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U.S. DEPARTMENT OF ENERGY

PRESENTS

MAXIMIZING THE RETURN FROM GENOME RESEARCH

JULY 23-24, 1993
HIGHLANDER INN
MANCHESTER, NEW HAMPSHIRE

MAXIMIZING THE RETURN FROM GENOME RESEARCH

A July 23–24, 1993, conference concerning intellectual property and technology transfer, with special attention to the interests of the biotechnology community.

PANELISTS

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MAXIMIZING THE RETURN FROM GENOME RESEARCH
Program Schedule

FRIDAY, JULY 23, 1993

12:30-1:00PM	Registration
1:00-1:30PM	Welcome and Overview
1:30-2:30PM	Origins of the Human Genome Project Robert Cook-Deegan
2:30:300PM	Break
3:00-4:00PM	Overview of Patent Protection in the Context of Other Intellectual Property Protection Kate H. Murashige
4:00-5:00PM	Overview of Federal Technology Transfer Lawrence Rudolph
5:15-6:15PM	Dinner
6:30-7:15PM	A Review of the Utility Requirement Under U.S. Patent Law Mark DeLuca
7:15-8:00PM	Congressional Perspective of the Biotechnology Revolution and the Human Genome Project Dennis Burke
8:00-8:45PM	Technology Transfer and the Human Genome Project Some Problems with Patenting Research Tools Rebecca S. Eisenberg
8:45-9:00PM	Break
9:00-9:30PM	Panel Discussion, with questions from registrants Moderator: Kate H. Murashige

SATURDAY, JULY 24, 1993

8:00AM	Continental Breakfast for hotel guests
8:45-9:00AM	Refreshments
9:00-9:15AM	Opening Remarks
9:15-10:00AM	Assessing and Licensing Federal Technology Ronald Barks
10:00-10:45AM	Perspectives on Technological Competitiveness Harvey Drucker
10:45-11:00AM	Break
11:00-11:45AM	The Human Genome Project and the Downside of Federal Technology Transfer Christopher J. Harnett
11:45AM-12:15PM	Panel Discussion, with questions from registrants Moderator: Lawrence Rudolph
12:30-1:30PM	Lunch
1:45-2:30PM	Breakout Sessions — What Stills Needs to be Addressed? • Technical Perspectives • Management Perspectives • Policy Perspectives
2:30-2:45PM	Break
2:45-3:30PM	Session Reports
3:30-3:45PM	Closing Remarks Moderator: Robert Cook-Deegan

Origins of the Human Genome Project*

The human genome project was borne of technology, grew into a science bureaucracy in the United States and throughout the world, and is now being transformed into a hybrid academic and commercial enterprise. The next phase of the project promises to veer more sharply toward commercial application, harnessing both the technical prowess of molecular biology and the rapidly growing body of knowledge about DNA structure to the pursuit of practical benefits.

Faith that the systematic analysis of DNA structure will prove to be a powerful research tool underlies the rationale behind the genome project. The notion that most genetic information is embedded in the sequence of DNA base pairs comprising chromosomes is a central tenet. A rough analogy is to liken an organism's genetic code to computer code. The goal of the genome project, in this parlance, is to identify and catalog the 75,000 or more files (genes) in the software that directs construction of a self-modifying and self-replicating system — a living organism. The main scientific justification for the genome project is not that it will explain all of biology. By the software analogy, studying the structure of DNA cannot directly approach problems of hardware — cells and organs — or of networks — social and environmental interactions. Biology has from its inception made clear the importance of adaptability. The complexity of the brain and its connections, with tens of billions of cells and trillions of connections, or the immense adaptability of the immune system, responding to countless external threats (including infectious organisms) and internal disruptions (including cancer), make clear that the human body is more than the simple expression of tens of thousands, or even hundreds of thousands, of genes.

The genome project is premised on the claim that genetic maps and new technologies will be among the most useful scientific approaches to highly complex biological phenomena, not that these maps will be the end of biology. The genome project is a biological infrastructure

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initiative, deriving from the fact that with so many investigators using genetic approaches to explore the biological wilderness, it is time to build some roads. The study of DNA structure does unapologetically promise reductionist explanations of some biological phenomena, tracing causes of disease, for example, to mutations in identified genes — that is, identifiable changes in DNA structure that affect biological function. This should not be confused, however, with a simplistic genetic determinism, with all its historical and political baggage. Indeed, the study of a wider variety of genes, diseases, and biological functions will surely dispel the simple-minded renditions of gene function, overwhelming it with myriad concrete examples of biological complexity that defy explanation by linear causal chains. Genes will nonetheless be nodes in many of the causal networks of interesting biological phenomena, and determining DNA structure is one of the surest and fastest ways to probe those networks. Gene maps are essential to this process; the genome project is aimed at providing those maps.

The earliest and most obvious applications of genome research are tests for genetic disorders, but less obvious diagnostic uses may prove at least as important, such as forensic uses to establish identity (to determine paternity, to link suspects of physical evidence of rape or murder, or as a molecular "dog-tag" in the military). Genome research also promises to find genes expeditiously, making the genetic approach attractive as a first step in the study not only of complex diseases, but also of normal biological function. Each new gene is a potential target for drug development — to fix it when broken, to shut it down, to attenuate or amplify its expression, or to change its product, usually a protein. Finding a gene gives investigators a molecular handle on problems that have proven intractable before.

Science administrators and members of Congress who shepherded the budgets for genome research (and their counterparts in other nations and international organizations) supported the project not only because of its medical benefits, but also because they saw it as a vehicle for technological advance and creation of jobs and wealth. The main policy rationale for genome

research was the pursuit of gene maps as scientific tools to conquer disease, but economic development was an explicit, if subsidiary, goal.

The genome project results from the confluence of tributaries that course through many provinces. The technical conception of the genome project derives mainly from precedents in molecular biology, but the story contains other major elements — the advance and dissemination of information technology, restructuring of the science bureaucracy, and increasing participation by commercial organizations. One way to trace these origins is to recount phases in the development of the genome project: how it got started, how it was redefined, and how it is now progressing. The history can be roughly divided into four stages: origins of the idea for a human genome project (the genesis), redefinition of its goals (a period of ideological conflict never completely resolved), emergence into a bureaucracy in the United States and several other nations (the Watson era), and transformation into a government-industry enterprise (still in progress).

Origins of the Idea

The genome project now embraces three main technical goals: (1) genetic linkage maps to trace the inheritance of chromosome regions through pedigrees; (2) physical maps of large chromosome regions, to enable the direct study of DNA structure in search of genes; and (3) substantial DNA sequence information, enabling the correlation of DNA changes with alterations in biological function. If history were logical, then the genome project would have grown from a discussion of each in turn, and how to bring them together into a coherent plan. History is not logical, however, and it was DNA sequencing technology rather than genetic linkage mapping that gave rise to the idea of a human genome project.

Three individuals independently came upon the idea of sequencing the human genome, that is, deriving the order of DNA bases comprising all human chromosomes. (Actually, this will, like other biological maps, be a composite or reference genome, as there is inherent variation

among individuals. While the order of genes and chromosome segments is generally quite stable, it is individual variations that are often of greatest interest. Gene maps help by laying out the overall structure, while much interesting biology comes from understanding how variations come about and what they cause.)

The seminal technology that led to the genome project was a group of techniques for determining the actual sequence of base pairs in DNA. In 1954, just a year after Watson and Crick described the double helical structure of DNA, George Gamow speculated that DNA sequence was a four-letter code embedded in the order of base pairs [Gamow, 1954 #1017]. In 1975, Fredrick Sanger announced to a stunned audience that he had developed a way to determine the order of those base pairs efficiently [1-3]. Alan Maxam and Walter Gilbert at Harvard independently developed a completely different method that same year. This method was announced to molecular geneticists late in the summer of 1975 at scientific conferences, and circulated as recipes among molecular geneticists until formal publication in 1977 [4]. Half a decade later, many groups began successfully to automate the process, in North America, Europe, and Japan. The first practical prototype was produced by a team at the California Institute of Technology in 1986, under the direction of Lloyd Smith, as part of a large team under Leroy Hood[5]. This prototype was quickly converted to a commercially available instrument by Applied Biosystems, Inc., and reached the market in 1987.

The new technologies for DNA sequencing spread through the biomedical research community like wildfire. By 1978, it was becoming apparent that sequence information needed to be catalogued systematically to make it useful to the scientific community. The idea of a database to contain this information emerged as a priority from a meeting at Rockefeller University that year. After several years of often intense and acrimonious discussion, twin databases were established under the European Molecular Biology Laboratory in Heidelberg at as GenBank at Los Alamos National Laboratory[6]. These databases were established just as personal computers were beginning to prove their immense power in biology laboratories. The

explosion of minicomputers in the 1970s and microcomputers in the 1980s fueled the attention to DNA sequence information, because computational methods were obviously the only way to analyze the deluge of DNA sequence information produced by sequencing techniques[6-9]. The technologies were thus present, but it took the spark of an idea of using them as part of a large organized effort to ignite the fire, out of which rose the human genome project.

Robert Sinsheimer, then chancellor of the University of California, Santa Cruz, thought about sequencing the human genome as the core of a fund-raising opportunity in late 1984. He and others convened a group of eminent scientists to discuss the idea in May 1985[10]. This workshop planted the idea, although it did not succeed in attracting money for a genome research institute on the campus of UCSC. Without knowing about the Santa Cruz workshop, Renato Dulbecco of the Salk Institute conceived of sequencing the genome as a tool to understand the genetic origins of cancer. Dulbecco, a Nobel-Prize winning molecular biologist, laid out his ideas on Columbus Day, 1985, and subsequently in other public lectures and in a commentary for *Science* magazine[11; 12]. The commentary, published in March 1986, was the first widely public exposure of the idea, and gave impetus to the idea's third independent origin, already gathering steam.

Charles DeLisi, who did not initially know about either the Santa Cruz workshop or Dulbecco's public lectures, conceived of a concerted effort to sequence the human genome under the aegis of the Department of Energy (DOE). DeLisi had worked on mathematical biology at the National Cancer Institute, the largest component of the National Institutes of Health. How to interpret DNA sequences was one of the problems he had studied, working with the T-10 group at Los Alamos National Laboratory in New Mexico (a group of mathematicians and others interested in applying mathematics and computational techniques to biological questions). In 1985, DeLisi took the reins of DOE's Office of Health and Environmental Research, the program that supported most biology in the Department. The origins of DOE's biology program traced to

the Manhattan Project, the World War II program that produced the first atomic bombs, and concern about how radiation caused genetic damage.

In the fall of 1985, DeLisi was reading a draft government report on technologies to detect inherited mutations, a nagging problem in the study of children to those exposed to the Hiroshima and Nagasaki bombs, when he came up with the idea of a concerted program to sequence the human genome[13]. DeLisi was positioned to translate his idea into money and staff. While his was the third public airing of the idea, it was DeLisi's conception and his station in government science administration that launched the genome project.

Redefining the Technical Goals

Molecular biologists did not welcome the idea with open arms. While many, especially those who studied medical genetics and the inheritance of genetic diseases, were enthusiastic, the broader community of protein biochemists and even molecular geneticists were far more skeptical. The year 1986 was a time of setback and redefinition for the genome project. The nadir of the project's trajectory came at a meeting at Cold Spring Harbor Laboratory in June 1986. A rump session was called to discuss Dulbecco's editorial. Walter Gilbert, who had been infected with the Santa Cruz bug, laid out a rationale for the project and then began to describe its technical goals and price tag. The discussion quickly veered into the politics of biomedical research — the dangers that large projects posed for budgets to support small investigator-initiated research (the space shuttle used as the negative icon) and the questionable competence of DOE to run such a project. David Smith, as the DOE representative, faced a largely hostile audience, although he also got many private expressions of support.

The controversy provoked a number of events on the policy front, and the debate moved to Washington, DC. The Howard Hughes Medical Institute, which had begun to get interested in the genome project, held a well-attended international forum in July 1986. In October, NIH hosted a discussion in conjunction with a meeting of the NIH Director's Advisory Committee.

These two meetings exposed considerable rancor among the ranks of prominent molecular biologists, but they also began the search for common ground, and laid the groundwork for a two-year succession of countless meetings that redefined the human genome project. The redefinition took place most conspicuously in a committee of the National Research Council (NRC).

In September, 1986, two projects were initiated to study the idea. The NRC, the largest operational arm of the National Academy of Sciences, approved a study. The NRC appointed a committee of extremely prestigious researchers chaired by Bruce Alberts of the University of California at San Francisco. This study committee vigorously debated the merits of a concerted scientific program, carrying out in microcosm the debate transpiring more broadly in the scientific community.

The NRC committee took a commonsense approach, looking at the scientific and technical steps that would be necessary to construct comprehensive maps of the human genome and to make sense of the resulting information. They started by bringing together those constructing various kinds of genetic maps in different organisms. The idea of a human genetic linkage map grew out of work in viruses, bacteria, yeast, and other organisms. The key insight grew from a 1978 inspiration shared between David Botstein, then at the Massachusetts Institute of Technology, and Ronald Davis of Stanford. In a discussion at Alta, Utah, they speculated that researchers could find natural DNA differences among individuals in families, most of which would not necessarily lead to clinically detected differences, to trace the inheritance of chromosome regions through those families.

Each person has a pair of each of the 22 nonsex chromosomes. (Women also have a pair of X chromosomes, while men have an X and a Y.) Botstein and Davis suggested that if detectable differences could be found for discrete chromosome regions, then one could figure out which of each parent's chromosome pair was inherited by each child. A map of such differences would enable geneticists to determine the approximate location of disease-associated and other genes,

even if they had no prior clues about the gene's function [14]. By late 1979, the first such DNA marker was found by Arlene Wyman and Raymond White, working in Worcester, Massachusetts[15].

These heterogeneous DNA markers were quickly used to hunt for disease genes, demonstrating the utility of the gene mapping idea. Suppose, for example, that some adult progeny of the same mother (or father) Huntington's disease also developed it, while other children did not. If the affected children all inherited DNA from the same region of chromosome 4, while those unaffected inherited the other copy of that DNA, this would be strong statistical evidence that DNA in that chromosome 4 region contained the Huntington's disease. This is exactly what James Gusella and others discovered in 1983, when they linked Huntington's disease to the tip of chromosome 4[16]. The DNA marker they used to track the passage of chromosome 4 in families was not the gene itself, but a nearby region that just happened to differ among family members so that the investigators could tell the chromosomes apart. Finding the gene itself took another decade of arduous work, but it was ultimately successful, made possible only because genetic linkage narrowed the zone of DNA to scan for the offending mutation[17].

The second cluster of mapping techniques centered on structural catalogs of DNA fragments, rather than markers to track inheritance through pedigrees. The general idea was to take native chromosomal DNA, break it into fragments that could be copied by various cloning techniques, and then put the DNA fragments (now plentiful enough to study in the laboratory) back in order. If this could be done for all the chromosomes, then once a gene's location were narrowed to a particular region by genetic linkage, then the DNA from that region would already be available in a test tube for direct analysis.

The techniques for physical mapping were again derived from work on viruses and bacteria, and by the mid-1980s, pioneering groups had moved into constructing physical maps of larger and more complex organisms. Maynard Olson and his colleagues at Washington University were working on a physical map of yeast, which was a very powerful model for the

genetics of organisms with nucleated cells[18]. In Cambridge, UK, Alan Coulson, John Sulston and their colleagues were working on a physical map of the nematode *Caenorhabditis elegans*[19]. *C. elegans* had been identified by Sydney Brenner as a powerful model to apply genetic techniques to study development and behavior of organisms containing differentiated organs, including a primitive nervous system[20]. John Sulston had mapped the lineage of every cell in the body of one developmental stage[21; 22], and others at Cambridge had traced the connections of the entire nervous system[23]. While the entire genomes of yeast and nematode were only the size of a singe human chromosome, many believed that similar techniques would prove applicable for the entire human genome, more than an order of magnitude larger. The prospects for physical mapping brightened in 1987, when David Burke and Georges Carle, working with Maynard Olson, developed a technique to clone DNA fragments hundreds of thousands of base pairs in length[24], considerably reducing the complexity of constructing large-scale physical maps.

The NRC committee ultimately redefined the project to embrace the entire set of genetic maps, giving much greater prominence to genetic linkage mapping and physical mapping than to sequencing. The committee also underscored the importance of organisms other than the human[25]. The committee recommended an annual budget of $200 million for 15 years, supporting the budget recommendations of a previous DOE advisory committee[26]. The budget recommendations of the two reports were quite similar, but where the DOE advisors urged DOE to take the lead, the NRC committee recommended only that there be a lead agency, and proffered NIH, DOE and NSF as the three options.

The congressional Office of Technology Assessment (OTA) project on the human genome initiative was approved in the same hour of the same day as the NRC study. While the NRC committee crafted a scientific strategy and made specific recommendations, the OTA report focused more on its policy rationale (why Congress should or should not support it) and the attendant policy issues. OTA surveyed international activity, and dwelt far more on issues of technology transfer, ethical and social implications of genome research, and research

management[27]. OTA's only substantive difference with the NRC report centered on the notion of a "lead agency." OTA warned that if a lead agency meant control of all funding, then picking one would invite internecine warfare between NIH and DOE, the most likely result of which would be death of the project. OTA did not offer specific recommendations, but in congressional testimony, it clearly favored a truly collaborative effort worked out between the two agencies, with a congressionally mandated task force as the backup option if the agencies failed to produce an acceptable agreement[28].

The genome project rose like the Phoenix from the ashes of Cold Spring Harbor. A vigorous two-year debate culminated in a pair of reports that smiled on, indeed pointed out the inevitability of, systematic gene mapping on the scale of the entire human genome. The next step was to translate the scientific strategy into a funded set of coordinated programs.

Establishment of Government Programs with Process Goals

The first move toward a genome bureaucracy came in the fiscal year 1987 DOE budget. DeLisi set aside $5.5 million of discretionary funds already appropriated, reprogramming them for his newly conceived genome research program. The first congressional action came with the fiscal year 1988 budgets, during hearings in the Spring and summer of 1987. DeLisi cleared a several-year program of genome research funding through the Department and then with the White House Office of Management and Budget. This was incorporated into the President's budget, and duly appropriated, with earmarked spending authority beginning in October 1987. On the NIH side, no request for genome research funding went into the President's budget request, but in response to questions from the House Appropriations subcommittee, Wyngaarden indicated that NIH could use $30 million for gene mapping if Congress chose to appropriate $500 million or more in excess of the Presidential request. Nobel laureates James D. Watson and David Baltimore met with Members and staff from both House and Senate Appropriations Committees in May 1987, primarily to seek additional funding for AIDS research, but Watson also asked for $30 million in genome research funds. The House duly earmarked $30 million,

but the Senate only earmarked $6 million, and a compromise between the two houses split the difference.

