. But, over the past year, some researchers were concerned that that was just what was happening. Watson was more of a genetic visionary than a practising researcher or manager, and his strength, both at the genome project and as director of the Cold Spring Harbor Laboratory on Long Island, New York, was not in day-to-day operations.

Watson's departure may make a place in the genome project for cDNA and its chief advocate, Craig Venter (at right, with NIH's Mark Adams)

His clash with Healy over cDNA patents last year was only the most apparent of his legendary disagreements with members of the genome community. He also opposed cDNA sequencing itself, arguing against churning out portions of expressed genes without knowing their function. And his determination to focus on obtaining a physical map of the entire genome assumed that gene sequencing technology would see great improvement over the past few years, something that has not happened.

"According to his text, we'd get revolutionary improvements in the technology, and that has not materialized," says Paul Berg, director of the Stanford University Beckman Center and current chair of the genome project's advisory committee. Sequencing cDNAs offered a cheap and easy way to find expressed genes that could be used as markers in genetic mapping, and an alternative to the straight-ahead, sequence-to-the-end approach that Watson advocated as the eventual goal.

But Watson disapproved of cDNA sequencing as being insufficiently rigorous, and he fought its leading proponent, J. Craig Venter of the NIH. Since then, the DOE (which supports about a third of the US genome project), France, the United Kingdom and Japan have all embraced cDNA sequencing. Only NIH have resisted.

Now, says Berg, "I think that there will be a much more receptive atmosphere to cDNA work." In his effort to give the genome project direction and momentum in the face of early opposition, Watson "may have focused too narrowly", Berg says. "He wanted to keep people's noses to the grindstone. And we might not have been so far along today, if it were not for his single-mindedness and doggedness." Berg predicts that the genome project will in future be more tolerant of other approaches, including more studies of gene function and biology.

Small genome centres may also come into favour. Several teams in Europe that are studying the yeast chromosome have shown that a dozen researchers with an automated gene sequencer, if they collaborate will similar teams, can be as productive as a large group, says Venter. "Originally, it seemed like exactly the wrong approach — exactly the opposite of the high-tech strategy" that Watson advocated, he says. But once the small teams learned to work with each other, they were able to move on to different projects with a flexibility that large laboratories can only hope for.

NIH are deciding how large to make the next set of genome centres. Many researchers argue for a balance between large and small laboratories, rather than a focus on laboratories with a 'critical mass' of researchers, about 20 PhDs, such as is headed by Eric Lander at the Whitehead Institute of Biomedical Research in Cambridge, Massachusetts.

In his resignation letter, Watson promised to continue to support the project enthusiastically, and to advise NIH informally. But his resignation takes effect immediately, and last week Healy appointed Michael Gottesman, currently chief of the Laboratory of Cell Biology at the National Cancer Institute, to be acting head of the National Center for Human Genome Research.

Healy also announced that the search for a permanent director would begin immediately. Although several prominent researchers (including Victor McKusick, a geneticist at Johns Hopkins University) have been mentioned in the past as possible replacements for Watson, the likeliest candidate right now is Daniel Nathans. He is a Nobel Laureate like Watson and, like McKusick, a Johns Hopkins geneticist, as well as being a member of the President's Council of Advisors on Science and Technology, on which Healy served before becoming director of NIH.

Christopher Anderson

GENOME PROJECT

Friends Say Jim Watson Will Resign Soon

The long-rumored resignation of James Watson, director of the National Center for Human Genome Research at the National Institutes of Health (NIH), appears to be imminent. Word spread across the country last week that the outspoken Nobel laureate, who has led the NIH genome effort since its inception in 1988, will step down this week or next. Watson would not comment, but many of his closest friends believe Watson is out—if not now, then soon.

PETER CUNNINGHAM

Jim Watson

Watson has wanted out for some time, his friends say. They note that the burden of holding two demanding jobs—he is also director of Cold Spring Harbor Laboratory—has taken both a physical and mental toll. In fact, at the January meeting of the NIH genome advisory committee in Irvine, Watson mused aloud about whether the project was well enough established so he could step down.

Watson also has a well-known propensity for resigning and then changing his mind—when he is angry. "Jim has resigned from everything about five times," says one friend, pointing out that Watson threatened to quit this job 2 years ago when the genome project was under fire from scientific critics.

This time, however, the threat seems to be real. The root problem, rumors aside, would appear to be Watson's basic incompatibility with NIH director Bernadine Healy. It is no secret that Watson's relationship with Healy, not great to begin with, has soured in recent months. They have been at loggerheads over NIH's recent move to patent thousands of gene fragments (*Science*, 22 November 1991, p. 1004), which Watson has denounced as sheer lunacy and Healy has strongly defended.

Not thrilled. Nor is Healy said to be thrilled by Watson's vocal criticisms of Frederick Bourke, a businessman who is attempting to lure several leading genome scientists into a sequencing company (*Science*, 7 February, p. 677). The equally outspoken Bourke has written to Healy, blasting Watson for his criticisms, which he considers out of line for a federal employee. Healy was sufficiently concerned to pass the letter on to Jack Kress, special counsel for ethics in the Department of Health and Human Services (HHS), says her spokeswoman, Joanna Schneider.

But the precipitating event of the current crisis seems to be Watson's yearly financial review, now under way, which has turned up some apparent conflicts of interest—reportedly, holdings in several biotech companies. Ethics watchdog Kress, who reviews the financial statements for HHS, told *Science* that he had approved Watson's holdings a-year-and-a-half ago. Since he has had this post, Kress added, Watson has openly declared his substantial holdings. But this year, Kress noticed a few red flags that he says arose both from changes in Watson's holdings and changes in the law, which has become more stringent.

To Kress, "This is very common, nothing out of the ordinary. I had a meeting last week with Dr. Watson. I said here are a couple of things that concern me. Let's talk in a couple of weeks. I made it very clear to him that in no way, shape, or form did I find anything ethically improper about anything he was doing."

By several accounts, Watson took the chat more seriously. Kress, too, says Watson told him at the time that he was thinking of resigning anyway. To Kress, the apparent conflicts shouldn't have precipitated such an action. There are several options for dealing with them, he insists: Watson could sell the stocks, recuse himself from any decision that might affect the company or companies or Healy could sign a waiver that would essentially say that Watson's financial interests are so insubstantial that they would not affect the performance of his duties.

