Teamsters to Unveil Anticorruption Plan

Union Chief Hoffa Aims To Bring End to Years Of Federal Oversight

By Glenn Burkins
Staff Reporter of The Wall Street Journal

WASHINGTON—Teamsters President James P. Hoffa, eager to end more than a decade of federal supervision of his union, will outline a plan today to combat internal corruption and stamp out any vestiges of organized crime left in the union.

James P. Hoffa

The plan will call for a union code of conduct, an ethics board and an internal system to punish abuses, among other steps. There also will be a study to determine what progress the union has made so far in severing ties to organized crime.

The former Detroit lawyer and son of legendary Teamsters President Jimmy Hoffa will unveil the proposal at a meeting of Teamsters leaders in Chicago.

The nation's largest private-sector union with more than 1.4 million members, the Teamsters have been under government supervision since 1988, when union leaders signed a consent degree with the Justice Department promising to break the union's long ties to organized crime. Since then, more than 100 members and officers have been expelled for associating with alleged mob figures. Dozens of Teamster locals have been put into trusteeship because of corruption or mismanagement.

The union has spent millions of dollars to comply with various conditions of the consent decree, and Mr. Hoffa believes it is now ready to police itself. Since taking over the union's top post 10 months ago, he has made ending federal oversight one of his top goals.

Teamsters spokesman Chip Roth said the union sought no government input while developing the plan. But it has kept several federal agencies abreast of its progress, he said, including the U.S. attorney's office in Manhattan, which administers the consent decree, as well as the Independent Review Board, the three-member, government-appointed panel established under the decree to oversee the clean-up effort.

John Cronin, the review board's administrator, said it is far too early to comment on how well Mr. Hoffa's plan might work. "Right now, it's just a plan," he said.

The U.S. attorney's office in New York said it would have no comment on the union's announcement.

Mr. Hoffa's timing may prove fortuitous politically. Taking the initiative for speeding anticorruption efforts could convince the White House to speed up an end to government oversight. The Teamsters remain one of the last big unions still uncommitted to backing Vice President Al Gore's Democratic presidential candidacy. The Clinton administration, including the vice president, has been openly courting the union, but union officials deny there are any political connections to today's announcement.

Mr. Roth says Mr. Hoffa deliberately failed to mention the consent decree last fall when President Clinton spoke at a New York dinner honoring the Teamsters president. "I honestly hope it's not a political decision," he said. "We have not asked for and will not ask for any special consideration on this."

Last July, Mr. Hoffa hired Edwin H. Stier, a former federal prosecutor, to head the union's anticorruption drive. He also hired Jim Kossler, a former Federal Bureau of Investigation agent, to help Mr. Stier. Mr. Kossler will lead the study assessing the union's clean-up efforts so far, which union officials hope will be ready in July.

Details of the Hoffa plan, including the code of conduct and makeup of the ethics board, are still emerging. According to an outline of the plan, Mr. Hoffa hopes to finish much of the work by late summer, with final approval by the Teamsters board by year end.

A More Perfect Union?

Key provisions of the Hoffa plan:

- **Establish a** Teamsters code of conduct and an ethics board to monitor violations.
- **Conduct a** national study to identify all locals and union organizations with past ties to organized crime.
- **Send representatives** to the union's roughly 550 locals to educate members about the ethics program.
- **Share findings** and results with government agencies, including the Justice Department.

Celera Pledges Human-Genome Map by Year End

By Robert Langreth
Staff Reporter of The Wall Street Journal

Celera Genomics Group said it has sequenced 90% of all human genetic material in just four months, and expects to finish assembling the human-genetic blueprint by the end of the year.

Celera, led by gene-research pioneer J. Craig Venter, is racing government researchers to map the entire complement of human genes. Celera's timetable for completing the blueprint is a year earlier than its previous projections. Mr. Venter said Celera will outpace the government's Human Genome Project, which is scheduled to finish its work some time before 2003.

At the Human Genome Project, officials said Celera's announcement won't affect their plans.

The news sent Celera's stock soaring, as it closed at 4 p.m. up $54.0625, or 29%, at $241 on the New York Stock Exchange. Celera, which is based in Rockville, Md., is a separately traded unit of PE Corp., Norwalk, Conn., whose stock was up $16, or 13%, at $139 on the NYSE.

The much-ballyhooed race to sequence the genome is really just a first step in a gigantic scientific effort aimed at developing gene-based cures for diseases. Once all the gene-sequence data are gathered, scientists face the daunting task of making sense of it all, a process that could take decades.

Still, investors, hungry for the next hot high-tech wave, have flocked to shares of Celera and other so-called genomics companies in recent weeks, boosting stock prices enormously.

While the development is an impressive first step, Celera has a way to go before the human-genome sequence is actually finished. So far it has determined the sequences of millions of random fragments of human DNA. But it doesn't yet know how these all come together to form the human genome.

Dr. Venter said the company will spend several more months sequencing human-DNA fragments, essentially mapping the entire genome several times. That will give it enough overlapping fragments to allow researchers, using supercomputers, to begin assembling these puzzle pieces into a coherent whole.

Once the company has completely sequenced the genome, Dr. Venter said, it will release the data, free, on the Internet. But it will sell more detailed information about human, animal and plant genetics to pharmaceutical companies and universities, as well as individuals.

Several drug companies already are paying Celera to subscribe to its databases and gain immediate access to human-DNA sequence information as it becomes available. Drug companies are hoping the genetic information will give them fresh targets that will help them find new drugs to treat diseases ranging from cancer to heart disease.

As for the government's Human Genome Project, it plans to complete its so-called rough draft of the genome by this spring, and complete a final version within three years.

"Nothing has changed from our perspective," said Kathy Hudson, assistant director of the National Human Genome Research Institute, which helps run the project.

Dr. Hudson said that the Human Genome Project needs to continue for several reasons, most importantly to guarantee public access to the genetic blueprint. Since Celera is a private company, there is always a risk it could change its mind and not fully release human-genome data, she noted. Also, she said that the Human Genome Project will release much data about how human genes vary between people. Celera plans to keep this type of information private so it can sell it. Dr. Venter said he is committed to releasing the human gene sequence to the public.

Microsoft To Settle Suit By Caldera

By Lee Gomes
Staff Reporter of The Wall Street Journal

Microsoft Corp. agreed to pay an estimated $275 million to settle an antitrust lawsuit by **Caldera** Inc., heading off a trial that was likely to air nasty allegations from a decade ago.

Microsoft and Caldera, a small Salt Lake City software company that brought the suit in 1996, didn't disclose terms of the settlement. Microsoft, though, said it would take a charge of three cents a share for the agreement in the fiscal third quarter ending March 31. Since the company has roughly 5.5 billion shares outstanding, the cost of the deal would appear to be about $165 million. Michael Kwatinetz, an analyst at Credit Suisse First Boston, estimated Microsoft paid about $275 million, based on its tax rate.