The genome project was thus established by congressional action at both NIH and DOE, beginning with the 1988 budget. DOE had long before established a genome program office; in October 1988, Wyngaarden appointed Watson an associate director for NIH in charge of genome research coordination. The newly appropriated funds were to be spent through the National Institute of General Medical Sciences in fiscal years 1988 and 1989, but Watson's office was to coordinate these funds with over $300 million being spent on genome research throughout the NIH institutes. In October 1989, the Department of Health and Human Services established the National Center for Human Genome Research at NIH, giving it authority to expend federal research funds directly, beginning with the 1990 fiscal year, rather than channeling them through the National Institute of General Medical Sciences.

The National Science Foundation had a major instrumentation program, substantial interests in plant and animal genome research, and considerable strength in computational biology, but it did not earmark funding or create a new management structure.

Outside the United States, an Italian genome program began in May 1987[29], tracing its roots to Renato Dulbecco's talk for the Italian Embassy in Washington, DC on Columbus Day 1985. In the USSR, Alexander Bayev and Andrei Mirzabekov presented the idea for a genome program to government officials in December 1987, and secured support for a new program after Bayev addressed the General Assembly of the USSR Academy of Sciences in March 1988, and subsequently obtained approval from the USSR Council of Ministers in December 1988[30]. When the USSR dissolved, the genome project survived, as a component of the Russian science program.

The United Kingdom launched its genome program in February 1989, combining forces between the government's Medical Research Council and the private Imperial Cancer Research

Fund in London[31; 32]. British molecular biologist Sydney Brenner wrote a letter to the European Commission in February 1986 to urge creation of an EC program aimed at a "Map of Man"[33]. Genome research programs on bacteria, yeast, and other organisms developed at EC over the next year. The human genome research program elicited concern in the European Parliament about its social and ethical implications. The EC program ultimately set aside over 7 percent of its budget to scrutinize these impacts, changed its name from "predictive medicine" to "human genome analysis" to address concerns among the German Green Party. With these changes and some other minor stipulations, the EC human genome program began in June 1989[34-37].

The process in Japan was complex. Japan was the first nation to have a government program dedicated to automating the process of DNA sequencing. Akiyoshi Wada was appointed director of a program that began in April 1981 for this purpose, sponsored by Japan's Science and Technology Agency and carried out at the RIKEN Institute in Tsukuba City. (By contrast, the first government funds for automation of DNA sequencing came in a 1984 grant to Caltech.)

When debate about the genome project began in North America and Europe in 1985, and especially when it picked up in 1986 and 1987, Japan's Ministry of Education, Science, and Culture (Monbusho), which supports the vast majority of university-based scientific research, appointed an advisory committee chaired by Osaka University professor Kenichi Matsubara. Monbusho began a modest genome research effort in April 1989, and the Science and Technology Agency expanded its genome research efforts that same year. The Ministry of Health and Welfare initiated an intensified effort to support hunts for disease-associated genes, and the Ministry of International Trade and Industry began planning for its own genome initiative in 1990, although its initiation was delayed by competition for funds. Japan's agriculture ministry began an effort to map the rice genome, funded largely by private funds gathered at sporting events.

France announced plans to mount a government-supported genome research effort in June 1990, and set aside funding beginning in October that year[38]. This augmented a relatively small grants program for genome research commenced in 1988. Canada joined the chorus in 1992[39]. Several European nations also augmented their funding for human genetics during this period,[36; 40] contributing to an accelerating pace of gene discovery. In June 1990, Latin American scientists formed a regional network to encourage collaboration on genome research with laboratories in North America and Europe and among themselves[41; 42].

The genome project thus grew rapidly into an international effort supported by many governments and the EC. There was strong consensus on the need for complete genetic linkage and physical maps, and general agreement about the need for new sequencing technologies. There was disagreement, however, about the degree to which large-scale DNA sequencing should be initiated and outright controversy about the best scientific strategy to pursue in large-scale sequencing efforts.

As the genome project was transformed from a series of meetings and policy reports into an actual scientific program, it added several process goals The technical goals for gene mapping remained, but several policy goals were added. One distinctive aspect of the genome project was its explicit attention to technology development in addition to science. Attaining the technical goals depended on new technologies, and developing new biological methods, instruments, automata and robots, and other new technologies became an explicit objective.

An unprecedented commitment to support research on social, legal, and ethical implications of genome research became the second process goal. Discussion about the social implications of human genetics had attended the genome debate from its earliest phases in Washington, and the history of eugenics cast a long shadow over the genome debate, particularly in German-speaking Europe. Both the NRC and OTA reports explicitly acknowledged the importance of social and ethical issues, and the need to address them head-on as the genome project progressed.

James Watson announced that the NIH program would include a budget set-aside for such research when he was announced as associate director for human genome research in September 1988. Other programs throughout the world, except the UK program, followed suit. (In the UK, such discussion was generally delegated to the private Nuffield Council, established to mediate a national debate on matters of bioethics.) This development deserves a separate treatment, but one particular aspect of this program deserves special mention here — a renewed commitment to technology transfer.

Ensuring that the fruits of genome research were quickly translated into useful applications (and thence into jobs and wealth) became a second process goal for the human genome project. Even as the various government programs noted above began to take shape, private interests also began to mount genome research programs, some of them more significant than publicly funded programs in their nations. In the United States, the Howard Hughes Medical Institute focused on issues not drawing sufficient attention from government, concentrating on databases and helping support the initiation of the Human Genome Organization to coordinate international efforts. In the UK, the Imperial Cancer Research Fund was an equal partner with the government Medical Research Council early on, and the private Wellcome Trust made even larger investments in new genome research and informatics centers in 1992 and 1993. In France, the most vigorous genome research effort was supported by the Centre d'Etude du Polymorphism Humain (CEPH), which formed a partnership with the private French Muscular Dystrophy Association to establish the Genethon, a highly automated genome research facility outside Paris. This effort was started quickly, and dwarfed the government genome research program. In Japan, the Saitama Research Center, the Chiba prefectural government, and other private groups began genome research efforts separate from the various government-sponsored programs.

The international efforts were united in a desire to share map and DNA sequence data widely. The idea behind gene maps was to use them as tools to speed research, and to reduce the need for multiple laboratories throughout the world to develop maps of the same regions when

hunting for different genes. Maps would only be as useful insofar as they were complete, and completeness depended on sharing data freely and rapidly. CEPH was formed in 1984 to forge an international collaboration for genetic linkage maps of human chromosomes[43]. The groups searching for various genes also formed international collaborations, intended to speed sharing of data and materials. This international ethic of sharing, however, had to contend with a growing set of commercial attachments that seemed likely to alter the rules governing collaboration within and across national borders.

Commercial Pursuits

Most of the initial efforts were funded by nonprofit groups hoping to further research. Beginning in 1992, however, a new wave of genome research centers began to take shape, only these were often supported by venture capital or private corporate funds. Existing genome research centers also developed ties to industry. In mid-1992, J. Craig Venter announced his intention to form The Institute for Genomic Research (TIGR). (His work formed the basis for the patent application for expressed sequence tags, which is discussed below.). This new institute was then the largest private investment, and its work was linked through agreements on intellectual property rights to a somewhat larger for-profit unit, Human Genome Sciences, Inc. Human Genome Sciences, Inc., in turn, announced an agreement in excess of $130 million with Smith-Kline-Beecham in May 1993, and William Haseltine was selected as Chief Executive Officer. Another company, InCyte, began a major program in genome research during 1992 and into 1993. Several private firms, including Mercator, Darwin Molecular, Genomyx, and others, pursued plans to develop instruments or pursue pharmaceutical development strategies that involved some mix of genome research.

Corporate funds were not attracted merely by hot science, but also by the prospects of diagnostic applications and more expeditious drug discovery. In every nation where the genome project was presented to its government, including the USSR, promoters pointed to the potential for genome research to create jobs and wealth through new technology. The true potential for

wealth, however, lay not in the new technologies, but in applying them to practical uses. There would doubtless be a spate of new instruments and reagents that could be sold, but this would be a relatively small research market in comparison to medical diagnostics, and smaller still in comparison to therapeutic pharmaceuticals or agriculture. In the medical arena, the most compelling rationale for corporate investment was not in technologies being pursued, but in the terrain being mapped, that is, genes embedded in the human genome. Private investments presumed a means to stake claims on that territory. Those claims would necessarily change the complexion of research, altering the rules by which materials and data were exchanged. The claims being staked were in the form of patents or trade secrets.

Each national government had thus been encouraged a genome research program not only to expedite biomedical research, but also to promote national economic development. These goals could not both be pursued to their logical ends without conflict, as national economic development would by definition mean winning an international economic competition, which was not entirely compatible with unfettered international sharing of data, information, and technology.

The seriousness of the conflict was brought to the surface by an international controversy provoked by a US patent application filed by NIH in June 1991. This patent application will be discussed at greater length and with greater authority by others in this conference, but several points should be made clear here. First, much of the public controversy was poorly framed in ethical terms. Sanctimonious claims were made about direct links between human genes and human dignity. DNA is a universal genetic code, and it will be difficult if not impossible to distinguish human genes from those derived from other organisms. This argument cannot be taken too far, as it is obvious that the human genome in aggregate contains the plans for a human instead of a monkey or nematode or yeast, but it is equally clear that very few, if any, genes will be exclusively human in origin. A classic 1975 paper by King and Wilson showed that the average protein sequence differed only one percent between humans and pygmy chimps, and the

difference at the DNA level was only slightly greater [King, 1975 #915]. The obvious implication was that humans differed more in the timing and quantity of gene expression, rather than which genes there were.

It is far from clear what a proscription on patenting "human" genes would entail, how it could be made meaningful in the law, and whether it would do any good. In most cases, patenting an animal gene and then slightly modifying it for another patent would cover the same material as a human gene. A simple genetic determinism would seem to lie at the root of this equation of DNA with dignity. The factors that distinguish humans from other organisms seem more likely to be nuances of gene expression, development, and environmental response than the collection of genes in the human genome. The brain, for example, is an organ seemingly adapted to be able to change its structure and function in response to environmental stimuli, even more than other organs. No CD-ROM containing Lincoln's DNA sequence could tell us much we would care to know about why he became an historically important figure.

The NIH patent dispute did surface a true international policy dilemma nonetheless, but it was not in patenting policy *per se* but in conflicts between the goal of quickly constructing comprehensive maps and databases as a worldwide scientific effort, and the goal of linking genome research to each nation's domestic economic development. It was not a simple conflict with data-sharing, since investigators in each company could release data as soon as patents were filed. Rather, it was the incentive for each nation to structure its science effort so as to secure its intellectual property rights before the others. Data could be shared only after stakes were claimed, and this could theoretically provoke an international genome gold rush.

If one of the purposes of an international effort was to reduce the duplication of effort that necessarily follows from a purely competitive strategy, then this efficiency was at risk. Taken to an absurd extreme, each nation might choose to attempt to patent the pathways to all human genes before making its data available to others. In this case, all nations would have to map the entire genome. Every nation would be aiming at the same goal, expending its resources to win

the race, but only the winning effort would secure the intellectual property rights. This is a recipe for inefficiency, a true multi-player prisoner's dilemma.

A final point about the NIH patent application is that the policy dilemma was sure to surface. If NIH had not filed a multi-gene patent application, private firms surely would have. The terms of the debate might have been different, and it might have been long delayed and less conspicuous, as the patent application need not have been publicly known for some time, but the debate was nonetheless inevitable. Whether a quieter and later debate might have been better or worse is a matter about which we can surely speculate, but will never be certain.

One of the most interesting aspects of technology transfer related to the genome project is how the project is caught in a changing of the rules. To make this point more starkly, we can perhaps discuss what might have been different if the techniques for DNA sequencing had been patented, as surely they could have been. These techniques are at least as central to research as the polymerase chain reaction that was patented. In the long list of citations to technical orgins of the human genome project, some items have been patented, and others not. The Cohen-Boyer patent for recombinant DNA was a centrally important technique of molecular biology. It was patented, but then licensed for relatively low fees. The polymerase chain reaction, discovered at Cetus Corp. in 1983 and then sold to Hoffmann-La Roche in 1991, was patented and then controlled through a complex set of relatively high-fee licenses for various applications and reagents. The two main techniques for DNA sequencing itself developed in 1975, however, were surely patentable but were never patented. Laboratory instruments, such as DNA sequenators and DNA synthesizers, were sold, with the price of the instrument and its reagents covering patent fees. These disparate ways of handling research methods and tools clearly affected who could use them, and perhaps also the pace of discovery and application, but how and to what degree was a matter of speculation and ideology more than empirical analysis.

It is far from clear what can explain these differences, aside from historical happenstance and the changing norms of biomedical research between the 1970s and the 1990s. It is even

more evident that there is not analytical answer to the question: is it good for science to patent discoveries? Or the question: is it good for the nation to patent research tools? Or even the question: is it good for technology tranfer to patent discoveries? Answers to these questions will no doubt differ from case to case, but analysis of the factors that distinguish cases might well lead to more sophisticated, and more successful, national policies and international agreements regarding intellectual property and the sharing of data, materials, and technologies.

Those grounded in the pharmaceutical industry often take the benefits of patenting as an article of faith, as well they might since the entire industry truly rests on a foundation of patent protection for chemical entities. There is nonetheless a disturbing dearth of literature on the transaction costs of patenting, or the untoward effects on the research enterprise from a need for complex cross-licensing and constraints on sharing of data and materials, especially in the domain of research tools. Those grounded in the ethos of science, in contrast, take the benefits of free exchange as an article of faith, but there is here a dearth of data about the therapeutic innovations foregone for lack of private investment.

Patent law has historically proven to be a flexible instrument, and a powerful engine for innovation, but it is equally clear that much of the debate about patent policy and technology transfer takes place in the absence of empirical data about outcomes, let alone analysis of long-term social impacts. The permissive interpretation of biotechnology patent law of the 1980s combined with a series of "technology transfer" statutes and executive orders to make a volatile mix. These trends moved policy strongly toward heavier reliance on patents, but with little analysis of their impact on the pace of discovery or on international science. Where facts are sparse, ideology fills the void. Even a cursory inspection of technology transfer policies relating to genome research leads to one obvious conclusion: all nations will be better off if the contending ideologies are disciplined by carefully designed empirical research.

US Genome Research Budgets at NIH and DOE

Based on budget documents prepared for the House and Senate Appropriations Committees 1987-1993, and projections by the Department of Energy and National Center for Human Genome Research.

Fiscal Year	DOE ($ million)	NIH ($ million)
1987	5.5*	-
1988	10.7	17.2
1989	18.5	28.2
1990	27.2	59.5
1991	47.2	87.4
1992	61.4	104.8
1993	63.1	106.1

* The first year's funding at DOE came from funds that Charles DeLisi reprogrammed from research budgets within the Department, and did not require congressional action. The first congressionally earmarked funding for both NIH and DOE came in Fiscal Year 1988.

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OVERVIEW OF PATENT PROTECTION IN THE CONTEXT OF OTHER INTELLECTUAL PROPERTY PROTECTION

by Kate H. Murashige

There are four commonly recognized systems for protecting "intellectual property". These four are trademark, patent, trade secret and copyright. Three of these systems, trademark, patent and copyright, are controlled by federal statute in the United States. Two of them, patent and trade secret, are directed to the same types of subject matter -- namely processes, compositions of matter, articles of manufacture and machines. The subject matter of copyright may also be embodied in articles of manufacture such as jewelry, recordings, and film. I suppose these could also be considered compositions of matter. Both the nature of the protection afforded, and the appropriateness of one system or another for a particular subject matter is often quite straightforward.

Trademarks

Trademark systems of protection are the most easily distinguished from the remaining three. Both federal and state governments maintain systems for the registration of trademarks, but the registration isn't necessary to obtain a trademark right. Trademarks are designed to inform the consumer of the origin of goods or services. They are considered proprietary to their owners because they are associated with the goodwill of the business engendered by the goods or services labeled by the mark. Brand names are the most familiar example, but they are not the

only use of the trademark statutes. The recent Supreme Court decision in Two Pesos, Inc. v. Taco Cabana, Inc., 23 USPQ2d 1081 (S. Ct. 1992) held that Taco Cabana had protection under section 43(a) of the Lanham Act for the distinctive decor in its chain of Mexican restaurants as would a conventional trademark. In any event, the application of trademark law to biotechnology so far seems to have raised no particular new issues as compared with application of trademark law elsewhere. Indeed, as the majority of biotechnology companies presently has few if any goods or services on the market, trademark protection is premature in a large number of instances.

Copyright

As its name implies, copyright is designed to protect the copyright holder against copying of the expression of the copyright holder's ideas by others. It has a defined term of such protection for works of authorship, paintings, musical compositions and the like. It can also be used to protect ornamental objects. The protection is expected to extend to the expression of an idea, not to the idea itself. Functionality is the enemy of copyright. If an idea can be expressed in only one (or a few) ways, the possibility of copyright protection is significantly weakened.

The only intrusion of copyright law specifically into a biotechnology context relates to a suggestion, first made at least a decade ago, that DNA sequences (and I suppose amino acid sequences) might be subject to protection under the copyright

law. Probably because a copyright protects only against copying and not against independent discovery, this suggestion appears to have gotten lost in the rush to obtain patent protection for genes. It may be useful to dust off this idea again in the light of the current flurry to sequence large numbers of DNA molecules obtained from expression libraries.

The application made by the NIH claiming "expression sequence tags" or "ESTs", retrieved and sequenced by Dr. Craig Venter and Dr. Mark Adams, has received wide publicity. Inspired, presumably, by the attempt to sequence the entire human genome, and recognizing the fact that approximately 99% of the human genomic DNA does not encode any proteins, Venter and Adams set about obtaining DNA sequences by reverse transcribing the messenger RNA found in brain cells. Because the messenger RNA embodies only genes that are on their way to becoming proteins, the 99% nonsense sequences are automatically eliminated and the sequenced material is putatively derived from the 1% of the genome that encodes protein (and its associated translation regulating elements). Venter and Adams were able to retrieve and sequence this reverse transcribed cDNA with astonishing efficiency and the initial NIH application contained approximately 300 sequenced "ESTs". The number has now grown to many thousands; Drs. Venter and Adams have left the NIH and continue their work in the context of a private institute. In the meantime, other companies such as Incyte Pharmaceuticals in Palo Alto, California and a Japanese company, and probably others, have entered the race to obtain sequences associated with

the estimated approximately 100,000 genes embedded among all the nonsense in the human genome. The hue and cry raised by the prospect of protecting so many DNA sequences by patent has resulted in a proposal to place a two-year moratorium on patents related to the human genome (a proposal that was not enacted) and in a study by the Office of Technology Assessment on the implications of this work.