Kress discussed those options with Healy in late February, at which time he raised the option of a waiver, which he portrayed as a routine step. Not routine to Healy, however. Her spokeswoman, Schneider, says that Healy believes that "there are questions surrounding his financial statement that clearly need to be answered and worked out." And Schneider says that Healy considers the waiver a "pretty serious move" and has asked Kress for more information.

Healy has not spoken to Watson about the matter—and that, say Watson's friends, is indicative of the problem. "They both lost their cool and stopped talking," says one. That may end this week, when Watson has asked for a meeting. But it may not change the outcome being widely predicted by those close to Watson. They believe he will leave, and the only question is when. Some suspect that once Watson calms down, he will decide to stay until a successor is named and the project is solidly on its feet. And everyone agrees that Watson is mercurial—a decision made in anger today could be reversed tomorrow.

–Leslie Roberts

SCIENCE EDUCATION

Science Teachers Offer a New Plan

Perhaps you're sick of reading about the dismal state of science education in the United States and are ready for a proposal. Enter the National Science Teacher's Association (NSTA) with their plan for improving U.S. science literacy, described in the book "The Core Content, A Guide for Curriculum Designers," which was published last month. It's the latest development in NSTA's "Scope, Sequence, and Coordination of Secondary School Science Program," known as SSC for short, which was begun 2 years ago with the aid of $15 million from the Department of Education and the National Science Foundation (NSF).

According to SSC's director of research and development, Russell Aiuto, science students are usually exposed to one discipline at a time and rarely see the relationships between subjects necessary for a deep understanding of scientific ideas. But SSC aims at getting around that problem by giving students simultaneous exposure to different scientific disciplines thoughout grades 6 to 12. "When evolution is taught, so is the history of the earth," Aiuto explains. "The current layer cake approach—biology in the 9th grade, chemistry in the 10th, and physics in the 11th—is a remnant from 1891."

And according to surveys made by SSC staff, the program is already successful in one regard. Students exposed to the new approach in pilot studies, as well as their teachers and parents, like it. Houston, the site of one pilot study, is so enthusiastic it plans to extend the program to all its secondary schools, and about 1000 of the 16,000 school districts in the United States have requested information about SSC. That interest could be a good sign, and not just for SSC. "What [NSTA's] doing may turn out to be very helpful to us, if they can get the notion into secondary educators that there may be different ways of doing things," says James Rutherford, head of the American Association for the Advancement of Science's Project 2061, SSC's chief competitor for funding.

But for all the positives, it's still too early to tell whether the SSC program is improving science literacy or enticing more students to become science majors. Nor do SSC's organizers think their new book is the last word in science education reform. To see what changes might be necessary, they want feedback both from people outside the pilot programs who try to use the SSC approach and also from 11th- and 12th-graders when they finish the courses.

–Robin Eisner

Robin Eisner is a science writer based in Boston.

Watson, Head of U.S. Genome Project, Faces Questions Over Stock Holdings

B8 4.9.92

By HILARY STOUT
Staff Reporter of THE WALL STREET JOURNAL

WASHINGTON – The Department of Health and Human Services ethics office is looking into a possible conflict of interest over stock in biotechnogy companies owned by James Watson, the Nobel laureate who runs the government's multibillion-dollar effort to identify all human genes.

Bernadine Healy, director of the National Institutes of Health, which is operating the human genome project, earlier this year asked the ethics office to examine the holdings listed on Dr. Watson's financial disclosure forms to determine whether they violate the government ethics statute, a spokeswoman for Dr. Healy said. Last night, an HHS spokesman said the matter "is still under review."

The probe comes against the backdrop of a festering behind-the-scenes battle between Dr. Healy and Dr. Watson. The journals Nature and Science report this week that the famous scientist, co-discoverer of the structure of DNA, is ready to resign over the flap.

Drs. Healy and Watson have been at loggerheads over a number policy issues. One disagreement centers on an NIH effort backed by Dr. Healy to patent man-made copies of hundreds of new-found genes. Dr. Watson also stirred controversy by his opposition to a proposal for a private company to take over a project for developing advanced techniques for determining the sequence of the molecules that make up the genes. But a spokeswoman for Dr. Healy denied that any disagreement influenced the NIH director's decision to question his financial holdings.

"They have had a policy dispute in the past, there's no doubt about it," said the spokeswoman, Johanna Schneider. "But that has not influenced this decision."

Ms. Schneider said that Dr. Healy hasn't received a response from the ethics office. And the HHS spokesman said that the ethics officer, Jack Kress, has reviewed the case and discussed with Dr. Watson "options for resolving the questions." He added, "At this time, the options are still under consideration and Dr. Watson's disclosure form remains under review."

Neither Dr. Watson nor Mr. Kress returned telephone calls seeking comment.

Dr. Watson's financial disclosure forms weren't immediately available. Ms. Schneider declined to identify his holdings in biotechnology and genetics companies, but she said that they were "substantial." Ms. Schneider also said that she didn't know if any of the companies had contracts with the government. But she added, "The [genome] project itself has a direct impact on the industry. . . . It is one of the newest industries, and it's growing and it's so volatile in terms of stock."

A spokeswoman for the genome project, Leslie Fink, confirmed that Dr. Watson has been thinking about leaving NIH, but she dismissed the idea that the conflict-of-interest probe would cause him to resign.

"He's been talking about resigning," said Ms. Fink. "His intention when he came on was to be here something like four years, and we're getting close to that. . . . As the program has gotten up and going, and he feels good about it, he's started to talk more about leaving." Ms. Fink contended that Mr. Kress had determined that no rules have been violated.

Dr. Healy is also said to be upset over a clash between Dr. Watson and Frederick Bourke, a Connecticut businessman who wanted to start a company to develop a technology for sequencing DNA. Mr. Bourke tried to hire two prominent gene sequencing researchers, who are heading a project to map the genome of a worm. Dr. Watson apparently tried to block the effort. Mr. Bourke sent a letter to Dr. Healy complaining of Dr. Watson's activities and alleging that he encouraged the British pharmaceutical company Glaxo to start its own gene sequencing company using one of the scientists Mr. Bourke was trying to hire. Mr. Bourke also alleged in the letter that Dr. Watson owned shares of Glaxo stock.

Dr. Watson is one of the most esteemed scientists in the world. In 1951, at the age of 24, he and Francis Crick, a British scientist, made one of the greatest scientific discoveries of the century, uncovering the structure of DNA, the basic building block of heredity. The genome project he now heads aims to map the human body's 100,000 or so genes and figure out precisely how they are constructed.

WSJ 4-9-92 p. C11

Bio-Technology General Corp.