While the amount of money is small for a company of Microsoft's size, the settlement suggests the software giant may be more willing to resolve its legal problems privately. It is also in talks to settle the broader antitrust case brought by the Department of Justice and 19 states. Those talks, which continued this week in Chicago under a court-appointed mediator, Judge Richard Posner, have yielded little movement so far, and the sides remain far apart, people close to the talks said.

The Caldera settlement also marks a vindication of sorts for Raymond Noorda, a retired industry leader and longtime Microsoft opponent who helped bankroll the litigation. Mr. Noorda, former chief executive officer of Novell Inc., founded closely held Caldera and is its biggest shareholder. Through a series of maneuvers, Caldera obtained the rights to DR-DOS, an operating system that Novell bought that was once a rival to Microsoft's MS-DOS operating-system software.

The suit in U.S. District Court in Salt Lake City alleged Microsoft competed unfairly against DR-DOS, and asked for monetary damages that had the potential for reaching into the billions of dollars.

The Caldera suit is technically unrelated to the Department of Justice action against Microsoft, which covers the company's response to the growth of the Internet during the mid-1990s. But many of the themes of the two actions were the same, especially as they involved Microsoft's response to competitive threats.

With the Caldera trial scheduled to start on Feb. 1, analysts and antitrust lawyers suggest Microsoft had many reasons to settle before then. It didn't want its well-publicized troubles with the federal government to affect the jury in the Caldera trial. It didn't want more revelations about its behavior becoming public while U.S. Dis-

Continued From Page A3

trict Judge Thomas Penfield Jackson, who rebuked the company in a finding of fact in November in the government case, was considering what remedy he should apply to Microsoft. What's more, it likely wasn't eager for any adverse decision in the Caldera case to become evidence in the more than 40 private antitrust lawsuits filed against it in the wake of Judge Jackson's finding.

"It's a solid strategy to settle up before facing potentially extraordinary damages," said Hillard Sterling, a Chicago attorney specializing in antitrust law.

Microsoft said it settled the suit "to put this issue behind us," said Tom Burt, the company's general counsel, in a statement. "Rather than litigating, we prefer to focus on building great software for our customers in this dynamic and competitive industry."

'You Can Stand Up to Microsoft'

Bryan Sparks, Caldera's CEO, said the settlement "proved that you can stand up to Microsoft and win. We told our story and exposed a lot of their behaviors."

Caldera's suit claimed Microsoft used licensing practices with computer makers that discouraged them from purchasing alternatives to MS-DOS. In 1994, Microsoft agreed to modify some of those practices following a Justice Department investigation. Caldera also claimed Microsoft had improperly tied its Windows software to MS-DOS, and developed technology that produced an error message if consumers used Windows with the rival DR-DOS operating system.

The Caldera case hasn't gone well for Microsoft. Dee Benson, the U.S. judge overseeing the proceedings, had rejected most of the company's pretrial motions. The jury trial also was set to take place in Utah, Caldera's home turf. "They may have decided that they didn't need another round of bad publicity," said Sam Miller, a former Justice Department attorney now in private practice in San Francisco.

Mr. Kwatinetz, of Credit Suisse, added the pact "would be consistent with the types of things that the Justice Department would like to see in a settlement. It's kind of mMicrosoft] saying, 'We are a different company now.' "

Stephen D. Susman, the flamboyant Houston attorney who represented Caldera, agreed the settlement was a signal Microsoft also was making progress in its talks with the government. While he declined to discuss the amount of the payoff, he said it was enough that "everyone involved with it could be celebrating in Tahiti."

The agreement was hammered out at a lengthy negotiating session on Friday at the Seattle office of Jim Smith, an attorney acting as a court-appointed mediator in the case. Mr. Susman said he arrived at the session initially suspicious Microsoft would use the day simply to distract him from his pretrial preparations. But it quickly became apparent, he said, the company was serious about settling the matter, as they soon came up with counteroffers to Caldera's proposed settlement amounts.

The pact was reached at 8 p.m. Friday night; Judge Benson signed off on the agreement yesterday.

Risks for Microsoft

Caldera was originally asking for monetary damages that could easily have escalated into the billions of dollars. It argued in pretrial proceedings that because DR-DOS at one point had 20% of the operating-system market, it should be entitled to 20% of Microsoft's profits from successor products to MS-DOS, which include Windows 95 and Windows 98. What's more, antitrust law allows a jury to triple a monetary damage against a company.

Caldera, which is 80%-owned by Mr. Noorda, obtained the right to sue Microsoft from Novell, the networking company that itself once owned DR-DOS. In connection with that agreement, Novell gets 18% of the Microsoft settlement. Mr. Noorda wasn't available for comment yesterday, though a spokesman said he "is very pleased it has come to an end, and is looking forward to competing aggressively" against Microsoft.

Mr. Noorda is competing with Microsoft via two companies he has established, which both share the Caldera name, leading to considerable industry confusion. Caldera Inc., the entity involved in the lawsuit, owns the assets connected with the DR-DOS product; through its Lineo Inc. subsidiary, it also sells software aimed at the market for a new generation of "embedded" computers.

But there is also Caldera Systems Inc., a completely separate company that is focusing on the Linux software market. Yesterday, Caldera Systems announced it had filed with the Securities and Exchange Commission to go public, joining a bandwagon of Linux companies raising money in the equity markets. Caldera Systems also announced $30 million in new investments from a variety of companies, including **Sun Microsystems** Inc. and **Citrix Systems** Inc.

—John R. Wilke contributed to this article.

cc Eric, Chris, + return
-BR

THE WHITE HOUSE

WASHINGTON

October 1, 1999

HEALTH— GENETIC PATENTING

MEMORANDUM FOR THE PRESIDENT

FROM: NEAL LANE Neal

SUBJECT: GENOME PATENTING

This memorandum responds to your query regarding the merits of genome patenting. Genome patenting is a complex issue that has been debated since large-scale DNA sequencing became feasible in the late 1980s.

What *is* patentable?

Patents have been granted to applicants who can show that they have obtained a genomic DNA sequence, can describe the protein product encoded by that gene, and can demonstrate the function of the protein in a living organism. Substantial uncertainty exists regarding the patentability of partial or full gene sequences when the applicant does not disclose information regarding the function or utility of the gene and its encoded protein product. The U.S. Patent and Trademark Office (PTO) has granted at least one patent on a partial gene sequence but is rethinking its position. PTO convened a public hearing on Nov. 5, 1998 to obtain public comments on draft guidelines describing the necessary elements for obtaining a patent on genome sequences. I understand PTO plans to issue new draft guidance by November 1.

In 1991, NIH filed patent applications claiming over 6,000 partial gene sequences obtained in the laboratory of Dr. J. Craig Venter but has never appealed PTO's denial of these patents. Under Harold Varmus, NIH adopted a policy promoting open access to research tools, including genomic sequence data.