One consideration that might be given to the protection of these ESTs is the application of copyright law. Copyright protection would essentially prevent others from "stealing" the sequencing work already done, but would not prevent the use of independently recovered forms of the relevant genes and ESTs. Since it is no longer necessary to apply a copyright notice in order to obtain copyright protection, this may already be inherent in the sequences themselves.

Aside from the foregoing, copyright protection as applied to biotechnology is not particularly exciting. It would apply in conventional ways such as protecting advertising brochures, business descriptions, etc. from direct copying.

Trade Secrets

The protection afforded by trade secrets is generally governed by state law and is a mix of statutory and judicial provisions. Trade secrets are applicable to any kind of information which relates to the business of the trade secret holder and which is properly secured by that holder with appropriate guarding from discovery by unauthorized persons. In

a sense, trade secret protection is the converse of patent protection which requires full and complete disclosure of the subject matter to be protected. There is no statutory system for providing such protection. Since trade secrets are not protected by a statutory scheme, the protection extends for an indefinite length of time -- i.e. until the secret is out.

Much of the trade secret protection that is important to biotechnology companies is similar in nature to that ascribable to any commercial enterprise -- plans for future business development, areas in which future research will be conducted, plans for expansion or building of facilities, certain financial records, and the like which have to do with the manner in which the particular company intends to conduct its business, is conducting its business, or has conducted its business. This type of trade secret is presumably not available to nontrade institutions such as universities and research foundations. While there appears to be no case law directly on point, it may very well be that with the increased tendency of such institutions to participate in commercial development through outlicensing programs, and even equity investments in commercial enterprises, this distinction may no longer be viable.

A different type of subject matter which is also susceptible to trade secret protection overlaps that for which patent protection may be obtained. This type of subject matter often includes ways to produce products, ways to conduct assays, particular materials useful in manufacture, and even the composition of materials that are to be sold. This latter

category makes sense, of course, only if the product cannot be reverse engineered and its composition discovered from analysis of the product itself.

The significant characteristic of trade secrets is that the ability of the holder to keep the secret secret is the ultimate requirement. The holder is not protected against independent discovery of the trade secret from its own inadequate schemes for insuring secrecy. Thus, with respect to the latter point, it will be necessary for the holder of the trade secret to initiate and maintain certain institutional practices which may or may not be acceptable, such as requiring employees to sign confidentiality agreements, requiring visitors to wear badges and be escorted, requiring exit interviews for employees leaving the company, requiring identification of what is and what is not under trade secret protection, and other perhaps burdensome and rather ill-defined measures to assure confidentiality. Even with respect to "patent type" subject matter, universities or research institutions may be reluctant to institute measures which seem in contradiction to their presumed duty to spread knowledge. Acknowledging the availability of "know-how" in the context of a license to a commercial enterprise may be offensive, since presumably a university, at least, is obligated to teach the general public what it finds out and what it knows.

The propensity of participants in biotechnology to take a dim view of anything that inhibits communication with colleagues is also well known. This may be diminishing as the industry continues to distance itself from academic environments

and increases its associations with traditional pharmaceutical companies. As this occurs, the tendency of persons involved in the research and development of products to treat their knowledge as common property with their academic colleagues will diminish.

With respect to the first consideration -- lack of protection against independent discovery -- keeping trade secrets in biotechnology seems to have elevated risk factors. Trade secret protection seems most appropriate for subject matter that is unlikely to be discovered by anyone else because it is so specific to a particular process or product that it is unlikely that a duplicate set of experiments will be conducted. It is quite inappropriate for a generic improvement that is likely to be stumbled upon by anybody in the field. For example, if, in the production of a particular recombinant protein, it is found that a particular fusion partner permits very high expression in a particular host organism (and the fusion partner is cleaved before the product is marketed), it may very well be that the probability of competitors discovering this is quite low and trade secret protection will be fine. On the other hand, if it is found that a particular type of cell is extremely effective in yielding large product yields for recombinant products in general, it is probably a mistake to attempt to keep this a secret. The chances for independent discovery by others are great and, should these independent discoverers decide to obtain a patent themselves, the holder of the trade secret might find it necessary to stop using the cell as a production host to avoid infringement of the patent.

In general, then, trade secret protection for subject matter which could otherwise be patented is possible only when commercialization of the product or process or service does not automatically reveal the trade secret and is most appropriate when the likelihood of independent discovery is vanishingly small. Otherwise the risk is run not only of losing trade secret protection, but also of being prevented from practicing what used to be the secret by a competing patent.

The Patent System

The patent system is established in the United States (and in other jurisdictions) by statute. In the United States, Title 35 of the U.S. Code provides a 17-year monopoly to the patentee during which the patentee may exclude others from making, using or selling the claimed subject matter in the United States. This is not a license to conduct the invention by the patentee; patentees may be prevented by patents held by others from practicing their own inventions. The monopoly is not extraterritorial, either. The only "long-arm" provision of the U.S. statute relates to process claims. Since 1988, it has been an act of infringement to import or sell a product made by a process protected by a U.S. patent claim. In addition, before 1988, and still today, it is possible to exclude from importation the product of a patented process, even though the process protected by U.S. patent has been conducted abroad.

The significance of this long-arm protection in the context of biotechnology is quite well known. The initial

attempts by Amgen to prevent importation using these "process" provisions of erythropoietin made with their patented DNA and cells was rebuffed. Since the claims in the Amgen patent had to do only with the materials for manufacture of erythropoietin, and not a process for its manufacture, they were considered not to be in a category that permitted the exclusion of the gene product.

The 17-year monopoly is considered a *quid pro quo* for full disclosure of the invention to the public. This disclosure is made through an application filed with the U.S. Patent and Trademark Office which is required to "contain a written description of the invention and of the manner and process of making and using it, in such full, clear, concise and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention." 35 USC 112, first paragraph.

Applications which fail to comply with this section of the statute cannot form the basis for the grant of a patent as defined by the claims included in the application. The claims have to be directed to a composition of matter, a process, a machine, or an article of manufacture. 35 USC 101. Of course, the subject matter does not have to be claimed in those terms. It is simply to be claimed in such a way that the claims particularly point out and distinctly claim the subject matter which the applicant regards as his invention. 35 USC 112, second paragraph. Claims of relevance in biotechnology can be directed

to proteins, DNA molecules, cells, mice, antibodies, methods of treatment, methods of recombinant production, oligosaccharides, oligonucleotides, and so forth. They can also be directed to assay devices, chromatographic columns, methods to conduct electrophoresis, panels of peptides, and methods of diagnosis. All of the foregoing are, if properly claimed, "statutory subject matter".

It might be noted that not all of these are statutory subject matter everywhere. Methods of treatment, for example, are unpatentable in most jurisdictions. It is an arbitrary statutory decision what will and will not be included.

The subject matter of successful claims must meet other criteria: specifically, the subject matter must be new, useful, and nonobvious. The novelty requirement is the least troublesome; the claimed subject matter simply must not have existed somewhere in the form in which it is claimed. In the context of biotechnology, the most obvious concern is the patentability of natural products, which, at first glance, appear to have preexisted. This is true only up to a point, and the precedent is well established that if these materials can be claimed in a manner which distinguishes them from their status as they occur in nature, there is no barrier to patentability. Early cases, prebiotech revolution, set the groundwork for this where prostaglandins and vitamin B_{12} were, when claimed as pure compounds, considered distinguishable from the gemishes in which they were originally found. Similarly, patents have now issued on DNA encoding erythropoietin, pure TPA, DNA encoding TPA, and

so forth. There is no longer any question that the existence of the essential features of the claimed subject matter in a natural state is not a barrier to patentability in properly constructed claims.

The Utility Requirement

35 USC 101 requires that claimed inventions be "useful". There doesn't seem to be any question that if, for example, a compound can be shown to kill weeds, or to reduce inflammation, or to cure an infection, it is useful to the general consuming public. It also seems clear that if a compound is useful as a laboratory reagent, for example as a dye to detect the presence of a protein on a chromatogram, it is useful to the research community. It is also clear that if a compound is "useful" only to find out what it is good for, that "utility" is not sufficient.

A related question relates to the level of proof required to demonstrate that the utility asserted for a claimed method or compound is in fact accurate. It is clear, in the context of applying for patent protection, that the burden is on the examiner to show that the asserted utility is not credible. In re Langer, 183 USPQ 288 (CCPA 1974); In re Marzocchi, 169 USPQ 367 (CCPA 1971). This burden is not particularly great, apparently, depending on what the asserted utility is and how the Patent Office chooses to treat it.

The putatively controlling case on questions of utility is Brenner v. Manson, 148 USPQ 689 (S. Ct. 1966). Manson, the

applicant, invented a process for making a steroid which was a homolog of another steroid that had tumor inhibiting effects in mice. Perhaps the Manson application itself did not assert any utility, but possibly in response to a rejection, applicant submitted an article in the Journal of Organic Chemistry describing the class of steroids to which the steroid prepared by the claimed process belonged. Some members of the class had antitumor activity. The Court held that this was an inadequate showing that the steroid that was the product of the claimed process, too, would have such an effect. Since the intended product could not be shown to be useful, the Court held the process that produced it wasn't useful either.

What the Court evidently wanted to do was to stem what it perceived as a tide toward requiring no statement or showing of utility at all. There was an earlier CCPA holding in In re Nelson, 126 USPQ 242 (CCPA 1960) where the court reversed a Patent Office rejection, for lack of utility, of a claim to steroid intermediates, where the steroids that would be produced from them had no disclosed utilities. In the decision below in the instant case, the CCPA had held that it was sufficient that a claimed process result in the intended product and that the product is not detrimental to the public interest for utility to be found (In re Manson, 142 USPQ 35 (CCPA 1964).

The discussion offered by the Court in Brenner v. Manson addresses policy considerations stating, finally, "Unless and until a process is refined and developed to this point -- where specific benefit exists in currently available form --

there is insufficient justification for permitting an applicant to engross (sic) what may prove to be a broad field."

Contemplation of this decision affirms that its implications are really quite unclear, beyond the simple statement that, "it is insufficient to meet the utility requirement to show that a claimed process successfully produces its intended product when there is no specified or known use for the intended product," the waters become murky. The case does not directly address the standard of evidence required for establishing the asserted utility. It does hold that in the context of its facts, extrapolation from homologous compounds is not enough. But it is totally silent as to whether *in vitro* or *in vivo* tests are needed to establish therapeutic utility of a steroid or other compounds. It does not address the question of whether adequate utility would have been found had the applicant asserted, for example, that the steroid was useful as a control standard in a diagnostic assay for steroids in general. Perhaps if Manson had not been misled by the trend in the CCPA away from requiring an assertion of utility, a utility could have been asserted in his application that would have passed muster.

It is the element of adequate proof of therapeutic utility that causes the most problems for applicants attempting to protect biotechnology inventions. It is not as if the applicant does not know what kind of therapeutic utility the invention will have. It is rather that the Patent Office often demands levels of proof that are too expensive or too time consuming for applicants to assemble prior to the application for

patent or even during the prosecution thereof. For example, in Ex parte Balzarini, 21 USPQ2d 1892 (BPAI 1992), the Board upheld a rejection of claims directed to a pharmaceutical composition asserted to be effective to treat retroviral diseases in an animal or patient. The specification only contained *in vitro* tests. The Board held that these tests were not adequate proof of *in vivo* efficacy.

This approach by the Patent Office appears quite common, especially in claims to compositions asserted to be effective as vaccines, as antivirals, as antitumor agents, and the like. It is not clear why this is so, since therapeutic protocols which fail to work are applied every day in every hospital in the country. The protocols are evidently considered useful although manifestly they do not work, certainly not in every case or even in a substantial number of cases. Nevertheless, the posture of the Patent Office has been consistently to question assertions of such therapeutic utility -- almost invariably, if the claims themselves are directed to methods of treatment and quite often if the therapeutic utility is the only use disclosed for a claimed composition of matter.

The dilemma faced by an applicant seeking to develop a new therapeutic compound is often resolved by disclosing, in addition to the real purpose for which the invention is intended, a "safe" utility that can be established without question. Such a "safe" utility might be that suggested for Manson's steroid above -- as a control in a quantitative assay for steroids in

general. A compound thought to be toxic to cancer cells might be useful in a screening method for cancer cell growth factors that overcome the effect of the toxin. A DNA molecule might be considered useful as a reagent to prime DNA synthesis in a controlled manner in the production of specifically binding DNA from mixtures. Sometimes construction of these "safe" utilities works. Sometimes the Patent Office won't buy it.

For example, in Ex parte Kranz, 19 USPQ2d 1216 (BPAI 1990) the Board itself issued a rejection based on lack of utility to claims that were directed to a process for making a targeted cell susceptible to lysis by a cytotoxic T-lymphocyte. The claim itself did not require *in vivo* application of the technique; the claims were worded so as to cover laboratory procedures. But the Board said that the appellant's specification and brief "clearly indicate that the claimed process has as its practical objective a use *in vivo* specifically against cancer cells as the targets." So the Board issued a rejection, based on asserted inadequate proof of efficacy, of a method that was not even being claimed!

The question of patentable utility has been raised repeatedly in connection with the multiplicity of DNA sequences called expression sequence tags (ESTs) now sought to be patented by the National Institutes of Health. Most of the ESTs are not associated with genes encoding proteins whose functions are known. Various utilities have been asserted including the use of the ESTs for chromosome mapping and as probes to retrieve genes which purportedly encode proteins that have some function since

the genes are expressed in real tissues. The issue in this context is still unresolved.

I am aware of no recent Federal Circuit decisions relating to the standard of proof for therapeutic utility; the Board of Patent Appeals and Interferences has fairly consistently upheld rejections where the examiner has asserted insufficient evidence to support a stated utility. See, Ex parte Busse, 1 USPQ2d 1908 (BPAI 1986); Ex parte Rubin, 5 USPQ2d 1461 (BPAI 1987); Ex parte Maas, 9 USPQ2d 1746 (BPAI 1987); Ex parte Stevens, 16 USPQ2d 1379 (BPAI 1990) and Ex parte Sudilovsky, 21 USPQ2d 1702 (BPAI 1992). The only case in the foregoing which reversed a utility rejection was Ex parte Rubin where claims were to a method for improving the effectiveness of interferon in the treatment of neoplastic conditions by administering an agent for inhibiting tyrosinase. The application provided *in vitro* tests which showed that tyrosinase denatured interferon, a known antitumor agent. The Board here held that the utility described was not inherently incredible and that factual evidence was required if the claims were to be rejected on this basis.

Shop Right

The shop right issue arises in the patent context, but has nothing to do with the nature of the protection afforded or the nature of the subject matter that can be protected or its criteria for protectability. It has to do with what does and does not constitute infringement of an issued patent -- whether

or not certain entities may or may not be among those excluded from making, using and selling the claimed invention.

The issue arises in the context of the employed inventor when the employer fails to acquire ownership of the invented subject matter. It probably does not arise with great frequency in the context of the biotechnology industry since virtually all companies are aware of the necessity to obtain an employment agreement with their employees that requires assignment of any inventions made in the course of employment to the employer. Various states may have statutory provisions which limit the scope of circumstances in which such assignment can be required, but none prevents requiring assignment where the invention was clearly made under the financial sponsorship of the employer. It is standard practice to require such agreements as a condition of employment and I am not aware of any company with any kind of financing that does not require assignment to itself of inventions made in the course of employment. If the employer winds up owning the invention the issue of shop right does not arise.

In the United States, unlike other jurisdictions, the inventors must be the applicants for patent protection. This requires that the inventors themselves sign the oath swearing that they are the original and first inventors of the claimed invention and that they have reviewed the application to be submitted and understand it. This does not prevent their assigning all their rights in the invention to their employer or anyone else who from then on can control the prosecution of the

application to the exclusion of the inventors. The assignee cannot only control prosecution, but can further assign the invention to anyone and can disclaim all or a portion of it. Once the inventors have assigned the invention, their control over it is lost.

Even absent an executed agreement that inventions made by employees will be assigned to the employer, there may be an implied obligation to do so if the inventor was actually hired to invent. This is a judicially created rule, and it appears to be most clearly applicable when the employee was employed to invent specifically what he did indeed invent. Standard Parts Company v. Peck, 264 U.S. 52 (1924). This decision has been followed by a multiplicity of lower federal courts. It is less certain that the employer is entitled to assignment if the employee is simply generically hired to do research. De Jur-Amsco Corp. v. Fogle, 109 USPQ 263 (3d Cir. 1956). A number of factors can be listed affecting the decision. In any event, should it be held that the employer is entitled to assignment based on the "employed to invent" principle, the issue of shop right doesn't arise either.

The issue of shop right arises only when the employee retains the ownership of the patent to the invention which is made, at least at some level, at the expense of the employer. Under those circumstances, the employer is considered to have a shop right in the invention -- i.e. a nonexclusive, royalty-free nontransferable license to make and use the invention without infringing the patent. The meanings of nonexclusive, nontransferable and royalty-free are fairly clear; however, the

total scope of this license is not. Clearly it extends to conducting business as usual by the employer; however, whether it will extend to business successors or expansion of the original business scope is unclear.

International Aspects

This is global economy, but patents are territorial. They do not provide exclusivity for their holders beyond the borders of the jurisdiction in which the patent is issued. The sole exception to this is the process provisions mentioned above. Jurisdictions other than the United States have had this general principle in force for some time since it has long been considered in most of them that the product of a protected process is also covered by the claims. Thus, a product made by a process patented in France would infringe that patent even if the process were conducted in the United States and the product merely imported into France.

Although it is recognized that much time and money could be saved with a uniform patent system at least covering the industrialized countries, a harmonization of existing patent systems appears to be proving difficult, not to mention providing an independent mechanism for an international patent. European nations have made a first step in the form of the European Patent Convention which went into force in 1978 and which provides a common examination and granting procedure for its 14 member countries. However, the grant of a European patent results only in a "bundle" of national patents which must be enforced on a

country-by-country basis. The members of the convention intended to provide an alternative of a "community patent" in the last year but failed to implement this.

An additional step has been the implementation of a Patent Cooperation Treaty that provides for a common application to be filed applicable to all member countries (which include most of the jurisdictions important to biotechnology applicants). However, the examination procedure conducted in connection with this international application is nonbinding on jurisdictions in which the corresponding patent is eventually filed.