NEW YORK—Bio-Technology General Corp. said it received approval to market its recombinant human growth hormone for short stature in France.

Bio-Technology General has already received technical and marketing approval in several other European countries, and a company spokesman said it expects further approvals "in the coming months."

Bio-Technology General began selling the hormone in South Korea and Israel last year. It will not be able to enter the U.S. market until 1994, when the protected status of similar Genentech Inc. and Eli Lilly & Co. drugs expires.

HEAD OF GENE MAP THREATENS TO QUIT

Watson, Who Helped Discover DNA, Now Faces Pressure on Financial Holdings

4-9-92 p. A26

By PHILIP J. HILTS
Special to The New York Times

WASHINGTON, April 8 — Dr. James D. Watson, the co-discoverer of the structure of DNA, is threatening to resign this week as head of the government project to map the human genome or gene set, officials close to him say.

Dr. Watson had intended to resign from the leadership of the gene program some time later this year, but has threatened to do so now after hearing that the National Institutes of Health was looking into possible conflicts of interest he might have because he holds stock in several pharmaceutical and genetic engineering companies.

Among the companies in which he or his immediate family has a financial interest are Amgen Inc., Glaxo Inc., Eli Lilly and Company, Oncogen and Merck & Company, an official of the Department of Health and Human Services said. Dr. Watson recused himself from direct decisions in some of the companies, but not in others, the official said.

His decisions as head of the project could have a substantial effect on the companies in which he has an interest, officials of the National Institutes of Health said.

Potential Beneficiaries

The companies are also doing sequencing work, these officials said, and are seeking human genes to use them in making drugs. Thus, they are both competitors with the government project and potential beneficiaries of its progress.

The threatened resignation, first reported in Science and Nature magazines, has caused some worry among scientists that the action could harm the prestige and financing of the project.

Dr. Watson has become so personally identified with the project that his departure may well open the project up to a new debate about its merits, Congressional staff members said.

Even critics quickly concede that the project's status and wide degree of backing are attributable to Dr. Watson's personal prestige and political connections.

Catherine Squires, a professor of biology at Columbia University who is a critic of the genome project, said today: "His stature in pushing this concept is one of the things that really carried that project. He is a good administrator, a smart and charming man, and in terms of politics he has been an excellent director of the project. The project has gotten where it has, which in my opinion is further than it should, because of who he is."

She said she hoped that Dr. Watson's departure, if it happens, would reopen the debate about the project because in her view it diverts money from more important biological research and toward the non-scientific "drudge work" of sequencing and mapping genes, most of which will turn out to be unimportant. The human genes are thought to be interspersed among much longer stretches of DNA that may have no essential purpose.

2,896 New Genes Discovered

The $160 million project is among the largest in the history of biology. As it progresses it is expected to map all of the 100,000 or so genes that are encoded among the billions of letters of DNA code in the human gene set.

As of last month the project has discovered 2,896 new genes, about 3 percent of all human genes, and have sequenced some of them. It also has mapped out large parts of three chromosomes.

The cost of sequencing genes under the project has dropped from an initial $2 to $5 per base pair down to the current estimate of $1 per base pair. The goal is to reduce the cost even further, to 50 cents or less per base.

The goal of sequencing the human gene set has been the subject of acrid debate among biologists. Critics maintain that that mapping the genes alone would be an almost useless exercise until the function of each gene is known, a task to be accomplished through conventional research on specific diseases.

Dr. Watson, who has been the head of the Genome Project since it began in 1988, has recently had some disagreements with Dr. Bernadine Healy, director of the National Institutes of Health, over whether the Government should try to patent every human gene as soon as it is discovered, regardless of whether its function is either known or useful.

Dr. Watson has called the idea "lunacy," but Dr. Healy has strongly supported comprehensive patenting to protect American rights to any drugs that might be developed from the newly discovered genes.

Recommendation Awaited

With that as backdrop, Dr. Healy recently received a letter from a businessman trying to start a gene-sequencing venture who suggested that Dr. Watson might have conflicts of interest. Dr. Healy turned the matter over to Jack Kress, the ethics officer at the Department of Health and Human Services.

Mr. Kress has not yet made his recommendation, but officials close to Dr. Healy said she would rather not resolve the matter by giving Dr. Watson a waiver, as Mr. Kress had suggested.

Another solution would be for Dr. Watson to recuse himself from matters involving the companies in which he has an interest, or to put his holdings in trust.

45,000 sites called potential hazards

Bost Globe 4-8-92 p. 6

WASHINGTON – More than 45,000 locations nationwide, including factories and hospitals, are potentially contaminated by radioactivity, according to the first government effort to chart the full national extent of the hazard. The eight-month study, commissioned by the Environmental Protection Agency, did not attempt to quantify the health risks at any specific location, or the degree to which radiation may have reached groundwater and croplands. Researchers based their findings on a survey of all available records of locations at which radioactive material was used, stored, manufactured or spilled. (AP)

INSIDE TV / BY PETER JOHNSON

Why Ellerbee held off disclosing breast cancer

USA 4-9-92 3-D

Linda Ellerbee thought about going public with news of her breast cancer several weeks ago, but hesitated.

She had taped last month's Nickelodeon kids' special in which Magic Johnson discussed having the AIDS virus "and didn't want to take the attention from that subject."

Ellerbee, a former ABC and NBC News correspondent, has gained lots of friends in the business over the years. When it came to keeping her secret, those same friends took off their news hats.

"Basically I have been getting an awful lot of calls and the press has been wonderful," Ellerbee said. "Everybody knew and nobody wrote anything."

But one of those old friends, ABC *PrimeTime Live* correspondent Sylvia Chase, talked Ellerbee into being the subject of an upcoming profile on ABC's *PrimeTime Live*. "Sylvia persuaded me it was a good way to tell a lot of people."

Biologist Watson Quits Position at NIH

Resignation Follows Disagreement Over Possible Conflict of Interest

By Malcolm Gladwell 4-11-92
Washington Post Staff Writer p. A9

James D. Watson, the Nobel Prize-winning biologist, has resigned as director of the National Center for Human Genome Research, Watson's resignation, submitted to National Institutes of Health Director Bernadine P. Healy yesterday, follows concerns raised by federal officials about whether Watson's stock holdings in, and involvement with, biotechnology companies might constitute a conflict of interest.

The genome project is a part of NIH, which is under the Health and Human Services Department. Two weeks ago, Watson met with an attorney in the HHS ethics office for a routine annual review of his financial holdings.