PTO and NIH have been at loggerheads over the criteria necessary to obtain patents on genomic DNA sequence data, although they agree more generally on the value of patents on the results of later-stage genome research in stimulating investment in health care product development.

What *should* be patented?

NIH discourages grantees from seeking patents on so-called raw human genomic DNA sequence data. In 1997, NIH, DOE and the U.K.'s Wellcome Trust, partners in the international Human Genome Project, adopted a policy (attached) requiring grantees funded specifically to generate large-scale human genomic DNA sequence to deposit such data in a public database within 24 hours of its generation, thus rendering it unpatentable. A September 20th *London Guardian* article inaccurately portrayed this as a new policy designed to preclude all gene patents. (Press guidance on this article is attached.)

The rationale for freely disseminating raw human genomic DNA sequence data is that such broad public access will *promote innovation* and encourage its use in the development of downstream products. Moreover, the non-profit supporters of genomic research believe patents on early-stage genome data are a *disincentive to innovation.* That is, drug companies and other innovators may be reluctant to invest in product development on the suspicion that, having done so, they will learn belatedly that a patent has been granted on a gene sequence critical to their product. This will necessitate negotiation of a license for marketing to proceed. This is not an unreasonable fear, as some companies describe such patenting as their principal goal, and it may be years before the existence of such patents becomes known. While most agree on the value of patents for genes about which there is known function or clear utility (for example, diagnostic genetic tests), exclusive licenses on these patents are controversial due to their potential for restricting the availability of new health care advances.

Not surprisingly, industry views on patenting the early results of genome sequencing are mixed, depending on the company's business strategy. A few companies hope to be able to obtain patents on large numbers of raw gene sequences. One significant occurrence is the April 15th announcement of a consortium formed among 10 of the world's foremost pharmaceutical companies to create a public database of the genetic markers that distinguish one person from another. These markers will be valuable for identifying specific genes involved in common and rare diseases, developing new diagnostic tests, and creating new "personalized" medicines, based on an understanding of minute genetic variations. Members of this consortium believe that it is preferable to have these indicators of human genetic diversity in the public domain, as opposed to dealing with the licensing issue at a later date. They clearly do not feel that making this information public hampers their efforts to develop downstream products based on genetic information or threatens their future intellectual property rights.

The Bayh-Dole Act and other technology transfer statutes give Federal grantees and contractors the right to apply for patents on the results of government-funded research. The NIH-DOE policy requiring rapid access to raw human genomic DNA sequence data precludes the patenting of such information, but once an investigator has determined the biological significance of such information, obtaining a patent is straightforward. It seems a reasonable course of action to continue the policy of making raw human genomic DNA sequence widely available to the largest possible number of inventors, thus stimulating further innovation and product development.

I believe PTO's guidelines will reflect a bright line approach allowing patents on gene sequences only when the inventor can demonstrate how such sequences might be used. I believe this approach is the right one for advancing science and for ensuring rapid development of products based on that science. The current climate of uncertainty regarding the boundaries of patentability is a disincentive to genomic product development, and issuing the guidelines will help resolve this problem.

Attachments

cc: John Podesta
Bruce Reed
David Beier

The National Human Genome Research Institute

NHGRI Policy Regarding Intellectual Property of Human Genomic Sequence

POLICY ON AVAILABILITY AND PATENTING OF HUMAN GENOMIC DNA SEQUENCE PRODUCED BY NHGRI PILOT PROJECTS (FUNDED UNDER RFA HG-95-005)

April 9, 1996

This document describes the policy of the National Center for Human Genome Research with respect to availability and patenting of human genomic DNA sequence produced under grants funded as a result of RFA HG-95-005. In conformity with the existing spirit and philosophy of the Human Genome Project and in response to the recommendations of advisors and the expressed wishes of the community, NHGRI seeks to make DNA sequence information available as rapidly and freely as possible.

Background

The Human Genome Project (HGP) is an international research effort, begun in 1990, which has the scientific goals of generating maps of the human genome[1] and producing the complete sequence of the human DNA by the year 2005. The project was undertaken in the U.S. following the advice of several scientific committees that emphasized its importance in creating a resource that "will facilitate research in biochemistry, physiology and medicine"[2], "have a major impact on health care and disease prevention"[2] and provide ""enormous scientific and technological advances..., having both basic and commercial applications" [3]. At NIH, the National Human Genome Research Institute (NHGRI) was founded to implement the HGP.

The HGP has progressed rapidly, even beyond optimistic expectations. The initial mapping goals are nearly completed and recent improvements in DNA sequencing technology and capacity have led many scientists, including NHGRI advisors, to conclude that complete sequencing of human genomic DNA should begin. Early in 1995, NHGRI issued RFA HG-95-005 to solicit grant applications for pilot projects to test strategies that can potentially scale up to sequence the human genome. The applications received in response to the RFA were peer reviewed in the fall of 1995 and approved by the National Advisory Council for Human Genome Research in January 1996. A set of grants will be funded by April 1996.

At the inception of the HGP, the planners emphasized that, in order to reap the maximum benefit from the HGP, human DNA sequence should be freely available in the public domain. The NIH Ad Hoc Program Advisory Committee on Complex Genomes stated that "Distribution of and free access to the databases (containing the sequence data) must be fully encouraged. Thus, the data must be in the public domain, and the redistribution of the data should remain free of royalties."[3] Similarly, the National Research Council stated: "...access to all sequences and material generated by these publicly funded projects should and even must be made freely available..."[2]. Most recently, an international group of scientists, from both the public and private sectors, who are already involved in genomic DNA sequencing, passed a unanimous resolution that "all human genomic DNA sequence information, generated by centers funded for large-scale human sequencing, should be freely available and in the public domain in order to

encourage research and development and to maximize its benefit to society"[4].

There are very strong scientific arguments that human genomic DNA sequence should be freely available and in the public domain:

o The human genomic DNA sequence is unique. Although there are many other types of information that contribute to the understanding of human biology, e.g., DNA sequence of model organism genomes, in the end, the only source of definitive information about the human is the human sequence.

o The human genomic DNA sequence is a vast resource. It contains a very large number of genes and an enormous amount of additional biological information. It is anticipated that the sequence resource will be the basis for many useful inventions and patentable products. It will take many researchers years to find and characterize all of the genes and other functional elements within the sequence and to use that information to develop products and other approaches that will improve the health of the American people.

o The human genome is a bounded resource. Once the genome has been sequenced, few or no opportunities will exist for discovery of new information that will not make reference to, or be dependent on, that first sequence. Thus, it is important to ensure maximum access of a large number of parties to the initial genomic DNA sequence as it is generated, to provide a broad opportunity for development of new products.

Policy

It is therefore NHGRI s intent that human genomic DNA sequence data, generated by the projects funded under RFA HG-95-005, should be released as rapidly as possible and placed in the public domain where it will be freely available. In order to implement this policy, NHGRI will require that grantees under RFA HG-95-005 adopt a policy of rapid release of data to public databases. This policy will be made a condition of the award.