A major hurdle in any of these attempts at internationalization has been the refusal of the United States to conform its patent system with that of almost all other jurisdictions in several important aspects. First, in the United States, the patent is awarded to the first inventor to invent the claimed subject matter; everywhere else except the Philippines it is awarded to the first inventor to file an application for the claimed subject matter. It should be noted that in no jurisdiction is a noninventor entitled to a patent. Copying someone else's invention and filing the copied subject matter in the Patent Office is nowhere countenanced. Second, the patent term in the United States runs from the date of issue; everywhere else it runs from the date of filing. This has the effect of permitting the applicant for patent to time the period of the monopoly awarded at the patentee's convenience. Third, the United States keeps applications in confidence until the patent issues; everywhere else, applications are published 18 months

from the initial priority filing date. This last distinction is perhaps unimportant since participants in the global economy file elsewhere anyway and thus realize that their applications will be published regardless of what the United States does.

Significance of Patent Protection

Although the property protected is perhaps intangible, patent protection is considered an asset of the patent holder. Quite often, the patent assets are the only assets of a young company grounded in a high technology endeavor and requiring a large dose of R&D expenditure prior to marketing any product at all. Therefore, obtaining an appropriate patent portfolio is an important instrument in attracting investment and assuring investors that when products and services are finally marketed, exclusivity will be assured to the company.

OVERVIEW OF FEDERAL TECHNOLOGY TRANSFER

Mr. Lawrence Rudolph*

Any opinions, findings, and conclusions or recommendations expressed in this material are those of the author(s) and do not necessarily reflect the views of the National Science Foundation.

Federal technology transfer can be understood, if at all, only as the temporary product of a number of often conflicting forces. It is not pretty. It is not smart. But it is there and must be considered.

First, I should explain that this issue has two components — Government Patent Policy, which might be described as the "input" side since it controls the Federal agencies' acquisition of rights to inventions, and technology-transfer policies and authorities, which form the "output" side. Some of the problems with Federal technology transfer stem from the fact that contradictory policies have been adopted for these two sides.

What I will do here is give you a rough idea of current policies and procedures by taking you through a brief review of what has been done over the past 13 years through statutes, pronouncements, and executive orders that have spoken to both Government Patent Policy and the transfer of federally-owned technology. Then I will briefly note what some agencies are doing in this area now.

Enacted by a "lame duck" Congress and President in December 1980, the Bayh-Dole Act,[1] **[Slide 1]** required agencies to adopt what was then referred to as a "title in contractor" policy for small business and nonprofit organizations, such as universities. What this meant was simply that small businesses and nonprofits were given a statutory right to chose to retain title to inventions made during federally-assisted research and development so long as they were interested in patenting and attempting to commercialize those inventions. This policy was based on a belief, supported by evidence gathered by a Federal interagency committee,[2] that private entities, given the incentives of the patent system, would do a better job of commercializing inventions than Federal agencies.

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1 Chapter 18 of title 35 of the U.S. Code, sometimes called P.L. 96-517.

2 Committee on Government Patent Policy of the Federal Council on Science and Technology, which was established to fulfill an annual reporting requirement in the 1971 Presidential Memorandum on Government Patent Policy, discussed later.

In reality, long before Senators Bayh and Dole introduced the first version of their bill in the 95th Congress, many agencies already allowed contractors to retain patent rights to their inventions. For example, the Department of Defense followed a "title in contractor" policy since World War II. The National Institutes of Health and the National Science Foundation also effectively had that policy through Institutional Patent Agreements and post-invention waivers of rights, which were known as "deferred determinations."

Other agencies, such as the Department of Agriculture, the National Aeronautics and Space Administration, and the Department of Energy, however, had long-established policies, sometimes required by statute, of normally claiming ownership to inventions made with their support — so-called "title in the Government" policies. These agencies licensed these inventions either on a non-exclusive, royalty-free basis, which of course was equivalent to dedicating them to the public, or with some exclusivity and royalties.

You can see that, despite a Presidential Memorandum on Government Patent Policy issued by President Kennedy in 1963 and revised by President Nixon in 1971, there was no uniform Government-wide treatment of inventions. Although as noted previously a consensus in favor of leaving rights with inventing organizations slowly developed, agencies went their separate ways under those Memoranda. In fact, the Bayh-Dole Act was reportedly prompted by concern in the academic research community that Joseph Califano, the Carter Administration's first Secretary of Health, Education, and Welfare, would change NIH's "title in the contractor" policy.

The Bayh-Dole Act for the first time established a largely uniform Government-wide policy on treatment of inventions made during federally-supported research and development. Not totally uniform, however, since limited flexibly was provided. For example, agencies could continue to exclude from coverage of the Bayh-Dole Act operating contracts for federally-owned laboratories — so-called government-owned, contractor-operated, or GOCO, facilities. Also, agencies were empowered, but not required, to leave invention rights with inventors when awardees did not want them and different agencies adopted different practices on that.

A little-remembered part of the Bayh-Dole Act is its endorsement of the 1971 Presidential Memorandum on Government Patent Policy and authorization of past and future dispositions of invention rights under it.[3] This was felt necessary by some in order to provide a statutory basis for disposition of Government property -- patent rights.

Although the "title in the contractor" policy of Bayh-Dole was already that of the National Science Foundation and we have, in fact, done everything we can to allow our contractors and grantees to retain principal legal rights and the attendant incentives for commercialization, I must note that not everyone is happy with the Act's policy and effects. Some Members of Congress still believe that things produced with public funds should be "dedicated to the public" — that is,

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3 Section 210(c) of title 35 of the United States Code. This section was amended n 1984 to refer to the 1984 Memorandum, discussed below.

made available to everyone with no exclusive rights — and that no one should profit as a result of Government funding. They fear the situation where "The Government pays the cost of digging the mine, the contractor gets the gold, and the taxpayer gets the shaft!". This raises some interesting questions. Should no one profit from a federally-supported activity? Should there be just a little profit? Or, in the words of one bureaucrat, "Do you want us to fund only losers?". A few academics are also unhappy with the Act because it explicitly encourages universities to commercialize inventions, thereby focusing on profit rather than knowledge. Some have wondered if the academy sold it birthright for a mess of patents. Those most happy with the Act, of course, are those who conceived and promoted it — largely university and Government intellectual property specialists.

Not long after the Bayh-Dole Act was enacted, President Reagan issued a "Government Patent Policy" memorandum on February 18th, 1983 **[Slide 2]**. This was done principally because the Administration was unsuccessful in persuading Congress to expand the coverage of the Bayh-Dole Act. This Presidential Memorandum directed agencies that were not prevented by statute to treat all contractors, not just small businesses and nonprofits, in accordance with the Bayh-Dole Act. In essence, this measure functionally expanded the Bayh-Dole Act to all sizes of contractors as well as to individuals.

The next step in the chronology was the Bayh-Dole Act Amendments of 1984,[4] **[Slide 3]** which limited the agencies' ability to exclude from the Act's coverage contracts with universities to operate federal laboratories. In other words, nonprofit GOCOs would now get the same type of coverage that the Bayh-Dole Act originally provided. These amendments also made the Department of Commerce the lead agency in patent matters for the U.S. Government.

As lead agency, Commerce promulgated guidelines,[5] **[Slide 4]** which all agencies must observe, on administering rights to inventions made during federally-supported R&D, including a standard clause which I am sure many of you have seen. Although these guidelines are mandatory only for awards to small businesses and nonprofit organizations, agencies, such as mine, that are not subject to any conflicting statute can apply them to all awardees as directed by the Presidential Memorandum.

Staying on the input side but shifting gears slightly, the rules governing inventions made by Federal employees, in contrast to those governing contractors' and grantees' inventions, have been both uniform and stable. President Truman's 1950 Executive Order,[6] **[Slide 5]** which presumes that agencies normally will take title to inventions made by their employees as parts of

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4 98 Stat. 3335, 3364-68; title V of P.L. 98-620.

5 Part 401 of title 37 of the Code of Federal Regulations.

6 Executive Order 10096, as amended (3 CFR 1949-1953 Comp.), and implementing regulations of the Department of Commerce published as Parts 101 and 501 of title 37 of the Code of Federal Regulations.

their jobs, still governs. The only significant change here was made in 1986, when section 15 of the Federal Technology Transfer Act of 1986 directed agencies to allow their employees to patent inventions when the agencies do not intend to do so.[7]

Now let us move to the output side and once again start with the Bayh-Dole Act. **[Slide 6]** Few persons outside the Federal Government, and not many within it, realize that three sections of that law established rules for protection and licensing Federally-owned inventions.[8] As the 1984 amendments to the Bayh-Dole Act did for extramural inventions, these provisions removed all doubt as to the constitutionality of agencies patenting and exclusively licensing inventions.

Backing up a little bit, two months before the Bayh-Dole Act was passed, Congress enacted the Stevenson-Wydler Technology Transfer Act of 1980.[9] **[Slide 7]** This is the basic Federal technology transfer law.

A principal policy established by Stevenson-Wydler is that agencies should ensure the full use of the results of the nation's Federal investment in research and development. Another is that the Government should strive, wherever appropriate, to transfer federally-owned or -originated technology to both state and local governments and to the private sector. Some have questioned whether those policies are consistent with the "title in the contractor" policy of Bayh-Dole, which removes from agency control intellectual property rights that would be useful in transferring and promoting federally-owned or -originated technology. Others wonder whether adding technology transfer as another mission of every Federal agency was wise, since doing so inherently detracts from an agency's ability to focus on more important roles. Of course, once again those who conceived and promoted the Act — this time Government intellectual property specialists combined with Federal laboratory administrators — were happy with the importance it assigned their roles.

On a more practical note, Stevenson-Wydler also required agencies to establish Offices of Research and Technology Applications (ORTAs) at their federal laboratories, and to devote a percentage of their R&D budgets to technology transfer. Another aspect of this Act was establishment of a Center for the Utilization of Federal Technology, which, in turn, coordinates ORTAs. This center was established within the Department of Commerce. Subsequently (in 1986) that role was reassigned to what is now known as the National Institute of Standards and Technology.

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7 Section 15 of the Federal Technology Transfer Act of 1986, 15 U.S.C. 3710d.

8 Section 207 through 209 of title 35 of the U.S. Code, implemented by the Department of Commerce regulation published as part 404 of title 37 of the Code of Federal Regulations.

9 Sections 3701 through 3714 of title 15 of the U.S. Code.

OVERVIEW OF FEDERAL TECHNOLOGY TRANSFER

And so we come, in 1986, to the Federal Technology Transfer Act. **[Slide 8]** This Act amended the Stevenson-Wydler Act and affects only federally-owned laboratories — not GOCOs, which, you will recall, are Government-owned, contractor-operated facilities, but GOGOs, that is Government-owned, Government-operated labs.

Having supplied you with two widely-used acronyms for federally-owned laboratories, I would be derelict if I did not supply you another — FFRDC or Federally-Funded Research and Development Center. That is a term my agency coined to cover facilities that derive most of their funding from the Federal Government no matter who owns or operates them.

The most important feature of the Federal Technology Transfer Act was its authorization of Cooperative Research and Development Agreements — or CRADAs — between federal labs and non-federal entities.[10] It also authorized award programs for federal employees who were responsible for inventions and required royalty sharing with employee-inventors whenever the agency retains ownership of their inventions. Finally, as noted earlier, the Tech Transfer Act directs agencies to allow their employees to patent their inventions when the agencies themselves do not patent or otherwise promote commercialization.

To implement the Federal Tech Transfer Act, the President issued Executive Order 12591, "Facilitating Access to Federal Technology" in April 1987.[11] **[Slide 9]** This directed Federal agencies to encourage and facilitate cooperative research and technology transfer through their laboratories. The Order required that technology access and intellectual property protection be considered in any negotiation of an R&D agreement with foreign individuals or governments. The last is an important tool of this country's efforts to persuade other nations to provide — in law and in practice — effective protection for intellectual property and to allow American scientists and engineering entry into their laboratories.

The National Competitiveness Technology Transfer Act of 1989[12] **[Slide 10]** amended the section governing CRADAs to authorize the Department of Energy's GOCO labs to enter into CRADAs on the same basis as its government-operated, government-owned laboratories. As an aside, this statute also created an exemption from the Freedom of Information Act for certain categories of information developed during cooperative research, permitting Federal labs to withhold such information from disclosure for a specified period.

Other laws — such as the American Technology Preeminence Act of 1991[13] — made minor amendments to the Stevenson-Wydler Act, including extending it to Legislative Branch agencies and modifying required CRADA terms.

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10 15 U.S.C. 3710a.

11 E.O. 12591, 3 CFR 1987 Comp., p. 220, as amended.

12 103 Stat. 1674, November 29, 1989, P.L. 101-189.

13 106 Stat. 7; February 14, 1992, P.L. 102-245.

OVERVIEW OF FEDERAL TECHNOLOGY TRANSFER

Congress is constantly tinkering with the laws governing technology transfer. **[Slide 11]** In the last Congress, eighty bill were introduced that referenced or amended the Stevenson-Wydler Act, among two hundred and forty-three measures introduced that somehow affected technology transfer. Thus far, one-fourth of the way through the current Congress, twenty-one bills amending or mentioning Stevenson-Wydler are among the fifty-four ones introduced that concern technology transfer. What this tells us and should tell the public as well is that the use of federally-owned technology to promote economic competitiveness and growth is certainly very popular, both in Congress and with this Administration as well.

Three pending bills are worth noting.

H.R. 820, containing the "National Competitiveness Act of 1993", "Manufacturing Technology and Extension Act of 1993"; and "Civilian Technology Development Act of 1993", was introduced by Rep. Tim Valentine (D-NC) on Thursday, February 4, 1993 and was passed by the House of Representatives on May 19, 1993, by a 243-167 vote. It is a package of proposals that seeks to boost America's international competitiveness by strengthening our technology base and fostering the development of advanced products, particularly in manufacturing. Among other things, it would establish a National Technology Outreach Program to assist manufacturers and research centers in upgrading their technology base by facilitating the sharing of new technology and expertise through an interactive information and communications system. It would direct my agency to set up new engineering centers dedicated to manufacturing research and development, establish an Advanced Manufacturing Technology Development Program within the Department of Commerce to promote the development and application of advanced manufacturing technologies and processes, expand Commerce's Advanced Technology Program to provide greater support for pre-commercial research and development of generic technologies, strengthen the National Institute of Standards and Technology's technology transfer program, and establish a program to coordinate the collection of information on foreign science and technology, 'benchmark' foreign research and development capabilities against those in the United States, and disseminate this information to U.S. industry. Since the Senate has passed a similar measure and President Clinton has indicated his support, H.R. 820 is likely to be enacted soon.

Of particular interest to one of our hosts is H.R. 1432, the "Department of Energy Laboratory Technology Act of 1993". It would establish missions for the Department of Energy research and development laboratories, provide for the review of laboratory effectiveness in realizing such missions, and reorganize and consolidate DOE technology-transfer activities. According to its sponsor, Rep. George Brown (D-CA), this bill has four key objectives: providing an updated and focused set of missions for the laboratories; improving the organization of DOE's research, development, and technology transfer functions; enhancing collaboration between the DOE laboratories and industry by streamlining the technology-transfer process; and ensuring that the activities of the DOE laboratories, and all Federal laboratories, are regularly evaluated and, so far as possible, coordinated. The Department is supporting this bill, which seems likely to be enacted in this session of Congress.

Also worth mentioning, although its prospects for enactment are dim, is H.R. 523, the "Technology Transfer Improvements Act of 1993", introduced by Rep. Constance A. Morella (R-MD) on Thursday, January 21, 1993. It would amend the Stevenson-Wydler Technology Innovation Act of 1980 to enhance technology transfer for works prepared under certain cooperative research and development agreements by allowing Federal agencies to claim copyright in any computer software prepared in whole or in part by employees of the United States Government in the course of work under a Cooperative Research and Development Agreement. This would be the first time that copyright in a "work of the United States Government" was allowed under American copyright law.

I would like to turn now to agency tech transfer activity itself. Technology transfer efforts for federal laboratories are, as I mentioned before, prescribed and detailed at some length by the Stevenson-Wydler Act. The Act requires Office of Research and Technology Applications to be created at each GOCO and at each GOGO over a certain size.

Also all Federal agencies are "taxed" to support the Federal Laboratory Consortium. That is an interagency group which acts as a clearinghouse and helps to discuss tech transfer issues that get raised between government agencies, as well as the terms of CRADAs.

Tech transfer activities themselves vary greatly from agency to agency, depending on missions and capabilities. The National Science Foundation, is barred from operating any laboratory itself. Its mission, moreover, is to promote research capability and education, not to further any particular area of technology. As a consequence, NSF has no in-house scientific research or tech transfer efforts at all.

The Department of Agriculture, on the other hand, has a long history of developing farm-related technology and disseminating it to farmers. The Agricultural Research Service and the Forest Service have entered into hundreds of CRADAs since the Federal Technology Transfer Act became law.

The Department of Commerce has Offices of Research and Technology Applications in all its laboratories and has entered into CRADAs with private industry for research in several areas. Commerce's National Institutes of Standards and Technology, regional Centers for the Transfer of Manufacturing Technology, and, of course, its Advanced Technology Program all participate.

After years of congressional prodding, the generous sponsor of this conference — the Department of Energy — is paying more and more attention to technology transfer. Each DOE laboratory has a Technology Transfer Office that actively promotes inventions and ideas. As we all know from media reports, DOE's labs are working overtime to avoid extinction as part of the "peace dividend", since there are few if any private sector jobs for which "made atomic bombs" is a valuable resume item. The Cable News Network reported late last month that DOE labs have entered into over three hundred CRADAs in their attempts to convert sword-makers into plowshare manufacturers. To put things into perspective, however, the research funding involved in those three hundred agreements amounted to only three percent of the labs' budgets.

The National Institutes of Health's Office of Technology Transfer promotes and licenses technology developed at all of its GOCO labs. The Public Health Service makes extensive use of the CRADA authority, but not without some controversy. A recent *Washington Post* article on a DC-area biotech firm that was among the first companies to enter into a CRADA with NIH noted that such partnerships have been criticized because participating firms may gain what some consider an unfair competitive advantage from Government-funded research.[14] The article also reported that CRADAs are not without headaches for the private sector; since participating firms have less influence than they might want over the direction of research and must accept complex rules about conflicts of interest and proprietary control over the knowledge gained by such research.

Finally, I would like to mention that the Department of State, which supports no scientific research itself, so has no technology of its own to transfer, but nevertheless is actively involved in encouraging both scientific and technological cooperation between the United States and foreign agencies, foreign universities, and firms. That is done through agreements that they negotiate in the science and technology area, using the carrot of technology agreements with Federal agencies and laboratories as well as the well-publicized stick of trade sanctions.