Watson, 64, who announced his decision to resign on Wednesday, said that he was insulted by aspects of that meeting and he no longer felt "wanted" in the position as head of the government effort to map the human genome, which he had held for almost four years.

"Dr. Watson is an historic figure in the annals of molecular biology, and the NIH has benefited from his leadership," Healy said in a statement issued yesterday. "We have been fortunate to have had his expertise and scientific judgment, which have been invaluable to the establishment of the National Center for Human Genome Research."

Healy's statement said that Michael M. Gottesman, chief of the Laboratory of Cell Biology at the National Cancer Institute, has been appointed as Watson's temporary replacement. The statement also said that the search for a permanent replacement will begin immediately.

DNA PIONEER QUITS GENE MAP PROJECT

Watson Resigns After Federal Review of His Holdings in Biology Companies

N.Y. Times 4-11-92 p 12

WASHINGTON, April 10 (AP) — Dr. James D. Watson, winner of the Nobel Prize as co-discoverer of the structure of DNA, resigned today as director of the project to map the entire human genetic sequence.

The resignation follows a review of Dr. Watson's investment portfolio and a statement from the Department of Health and Human Services that there were questions about his holdings.

In his letter of resignation, which was effective immediately, Dr. Watson said he "considered it a great pleasure and opportunity to have served."

The National Center for Human Genome Research, which runs the gene-sequencing project, said in a statement that Dr. Watson had presented his letter to Dr. Bernadine Healy, director of the National Institutes of Health, and had recommended that "a scientist of the highest reputation and integrity be appointed as soon as possible to succeed him."

Dr. Healy announced that Dr. Michael M. Gottesman would serve as acting head of the Federal gene research agency. Dr. Gottesman is now chief of the laboratory of cell biology at the National Cancer Institute. A search is under way for a permanent replacement for Dr. Watson, Dr. Healy said.

The N.I.H. director also described Dr. Watson as a "historic figure in the annals of molecular biology."

"We have been fortunate to have had his expertise and scientific judgment, which have been invaluable" to the gene project, Dr. Healy said.

Dispute With N.I.H. Chief

It was Dr. Healy who triggered a review of Dr. Watson's investments. Earlier this week, a spokeswoman for the health institutes, Johanna Schneider, said that Dr. Healy asked an ethics officer at the Department of Health and Human Services to review Dr. Watson's financial disclosure form, a report required of high Government officials. Dr. Healy was concerned about investments Dr. Watson had made in biotechnology companies, the spokeswoman said.

[A department official said this week that among the companies in which Dr. Watson or his immediate family has a financial interest are Amgen Inc., Glaxo Inc., Eli Lilly and Company, Oncogen and Merck & Company. Dr. Watson recused himself from direct decisions in some of the companies, but not in others, the official said.

[Officials of the National Institutes of Health have said Dr. Watson's decisions as head of the project could have a substantial effect on the companies in which he has an interest because they are also doing gene sequencing work. Thus, they are both competitors with the Government project and potential beneficiaries of its progress.]

Dr. Watson was named the first director of the gene research agency in 1989. The agency was created to coordinate Federal efforts to map and sequence all of the genes that control inherited human characteristics. The project is expected to take years and cost billions of dollars.

After Dr. Healy took over as director of the health institutes last year, she and Dr. Watson became ensnarled in a policy disagreement that Dr. Watson took no pains to conceal. Dr. Healy ordered the institutes to apply for patents for any genes that were identified by research it had supported. Dr. Watson has called the idea "lunacy."

Watson Resigns as Head of U.S. Gene-Mapping Project

Pioneering DNA Researcher Faced Probe on Holdings In Biotechnology Firms

By HILARY STOUT
Staff Reporter of THE WALL STREET JOURNAL

WASHINGTON—James Watson, the Nobel Prize-winning biologist who co-discovered the structure of DNA, resigned as head of the government's project to map the human genetic code following questions about his stock holdings in biotechnology companies.

His departure from the National Institutes of Health's Center for Human Genome Research comes after a series of policy disagreements with Bernadine Healy, who became the NIH director last spring. Dr. Watson has denounced her decision for the NIH to apply for a patent on thousands of gene fragments identified by one of its scientists who isn't involved in the genome project. Dr. Watson has called the patent application "sheer lunacy," and has predicted a frantic scramble among scientists and private companies to lay claim to human genes.


James Watson

In addition, Dr. Healy has been said to be upset over a clash between Dr. Watson and Frederick Avery Bourke Jr., a Connecticut businessman who wanted to start a company to develop a technology for sequencing DNA. Mr. Bourke tried to hire two prominent gene sequencing researchers, who are heading a project to map the genome of a worm. Dr. Watson apparently tried to block the effort. Mr. Bourke sent a letter to Dr. Healy complaining of Dr. Watson's activities and alleging that he encouraged the British pharmaceutical company Glaxo Holdings PLC to start its own gene sequencing company using one of the scientists Mr. Bourke was trying to hire. Mr. Bourke also alleged in the letter that Dr. Watson owned shares of Glaxo stock.

Pledge of Support

Associates of Dr. Watson say he has been considering resigning for many months. Some of his colleagues say he never intended to stay in the genome job for more than a few years, but they believe the continuing disagreements may have hastened his departure. The 64-year-old scientist also runs the closely held Cold Spring Harbor Laboratory in New York state, and will continue in that job.

"I remain firmly committed to the success of the Human Genome Project," Dr. Watson wrote in a four-sentence resignation letter submitted Friday to Dr. Healy. "I hope and expect to continue to support the project enthusiastically and, if called upon by my successor, to advise NIH informally."

Dr. Healy named Michael Gottesman, chief of the National Cancer Institute's cell biology laboratory, as acting head of the federal gene research agency until a permanent successor is chosen.

The NIH director in a statement called Dr. Watson a "historic figure in the annals of molecular biology." She added, "We have been fortunate to have had his expertise and scientific judgment, which have been invaluable."

Financial Review

Earlier this year, Dr. Healy questioned stock holdings in biotechnology and gene sequencing companies listed on Dr. Watson's annual financial disclosure form, and she asked a Department of Health and Human Services ethics officer to review the matter.

Last week, Dr. Healy denied through a spokeswoman that her motive for questioning Dr. Watson's stock holdings stemmed from either personal or policy disagreements. She said that his holdings were a serious cause for concern because the genome project directly influences the volatile biotechnology industry.