In NHGRI s opinion, raw human genomic DNA sequence, in the absence of additional demonstrated biological information, lacks demonstrated specific utility and therefore is an inappropriate material for patent filing. NIH is concerned that patent applications on large blocks of primary human genomic DNA sequence could have a chilling effect on the development of future inventions of useful products. Companies are not likely to pursue projects where they believe it is unlikely that effective patent protection will be available. Patents on large blocks of primary sequence will make it difficult to protect the fruit of subsequent inventions resulting from real creative effort. However, according to the Bayh-Dole Act, the grantees have the right to elect to retain title to subject inventions and are free to choose to apply for patents should additional biological experiments reveal convincing evidence for utility. The grantees are reminded that the grantee institution is required to disclose each subject invention to the Federal Agency providing research funds within two months after the inventor discloses it in writing to grantee institution personnel responsible for patent matters. NHGRI will monitor grantee activity in this area to learn whether or not attempts are being made to patent large blocks of primary human genomic DNA sequence.

During this pilot period, NHGRI will be soliciting opinions and collecting evidence from the broad scientific and commercial sectors to allow an evaluation of whether the approach described above is sufficient to ensure that sequence generated by these grants is maximally useful to the research and commercial sectors. If not, NIH will consider a determination of exceptional circumstance to restrict or eliminate the right of parties, under future grants, to elect to retain title.

The National Human Genome Research Institute

NHGRI Policy on Release of Human Genomic Sequence Data

March 7, 1997

At the Second International Strategy Meeting on Human Genome Sequencing (Bermuda, 1997), attendees affirmed the principle that was set out at the First (1996) International Strategy meeting, that primary genomic sequence should be rapidly released. Specifically, the report of the first meeting stated that "sequence assemblies should be released as soon as possible; in some centres, assemblies of greater than 1 kb would be released automatically on a daily basis." The discussions at the 1997 meeting confirmed NHGRI's conclusions that it is extremely important for its large-scale sequencing program to be functioning in a manner consistent with this principle, that such rapid release is technically feasible, and that such unfinished DNA sequence data have already been found to be useful by the larger scientific community. NHGRI has determined, therefore, that its grantees engaged in large-scale genomic DNA sequencing should now be automatically releasing sequence assemblies of 2 kb or larger within 24 hours of their generation. (the trigger for data release is 2 kb, instead of 1 kb, in order to ensure that the released sequence be comprised of at least two sequence reads. Investigators who wish to release smaller assemblies may do so.) Any laboratory funded by NHGRI for large-scale human genomic sequencing must develop and submit to NHGRI a plan to implement such a data release program, which must be implemented within one month of its being approved by NHGRI. No non-competing or competing renewal will be funded until an acceptable plan has been approved. Mandatory data release as described above will be made a condition of the award for any grant funded by NHGRI for large-scale human sequencing.

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Human Gene Patents
September 20, 1999

Context: *Today's* London Guardian *ran a story stating that Prime Minister Tony Blair and President Clinton are negotiating a deal to obtain intellectual property rights on the human genome, thereby precluding private sector ventures in this area. U.S. and U.K. government officials have been discussing the possibility of issuing a statement endorsing data access principles already adopted by an international consortium of human genome researchers, but the article's references to government efforts to block private sector patents are inaccurate. The President and Prime Minister have not been involved in these discussions.*

Background: The international Human Genome Project is funded primarily by the National Institutes of Health and Department of Energy in the U.S., and the Wellcome Trust, a non-profit philanthropy in the U.K. Researchers funded by these organizations developed the so-called "Bermuda Principles" under which human genome sequence data is deposited in a publicly-accessible database within 24 hours of being generated. For the past year not-for-profit partners have been discussing the possibility of a memorandum of understanding with Celera Genomics, a U.S. company beginning human genome sequencing. However, data access has remained a sticking point in development of the M.O.U. The public Human Genome Project does not maintain intellectual property rights to the data.

Is the President discussing a deal with the U.K. Prime Minister to stop entrepreneurs from profiting from gene patents?

A. No. The President has not been engaged in these discussions. Government officials in both countries are in general agreement that DNA sequenced data developed under the Human Genome Project ought to be made freely available so as to promote progress in biomedical research and the rapid application of such information to the development of treatment, prevention and cure of human disease. We believe that a joint statement in support of this data access policy might be valuable.

Q. Who will own the data from the Human Genome Project?

A. All data are to be deposited daily in publicly accessible databases to ensure that scientists around the world have unfettered access, free of charge, to the wealth of information and can use it in their research to understand human disease, develop new diagnostics and therapeutic interventions, and improve the health of our citizens.

Because data are deposited daily in publicly accessible sites, no patent protection on raw fundamental genome information arising from the Human Genome Project will be sought by participants.

Gwen Smith

Bill Clinton

Neil Lane can you reply? John

Genome patenting

~~[illegible]~~ (Bruce

Do we have a position on Genome patenting
There have been several
articles on why it's
bad for medical research
& commercial development
Big issue —
BC

9-23-99

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Podesta
Reed

President of the United States

THE PRESIDENT HAS SEEN
9-7-99

The New Y

ay, August 29, 1999

Money&I

Section 3

cc: CHRIS, ERIC, SARAH + file

Chris –
Is there anything we should do on this? It dwarfs stem cells as a potential issue, 2000 SOTU? BR

Shouldn't we do something to protect public interest?
Change patent laws?
Any exec action possible?

The Race to Cash In On the Genetic Code

As DNA Gives Up Secrets, Pursuers Turn Entrepreneurs

Rival Strategies

The leading genomics companies have contrasting business models: two aim to develop drugs (■); two aim to sell data about genes (■).

[redacted]

HEADQUARTERS Cambridge, Mass.