That concludes our brief history of Government Patent Policy and technology-transfer legislation and quick summary of some agencies' technology-transfer activities.

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14 "Genetic Therapy's New Hire Seeks Market for Biotech Products??", *Washington Post*, "Washington Business" section, Monday, June 28, 1993, page 11.

Government Patent Background

BAYH-DOLE ACT

Chapter 18 of title 35 of the United States Code (P.L. 96-517) December 1980

- **Applies to small businesses and non-profit institutions (notably universities**
- **Establishes right to keep title to inventions made during federally-funded R&D**

Government Patent Background

Presidential Memorandum

Entitled "Government Patent Policy"

February 18, 1983

Direct agencies to apply the policy of Bayh-Dole Act to all awardees, to the extent permitted by applicable statutes

Government Patent Background

Bayh-Dole Act Amendment

P.L. 98-620

November 1984

Extended coverage to university-operated Government-owned-contractor-operated laboratories

Made Department of Commerce lead agency.

Government Patent Background

Department of Commerce Guidance

Part 401 of title 37 of the
Code of Federal Regulations
March 1987

- Prescribes standard award provision
- Provides guidance for administering rights to inventions

Government Patent Background

Employee Inventions

- Executive Order 10096, "Providing for a Uniform Patent Policy for the Government with respect to inventions made by Government Employees and or the administration of such policy", 3 CFR 1949-1953 Comp., p292, as amended.
- Department of Commerce regulation "Uniform Patent Policy for domestic rights in inventions made by Government employees", 37 CFR Part 501.
- Department of Commerce regulation "Acquisition and protection of foreign rights and inventions", 37 CFR Part 101.

Government Patent Background

Bayh-Dole Act

Licensing Provisions

Section 202-209 of title 35 of the United States Code (P.L. 96-517) December 1980

- **Authorizes agencies to grant exclusive or partically-exclusive licenses after notice in the *Federal Register***
- **Implemented by Department of Commerce regulation "Licensing of Government owned inventions", 37 CFR Part 404.**

Federal Technology Transfer Laws

Federal Technology Transfer Laws

Stevenson-Wydler Technology Transfer Act

Sections 3701 through 3714 of title 15 of the United States Code

December 1980

- Federal Government to ensure full use of the results of the Nation's Federal investment in research and development.
- ORTAs -- Office of Research and Technology Applications -- established at each Federal laboratory.
- Budget "set-aside" for technology transfer mandated.
- Center for the Utilization of Federal Technology established.

Federal Technology Transfer Laws

Federal Technology Transfer Act

October 1986

- Government-owned, Government operated ("GOGO") laboratories allowed to negotiate Cooperative Research and Development Agreements ("CRADAs") with businesses.
- Royalty-sharing with Federal employee-inventors required.

rights is likely to impede commercial development of clinically useful products and processes related to Venter's discoveries.

Possible Scope of Patent Protection

NIH's ability to license the Venter technology depends, in large measure, on the scope of the claims, if any, that are eventually allowed by the Patent Office. In its initial response to the Venter applications, the Patent Office reportedly(24) rejected the NIH claims because they did not satisfy the three fundamental requirements for patentability -- novelty, utility and non-obviousness.(25) The NIH was expected to file a response to the initial Patent Office rejection by February, and a final decision of the Patent Office would then be expected in late 1993 or early 1994.

Because Venter's partial cDNA sequences do nothing to elucidate the biological activity of the genes, the issue of patentable utility with respect to the Venter disclosure has drawn considerable attention from commentators.(26) NIH argues that the Venter invention has patentable utility

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(24) See, Leslie Roberts, "Rumors Fly Over Rejection of NIH Claim," 257 Science 1855 (September 25, 1992).

(25) See, 35 U.S.C. §§ 101, 102 and 103.

(26) See, e.g., Thomas D. Kiley, "Patents on Random Complementary DNA Fragments?," 257 Science 915 (August 14, 1992).

because the disclosed partial cDNA sequences can be used: 1) as polymerase chain reaction (PCR) primers; 2) to isolate the coding sequence of cDNAs; 3) to isolate complete genes; 4) to determine the position of genes on the human chromosome; 5) to produce antisense oligonucleotides and triple helix probes; and 6) in forensic applications.(27)

While the utility requirement is typically considered a low hurdle to patentability,(28) the United States Supreme Court has held that the utility requirement is not satisfied if an invention is useful only in research.(29) If, therefore, the Patent Office believes that Venter's sequences are useful merely as a means for making discoveries, the claims may be rejected for lack of utility.(30) Moreover, the Patent Office has, on occasion, applied unusually stringent utility standards to promote what it considers to be public policy objectives.(31)

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(27) Patent application of Craig Venter, "Sequences Characteristic of Human Gene Transcription Product." A partially redacted version of this patent application is publicly available through the NIH Office of Technology Transfer.

(28) See, e.g., Stiftung v. Renishaw PLC, 945 F.2d 1173 (Fed. Cir. 1991); Envirotech Corp. v. Al George, Inc., 730 F.2d 753 (Fed. Cir. 1984).

(29) Brenner v. Manson, 383 U.S. 519 (1966).

(30) Id. at 383 U.S. 536, "But a patent is not a hunting license. It is not a reward for the search, but a compensation for its successful conclusion."

(31) The Patent Office has recently adopted an informal
(continued...)

Considering the high-profile and controversial nature of the present case, the Patent Office may again be inclined to apply stringently the utility standard.

As noted above, the claims of both Venter patent applications encompass much more than the disclosed ESTs. The specifications of the Venter applications describe, in detail, procedures for identifying and sequencing the ESTs, procedures for identifying the sequence of a gene using an EST as a starting point, and procedures for accomplishing gene expression. The Venter disclosure, however, does not identify the full length sequence of previously unknown genes, identify the polypeptides coded by those genes, or teach the biological activity of those genes or polypeptides. As such, there is considerable doubt that Venter will be entitled to claims directed to full length genes or polypeptides coded by those genes.(32) Indeed, recent case law suggests that, even assuming the novelty, utility and nonobviousness standards are satisfied, Venter would not be entitled to claims that extend much beyond the

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(31)(...continued)
"policy" under which claims directed to treatment of HIV infection are rejected for lack of utility where the claimed effectiveness is supported only by in vitro data. See, e.g., In re Balzarini, 21 USPQ2d 1892 (B.P.A.I. 1991); A similar "policy" relating to anti-cancer compounds in the 1970s was brought to an end by In re Jolles, 628 F.2d 1322 (C.C.P.A. 1980).

(32) See, e.g., Rebecca S. Eisenberg, "Genes, Patents, and Product Development," 257 Science 903 (August 14, 1992).

specifically disclosed ESTs.(33) Thus, it appears that even if NIH can prevail on the issue of utility, the scope of the claims that may be allowed are likely to be substantially narrower than the claims filed in Venter's applications.

Possible Licensing Consequences

Federal patent laws in effect since 1980 have permitted and encouraged licensing of government owned patent rights.(34) Under the FTTA, federal laboratories can agree to grant intellectual property rights in advance to collaborators who are party to a CRADA.(35) The NIH technology transfer policy relies heavily on the patent system, and in its general licensing policy, NIH states that, "Congress and the President have chosen to utilize the patent system as the primary mechanism for transferring Government inventions to the private sector."(36) Indeed, NIH officials have suggested that patent protection for the cDNA sequences is necessary to induce potential licensees to commit the time and financial resources to develop

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(33) See, e.g., Fiers v. Revel, 984 F.2d 1164 (Fed.Cir. 1993); see also Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed.Cir. 1991)

(34) See, Government Patent Policy Act of 1980, P.L. 96-517, 94 Stat. 3015 (codified at 35 U.S.C. § 200-212 (1990)).

(35) See, supra, note 4 at 307, 309.

(36) See, supra, note 4 at 309.

commercially viable products derived from the NIH's cDNA discoveries.(37)

Federal statutes directed to technology licensing balance the need for exclusivity to induce commercial development against the possible adverse consequences of an unnecessary monopoly. Consequently, NIH licensing policies, in most circumstances, favor non-exclusive licenses over exclusive licenses.(38) However, consistent with a fundamental principle of the patent system(39), NIH is willing to "grant exclusive commercialization licenses under their patent or other intellectual property rights in cases where substantial additional risks, time and costs must be undertaken by a licensee prior to commercialization."(40)

Federal law, however, permits a federal agency to license its inventions on an exclusive basis only if it is determined that: 1) the public interest is served by the

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(37) Testimony of Dr. Bernadine Healy before the Senate Judiciary Subcommittee on Patents, Trademarks and Copyrights, September 22, 1992.

(38) See, supra, note 4 at p. 310.

(39) See Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861 (Fed. Cir. 1985), "The patent system, which is rooted in the United States Constitution serves a very positive function in our system of competition, i.e., 'the encouragement of investment based risk.'" (citations omitted); U.S. Const. Art 1. Sec. 8, Cl. 8: "The Congress shall have power ... to promote the progress of science and useful arts, by securing for limited times to authors and inventors exclusive right to their respective writings and discoveries."

(40) See, supra, note 4.

exclusive license in light of the prospective licensee's plans and ability to promote the public's utilization of the invention; 2) the practical development of the invention has not or is not likely to be expeditiously achieved under a non-exclusive license; 3) the exclusive license is required to attract capital and stimulate interest needed to develop the invention; and 4) the proposed scope of the exclusive license is not broader than is necessary to accomplish development of the invention.(41) Moreover, NIH reserves the right to revoke an exclusive license if the licensee fails to make reasonable progress in developing the invention or if the licensee cannot satisfy unmet public health needs.(42)

Attempts by NIH to license any patent that may issue from the Venter applications will be problematic. As discussed above, the claims of such a patent are likely to be narrow. One commentator has suggested that claims limited to the specifically disclosed ESTs and their equivalents may not be "broad enough to offer effective protection to firms seeking to bring related products to market...."(43) The private sector, therefore, may not be interested in licensing the Venter technology, either

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(41) 35 U.S.C. § 209(c)(1); see also 37 C.F.R. § 404.7.

(42) See, supra, note 4 at 311.

(43) See, supra, note 32.

exclusively or non-exclusively. As such, the NIH patent protection will do nothing to advance the development of commercial products or processes and may indeed hinder such developments by contributing to the "thicket of patent rights that firms must negotiate their way past before they can get products on the market."(44)

On the other hand, if NIH is somehow entitled to broader patent coverage (or if private sector participants are nonetheless interested in licensing a narrow NIH patent), then NIH must determine whether an exclusive or non-exclusive license is appropriate. Because the vast majority of the 2,700 genes corresponding to Venter's EST's are not likely to be immediately significant for clinical applications, the Venter patent applications clearly present a situation where substantial (and risky) expenditures of time and money are necessary before any commercially viable product may be marketed. Therefore, potential licensees may not be inclined to expend resources without an exclusive license.

As discussed above, the technology disclosed and claimed in the Venter applications is not well developed and encompasses vast subject matter -- Venter's claims may

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(44) Id. at 904. See also, Leslie Roberts, "Scientists Voice Their Opposition," 256 Science 1273 (May 29, 1992). Michael Roth, a patent attorney at Pioneer Hybrid comments that the NIH patent approach "does not build a road to further advances, it just builds a toll booth along the way."

theoretically "read on" approximately 5% of all expressed human genes. An exclusive license to use Venter's EST's would, therefore, provide an extreme disincentive for non-licensees to investigate the biological significance of the 2,700 expressed genes and polypeptides corresponding to Venter's partial cDNA sequences. Such a disincentive may result in a "meta-monopoly" whereby a single entity would acquire de facto dominion over the eventual identification of 2,700 genes, their gene products and methods of exploiting their biological activity. Such a meta-monopoly may run afoul of the patent licensing laws(45) and would do nothing to promote development of useful products.(46) Exclusivity over Venter's discoveries may bring about a result decried by the Supreme Court in Brenner v. Manson:

> Such a patent may confer power to block off whole areas of scientific development, without compensating development to the public. The basic guid pro guo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is developed to this point--where specific benefit exists in currently available form--there is insufficient justification for

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(45) 35 U.S.C. § 209

(46) Craig Venter himself states that "The patent system wasn't designed to give me and a small group of people ownership of half the genome." See, supra, Roberts at note 44.

> permitting an applicant to engross what may prove to be a broad field.(47)

Thus, either exclusive or non-exclusive licensing schemes for any patents issuing from the NIH applications may stand in the way of ultimately developing clinically useful products related to Venter's ESTs. NIH should, therefore, seriously consider dedicating the Venter technology to the public as a means to ensure widespread access to that technology and to best eliminate impediments to the ultimate development of clinically significant products.

Conclusion

The NIH decision to seek patent protection for Dr. Venter's substantially undeveloped discoveries demonstrates that NIH's technology transfer activities are driven by the commercial objectives of its private sector collaborators. Merger of NIH and private sector objectives is an inevitable consequence of the NIH's implementation of the FTTA. Such a merger threatens to shift the focus of NIH research, compromise the objectivity of that research and, in certain circumstances, impede the ultimate introduction of products ultimately developed from NIH research. Therefore, NIH policies such as the cDNA patent decision

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(47) See, supra, note 29 at 534-535.

that overzealously promote private commercial interests should be reconsidered.

This author believes that the progress of science and the interests of the public are best served by maintaining NIH as an objective research institution rather than a vehicle for advancing the commercial interests of private biomedical research concerns. The biotechnology industry does not need NIH to protect its commercial interests -- those interests are adequately protected by numerous individual private companies and by their lobbying groups. The public, however, does need NIH to continue to perform high-level objective research in order to preserve the United States' status as the world leader in biomedical sciences.

A REVIEW OF THE UTILITY REQUIREMENT UNDER U.S. PATENT LAW

By Mark DeLuca*

Introduction

The discoveries and inventions arising from the Human Genome Project and parallel ventures will be required to comply with each of the requirements of the U.S. Patent Law in order to secure the exclusive rights derived from a U.S. Letters Patent. In particular, in order for nucleotide sequences that are discovered during the sequencing of the human genome to be patentable, they must be useful[1], novel[2] and unobvious[3]. In addition, the applicant for a patent must include in a patent application one or more claims which clearly and distinctly define the invention and a specification which supports the breadth of the claims, discloses the best mode for practicing the invention, and enables one having ordinary skill in the art to make and use the invention.[4]

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[1] 35 USC §101

[2] 35 USC §102

[3] 35 USC §103

[4] These requirements are collectively included in 35 USC §112

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Of these requirements for patentability, two relate to the use of the invention and these requirements are often referred to as the "utility requirement".[5] The purpose of this paper is to outline the case law related to utility requirements and to provide some framework and guidance for analyzing whether or not inventions, and the patent applications that claim them, meet the utility requirements for patentability. In the first part of this paper, I provide a historical background of the emergence of the modern rules for utility as it applies to chemical inventions, particularly chemical intermediates. This section provides a major portion of this paper because it defines the issue for an arguably analogous field. More importantly, it places a historical perspective on where the law is and how it developed in the hope of providing some basis to predict how it will be applied to new fact situations involving different inventions. In the second part of this paper, I discuss case law which sets out the standard for determining whether an invention has practical utility. In the conclusion of this paper, I have tried to set out some guideposts to be considered when analyzing the issues likely to arise when considering the requirements of utility for inventions and

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[5] The commingling of the requirement for usefulness under 35 USC §101 and the requirement that the specification teach "how to use" the invention under 35 USC §112 has been the subject of much criticism. As noted, the two requirements are distinct and require separate analyses. As used herein, the "utility requirement" is meant to refer to the requirement for usefulness required under 35 USC §101 which is the traditionally accepted definition of the term. The requirement under 35 USC §112, which is referred to as the "how to use" requirement. For convenience, when discussing both requirements, they are referred to herein as the "utility requirements".

discoveries that may be made during the sequencing of the human genome.

As noted above, the utility requirement is actually two separate and distinct requirements: first, the invention must be useful to satisfy 35 USC §101; and second, the applicant must teach "how to use" the invention to satisfy the first paragraph of 35 USC §112.[6] Applicants must satisfy both of these requirements in order to obtain a U.S. Letters Patent. Of the two requirements, the "how to use" requirement is generally less complicated to apply. The standard articulated in the statute provides more guidance and is, therefore, more easily interpreted. On the other hand, the requirement that the invention be useful invites more subjective interpretations making it the more problematic of the two. The standard for determining usefulness under 35 USC §101 is likely to be the more demanding requirement facing the applicants and their patent attorneys when attempting to claim that incomplete sequences that encode proteins of unknown function which are discovered during the sequencing of the human genome. Accordingly, most of the review contained within this paper deals with that aspect of the utility requirements.

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[6] The first paragraph of 35 USC §112 states:

> The specification shall contain a written description of the invention, and of the manner and process of making and *using it*, in such full, clear, concise, and exact terms as to enable one having ordinary skill in the art to which it pertains, or with which it is most connected, to make and *use* the same, and shall set forth the best mode contemplated for carrying out the invention. (Emphasis added)

The Emergence of the Modern Utility Requirement

The case law regarding the requirement that an invention be useful with respect to chemical inventions has evolved in the last half century. This evolution occurred with the emergence of modern chemistry and pharmaceutical science. Rigid standards are now imposed which were previously nonexistent. The case law indicates that a tumultuous, if not bitter, struggle occurred in which the standard of utility for chemical inventions changed after the first 150 years of U.S. Patent Law. Depending upon the philosophy one embraces, this change can be characterized as a radical departure from precedent or a change necessitated by technological advancement to conserve well established principles.

It has always been a requirement for patentability that an invention be useful. The early interpretation of the requirement that an invention be useful was 1) that the invention was operable, i.e. that it worked, and 2) that the invention represented some benefit to society, i.e. it was not against public policy such as being illegal, immoral, harmful or injurious to society. The opinion by Justice Story in *Lowell v. Lewis*[7], which was widely accepted as representative of the standard for utility, required that the invention provide a benefit to society in contradistinction to inventions which are illegal, immoral or

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[7] 1 Mason 182 (CC Mass. 1817)

harmful.[8] Thus, an invention was considered to be a benefit to society as long as it was not injurious to society.

In cases involving chemical inventions, a body of law has developed which imposes a different and higher standard than mere operability and harmlessness. Prior to 1940, an invention was assumed to be useful absent some indication otherwise. In particular, chemical inventions were considered to be inherently useful. With the emergence of modern chemistry, the utility requirements for chemical inventions has developed. In the 1940's, the Patent Office without legislative prodding began to impose a higher standard for complying with the utility requirement for chemical inventions.[9] Through a series of legal decisions at the appellate level which are discussed below, the Patent Office's stricter requirements for patentability, previously nonexistent, were established in the case law. The additional requirement that the invention be shown to have a substantial utility has been incorporated as a requirement for patentability. The substantial

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[8] In Justice Story's opinion in *Lowell v. Lewis*, it is stated that:

> All that the law requires is, that the invention should not be frivolous, or injurious to the well-being of society. The word useful, therefore, is incorporated in contradistinction to mischievous, or immoral.