Dr. Watson, who at 24 years old discovered the double-helix of DNA along with British scientist Francis Crick, was appointed the first director of the genome agency in 1989. Many scientists believe that his prestige was invaluable in getting the ambitious, unprecedented and controversial project off the ground. Its aim is to map all human genes, which may number as many as 100,000.

But some scientists and members of Congress worry that the $3 billion, 15-year project could divert funding from other scientific research.

Akorn Inc.

Akorn Inc., Abita Springs, La., said it expects to report a loss that may be as high as $6.5 million for the third quarter ended March 31, compared with profit of $301,000 a year earlier.

The company said it will take several cash and non-cash charges in the third quarter relating to the acquisition of Taylor Pharmacal Co., the reorganization of the company's manufacturing operations and closing of the Walnut Pharmaceuticals Inc. unit, in addition to costs associated with the recall of products made at the Walnut facility. A spokesman said the charges total about $6.5 million. About $4.5 million of the total are cash charges to be paid out in the next 24 months, he said.

For the year ending June 30, the pharmaceutical and ophthalmic-products manufacturer and marketer said it expects a pre-tax loss of $8.5 million. For 1991, Akorn had a loss of $4.6 million on $15.9 million of revenue.

Opposition to Businessman's Worm Genome Project Led to Conflict Charges

By JERRY E. BISHOP
Staff Reporter of THE WALL STREET JOURNAL

The resignation of Nobel laureate James Watson as head of the human genome project was precipitated by a wealthy Connecticut businessman who has his own ideas about genome research.

Frederick Avery Bourke Jr., 45 years old, is most often associated with Dooney & Bourke Inc., a Norwalk-based maker of expensive leather purses. But he also is a home builder, a fan of jigsaw puzzles and an influential in-law of the Henry Ford family.

Earlier this year, Mr. Bourke burst upon the abstruse world of genetic research with an audacious plan to create what one scientist calls "the IBM of biology." Mr. Bourke's idea is to start a company that would "sequence," or pick apart the three billion molecules that comprise human genes—collectively the "genome." The company would link up with another fledging effort backed by Microsoft Corp.'s founder, William Gates, that is developing the information-handling technology to keep track of those molecules.

It wasn't Mr. Bourke's concept that triggered his clash with Dr. Watson but rather the way he proposed to launch his company. Mr. Bourke's company would start off by pre-empting one of Dr. Watson's key projects, a collaborative effort with the British to sequence the genome of a tiny worm.

Dr. Watson's powerful opposition to Mr. Bourke's taking over the worm genome project prompted the businessman to charge that the Nobelist's holdings of certain drug and biotechnology stocks constituted conflicts of interest. The charges were made in a letter to National Institutes of Health director Bernadine Healy, who has clashed with Dr. Watson on policy issues, and led Dr. Healy to order an investigation. Dr. Watson has told friends that Mr. Bourke's charges were unwarranted and that he thought Dr. Healy was merely using the charges as an excuse to get rid of a cantankerous thorn.

Mr. Bourke's letter hasn't yet been made public and his exact charges remain something of a mystery. Attempts to reach Mr. Bourke in Norwalk were unavailing as were attempts to interview Dr. Watson.

One of the charges that Mr. Bourke was reported by the British science journal, Nature, to have made, is that Dr. Watson tried to persuade the big British drug company, Glaxo Holdings PLC, to start up a biotech company that would compete with Mr. Bourke's proposed company. A top Glaxo official denies that. Richard Sykes, research director at the company, said through a spokesman that he had met Dr. Watson at a international conference and chatted with him but that there was no mention of setting up any kind of biotech company and that Glaxo had never considered such a move.

A spokeswoman for Dr. Watson said that he did not have a copy of the letter, but it had been read to him. The letter apparently charged that his positions on several genome-related policies are shared by drug and biotechnology companies and that Dr. Watson holds stock in Amgen Corp., a biotech company, and Merck & Co., the big drug maker. For example, Dr. Watson is opposed to the NIH's attempt to patent hundreds of human genes uncovered by NIH scientists, an effort backed by NIH director, Dr. Healy. The biotech industry is similarly opposed to the gene patenting effort.

What sparked Mr. Bourke's interest in Dr. Watson's human genome project is unclear. Several months ago, according to various scientists, he began approaching several researchers who are involved in laying the groundwork for the ultimate phase of the genome project, the so-called DNA sequencing phase.

The initial aim of the genome project, which was formally launched in the U.S. in late 1990 under Dr. Watson's guidance, is to "map" or locate and identify all 50,000 to 100,000 genes that are hidden in the chromosomes of every human cell. Each gene consists of a segment of DNA, which is a necklace-like strand of submolecules called bases.

As the thousands of genes are mapped, however, scientists face the problem of determining the sequence of the DNA base molecules in each gene. The plan is ultimately to determine the sequence of the base molecules in the entire length of human DNA, estimated to be three billion bases long.

Such sequencing work is expected to be so tedious and voluminous as to be beyond the capacity or interest of academic scientists. So, almost from the beginning, the plan has been to contract out the sequencing work to private industry.

"I've been involved with him almost from the beginning" of the proposed company, says Leroy Hood, the California Institute of Technology biochemist and pioneer in developing automated machinery to sequence genes and proteins. "Initially, I was skeptical—not of the validity of the proposed company but whether this was the right time to do it," he adds. After talking with Mr. Bourke and with other scientists, he says, "I became convinced it is feasible." In fact, he says, there is widespread agreement that "this is a good thing to do and now is the time to do it."

Dr. Hood is the key link between Mr. Bourke and Microsoft's Mr. Gates. The Caltech scientist is founder of a small company, Applied Biosystems Inc., which is developing the automated sequencing machinery. Dr. Hood along with many of his Caltech co-workers are preparing to move to the University of Washington in Seattle, lured by a $12 million gift from Mr. Gates.

With the Gates endowment and the help of Mr. Gates's computer wizardry, Dr. Hood's team will work on the technology for the sequencing task. He hopes, for example, to develop machines that can sequence a million DNA bases a day, a hundred times more than can be done with current techniques. Techniques to record and interpret this much information require a major advance in computerized information handling, Dr. Hood explains.

Mr. Bourke's company would acquire machines from Dr. Hood and seek cost-plus government contracts to sequence human DNA. But the major potential of the company, Dr. Hood says, would be its primacy in access to the unprecedented information that will come from sequencing the human genome. Its first-view position could lead to a large business in information for medical diagnostic and therapeutic uses, he says. "In four to five years, the company would become a major information broker," he says.