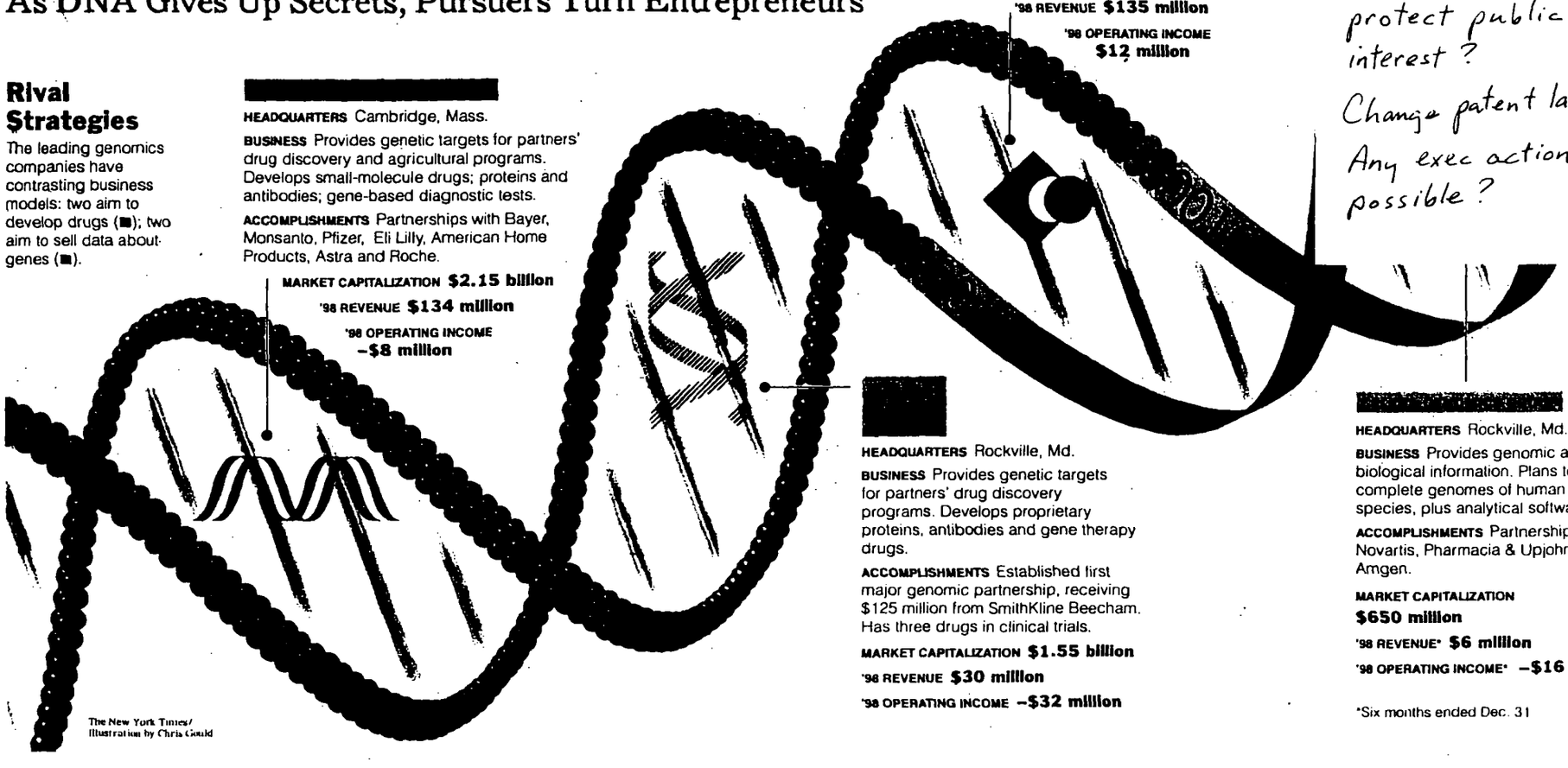
BUSINESS Provides genetic targets for partners' drug discovery and agricultural programs. Develops small-molecule drugs; proteins and antibodies; gene-based diagnostic tests.

ACCOMPLISHMENTS Partnerships with Bayer, Monsanto, Pfizer, Eli Lilly, American Home Products, Astra and Roche.

MARKET CAPITALIZATION **$2.15 billion**

'98 REVENUE **$134 million**

'98 OPERATING INCOME **–$8 million**



The New York Times/
Illustration by Chris Gould

[redacted]

HEADQUARTERS Palo Alto, Calif.

BUSINESS Provides data bases of gene sequences and related analytical software by subscription. Manufactures and sells drug discovery tools.

ACCOMPLISHMENTS More than 25 major pharmaceutical and biotechnology subscribers. First genome company to report earnings from operations.

MARKET CAPITALIZATION **$713 million**

'98 REVENUE **$135 million**

'98 OPERATING INCOME **$12 million**

[redacted]

HEADQUARTERS Rockville, Md.

BUSINESS Provides genetic targets for partners' drug discovery programs. Develops proprietary proteins, antibodies and gene therapy drugs.

ACCOMPLISHMENTS Established first major genomic partnership, receiving $125 million from SmithKline Beecham. Has three drugs in clinical trials.

MARKET CAPITALIZATION **$1.55 billion**

'98 REVENUE **$30 million**

'98 OPERATING INCOME **–$32 million**

[redacted]

HEADQUARTERS Rockville, Md.

BUSINESS Provides genomic and biological information. Plans to offer complete genomes of human and other species, plus analytical software.

ACCOMPLISHMENTS Partnerships with Novartis, Pharmacia & Upjohn and Amgen.

MARKET CAPITALIZATION
$650 million

'98 REVENUE* **$6 million**

'98 OPERATING INCOME* **–$16 million**

*Six months ended Dec. 31

By LAWRENCE M. FISHER

ROCKVILLE, Md.

BEFORE there was an Internet bubble, before biotechnology left a bad taste in money managers' mouths, capital was ventured and shares were sold in a group of companies that aimed to leapfrog the Government's multibillion-dollar effort to map the human genome. By sequencing and patenting genes ahead of the publicly financed laboratories, the investors thought, these companies would control the next era of health care — and make their founders and shareholders rich.

But now, as the international race to spell out the precise sequence of the three billion letters in the human genetic code sprints to the finish line, the markets are demanding that the gene merchants deliver the goods. Investors are starting to demand not just science, but a viable business model, too.

To the victors will belong an asset of almost unfathomable value: the source code of life itself. By sequencing the DNA in all 100,000 genes in the human body — that is, by divining the order of the four chemicals that make up the genes — scientists hope to treat diseases in much the same way that software engineers fix faulty computer programs: by isolating flaws in the code.

If the effort is successful, health care will shift from a paradigm of detect and treat, typically with toxic drugs that sometimes do no more than mask symptoms, to predict and prevent, with therapies of exquisite specificity aimed at the causes of disease. By identifying the genetic roots of illnesses like cancer and heart disease, some experts say, the science of the genome, or genomics, may make it possible for a child born today to live to 150 — or, some say, much longer.

"Death is a series of preventable diseases," said Dr. William A. Haseltine, chairman and chief executive of **Human Genome Sciences** here, declaring the philosophy behind the industry he is helping to invent.

Other genomics leaders have less trouble with that assertion than with Dr. Haseltine's contention that his company already has sequences for 95 percent of the human genes and is amassing a patent portfolio that will make it the gatekeeper for the entire biopharmaceuticals industry.

PLUNGING INTO THE DOUBLE HELIX

For investors, buying shares in genomics companies still requires a leap of faith. But the stocks could become great long-term holdings. *Page 6.*

Assertions like that have always irritated Dr. Francis S. Collins, the director of the Human Genome Project at the National Institutes of Health in Bethesda, Md. For some of the companies, he said, "financial viability appears to be tied to claims of exclusivity," while the Government's goal is to sequence all the human genes and place them in the public domain for the common good.