[9] In his dissenting opinion for the U.S. Supreme Court *Brenner v. Manson,* 148 USPQ 689 (1966), Justice Harlan notes the shift in Patent Office policy which led to the emergence of the new and higher standard for utility in cases involving chemical inventions. *Id.* at 697. The shift in the Patent Office is further discussed and recounted in detail in the dissenting opinion of Judge Rich in *In re Kirk*, 153 USPQ 266, 269-71 (CCPA 1967). Commentators have noted and discussed the same. See: 27(12) J.P.O.S. 831 (1945); 49(7) J.P.O.S. 533 (1967); and 51(12) J.P.O.S. 769 (1969).

utility required for patentability refers to the requirement that an invention provide a specific benefit that is in a currently available form. The case law provides guidelines for determining whether or not an invention possesses a substantial utility.

The case of *In re Bremner*[10] provided the springboard for the modern utility requirement. In *Bremner*, the claims on appeal related to a process of producing polymers of dihydropyran and to the compound produced by the process, polydihydropyran. The specification contained no assertion of utility for the compound and the claims were rejected for that reason. After the Board of Appeals affirmed the final rejection, the applicants appealed to the Court of Customs and Patent Appeals. The issues that were decided by the court were whether it was necessary for the utility of a claimed invention be disclosed in an application and, if so, whether the applicants satisfied that requirement. The CCPA held that

> the law requires that there be in the application an assertion of utility and an indication of the use or uses intended.

The court, citing Article I, section 8, subsection 8 of the U.S. Constitution and case law precedent, went on to state that

> it was never intended that a patent be granted upon a product or a process for producing a product, unless the product be useful.

The court then found that the application did not contain a disclosure of utility and affirmed the decision of the board.

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[10] 86 USPQ 74 (CCPA 1950)

Relying on a decision by the CCPA in *In re Bremner*, the Patent Office began establishing increased requirements for utility. In *Ex parte Tolkmith*[11] the Patent Office Board of Appeals affirmed a Patent Office rejection of claims to a compound asserted to be useful as an "intermediate" and as "a constituent of parasiticide compositions". The rejection was based upon the 35 USC §112 "how to use" requirement. With regard to the utility of the compound as an intermediate, the Board, citing *Avakian v. Fahrenbach*[12] which followed *Bremner*, found that since the products made using the claimed compounds had no known utility, the asserted utility of claimed compounds as intermediates was insufficient to satisfy the requirement for disclosure of utility. With regard to the asserted use of the compounds in parasiticide compositions, the Board reasoned that the disclosure was too inadequate to satisfy 35 USC §112 since there was no specific disclosure as to how to use the compounds in parasiticide compositions. The Board stated that the terms used in the application were so vague and indefinite as to require speculation and experimentation for use. The applicant was required to teach how the compounds can be used as parasiticide

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[11] 102 USPQ 464 (Pat. Off. Bd. App. 1954)

[12] This decision of the Commissioner of Patents for Interference number 84,159 is contained in the file of U.S. Patent Number 2,620,340 issued 1951. In his dissent in *In re Kirk*, 153 USPQ 266, 270-71 (CCPA 1967), Judge Rich criticizes the propriety of basing the decision in *Tolkmith* on the decision in *Avarkian*. Judge Rich stated that the *Avarkian* decision does nothing but restate the requirement of *Bremner* that there be an assertion of utility and intended use or uses which is clearly met in *Tolkmith*.

compositions. The Board found insufficient disclosure with respect to the function of the compounds and the parasites to be targeted.

The 35 USC §112 "how to use" requirement was found to have been met in *Ex parte Ladd*[13]. In that decision, the Board reasoned that where the applicant's invention is a new compound whose members are well known to be useful for a particular purpose and the prior art reveals that one having ordinary skill in the art can use the claimed compound for that purpose, then disclosure of the claimed compound may be sufficient to meet the requirements of 35 USC §112.

In at least one commentary[14], the decision in *Ladd* has been characterized as eliminating the requirements established in *Tolkmith* that the final product be known and specified. The two decisions can be viewed as consistent with each other and the statute. In order to satisfy the "how to use" requirement of 35 USC §112, the disclosure must be sufficient to enable one having ordinary skill in the art to use the claimed invention. This construction echoes the statute and places a burden on the applicant to ensure that the disclosure contains no less than that which allows the public to derive some benefit from the invention. Thus, the critical holding in *Tolkmith* the utility requirement is

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[13] 112 USPQ 337 (Pat. Off. Bd. App. 1955)

[14] 63(7) J.P.O.S. 479 (1961)

not met unless compounds which are only use is as chemical intermediates can be used to make end products with known uses.[15]

In re Nelson[16] gave the CCPA the opportunity to reverse the trend that was taking place in the Patent Office. In that decision, the CCPA provided an extensive discussion of the utility requirements, the disclosure requirements, the *Bremner* decision, and an earlier U.S. Court of Appeals, District of Columbia case[17]. The claims in *Nelson* related to synthetic steroids which were asserted to be useful in the synthesis of other steroids. The disclosure included descriptions of the use of the claimed steroids in reactions to make other steroids although no use for the products was asserted. The court in *Nelson*, expressly noted *Bremner* but refused to follow the Board's decisions in *Tolkmith* and *Ladd* which were cited by the Patent Office to support the rejection of Nelson's application. The *Nelson* court held that claims to chemical intermediates useful to make other compounds were in compliance with 35 USC §101.[18] Further, the court held that the

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[15] The rejection in *Tolkmith* based upon the lack of utility for chemicals asserted to be useful as intermediates where no known utility exists for products should have been based upon 35 USC §101. The rejection based upon 35 USC §112 is the type of commingling of the two requirements that has been criticized.

[16] 126 USPQ 242 (CCPA 1960)

[17] *Petrocarbon Limited v. Watson*, 114 USPQ 94 (CA DC 1957) (holding that the applicants in that case failed to comply with the "how to use" requirement of 35 USC §112).

[18] Responding to the Patent Office's position that there must be a presently existing practical utility, that majority in *Nelson* held that the claimed compounds were "*useful to chemists doing*

disclosure teaching how to use the compounds in reactions was sufficient to satisfy 35 USC §112. The court held that the applicants in *Nelson* sufficiently stated the intended use of the claimed compounds - that they were chemical intermediates useful for research - as required by *Bremner*. The court in *Nelson* was unable to find their holding consistent with the holding in *Petrocarbon Limited v. Watson,* which the Patent Office urged to be authoritative precedent. The CCPA therefore expressly declined to recognize it as precedent[19].

The decision in *Nelson* was followed by *In re Manson*[20], a case involving an application claiming a process of making certain steroids. The applicant in *Manson* requested an interference with another group of inventors who claimed the same invention. The Patent Office found that the application in *Manson* did not disclose a utility for the compounds made by the claimed process and was therefore unpatentable.[21] The Board affirmed the denial and the CCPA reversed, holding the application in *Manson* met the utility requirement.

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research" and thus "[s]uch intermediates were "useful" under section 101." *Nelson, supra*, at 250.

[19] *Nelson, supra* at page 255.

[20] 142 USPQ 35 (CCPA 1964)

[21] Manson thus was denied the interference since patentable subject matter must be claimed by the parties in an interference.

In *Brenner v Manson*[22] the U.S. Supreme Court granted *certiorari* citing the "running dispute over what constitutes utility of chemical process claims" and referring to both the conflict between the Patent Office and the CCPA and between the CCPA and the CA DC.[23] The Court reversed the CCPA and held that *Manson* did not meet with the requirements of utility. The Court framed the dispute between the Patent Office and the CCPA as a conflict over the patentability of chemical processes which yield products without a known utility except "as a possible object of scientific inquiry". The Court also stated that the CCPA moved away from the standard in *Bremner* and noted the CCPA was moving toward a standard requiring only that the process produce an intended result not detrimental to the public interest[24]. As noted above, Justice Harlan in dissent contradicted the characterization that CCPA was imposing a new standard.

The reasoning behind the Court's holding in *Brenner v. Manson* relies upon the belief that the society benefits from the patent system through a *quid pro quo* where an inventor is rewarded with exclusive rights in exchange for making public an invention which is substantially useful. The Court found that the public did not derive sufficient benefit from the invention to justify conferring exclusive rights to the applicant. Further, the Court

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[22] *Brenner v. Manson, supra* at 691

[23] *Id.* at 691

[24] *Id.* at 693 and 694

warned that such a grant may block off large areas of scientific inquiry without compensating the public.[25] Finally, the Court stated that

> a patent is not a hunting license. It is not a reward for the search, but compensation for its successful conclusion.[26]

In the cases *In re Joly*[27] and *In re Kirk*[28], the CCPA using *Brenner v Manson* as controlling precedent held that compounds useful as intermediates failed to comply with the utility requirement because no utility was asserted for the products produced using the intermediates. The applicants in both cases urged that *Nelson* was the controlling precedent. The court held that if *Nelson* were viable precedent it might control but that *Nelson* was inconsistent with *Brenner v. Manson* and was thus overruled. The CCPA had, following *Brenner v. Manson*, effectively overturned *Nelson*. Judge Smith and Judge Rich, joining each other, issued vigorous and extensive dissents in *In re Joly*[29] and *In re Kirk*[30], respectively. These dissents called for a narrow construction of the decision in *Brenner v. Manson* and outlined the shortcomings of the results. The dissenters accused the majority

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[25] *Id.* at 695

[26] *Id.* at 696

[27] 153 USPQ 45 (CCPA 1967)

[28] 153 USPQ 48 (CCPA 1967)

[29] 153 USPQ 243 (CCPA 1967)

[30] 153 USPQ 266 (CCPA 1967)

of expanding the holding of *Brenner v. Manson* beyond the intent of the U.S. Supreme Court and in contradiction to the 150 years of codified patent law and the case law that accompanied it. Nevertheless, *In re Joly* and *In re Kirk,* controlled by *Brenner v. Manson,* became the accepted standard and, as one commentator conclusively noted, "one hundred fifty years of precedent had been overcome."[31]

The wisdom of the holding in *Brenner v. Manson* and the subsequent holdings in *Joly* and *Kirk* can be debated convincingly as can the reasoning for the opposite result. Judge Rich's dissent in *Kirk* outlines the shortcomings of the decision by the majority. However, the policy reasons behind the departure from 150 years of precedent is compelling. Whether or not one agrees with what has happened, however, it is reasonably well settled that the modern utility requirement for chemical cases requires that an invention be useful by providing a specific benefit that is currently available.

Practical Utility

Defining what constitutes a specific benefit in currently available form provides a further challenge toward elucidating the utility requirement. The case law leading to the promulgation of the modern standard teaches what is not a specific benefit in currently available form. The following cases allow for some

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[31] 51(12) J.P.O.S. 768 (1969)

insight into what affirmatively constitutes a specific benefit in currently available form.

In *Nelson v. Bowler*[32] the issue of utility was raised in an interference proceeding in which the two parties claimed identical synthetic prostaglandins. Specifically, the issue was whether or not one party, Nelson, demonstrated utility which was sufficient to establish a reduction to practice of the claimed compounds. Nelson had demonstrated that his compounds were active in *in vitro* and *in vivo* assays. In a decision by the Patent Office Board, Nelson was not granted priority because it was held that the assays were insufficient to show adequate proof of practical utility. The court distinguished *Nelson v. Bowler* from other cases[33] in which assays were used by finding that the assays used in those other cases were less reliable as indicators of utility. The CCPA reversed and held that the pharmacological activity shown by the compounds in the *in vitro* and *in vivo assays* did establish practical utility. This decision is most relevant in supporting an assertion of utility in the context of pharmaceutically active compounds but it contains general language about practical utility.

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[32] 206 USPQ 881 (CCPA 1980)

[33] *Rey-Bellet v. Englehardt*, 181 USPQ 453 (CCPA 1974) which the court found that the tests employed provided uncertain results and did not provide an adequate correlation between the test results and pharmacological activity; and *Knapp v. Anderson*, 177 USPQ 688 (CCPA 1973) in which the tests used to support the assertion of practical utility were outside the "intended functional setting" and the losing party did not establish that the test results correlated with the intended utility.

The CCPA provided a definition of practical utility in the opinion, stating:

> "Practical utility" is a shorthand way of attributing "real world" value to claimed subject matter. In other words, one skilled in the art can use a claimed discovery in a manner which provides some immediate benefit to the public.[34]

In *Cross v. Iizuka*[35], the Court of Appeals for the Federal Circuit (CAFC) discussed the issue of practical utility in the context of compliance with the how to use requirement of 35 USC §112. In that case, the two parties, claiming the same imidazole derivatives, were involved in an interference proceeding. Each party moved to be accorded the filing date of their respective foreign priority patent applications and each party charged that the other party's foreign application failed to comply with utility requirement. The board, following *Nelson v. Bowler* held that Iizuka had provided a practical utility by establishing sufficient evidence of pharmacological activity and declared Iizuka, who had an earlier foreign priority date, was the senior party. Cross appealed and asserted that Iizuka failed to comply with the "how to use" requirement of 35 USC §112. The CAFC held that since the practical utility was demonstrated in an *in vitro* assay, the standard to determine whether the application satisfies 35 USC §112 is whether or not one having ordinary skill in the art is

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[34] *Nelson v. Bowler, supra* at 883

[35] 224 USPQ 739 (CA FC 1985)

sufficiently enabled so that they may use the compounds in the assay.

Nelson v. Bowler and *Cross v. Iizuka* demonstrate that the threshold for practical utility is an absolute standard and not one of degree. The "real world" value that the court found in the compounds in *Nelson v. Bowler* was their pharmacological activity; specifically, the ability of the compounds to make a gerbil's colon muscle twitch. No equivalent "real world" value can be assumed, however, in chemical intermediates which are used to make end products with no known utility. Compounds such as those in *Joly* which can be used to make new compounds of unknown utility do not possess the real world value despite the fact that they can be commercially exploited by virtue of the demand for them by research chemists. The utility lies not in the what can be done with the new materials but what they tell us.

The Court in *Brenner v. Manson* framed the issue as determining

> the test to be applied to a chemical process which yields a known product whose utility - other than as a possible object of scientific inquiry - has not yet been evidenced.[36]

The court in *Kirk* echoed this sentiment. The usefulness of compounds whose only utility are as objects of further scientific study was insufficient. The court in *Nelson v. Bowler* held that

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[36] *Brenner v. Manson, supra* at 693

> knowledge of pharmacological activity of any compound is obviously beneficial to society.[37]

The utility of the compounds in *Nelson v. Bowler* was their *in vitro* and *in vivo* activities, not any therapeutic activity. The identification of the *in vitro* and *in vivo* activities removed the compounds from the realm of those whose only utility are as objects of further scientific study and placed them in the realm of compounds with practical utility. The knowledge of their pharmacological activity was sufficient to establish the successful conclusion of the search justifying compensation in the way of a patent as proscribed by *Brenner v. Manson*.

Conclusion

In cases in which genetic sequences which have a known utility or which encode proteins with a known utility, the utility requirements which are necessarily complied with in order for an inventor to receive a patent may met with little difficulty. A practical utility must be asserted and the specification must contain sufficient disclosure to enable a skilled practitioner to use the invention for its asserted utility.

Conversely, the patentability of genetic sequences which have no known utility or which encode proteins with no known utility is problematic. If such gene sequences are defined as equivalents of chemical intermediates or starting materials, they will not comply with the utility requirement unless an immediate

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[37] *Nelson v. Bowler, supra* at 883

benefit can be defined beyond their use in scientific research. A practical utility must be asserted.

The modern utility requirement as developed in the case law clearly imposes a higher standard for patentability in cases involving chemical inventions. *Joly* and *Kirk*, following *Brenner v. Manson*, established the standard in which intermediates and processes of making intermediates are not useful unless a specific use can be asserted for the products made from the intermediates. Starting materials and methods of making starting materials are not patentable unless some end product is useful. *Nelson v. Bowler* and *Cross v. Iizuka* indicate what minimum threshold must be met to comply with the requirements for chemical cases asserted to have pharmacological activity. These cases offer some insight into the general meaning of specific benefit in currently available form. They demonstrate that although chemical intermediates may not be patentable, compounds which possess some beneficial activity are. It would appear that if *Joly* and *Kirk* stand for the establishment of a requirement for a practical utility, *Nelson v. Bowler* and *Cross v. Iizuka* stand for the proposition that the practical utility required is minimal.

The law established by these cases can be applied to cases claiming nucleotide probes. Nucleotide probes are not identical to chemical intermediates. Accordingly, the law as developed in *Joly* and *Kirk* for chemical intermediates does not automatically apply. However, an analogy can be made between

chemical intermediates and nucleotide probes. Both compounds lead to new compounds which have unknown utilities now but which may be discovered to have desired activities. If this analogy is pressed to its logical conclusion, the law as developed for the cases of chemical intermediates will be applied to cases asserted utility as nucleotide probes for unknown proteins. Absent some other utility, the usefulness of probes to identify unknown genes fails to meet the utility requirement.

The challenge to the inventors and their patent attorneys is to distinguish the inventions from the chemical intermediate cases and establish some practical utility which confers some immediate benefit. The very nature of genetic sequences and their relationship to whole genes and proteins distinguishes them from chemical intermediates at some level. The genetic sequences may be distinguished from chemical intermediates based upon the different roles the two types of molecules play in the discovery of new compounds. Genetic sequences in the form of probes can be described as tools instead of starting materials. Probes are not converted into new products in the way intermediates are. Rather the interact with other molecules in such a way as to "point" to other molecules. Whether this difference is significant with respect to utility is subject to debate. Whether or not the differences alone are sufficient to render *Joly* and *Kirk* inapplicable remains to be seen.

Assuming that the differences alone are insufficient to distinguish nucleotide probes useful to hybridize to unknown genes

from chemical intermediates useful for making products of unknown utility, some other utility will need to be asserted. Genetic sequences may be asserted to have uses other than solely as probes to discover complete genes. The standard is whether an invention provides a specific benefit in currently available form. The analysis will be made as to whether such a utility rises to the level of a real world value - whether it answers an important question. In view of the policy as articulated in *Brenner v. Manson* and amplified in *Joly* and *Kirk* against rewarding inventors whose sole contribution is the advance of scientific inquiry, the challenge for the inventors and their attorneys will be to maintain that the asserted utility provides some immediate accessible benefit.