Earlier this year, however, Mr. Bourke made a move that stirred opposition from Dr. Watson and genome project managers in Britain. To start his company, Mr. Bourke tried to recruit the world's leading DNA sequencers, an American, Robert Waterston of Washington University in St. Louis, and a British scientist, John Sulston of the Medical Research Council laboratory in Cambridge, England.

The attempt to hire away the pair angered Dr. Watson who has striven to make the genome program an international effort. Fearing Mr. Bourke would destroy a successful collaboration vital to the international genome effort, Dr. Watson intervened. He appealed to the Medical Research Council, the British equivalent of the U.S. National Institutes of Health, to raise Dr. Sulston's funding lest the scientist defect to Mr. Bourke's company. The MRC hasn't announced its decision but is believed to have agreed to Dr. Watson's request.

Codiscoverer of DNA's form quits US post

Boston Globe 4-11-92 p.3

ASSOCIATED PRESS

WASHINGTON – James D. Watson, who shared the Nobel Prize for describing the structure of the molecule that forms human genes, resigned yesterday as director of the National Center for Human Genome Research.

The resignation follows a review of Watson's investments and a statement from the Health and Human Services Department that there were questions about his holdings.

Dr. Bernadine Healy, director of the National Institutes of Health, triggered a review of Watson's investments. This week, an NIH spokeswoman, Johanna Schneider, said Healy asked an HHS ethics officer to review Watson's financial disclosure form, a report required of high government officials. Healy, the spokeswoman said, was concerned about investments Watson made in biotechnology companies.

Watson shared the Nobel Prize in Medicine in 1962 with Francis Crick for discovering the double helix shape of the deoxyribonucleic acid, or DNA, molecule that forms the human genetic code.

Watson was named the first director of the gene research agency in 1989, which was created to coordinate federal efforts to map and sequence all human genes.

Nobel winner resigns from gene mapping program

By PAUL RECER
Of The Associated Press

WASHINGTON — James D. Watson, winner of the Nobel Prize for first describing the structure of the human gene molecule, resigned yesterday as director of the National Center for Human Genome Research.

The resignation follows a review of Watson's investment portfolio and a statement from the Health and Human Services that there were questions about the scientist's holdings.

In his letter of resignation, which was effective immediately, Watson said he "considered it a great pleasure and opportunity to have served."

The center said in a statement that Watson presented his letter to Dr. Bernadine Healy, director of the National Institutes of Health, and recommended that "a scientist of the highest reputation and integrity be appointed as soon as possible to succeed him."

Healy announced that Dr. Michael M. Gottesman would serve as acting head of the federal gene research agency. Gottesman currently is chief of the laboratory of cell biology at the National Cancer Institute. A search was under way for a permanent replacement for Watson, Healy said.

The NIH director also described Watson as a "historic figure in the annals of molecular biology."

"We have been fortunate to have had his expertise and scientific judgment, which have been invaluable" to the gene project, Healy said. "We wish Dr. Watson well and thank him for his service."

It was Healy who triggered a review of Watson's investments. Earlier this week, an NIH spokeswoman, Johanna Schneider, said that Healy asked a HHS ethics officer to review of Watson's financial disclosure form, a report required of high government officials. Healy, said the spokeswoman, was concerned about investments Watson had made in biotechnology companies.

Watson was named the first director of the gene research agency in 1989. The agency was created to coordinate federal efforts to map and sequence all of the genes that control inherited human characteristics. The project is expected to take years and cost billions of dollars.

After Healy took over as director of NIH last year, she and Watson became ensnarled in a policy disagreement that Watson took no pains to conceal. Healy ordered the NIH to apply for patents for any genes that were identified by NIH-supported research. Watson was quoted in the media as saying he thought this plan "absurd."

Abbott sees no letup in profits

1,000 added to sales force to keep momentum going

By Steven Morris

Clipic. Trib. 4/11/92 pg. 1/2

Abbott Laboratories expects continued growth in sales and profits despite "challenges" in its infant formula business and a downbeat hospital environment, a top executive told shareholders Friday.

Abbott's key diagnostics division increased its market share last year "about a point," to 15 percent, more than twice that of its nearest competitor, Baerhringer Mannheim of Germany, said Thomas R. Hodgson, president and chief operating officer, in a report at the company's annual meeting.

In the market for infant formula, Abbott remains the leader but is facing "intense price competition" in the government-sponsored Women Infants Children program, while major rivals such as Gerber and Carnation are "driving for share" in the general consumer market, Hodgson said.

And in the "very soft" market for hospital products, which has been affected by decreases in hospital admissions and procedures, domestic sales nevertheless grew 10 percent and operating income grew "significantly faster," he said.

In general, all of Abbott's businesses are "well-positioned for future growth," Hodgson said.

The diagnostics division has placed 17,000 of Abbott's IMx machines in laboratories for immunology testing since its introduction in 1988. They generated reagent sales of $400 million last year, an increase of 84 percent from 1990. Abbott expects at least 3,000 more of the machines to be in place by year's end.

The company's pharmaceuticals business made "good gains," said Hodgson. The launch in the U.S. of the anti-infective Biaxin, which received Food and Drug Administration approval in November, is expected to double that drug's worldwide sales to more than $150 million by the end of this year.

Biaxin and Temafloxacin, a quinolone anti-infective introduced in January, received "rapid reviews and approvals" from the FDA.

The company "took significant steps" last year to improve its relationship with the FDA in light of the agency's "more demanding requirements," Hodgson said.

Such steps include keeping in closer communication in order to streamline the submission of information, said company spokeswoman Catherine Babington. "We try to have whatever information they want and in the form they want it whenever they come into our plants," she said.

Introduction of three medical nutrition products last year—Nepro

See Abbott, following page

Continued from preceding page

and Suplena for kidney patients and Glucerna for diabetics—helped boost that division's sales above $500 million, up 13 percent from 1990.

Hodgson described as a "critical step" for the success of the recent launches the addition of 1,000 sales representatives, bringing the worldwide sales force to 9,000.

Abbott had its 20th year of record sales and profits in 1991. The "strong momentum" carried into the first quarter, in which sales rose 13.6 percent and earnings per share 16.9 percent, said Hodgson.

Sales of products introduced in 1991 came to $665 million, with new pharmaceutical and diagnostic products accounting for about 63 percent of that total.

About $2 billion of last year's $6.8 billion in sales came from products launched in the last five years, said Hodgson.