Indeed, the whole concept of patenting the bits of biochemical information known as genes offends many from religious leaders to scientists, including James Watson, a co-discoverer of DNA, who resigned as the original head of the Human Genome Project over this issue. While the Patent Office has established rules meant to clarify what kind of genetic discoveries can be patented, the issue is by no means resolved.

The genomics companies have filed patents by the thousands, but only a few hundred have been published, fewer still issued and none of those yet defended in court. So any claims of strong patent positions remain unproven.

But genomics is all about big claims. Last year, Dr. J. Craig Venter, a former N.I.H. researcher, shook up the field when he started a new company, now called

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A Race of Entrepreneurs to Cash In on the Genet

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Celera Genomics Group, a separately traded subsidiary of the PE Corporation, which he said would complete the sequencing of the human genome in 2001, about two years ahead of the public labs.

Dr. Venter's announcement was greeted with considerable skepticism, but it prompted Dr. Collins to move up his goal for completion, too; he now expects a rough draft of the human genome by next spring and a complete genome a year later.

The acceleration of the public and private efforts has already led to a rough winnowing of the genomics field, with some companies disappearing in mergers and others trading at such low share prices that their ability to raise capital and remain independent is doubtful.

A couple of broad strategies have emerged, meanwhile, among the best-capitalized companies.

Human Genome Sciences and **Millennium Pharmaceuticals** Inc., of Cambridge, Mass., intend to sell drugs, developed with capital raised in a few high-value deals with pharmaceutical companies. Two others, **Incyte Pharmaceuticals** Inc., of Palo Alto, Calif., and Celera, in Rockville, sell only data that others use to identify potential drug targets.

Shares in Human Genome and Millennium have soared this year, while Incyte, once the market leader, has fallen, primarily because of the perceived threat from Celera, which has deep pockets and a similar business model.

"The human genome is going to be sequenced, with absolute certainty, within the next two years," said Dr. Eric Lander, director of the federally financed Whitehead/M.I.T. Center for Genomic Research in Cambridge and a founding scientist at Millennium. "The game has moved on. Now it's: How do you add value to the genome?"

The Code as a Cure

Perhaps the most obvious way to add value to the genome is to turn genetic discoveries into drugs, but so far Human Genome Sciences is the only company that has done so. The stainless-steel fermentation vats at its 80,000-square-foot manufacturing plant here in Rockville would be a common site at a traditional biotechnology company, like **Amgen** or **Genentech**, but they are unique among the genomics players.

These vats produce the proteins that are Human Genome's first two drugs. One, intended to protect blood-forming cells from the toxic effects of chemotherapy, is being tested in women with breast and ovarian cancer. The other is being tested as a wound-healing agent. Both are in the second of three phases of trials typically required of new drugs by the Food and Drug Administration; that means that they are at least two or three years away from the market.

> Prospects for patent battles, as well as miracle cures.

But it is Human Genome's third drug candidate that provides a glimpse of the real promise of genomics. Using a gene injected directly into a diseased area, it prompts the body to grow new blood vessels. The drug is being tested as an alternative to bypass surgery for treating blocked arteries in the heart and limbs.

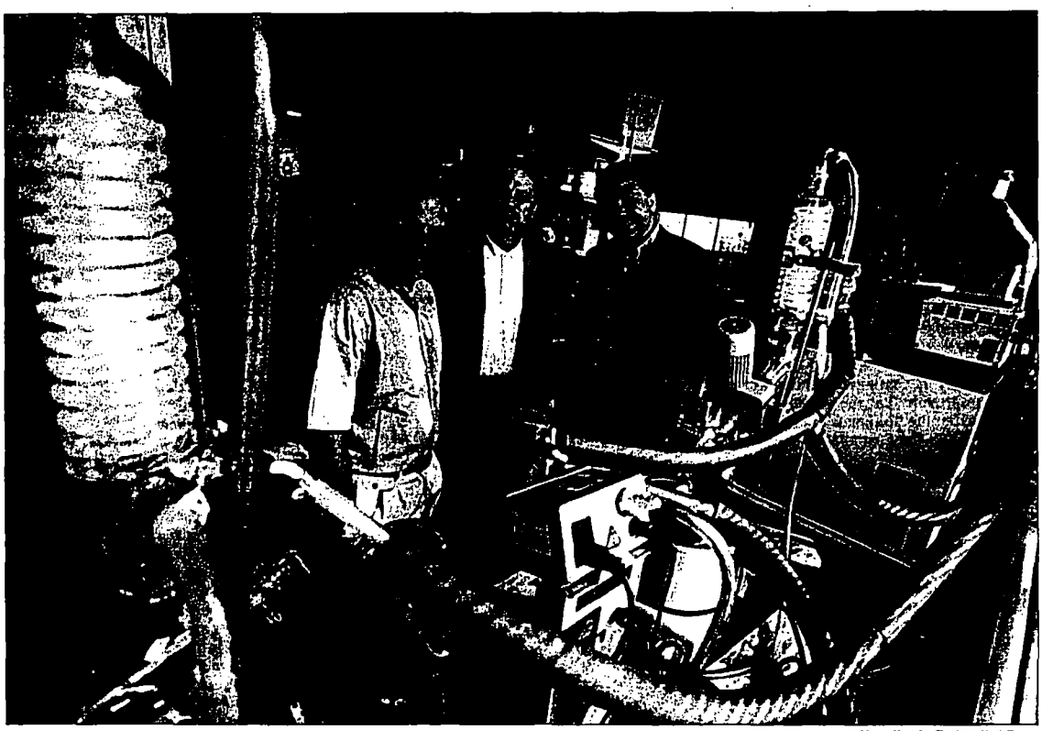
"At this point, we are the only company to create genomics assets and to use those assets to move drugs into the clinic," said Dr. Haseltine, who did pioneering work in sequencing the genome of HIV, the virus that causes AIDS, as a scientist at Harvard's Dana-Farber Cancer Institute.

But these three drugs, and three others that Human Genome hopes to begin testing next year, are only the tip of a very large iceberg. Dr. Haseltine said the company has discovered — and, more importantly, filed patents on — a vast data base of genes.