If an immediate benefit can be defined, the degree of utility is not relevant to the inquiry of compliance with the utility requirement. It is well settled that such a benefit need not be valuable in the commercial sense nor does the benefit have to be a comparative advance over what is already known.[38] The asserted utility need not represent an improvement over the prior art; in fact, it need not operate as well.[39] Moreover, although *Nelson v. Bowler* is most relevant in cases involving compositions

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[38] The law on this point is reviewed in *In re Nelson, supra* at 249-250, which position was not asserted to be overruled by *Brenner v. Manson*, as discussed in *In re Joly*, and *In re Kirk*.

[39] See *Chisum* §4.02[1]

with pharmacological activities, it provides guidance as to the broad meaning of a specific benefit in currently available form.

If an asserted utility complies with 35 USC §101, the specification must provide adequate disclosure for practicing the practical utility under 35 USC §112. Once the practical utility is defined, this task should be fairly straightforward for the inventors and their patent attorneys. Further, the invention must also be in compliance remaining requirements of patentability and the application must comply with the other disclosure requirements.

The law with respect to utility requirements is clear. A utility must be asserted and the specification must contain a disclosure sufficient to enable one skilled in the art to use the invention. An inventions whose sole utility is as an object of scientific inquiry does not meet the requirement that an invention be useful. Such is the case for chemical intermediates that useful to make compounds that have no known utility. If nucleotide probes that encode unknown genes are considered comparable to chemical intermediates, the well settled law with respect to intermediates will pose a formidable obstacle to the patenting of such probes. Differences in the roles of each respective molecule in the discovery of new compounds may allow the two types of molecules to be distinguished from each other. If not, some practical utility will have to be asserted. Such a practical utility need not represent any great advance but, rather, it must provide some use beyond research. In addition to asserting a utility in compliance with 35 USC §101, the specification must provide adequate

disclosure to allow for the invention to be used as intended.

Technology Transfer and the Human Genome Project: Some Problems with Patenting Research Tools*

July 24, 1993

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The Human Genome Project provides government funds for generating vast amounts of information in the hope that that information will ultimately be put to use in developing new products and processes for the diagnosis and treatment of human disease. The controversy surrounding the NIH patent applications on thousands of partial cDNA sequences derived in government laboratories highlights some of the complexities involved in achieving technology transfer in such a project.

Federal policy since 1980 has reflected an increasingly confident presumption that patenting discoveries made in the course of government-sponsored research is the most effective way to promote technology transfer and commercial development of those discoveries in the private sector. Whereas policymakers of prior generations may have thought that the best way to achieve widespread use of the results of government-sponsored research was to make them freely available to the public, advocates of the new pro-patent

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policy stress the need for exclusive rights as an incentive for industry to undertake the further costly investment necessary to bring new products to market. In this new way of thinking inventions that are made freely available to anyone who wants them are presumed to languish in government and university archives rather than to be actively exploited by all.

Yet the reactions of industry trade groups to the NIH cDNA patent applications suggest that there are some limits to this approach.[1] These trade groups are not composed of naive, idealistic scientists who have limited experience with patents and limited interest in product development. Their members are the same hard-nosed, pragmatic, profit-maximizing firms that the federal government is trying to entice into developing products out of government-sponsored inventions through its patent policy.

Position statements from the Pharmaceutical Manufacturers Association and from two biotechnology trade groups that have since merged, the Industrial Biotechnology Association and the Association of Biotechnology Companies, expressed views on the NIH patent applications that contradict the hypothesis that patent protection for those particular discoveries is necessary in order to protect the interests of firms that might develop related products in the future. The Pharmaceutical Manufacturers Association and the Industrial Biotechnology Association both urged that NIH not seek patent protection on DNA sequences whose biological function is unknown but instead place such sequences in the public domain. The third group, the Association of Biotechnology Companies, supported the NIH decision to

[1] See Eisenberg, *Genes, Patents, and Product Development*, 257 SCIENCE 903 (1992).

seek patent protection, but only as a means of generating revenues for the government and not as a means of ensuring the availability of exclusive rights in those sequences for firms. Indeed, even the ABC urged that the patents be licensed on a nonexclusive basis so as not to block development projects in industry. Although this position is nominally consistent with current federal patent policy, it contradicts its underlying rationale by conceding that, at least in this particular case, exclusive rights in discoveries could interfere with their effective commercial development. Generating royalty income for the government has never been among the justifications for patenting the results of government-sponsored research, and it would be a singularly unpersuasive justification inasmuch as the public would have to pay the royalties under such patents as consumers (in the form of higher prices for products) in order to collect them as taxpayers (in the form of revenues for NIH).

These reactions to the NIH cDNA patent applications suggest that even if patenting government-sponsored inventions will *sometimes* promote their subsequent development into commercial products, at other times it will retard progress toward that goal, and that *some* government-sponsored inventions will be exploited, even widely exploited, if left in the public domain. The course of scientific discovery and product development is incredibly complex and variable and unpredictable. Neither the old-fashioned approach of leaving all new discoveries in the public domain, nor the current approach of assigning exclusive rights in such discoveries to private parties, should be uniformly applied across the entire range of publically-supported discoveries. In our eagerness to avoid the inadequacies of the public domain approach, we may have moved too quickly and too emphatically in the opposite

direction, to the point where today patent rights in some government-sponsored discoveries may actually be undermining, rather than supporting, incentives to develop new products and bring them to market.

Prior to 1980 the policy and practice of the federal government with respect to patenting the results of government-sponsored research varied from one agency to the next, and sometimes from one institutional agreement to the next.[2] In 1980, Congress passed two statutes that have set the course for government technology transfer policy since that time. The first of these statutes, the Stevenson-Wydler Technology Innovation Act,[3] made technology transfer an integral part of the research and development responsibilities of federal laboratories and their employees. The second, commonly known as the Bayh-Dole Act,[4] focussed more explicitly on the role of patents in technology transfer, reversing the prior practice of some federal agencies of retaining public ownership of inventions made outside the government with federal funds. Under the Bayh-Dole Act, small businesses and nonprofit organizations who were sufficiently diligent in seeking patent rights and promoting commercial development of inventions were to retain patent ownership themselves. Large businesses making inventions with federal money were to receive only temporary title for 4½ years and thereafter could hold exclusive licenses from the government limited to specific uses that they selected for commercialization. In October of 1983, President Reagan extended

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[2]See Dobkin, *Patent Policy in Government Research and Development Contracts*, 53 VA. L. REV. 564 (1967).

[3] Pub. L. 96-480, 94 Stat. 2311 (1980).

[4] Pub. L. No. 96-517, 94 Stat. 3015 (1980).

the more generous terms that the Bayh-Dole Act had provided for small businesses and nonprofit organizations to all government contractors, including large businesses, so that now they too could retain patent ownership on inventions made in their laboratories with federal funds.[5]

Subsequent legislation and executive orders have continued to broaden and fortify the emerging pro-patent policy. Congress passed a series of amendments to Bayh-Dole in 1984 extending its provisions to inventions originating at government-owned, contractor-operated facilities and repealing limitations on the permissible duration of licenses from nonprofit organizations to large businesses on government-sponsored inventions.[6] Then, with passage of the Federal Technology Transfer Act of 1986, Congress authorized federal laboratories to enter into cooperative research and development agreements (CRADAs) with entities in both the public and private sectors and to agree in advance to assign or license to the collaborating party any patents on inventions to be made by federal employees in the course of collaborative research.

Subsequent legislation has attempted to close any loopholes that might leave potentially valuable discoveries in the public domain. Today, we have in place a system that virtually guarantees that wherever federally-sponsored inventions are made, whether in

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[5] Presidential Memorandum to the Heads of Executive Departments and Agencies, Subject: Government Patent Policy, 1983 Pub. Papers 248 (Feb. 18, 1983).

[6] Pub. L. No. 98-620, 98 Stat. 3335 [Trademark Clarification Act of 1984].

government, university, or private laboratories, if anyone involved in the research project wants the discovery to be patented, they may prevail over the objections of anyone who thinks the discovery should be placed in the public domain. Thus, for example, if a government agency or university has no interest in pursuing patent rights in a discovery, the individual investigator who made the discovery may step in and claim them.[7] If anyone sees money to be made through patenting a government-sponsored research discovery, if they have the sophistication and resources to pursue patent rights, chances are it will be patented.

Now, all of this makes a good deal of sense if we want *all* government-sponsored research discoveries to be patented. But I think there are reasons to question the effectiveness of patents as a means of promoting technology transfer in some contexts. At their best, patents provide essential incentives to undertake costly investments in product development. At their worst, they can create obstacles to subsequent research and development and add to a thicket of rights that firms must negotiate their way past before they can get their products on the market.

Patent protection is most likely to be an effective device for achieving technology transfer in the case of a patent that covers an end product for sale to consumers. It is least likely to be effective, and most likely to interfere with subsequent research and product development, in the case of a patent on a research tool that is to be used in subsequent stages of research and development but will not be incorporated into the end product as it is

[7] 35 U.S.C. § 202(d); 15 U.S.C. § 3710d.

ultimately sold.

The essence of the argument for patenting research discoveries as a means of promoting their subsequent development into useful products is that patents permit the firms that invest in product development to reap the rewards of their investment through profits without facing competition from free riders that have not shared in the costs and risks of development. Patent rights enhance incentives to develop products by allowing firms to keep would-be competitors out of their markets for a while. During the patent term, firms can charge monopoly prices, and thereby earn an enhanced return on their development costs and compensation for their risks. Thus patent rights are most likely to promote product development when they ensure the patent holder or licensee of a commercially effective monopoly in the relevant product market. Patents on some discoveries lend themselves more readily than patents on other discoveries to protecting the monopoly positions of innovating firms.

Generally, the most effective commercial protection, and therefore the most powerful incentive to invest in product development, is provided by a patent on an end product that is sold to consumers. Subject to the availability of substitute products that are outside the scope of the patent, such a patent confers a right to exclude competitors from the market for the patented product entirely, regardless of how they make it or what they use it for.

Somewhat less effective are process patents covering a specific use of an unpatented

product. So long as there are other uses for the product that are not covered by the patent, the patent holder cannot stop competitors from selling the unpatented product itself and thereby driving down its price. If the product is available in the market at competitive prices from a variety of sources, it may be impossible to monitor what purchasers are using it for.

Also less effective are patents on starting materials or processes used in making an unpatented end product. Such patents do not prevent a competitor from making the product from different materials or through a different process, or even from using the patented materials overseas and then importing the unpatented end product into the United States.[8] Such a patent may also be difficult to enforce because of practical problems in detecting and proving infringing activities in the manufacturing process that are not apparent from inspection of the end product as it is sold in the market.

Weaker still is a patent that claims products or processes that are used only during product development. Not only is it difficult to detect and prove infringement of such a patent, but often the only effective remedy even for proven infringement will be damages, because an injunction against future use of the invention will not thwart the efforts of a competitor who has already finished using the invention. One could argue for a substantial damage remedy if use of the patented product was an essential step in developing a lucrative product, and if infringement was willful the court has discretion to treble the amount of

[8] Amgen, Inc. v. U.S. Int'l Trade Comm'n, 902 F.2d 1532, 1538 (Fed. Cir. 1990).

damages.[9] But so long as the competitor no longer needs to use the patented invention in the manufacturing stage, an injunction against future infringement would not serve to keep the competitor off the market.

So firms that are interested in developing end products for sale to consumers are unlikely to see patents on research tools as a very effective means of promoting their market exclusivity. Instead, they will see such patents as potential stumbling blocks that they need to negotiate their way past in order to develop their products. Such patents may generate royalty income for their owners, and the prospect of earning royalties may make it more profitable to develop further research tools in the private sector, but it is unlikely to enhance the incentives of firms to develop end products through the use of those research tools.

Of course, one firm's research tool may be another firm's end product. This is particularly likely in the contemporary biotechnology industry, where research is big business and there is money to be made by developing and marketing research tools for the use of other firms. So, for example, even as the Pharmaceutical Manufacturers Association and the Industrial Biotechnology Association were calling upon NIH to leave its cDNA sequence information in the public domain, new firms were being formed to do further cDNA sequencing in the private sector, presumably with the hope of obtaining their own patent rights. It may well make sense to have this particular task performed in the private sector, and patents may enhance the incentives of firms to step in. On the other hand, it may make

[9] 35 U.S.C.A. § 284 (West 1984).

more sense to leave this information in the public domain, even if that means that the government has to continue to bear the cost of generating it.

There are reasons to be wary of patents on research tools. For one thing, although the ultimate social value of such inventions is difficult to measure in advance, it is likely to be greatest when they are widely available to all researchers who might have a use for them.[10] For years this country has sustained a flourishing biomedical research enterprise in which investigators have drawn heavily upon discoveries that their predecessors left in the public domain. It is in the nature of patents that they restrict access to inventions in order to increase profits to the patent holder. A significant research project might call for access to a great many research tools; the costs and administrative burden could mount quickly if it were necessary for researchers to obtain separate licenses for each of these tools.

Patents are unlikely to interfere significantly with access to research tools by subsequent researchers in the case of an invention such as a chemical reagent that is readily available on the market at a reasonable price from a patent holder or licensee. Many of the tools of contemporary biotechnology research are available by catalog under conditions that approach an anonymous market. Under these circumstances it may be cheaper and easier to obtain the tool from the patent holder or a licensed source than it is to infringe the patent by making it oneself.

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[10] See Eisenberg, *Patents and the Progress of Science: Exclusive Rights and Experimental Use*, 56 U. CHI. L. REV. 1017 (1989).

But not all research tools are readily available on a licensed basis in an anonymous market. Some esoteric research tools can only be obtained by approaching the patent holder directly and negotiating for a license. In this context patents potentially pose a far greater threat to subsequent researchers. Negotiating licenses for access to research tools may present particularly difficult problems for would-be licensees who don't want to disclose the directions of their research in its early stages by requesting a license. There is also a risk that the holders of patents on research tools will choose to license them on an exclusive rather than nonexclusive basis, in the process choking off the R&D of other firms before it gets off the ground. Such a licensing strategy may make sense for a start-up company that is short on current revenues, even if it is not value-maximizing in the long run from a broader social standpoint.

Another risk is that patent holders will try to use a device that has been increasingly popular with some biotechnology firms of offering licenses that call for the imposition of so-called "reach-through" royalties on sales of products that are developed in part through use of the research tool, even if the patented invention is not incorporated into the final product. So far patent holders have had limited success with such licenses. Firms have been willing to accept a reach-through royalty obligation for licenses under the Cohen-Boyer patent on basic recombinant DNA techniques, perhaps because the claims of that patent in effect extend to products developed through use of the patented technology. But reach-through royalty terms have met greater market resistance for the patents on the Harvard recombinant onco-mouse and polymerase chain reaction. Licenses with reach-through royalty provisions might appear

to solve the problem of placing a value on a research tool before knowing the outcome of the research project, but it takes little imagination to foresee the disincentives to product development that they could create if they become prevalent. Each reach-through royalty obligation becomes a prospective tax on sales of a product. The more research tools are used in developing the product, the higher the tax burden mounts.

For all of these reasons, exclusive rights may be expected to inhibit the optimal utilization of research tools and interfere with product development. Moreover, innovating firms are likely to have other patent rights of their own in new products that are far more significant to their market exclusivity (and therefore to their anticipated profits) than any competitive advantage they obtain as a result of exclusive access to a patented research tool. The earlier in the R&D stage an invention is used, and the more research that remains to be done in order to develop a product, the more likely it is that the innovating firm will make further patentable inventions of its own along the road to product development that are likely to be incorporated in the final product. The absence of exclusive rights in research tools is thus unlikely to undermine the incentives of innovating firms to use those tools to develop new products.

A complication arises in the case of inventions that have significant current value as research tools, but might also be incorporated into commercial products at some time in the future. It may be necessary to be able to offer exclusive rights in the ultimate commercial product to innovating firms in order to give them adequate incentives to develop the products.

This possibility may argue in favor of patenting inventions even if doing so is unnecessary to facilitate their present use as research tools, and even if it inhibits that use.

Intermediate strategies are possible to minimize any inhibiting effects on research. For example, one might add a research exemption to the Bayh-Dole Act that would protect subsequent researchers who use patented research tools developed through the use of government funds from infringement liability. Patent holders would still be able to enforce their exclusive rights against those who make, use or sell the inventions as commercial end products, including competitors who sell the invention to investigators for use as a research tool, but not against those who merely make and use the invention in their own research. Obviously, such an exemption would limit the value of patent rights in any government-sponsored invention that is useful primarily or exclusively as a research tool, although the protection against competitors who would sell the product to researchers provides some measure of protection. So long as other large scale producers can be excluded from the market, the patent holder will be able to reap the benefits of any significant economies of scale in production of the research tool. The lack of a remedy against researchers who make the invention themselves would still set an upper bound on the ability of patent holders to charge full monopoly prices, since at a certain point researchers might find it cost effective to make the research tool themselves rather than to buy it from the patent holder.

A variation on this approach would be to deny patent holders an injunctive remedy against research users, but permit them to recover a reasonable royalty as damages. This

would allow a tribunal to administer a more fine-tuned remedy to ensure that patent holders receive an adequate return in cases where economies of scale are insufficient to induce researchers who are completely exempt from infringement liability to deal with the patent holder. It has the drawback of creating uncertainty for patent holders and researchers as to the level of royalties that the tribunal will deem reasonable. In an environment where some patent holders are demanding reach-through royalty provisions in licenses for the use of research tools, the potential damage remedy might seem intolerable to innovating firms. And the prospect of opening up their financial books to prove how much of a royalty is reasonable is likely to be distasteful to firms on both sides of the dispute.

Of course, both of these approaches amount to compulsory licenses for research users of patented inventions, although only the latter is a royalty-bearing compulsory license. If they are perceived as such, they may be opposed throughout the industry. Universities and biotechnology start-up firms, who are most likely to be in a position to collect royalties on sales of research tools, will have a financial incentive to oppose any change in the law that reduces the value of patents on research tools. Pharmaceutical firms, who derive their profits from selling end products and have the most to gain from a policy that facilitates free access to research tools, oppose any form of compulsory licensing on principle, just as the National Rifle Association opposes any form of gun control. Perhaps the first alternative, which denies a damage remedy altogether, would seem less like a compulsory license provision than the second alternative, which limits damages to a reasonable royalty, although it is ultimately more hostile to the interests of patent holders.