Abbott's directors approved the purchase of up to 4 million shares of its common stock, contingent on the completion of the sale of Abbott's holdings in Boston Scientific Corp. The new authorization would be in addition to a 6 million-share buyback authorized in December.

Abbott previously entered into a contract to sell its 20 percent holding in Boston Scientific as that firm goes public.

NEWS & COMMENT

[redacted]

Washington Perspective

Exit Dr Watson, the genome chief

Spacious though it is, the National Institutes of Health could not indefinitely accommodate two such high-velocity personages as its combative director, Bernadine Healy, and Nobelist James D. Watson, at age 64 the permanent *enfant terrible* of American science.

Out of public view, the two have had a history of collisions concerning the proper separation of public and private responsibilities, a major sensitivity in this scandal-mongering capital. But now, amid considerable acrimony, their differences have publicly erupted, and Watson has stalked off, proclaiming himself hurt and unappreciated. "I would say this is the lowest moment of my life—to work so hard and be so badly treated", he lamented to the *Washington Post*. Sympathy for his plight should be tempered by the recognition that massive past glory armours the ego of the puckish Dr Watson. He is likely to emerge not only unscathed but perhaps even enhanced by this trauma. Before the battle smoke had cleared, Healy herself hailed Watson as "an icon of science".

The bureaucratic setting for the Healy-Watson showdown was his rare, if not unique, dual status as an employee of the United States Government *and* director of a non-government laboratory. In the first role, Watson served as the scientific architect and political drumbeater of NIH's genome extravaganza, holding the title of director of the NIH National Center for Human Genome Research. Watson was installed in that job by Healy's predecessor, James Wyngaarden, when it appeared that the leisurely paced NIH was about to be pre-empted in the genome business by ambitious researchers at—of all places—the Department of Energy. The Department, created long ago for bomb building, is ever on the lookout for new work.

Watson took charge. In just a few years, despite considerable scientific resistance and tough times for budget growth, the NIH genome programme soared from a few start-up millions to over $160 million a year, and is well on the way to the ultimate goal of consuming $2 billion over 15 years. It is generally agreed that the indispensable, magic ingredient was Watson's charm, drive, and dazzlement of our scientifically illiterate Congress—which easily warmed to the renowned author of *The Double Helix*. Remarkably, Watson led and sold the genome programme on a part-time basis, for, in his second role, he carried on as director of the Cold Spring Harbor Laboratory, on Long Island, New York. This is a private institution of high scientific repute—so high, in fact, that NIH has long supported research there, with grants now totalling some $15 million a year. Watson insists that he has rigorously avoided any involvement in dealings between the laboratory he directs and the government agency that employs him and provides money for his laboratory. Nothing to the contrary has been suggested, but simultaneous employment by giver and receiver usually rouses the posses of purism in Washington. The press and Congress, however, found Watson highly enchanting and his twin hats eluded the usual suspicions.

When Healy became head of NIH in April of last year, Watson had been on board for 3 years and his unusual status had weathered into a familiar part of the biomedical landscape. But Healy, who has shown sensitivity to Washington's obsessive concerns with conflicts of interest, says that from the start she was concerned about possible conflicts between Watson's public and private roles. Watson's arrangements with NIH, though unusual, had passed legal muster, Healy explained at a meeting with the press last week. However, she added, "that does not mean that there aren't some added burdens and difficulties about such a perhaps ambiguous situation, and I think some of that may be what's coming forward at the present time".

The "ambiguous situation" apparently was not enough to create a crisis, but it didn't soothe matters when several other events occurred. First, Watson denounced Healy's decision to scoop up patents for thousands of DNA sequences identified by NIH researchers. Healy said patenting was necessary to protect the Government's interests. Watson, in characteristically diplomatic language, described patenting as a "lunacy" that would impede research. Second, a periodic review of financial holdings—required of all senior government officials—revealed investments by Watson or his family in firms involved in biotechnology research, including, according to the *New York Times*, Amgen, Glaxo, Eli Lilly, Oncogene, and Merck. Whether or not Watson detached himself from decisions that might affect these investments, as he contended, his manoeuvring room on conflict of interest appeared to be narrowing. When the issue was raised, Watson said the holdings had long been known to government ethics officials, but were being cited because Healy wanted him gone. While threatening to resign, he said he would sell the stocks.

But then another controversy arose, this one created by a letter to Healy from a financier who contended that Watson had warned of "all-out war" when he heard that the money man was trying to lure a couple of Watson's genome researchers into a commercial venture. The writer accused Watson of being "excessively profane and vulgar".

Within the week that many of these events came to public attention, initially in *Science* and *Nature*, Watson resigned from NIH, declaring, "I have a fine reputation and they are trying to soil it when I have worked very hard for three-and-a-half years on behalf of my country".

His reign has been a triumph of political and scientific navigation through extremely difficult territory. Recognising that the genome project faced serious Luddite resistance, Watson shrewdly responded by setting aside 3% of its monumental budget for studies of ethical issues arising from biotechnology research, thus becoming the major bankroll for scholarship in this otherwise impoverished area. Rarely did he make a bad judgment or take a wrong turn.

His only major error may have been his reliance on past NIH directors as a guide to the present director. Healy's recent predecessors concentrated on encouraging more money from an already supportive Congress, and generally let the institution flow with the biomedical currents. Healy has enunciated many goals, ranging from immense growth for NIH to smartening up its slovenly internal procedures.

The current agenda includes an all-hands search for scores of millions of dollars of office and lab equipment unaccounted for in what Healy describes as a "wall-to-wall survey".

Two years ago, before Healy's appointment, I asked Watson whether the operation of the NIH genome programme was impaired by the long delay in filling the directorship of NIH—then enmeshed in abortion-related politics and concerns about the adequacy of the salary. No, the genome project was proceeding without difficulty, and he explained: "When I say it hasn't affected us, it reflects how little power the NIH director has". Referring to the 13 separate institutes in the NIH family, he said, "The Institute directors are pretty much masters in this . . . The director [of NIH] can't do anything—I think that's probably the chief reason people don't want the job. The salary is secondary, but it's the fact that you would take the job if you actually think you could do something, even though you lose money by the deal".

Daniel S. Greenberg

Round the World

Europe: Blood donation

Controversy over paid and voluntary blood donations will peak in June when the 26-nation Council of Europe and the EC Commission jointly release a report on European self-sufficiency in blood products. Both organisations are adamant that buying and selling blood or any other part of the body is unethical, whereas the blood products industry calls for a more pragmatic line. Industry says that although nobody likes to think of trading in blood, paid donations offer the only route to European blood product self-sufficiency. At present plasma imports into the EC alone are estimated at between 1·6 million and 1·9 million litres a year, mainly to Germany, Italy, and Spain. Industry also questions the difference between paying donors cash or giving them a paid morning off work.