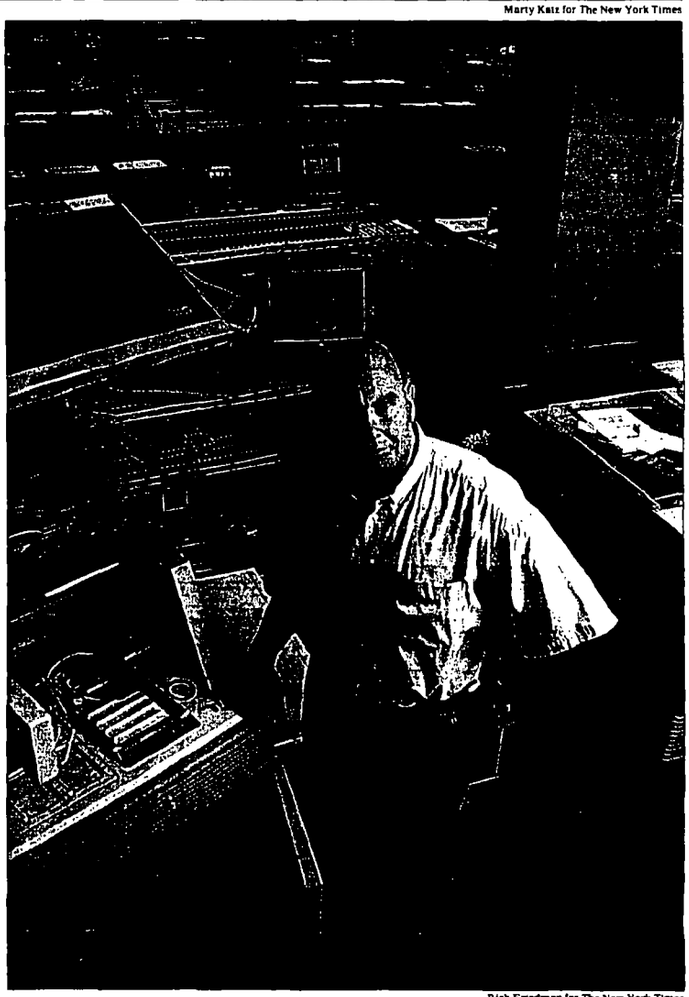
"Any company that wants to be in the business of using genes, proteins or antibodies as drugs has a very high probability of running afoul of our patents," Dr. Haseltine said. "From a commercial point of view, they are severely constrained — and far more than they realize."

Some drug industry executives dismiss this is as self-promotion, though as Human Genome's patents begin to be published, it is clear that the company is assembling an arsenal of intellectual property.

Still, Human Genome is itself constrained by the terms of a deal it struck in 1993 with **SmithKline Beecham** P.L.C., the British pharmaceuticals giant. For $125 million, then the largest biotechnology deal ever, SmithKline obtained exclusive rights to use Human Genome's gene discoveries to produce so-called small-molecule drugs, the kind that can be taken in pill form. The agreement expires in June 2001.



Marty Katz for The New York Times



Rick Friedman for The New York Times

Two companies working to make profitable use of the decoding of human DNA are Millennium Pharmaceuticals, led by, from left above, Steven H. Holtzman, Mark Levin and Dr. Eric Lander, and Celera Genomics Group, whose founder is Dr. J. Craig Venter, at right.

The deal left Human Genome free to develop drugs based on proteins — the easiest kind to take quickly to the clinic. But such drugs are commercially problematic, because they must be injected, and few patients want to take a shot if a pill is available. The company can also develop gene therapies, like its heart drug. But gene therapy has yet to produce an approved drug for anyone.

Nonetheless, Dr. Haseltine said the SmithKline deal was worthwhile, because it gave Human Genome the resources to grab a big lead in genomics. And when it expires, he will be free to strike new partnerships based on the same data base of genes. "Two years from now, we have a big opportunity to remonetize our asset and still have plenty of intellectual property to ourselves," he said.

Partners in the Marketplace

For now, however, the undisputed champion of deal making is Millennium, which has raked in over $1 billion in financing from partners like **Roche Holding** A.G., **Eli Lilly** & Company, **Monsanto** and **Bayer** A.G.

The arrangements are exclusive only for specific diseases (or, in Monsanto's case, for use in agricultural products), so Millennium remains free to pursue its own small-molecule drugs. It has also created subsidiaries for biotechnology drugs and for predictive medicine, like tests to identify genetic conditions showing a predisposition to diseases or adverse drug reactions.

Millennium's executives don't claim a lock on the intellectual property of the human genome, but their deal-making shows the value that drug makers see in the company's work.

A year ago, for example, Bayer agreed to pay Millennium up to $460 million over five years for 225 of what the industry calls validated genetic targets — that is, genes plus the accompanying biological data to show their relevance in areas like cardiovascular disease, cancer, osteoporosis, pain, liver fibrosis and viral infections. Targets that Bayer doesn't choose for drug development revert to Millennium.

"We did a huge search before we went with Millennium," said Wolfgang Hartwig, Bayer's executive vice president of pharmaceutical research. He said Bayer was attracted to Millennium's continual refreshing of its technology and to its freedom from the encumbrances of exclusive deals.

Millennium sprawls around Cambridge in leased space, most of it near the Massachusetts Institute of Technology. In its early days, the company made much of its connection to Dr. Lander and M.I.T.'s genome center. But today, Dr. Lander's role is more clearly advisory. The personalities who define the company are those of its chief executive, Mark Levin, a soft-spoken former venture capitalist, and his head deal maker and chief business officer, Steven H. Holtzman, a Rhodes Scholar with a degree in philosophy.

Mr. Levin tends not to make big claims, but he is building a big company, drawing on experiences early in his career at Genentech, the biotechnology pioneer, where he worked in process engineering in the mid-1980's.

"Genentech put in place the largest molecular biology lab in the world at the time," he said. "We've gone out and put together the largest critical mass in biotech today."

Later this year, Roche is expected to seek permission to begin trials of an anti-obesity drug developed from a genetic target supplied by Millennium. **Becton Dickinson** & Company in Franklin Lakes, N.J., will soon offer a melanoma test using technology from Millennium's predictive medicine unit.

But for all the depth and breadth of its science and technology, Millennium is conspicuously lacking a drug of its own in clinical trials.

"We're developing genes and targets and leads," Mr. Levin said. "By the end of 1999, going into 2000, you will see us make additional acquisitions, and these acquisitions will take us into the clinic."

Analysts note that while Millennium has the cash and high-value shares to acquire a drug — and many struggling biotech companies have drugs for sale — the best drug prospects attract multiple bids, and there are many far larger companies out shopping.

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The Knowledge Merchants

If Millennium and Human Genome aim to be the next Genentech and Amgen, Incyte and Celera have a different role model in mind: **Bloomberg** L.P. Just as Bloomberg sells information to the securities industry but isn't in the brokerage business, these companies sell data bases of genetic information to drug companies but never intend to produce drugs.

Incyte is based in Palo Alto, Calif., deep in Silicon Valley, and it is no coincidence that the heart of its headquarters is a vast, glass-enclosed room full of powerful computers. "At the end of the day, it's the information that matters," said Randy Scott, the president and chief scientific officer. "We are all about the application of Moore's Law to biology," he said — a reference to the observation that computer processing power doubles every 18 months. Applying that exponential growth to genomics should produce similar gains for drug discovery, Dr. Scott said.

Until recently, Incyte had something unique among genomics companies: operating income from sales of its products. Instead of signing huge deals to bankroll its own drug programs, Incyte sold subscriptions to Lifeseq, its genomic data base. Some 25 companies subscribed, including most of the leading pharmaceutical and biotechnology concerns, and Incyte showed steady earnings growth without big outlays on drug development.

But the creation last year of Celera — cash-rich and in no hurry to show a profit — put Incyte on the spot. While Incyte's data base offered gene fragments that point the way to full-length genes, Celera said it would provide whole genomes at a competitive price.

At the same time, the Government's Human Genome Project, now on an accelerated timetable, was placing thousands of genes in the public domain. And companies like **Pangea Systems** of Oakland, Calif., were supplying software tools to analyze this data, at a fraction of the cost of a Lifeseq subscription.

Facing a classic squeeze, Incyte management moved rapidly to improve its product, adding data from the Government's work, cutting the price and introducing new data bases. But the moves cost money, and as the company began reporting losses, investors fled, cutting the share price in half.

"I've been hearing this story — that Lifeseq's dead, it's all in the public domain — and maybe we even started to believe it ourselves," said Roy Whitfield, Incyte's chairman and chief executive. "But it's just not true." No customer has failed to renew its subscription, he said, and he predicted that profits — and investors — would return in the second half of next year.

Celera is the spoiler in genomics, or intends to be. The company plans to sequence the entire human genome and offer the data to subscribers. Other genomes of interest to scientists — like that of drosophila, a fruit fly used in many experiments — will be offered in a similar fashion. Dr. Venter's critics say Celera's hurry-up human genome will be full of gaps and errors, but the company has attracted three blue-chip subscribers: **Novartis** A.G., Amgen and **Pharmacia & Upjohn**.

As a sibling of **PE Biosystems Group**, also part of the PE Corporation, Celera received first access to PE Biosystems' latest automated gene-sequencing machines. (The two companies were created this spring in a reorganization of the old Perkin-Elmer Corporation.) Celera now has 300 of these $300,000 devices, some arrayed in neat rows, some lining the hallways still in their wooden shipping crates, some piled in elevators. The largest public genome center, Dr. Lander's lab at M.I.T. has 120 such machines, and most genomics companies have just a handful.

Combining the powerful equipment with an army of robots and vast amounts of computing power makes it practical and cost-effective to sequence whole genomes, Dr. Venter said.

The idea is that subscribers will pay Celera for partial genetic information as it becomes available, just as they have paid Incyte — but with the kicker that the company will ultimately supply complete genomes for many organisms. Companies can use this information royalty-free, except where it involves a gene sequence patented by Celera. Dr. Venter said he ultimately expects a mixture of revenues — from subscriptions, royalties on drug sales and even individual researchers paying to use the Celera Web site.

"They say I'm going to be the Bill Gates of biology. I'm not sure that's meant to be flattering," he said. Still, "the upside to this business is very, very large, and different from what anybody else is doing."

Many Eager Competitors

Wall Street loves to anoint winners, and given the impact of capital flow, these prophecies can become self-fulfilling. Despite talk that Celera or Human Genome may achieve a Microsoft-like dominance of biological information, many smaller companies are also pursuing opportunities.

The first real product of genomics was a diagnostic kit developed by **Myriad Genetics** Inc. of Salt Lake City, drawing on its discovery of two genes responsible for hereditary breast cancer. **Genome Therapeutics** Inc. of Waltham, Mass., has built a subscription business based on bacterial genomes. **Genset** S.A. of Paris has signed up two partners for what is called pharmacogenomics — the enterprise of applying genetic data to existing drugs to screen out people more likely to have side effects.

There are many more, and their continued proliferation suggests that genomics remains a fertile field.

"The current effort is rather like building the periodic table," said Dr. Collins, head of the Government's project, comparing the work to the fundamental plow work of chemistry.

"The real challenge of genomics — the real fun, the real payoff — is being able to take the periodic table and figure out how it works," he said. "All of that will be poorly understood and will be grist for research for decades to come."

Donna Bise for The New York Times

The Rev. Charles Wilson received a genetic treatment in a clinical trial.

A Vitalizing Gene, Straight to the Heart

Born with a genetic defect that caused his body to overproduce cholesterol, the Rev. Charles Wilson started having heart problems when he was 27. Over the next 30 years, he suffered a heart attack and had surgery many times. But by last summer, the blood supply to his heart was so reduced by atherosclerosis that he could barely get out of bed without severe chest pains.

"My doctor said to me, 'Charles, there's nothing else we can do; you've just got to sit still until technology catches up with you,' " said Mr. Wilson, 57, a Presbyterian minister who lives in Charlotte, N.C.

One day, though, he read a newspaper article about research on coronary gene therapy.

"I went looking on the Internet to find the actual report," Mr. Wilson said. "From that, I found the name of the doctor and the hospital."

He got in touch with Dr. Jeffrey M. Isner, chief of cardiovascular research at St. Elizabeth's Medical Center of Boston, and ultimately entered one of the first clinical trials of a drug developed through genomics.

Physicians in Boston made an incision in Mr. Wilson's chest and injected — directly into his heart — a gene that prompts the creation of new blood vessels. (Subsequently, the gene has been administered through a catheter.)

Although his recovery was slow at first, Mr. Wilson gradually gained strength.

"On the 42d day, as I was walking through the mall with my wife, when we had walked about a quarter-mile, I said, 'Honey, I haven't had any discomfort today,' " he said. "From that point on, I've been able to walk increasingly longer distances, faster and without pain." He now walks a mile and a half a day.

The gene he receives, VEGF-2, is being tested as a drug by **Human Genome Sciences** Inc. and is a product of **Vascular Genetics** Inc., which is a joint venture of Human Genome, Dr. Isner, St. Elizabeth's and Cato Holdings, a contract research organization. The drug is at least three to five years away from the market.

Although Mr. Wilson still has scar tissue and will have to take a variety of medications for the rest of his life, electronic scans of his heart show that it has grown new blood vessels in about 60 percent of the area that was previously blocked.

LAWRENCE M. FISHER

DRAFT

PROCLAMATION TO ENSURE THAT
DISCOVERIES FROM THE HUMAN GENOME
ARE USED TO ADVANCE HUMAN HEALTH

In the last decade of the twentieth century, scientists from around the world initiated one of the most significant scientific projects of all time: to determine the DNA sequence of the entire human genome, the human genetic blueprint. Progressing ahead of schedule, human genome research is rapidly advancing our understanding of the causes of human disease and will serve as the foundation for development of a new generation of effective treatments, preventions, and cures. To realize this promise, fundamental data on the human genome, including the human DNA sequence and its variations, must be made freely and broadly accessible to scientists everywhere. The human genome is the fundamental shared heritage of all humankind. Unencumbered access to this information is essential to enable discoveries that will reduce the burden of disease and promote health around the world. We applaud the decision by scientists working on the Human Genome Project to release information about the human DNA sequence and its variants rapidly into the public domain, and we call on all scientists worldwide to adopt this policy.

+ ~~one~~ 'heritage'.
+ affirm ~~to~~ basic + important value