The main reason the Council of Europe and the European Community, whose 13 states are also Council members, want self-sufficiency is because imported blood products, chiefly from the United States, come from paid donations. Furthermore, blood sales from developing countries such as Mexico and Cuba to the US stall efforts to set up transfusion systems in the third world. Officials moreover dispute industry's view that self-sufficiency can come only through paid donations. They point to Switzerland, which not only has achieved national self-sufficiency through a voluntary donation system but also helps to prop up the Greek transfusion system. Other European states, including the UK, Finland, Belgium, and the Netherlands, are no longer reliant on blood imports but do not pay donors. Nevertheless, many European countries are heavily reliant on industry for blood products, particularly factor VIII.

A draft of the self-sufficiency report was sent to European governments at the beginning of this month, but has already been slated by industry, which claims bias in the choice of author. The Council and Commission picked Professor van Aken from the Dutch Red Cross blood banks, because he wrote a similar report two years ago. They deny industry accusations that they have sided with the non-profit sector and counter that van Aken was hired because he is expert and not because of his Red Cross links. Industry remains unconvinced and has already pledged to write an alternative report. Blood product executives point out that van Aken's data on Germany, the European state most reliant on imports, will be incomplete because that country has a decentralised, privately run transfusion system. For an up-to-date picture Aken needed industry's help, which it was unwilling to give without having more say in the shape of the final report. Some executives also accuse the voluntary sector of hypocrisy since it sells leftover blood to industry.

Despite their reservations, industry executives were to meet representatives of the Council of Europe, the Commission, the voluntary sector, donor associations, and user-groups such as the Haemophilia Society in Strasbourg on April 16 to discuss Europe's self-sufficiency goals and analyse trends in van Aken's report. But the talks will be informal and seem likely to resolve few, if any, of the long-running issues in the blood products row.

Sarah Lewis

Europe: Impasse on biotechnology patents

The European Community deadlock on the issue of biotechnology patents deepened on April 8, when the European Parliament imposed a three-month deadline on its demands for key changes in legislation proposed by the EC Commission. The Strasbourg assembly voted through a series of 45 amendments to the draft directive on the Legal Protection of Biotechnological Inventions, with dissent coming mainly from the 27 members of the Green group, who argue that the Commission proposal is "far too flawed and outdated to be worthy of amending" (see *Lancet* Feb 8, p 355). However, having adopted the amendments, the assembly then agreed to delay its final vote to allow further negotiations with the Commission.

German Social Democrat MEP Mr Willi Rothley, spokesman for the assembly's Legal Affairs Committee and author of a study on the draft legislation, explained that although the Commission is prepared to concede more than 20 of the changes sought by MEPs, the assembly nevertheless wanted unequivocal safeguards on three issues: a prohibition on patents on the human body or its parts, a similar exclusion of patents on transgenic animals, and guarantees on the so-called "farmers' privilege" allowing use of seed or progeny of patented crops and livestock without payment of additional royalties. Mr Rothley insisted that the vote should not be seen as a rejection of genetic research. The assembly was accepting that it might be possible to obtain legal protection for procedures for isolating a gene—but the gene or genetic sequence should not enjoy patentability. Under the Parliament's rules, a final vote will have to take place within three months and the Commission would be pressured during the pause to offer further concessions. Given the strength of feeling demonstrated in the voting, the Commission risked total rejection of the directive, since even the Greens would support other political groups on the simple issue of endorsement of rejection. "The Commission will have to change its position if it wants to save this proposal", said Mr Rothley. For their part, the Greens foresee that EC legislation will be ineffective without an overhaul of the 16-nation European Patent Convention, under which a patent has already been granted on the Harvard "onco-mouse" used in cancer research. But British Conservative MEP Mr Amadée Turner, himself a patent lawyer, considers that it should be possible to challenge a patent granted by the European Patent Office in Munich, if it runs counter to the EC rules, once these have been transposed into national legislation in the 12 EC member states.

Arthur Rogers

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Life Science

April 14, 1992

WATSON RESIGNS AS DIRECTOR OF NCHGR

James Watson resigned Friday as director of the National Center for Human Genome Research at the National Institutes of Health (NIH). Watson began the NIH Human Genome project four years ago at the invitation of then NIH Director James Wyngaarden.

Michael Gottesman was appointed Friday as acting NCHGR director by NIH Director Bernadine Healy. Gottesman currently is chief of the Laboratory of Cell Biology at the National Cancer Institute. Healy announced that she will begin an immediate search for a permanent NCHGR director.

Watson met with Healy at 1:45 on Friday and presented her with his letter of resignation. In his letter Watson said, "I remain firmly committed to the success of the Human Genome Project. I hope and expect to continue to support the project enthusiastically and, if called upon by my successor, to advise NIH informally.

In a later statement, Watson said that "having accomplished the goal of launching the [genome] project, the time has come for me to step down. Performing the substantial duties as director of NCHGR while simultaneously serving as director of Cold Springs Harbor Laboratory has proved to be increasingly difficult and burdensome to myself and my family....I have discussed with a number of friends and colleagues over the last several months my intention to leave the project and return full time to Cold Springs Harbor." Watson noted in his statement that his "resignation at this time also provides Dr. Healy...the opportunity to appoint her own director for the project."

Healy said of Watson that he is "an historic figure in the annals of molecular biology, and the NIH has benefited from his leadership. We have been fortunate to have had his expertise and scientific judgement, which have been invaluable to the establishment of the NCHGR."

Secretary of the Department of Health and Human Services Louis Sullivan described Watson as "a key figure in the creation and development of the [genome] project....The project is critically important to all men and women who suffer from genetic diseases and conditions. It is certain that this work will eventually result in the relief of untold human suffering."

Sources close to both Healy and Watson say the two have had several policy disagreements. One recent and public disagreement centered on the decision by Healy for NIH to apply for patents on thousands of gene fragments identified by an NIH scientist. Watson disagreed with the decision and predicted a scramble to obtain patents on human genes.

The "New York Times" and the "Wall Street Journal" both have carried stories indicating that there was concern by Healy and NIH that Watson's holdings in pharmaceutical and biotechnology companies offered potential for the perception of conflict of interest on Watson's part.