Any retreat from the broad giveaway of patent rights under present law will inevitably be opposed by some people in industry. This does not necessarily mean that a retreat would interfere with technology transfer. The rhetoric surrounding current federal technology transfer policy suggests that whatever is good for industry must be in the public interest. This is a vast oversimplification of the issue. The biotechnology industry is not monolithic. Rights that enhance the profits of small start-up firms may interfere with the research of established pharmaceutical firms. The private sector responds to the profit incentives created by whatever policies the government puts in place. Whenever the government offers new property rights one would expect someone to step forward to claim them (and to protest when it threatens to take them away). It doesn't necessarily follow that those property rights are on balance creating new social value that will make all of us better off.

I believe that patents have a critical role to play in promoting technology transfer. But the incentives created by patent rights in government-sponsored inventions would do little to compensate for the damage we could do to our research enterprise if we allocate too much of our new knowledge to private owners and too little to the public domain. To quote from a recent opinion by Judge Kozinski of the United States Court of Appeals for the 9th Circuit:

> "Private property, including intellectual property, is essential to our way of life. ... But reducing too much to private property can be bad medicine. Private land, for instance, is far more useful if separated from other private land by public streets, roads and highways. Public parks, utility rights-of-way and sewers reduce the amount of land in private hands, but vastly enhance the value of the property that remains.

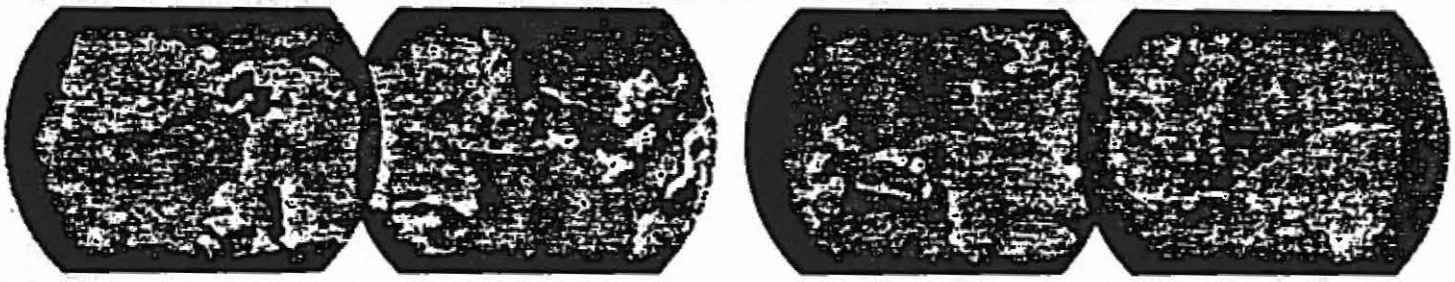
"So too it is with intellectual property. Overprotecting intellectual property is as harmful as underprotecting it. Creativity is impossible without a rich public domain.... Culture, like science and technology, grows by accretion, each new creator building on the works of those who came before. Overprotection stifles the very creative forces it's supposed to nurture."[11]

Government is uniquely situated to enrich our public domain. We should be wary of disabling the government from performing this critical function in our eagerness to enhance private incentives to put existing discoveries to use.

[11] Vanna White v. Samsung Electronics America, Inc. et al., 989 F.2d 1512, 1993 U.S. App. LEXIS 4928, slip op. at 6 (9th Cir. 1993).

LICENSING LAW AND BUSINESS REPORT

Edited by the law firm of Willian Brinks Olds Hofer Gilson & Lione
455 North Cityfront Plaza Drive, Suite 3600, Chicago, Illinois 60611



Vol. 15, No. 1 May-June 1992

ACCESSING AND LICENSING FEDERAL TECHNOLOGY [1]

Ronald E. Barks [2]

- The Federal Laboratory System
- Federal Law
- Company-Federal Laboratory Interactions
- Locating Federal Technology
- Accessing Federal Technology
- Federal Laboratory Licensing Considerations
- Pricing Considerations
- Results of Federal Licensing

1. Introduction

In an age of intense worldwide economic competition, U.S. companies have, in the federal laboratory system, an enormous pool of resources which they can leverage to their advantage. These resources consist of personnel, facilities, know-how, technologies, funding, and intellectual property. The magnitude of the federal laboratory system budget amounts to approximately $25 billion annually. These funds provide for research and development, conducted at over 700 federal laboratories, in

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[2] Ronald E. Barks directed the technology transfer and licensing office at Los Alamos National Laboratory for four years and is currently responsible for economic development programs. A Ph.D in materials science, Dr. Barks' career has focused on the linking of business, management and science. As a director of research and development, Norton Company, for twelve years, he was responsible for the development and transfer of product/process technology to plants in 14 countries. He is principal of Ronald E. Barks Associates, a consulting firm specializing in technology transfer and commercialization. A fellow and Vice President of the American Ceramic Society, Dr. Barks originated and conducts the annual Corporate Award Winners Workshops and Business of Technology panel discussions. He is a member of the Technology Transfer Society and The Licensing Executives' Society, serving as a faculty member on the latter's annual course in technology transfer.

Licensing Law and Business Report
is published by Clark Boardman Company, Ltd. 375 Hudson Street, New York, NY 10014 ISSN 0162-5764

fourteen federal agencies and centers. These laboratories are staffed by over 100,000 scientists and engineers who address virtually every area of science and technology. Federal Laboratory Consortium, *Handbook of Fundamentals for FLC Representatives*, 1992 at 5. A primary mission of the federal laboratories is the transfer of this federal technology and expertise to private sector companies for commercialization to improve the U.S. economy.

Successful partnerships between companies and federal laboratories, through licensing, will ultimately benefit the nation. Although there are many mechanisms for technology transfer, licensing of existing intellectual property, as well as that developed through Cooperative Research and Development Agreements (CRADA or CRDA), are the primary mechanisms used to acquire technology for commercial development.

The development of mutually beneficial licenses between institutions as different as industrial companies and federal laboratories are increasing. Moreover, such development can be enhanced by achieving an understanding of the respective cultures. The focus of this article is intended to assist the process.

2. The Federal Laboratory System

Federal laboratories are divided into two primary categories: Government-Owned/Government-Operated (GOGO) laboratories and Government-Owned/Contractor-Operated (GOCO) facilities. GOGO laboratories and centers represent 98 percent of the total laboratories in the system. Furthermore, GOGO employees are actually employees of the federal government. Thus, their patent and licensing practices are subject to a body of federal law and regulations which differ in some important ways from those pertaining to GOCO laboratories. The best example of this difference is in the area of software. Although federal and nonfederal employees at a federal GOGO laboratory may protect software-related inventions by patent, U.S. law generally prohibits federal employees from copyrighting software. Federal Laboratory Consortium, *Handbook of Fundamentals for FLC Representatives*, 1992 at 6–7. (See Table 1 for a listing of Agency technology transfer contacts.)

Conversely, GOCO laboratories reside primarily in the Department of Energy (DOE). Via contract, various universities and private companies manage and operate these laboratories for the DOE. (See Table 2 for list of the DOE-GOCO laboratories and contractors.) Employees of GOCO facilities are employees of the particular contractor, not the funding agency. Federal law and various contracts support the contractor's ability to take title to inventions generated at their facilities. Once the DOE has granted title for an invention, the contractor conducts patenting and licensing activities as a private sector entity rather than a federal agency. Advantages to this system manifest themselves in the ability of GOCO laboratories to copyright and license software developed by their employees. Specific details of these patent and licensing practices are usually provided to interested companies, by representatives of the technology transfer or licensing office, at the federal facility controlling the targeted technology.

3. Federal Law

Major laws passed by Congress since 1980 (See Table 3) encourage technology transfer from federal laboratories to private-sector companies and universities. These laws were previously reviewed in G.R. Peterson, *Rights in Federal Funded Inventions: Technology Transfer and Licensing Considerations for Universities and Industry*, LICENSING LAW AND BUSINESS REPORT (Vol. 12, Nos. 5 and 6, January–February 1990 and March–April 1990).

4. Company-Federal Laboratory Interactions

The number of companies seeking technology transfer opportunities at federal laboratories has increased tremendously in recent years. As a result, some important insights have been gained from these interactions.

Numerous companies are now approaching the federal laboratories seeking opportunities to achieve the following objectives via the acquisition of government technology:

- improvement of their competitiveness in world markets by leveraging their resources with those in the federal laboratories,
- reducing the risk of having to make their own investments in research and development, and
- acceleration of the product/process introduction to market.

On their part, the laboratories are looking to develop partnerships in response to the requirements of previously mentioned laws and in support of National Economic Enhancement Objectives, including:

- to create quality jobs in America;
- to maintain our standard of living; and
- to reduce the balance of payments.

Thus, the corporate and laboratory objectives are mutually supportive. Comments from industry visitors reflect this. "We need to achieve a national economy of effort. There is a need to leverage company resources with those of the National Laboratories and other companies." (Preceding comments made during Superconductivity Industry Workshops at Los Alamos National Laboratory on Oct.–Nov. 1982.) "From inception, the commitment to commercialize has to be inherent in the program as an objective." *Id.* The increasing use of CRADAs reflects this. "The speed of getting to market is a key issue. We will be killed in world markets if we are slow." *Id.*

Overall, in their interactions with federal laboratories, companies express the need for speed, certainty, simplicity and flexibility. These important issues are being addressed through new laws under consideration and through new policies and procedures by the Government Agencies.

Companies seek federal technologies that will provide them with an advantage in the marketplace and that will eventually generate profit. To have commercial value, however, the particular technology need not be the overall result of a major federal program. Such large federal programs represent a "technology push" approach to product/process development. For a company to take such a technology to market would represent significant development costs, high risk, and a considerable period of time. There are many examples of the transfer of such technologies from the laboratories to private companies, generally major corporations.

More commonly, companies seek technologies consistent with a "market pull" approach to product/process development. These technologies, which are the by-products of most federal programs, are characterized by incremental improvements relative to an existing technology, low level of risk, and relatively low levels of investment before the product/process goes to market. Firms of all sizes derive important commercial value from this approach to the abundance of technologies in the federal laboratory system. Sensors, specialty characterization devices, and personal convenience computer codes are examples of incremental technologies available to such an approach.

[a] The Value-Added Potential of Company-Laboratory Interactions

Experience dictates that companies derive added value from company-laboratory interactions in at least three different ways: (1) they gain knowledge of technology that may provide unexpected options relative to their application of interest; (2) accelerating product/process development to market; and (3) they gain additional mechanisms to acquire technology.

Federal research programs are usually directed to developing new knowledge through basic research and to providing solutions for problems specific to the needs of the sponsoring Agency. These approaches result in the development of technology rather than specific products or processes for a given application or market. Such generality has numerous advantages. First, it lends itself to the possibility of being applied in a number of different ways. Second, it will very likely be less constrained than the technological expertise in a company that is generally focused on a specific product or product line and thereby constrained by that focus. Furthermore, during laboratory visits, exchanges between laboratory and company scientists and engineers often provide valuable insights to solving a particular problem which a company may not have realized on its own.

Third, some excellent examples exist of accelerated product/process development. There are a number of versions of a product commercialization cycle. They usually show the product concept at the origin and through the course of years, progress through various stages of the learning curve including technology development, slow progress, low level of production, volume production and market maturity. The time related to this full cycle varies from industry to industry, generally in the two-five year period for consumer products, five-ten years for the biomedical industry, and ten-twenty years for the automotive, machine tool, and energy industries. When a company approaches the laboratory, it is usually in the product concept stage of a commercialization cycle. It may find that the laboratory will have a relevant technology it has been working with for years that has progressed well along the learning curve. Through the transfer of technology from the laboratory, the company can be brought to that same position on the commercialization curve quite rapidly. This saves the company a great deal of time, research investment, and risk. The result may be that a product will proceed to market in much less time than had the company worked completely on its own. Indeed, following are three examples of sophisticated Los Alamos technologies transferred, via licensing, to companies that brought them to market in under ten months:

- A sensor for the rapid measuring of superconductivity in materials.

LICENSING LAW AND BUSINESS REPORT

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Published bimonthly by Clark Boardman Callaghan
375 Hudson Street, New York, New York 10014

Subscription: $135 for six issues
Orders received from outside the United States must be accompanied by a check in U.S. dollars drawn on a U.S. bank.

ISSN 0162-5764

- A software/hardware combination that allows supercomputers from different manufacturers to communicate with one another in real time.
- A process that removes trans-uranic and other undesirable heavy metals from waste streams to produce water that meets Environmental Protective Agency standards for human consumption.

These examples demonstrate the possibility for rapid, effective transfers of government technology to private companies which result in products being brought swiftly and successfully to market. Often, such transfers result in new jobs and increased profits for these companies.

Not all companies, however, are interested in obtaining federal technology via licensing. A number of other technology transfer mechanisms are available at the federal laboratories. The different mechanisms are designed to meet the various individual needs of companies interested in obtaining technology. The simplest of these transfers involves the sharing of information via papers, workshops, seminars, etc. In addition, formal exchanges of personnel and consultants are provided, as well as the opportunity for use of laboratory facilities. Finally, more complex are the formal licensing and contractual mechanisms such as contract research, CRADAs, prototype development, startups and spinoffs, and consortia formation.

The most effective company visits to federal laboratories utilize a corporate teaming approach. The team consists of a member or members from both marketing and research, each having important roles. Marketing personnel are quick to recognize the business potential of a technology. Research personnel on the other hand are able to provide immediate verification as well as identify other useful applications for the technology. The net result is the establishment of a level of credibility for the technology, by the corporate team, leading to a more rapid decision concerning acquisition.

[b] Company Ownership vs. Acquisition of Federal Technology

When a company finds the exact technology it desires, it almost always seeks to obtain ownership in order to protect its commercialization investment. Companies express the magnitude of this investment, i.e., the "investment scaler," to mean that for every $1 of research, a company spends $10 to develop the product and another $100 to take it to market. The law does not allow a company to own technology developed with taxpayer's money. The government always retains a nonexclusive royalty free, irrevocable license to use the technology and any patent application covering it for government purposes by an assignment and confirmatory license. A company can, however, obtain exclusive use of a specific federal technology, via licensing. Generally, these exclusive licenses will be limited to a specific field of use in order to meet federal requirements for the broad application of the technology. Nonexclusive licenses are also available. These vehicles can be used to acquire federal intellectual property including patents, blue prints, engineering drawings, and in addition, copyrights from GOCO facilities. Consideration, in the form of proposed legislation, is also being given to including mask works, trademarks and copyrights for software for GOGO laboratories. (See Tables 6 and 7 for a listing of patent and licensing activities by the various federal agencies.)

[c] Technology Transfer and Commercialization

Company visitors have provided considerable insight on technology transfer, commercialization and the roles of the federal laboratories in these respective processes.

[1] Technology Transfer

The simplest definition of technology transfer is the conveying of a body of applied knowledge from one entity to another. The transfer is comprised of two stages. First, the technology developer educates or trains personnel from the entity to whom it is being transferred. Second, the developer also assists in any follow-up problem-solving that may be needed. Note that if provision for such follow-up support is not included in the license, failure of the transfer may result.

Within a company, technology transfer occurs between a research section and either a development or manufacturing section. When the technology is acquired from a federal laboratory, the latter may be perceived as a threat by the corporate research group of the receiving company. This, however, is not an accurate perception. Federal technology rarely occurs as a finished product or process ready to be transferred. It invariably requires adaptation and further development to the final product/process by the receiving company, a critical role supplied by their research and development section. Companies will generally request and welcome some degree of government laboratory assistance in technology transfer.

[2] Technology Commercialization

Technology commercialization from the industrial standpoint means the development and taking to market of a finished product/process for profit. This involves the full range of technical and business stages including marketing, research and development, manufacturing, and sales. Since technology transfer occurs between research and manufacturing, it can begin whenever the two sections feel it is appropriate. Furthermore, it can continue, in a supporting role, as far into the manufacturing and sales phases of the commercialization process as the company desires. Therefore, the extent of federal laboratory involvement in the commercialization of a technology will be determined by the company. Usually,

companies prefer that such involvement cease prior to the point where contact with their markets may occur.

Finally, it is possible to have a successful transfer of technology and still have a commercial failure. For a product to reach the market and be successful involves factors both internal and external to the company, any of which alone, or combined can lead to the commercial failure of the product/process.

5. Locating Federal Technology

There are several ways to locate federal technologies. The initial step generally involves a review of topical literature in the field of interest, including conference or symposia agendas, relevant professional society journals, trade association publications and shows, newsletters, etc. Technologies with acknowledged commercial potential are presented annually as winners of the prestigious R&D 100 Awards in *Research and Development Magazine* (Cahner's Publishing Co., a division of Reed Publishing, U.S.A.). Federal laboratories win a considerable number of these awards, thereby, demonstrating that there is significant commercially valuable technology in the federal system. The R&D 100 Awards help to identify laboratory capabilities in the field of interest, the names of the researchers, and specific technologies of interest.

Several government information centers for available technology also exist. The National Technical Information Service (NTIS) is operated by the Department of Commerce. "NTIS licenses patents for several federal agencies including Agriculture, Commerce, The National Security Agency in Defense, the Environmental Protection Agency, Interior, the Public Health Service in Health and Human Services, and Veterans Affairs," *Technology Transfer: Federal Agencies Patent Licensing Activities, United States General Accounting Office*. (Reprint to Congressional Requestors, GAO/RCED-91-80, at 16).

The *Commerce Business Daily* (CBD), produced by the Department of Commerce, contains information about federal contracts and technologies. The CBD has proven to be a very effective vehicle for alerting companies to the availability of technologies for licensing or the formation of CRADAs. Los Alamos advertises availability of these technologies in the Basic Research section. CBD can be obtained in university or public libraries or by writing the U.S. Department of Commerce, *Commerce Business Daily*, P.O. Box 5999, Chicago, Illinois 60680. It is also available as an on-line data base, CompuServe (CO-CBD).

In addition, the DOE's Energy Sciences and Technology Software Center provides information on available agency software. Moreover, the National Aeronautics and Space Administration's (NASA) magazine, *Tech Briefs*, is a very popular vehicle for portraying NASA's technologies. (See Table 1 for a list of contacts for these sources.)

The Federal Laboratory Consortium provides access to the entire federal laboratory system. Organized in 1974, it was formally chartered by the Federal Technology Transfer Act of 1986 to promote and strengthen technology transfer nationwide. All major federal laboratories and centers and their parent agencies are members. The Consortium provides a basic link between the individual laboratory members and the potential users of government-developed technologies. The backbone of the FLC is the individual laboratory or center representative. These individuals represent their own laboratory and, combined, form a network for national technology transfer. The FLC's strength is the ability to put potential users in contact with a laboratory person having a specific technical capability. The same protocol for accessing technology through the laboratories applies to the FLC as well. National contacts and the six regional coordinators of the FLC are shown in Table 4.

A recent addition to the government's array of institutions designed to support industrial/federal laboratory interactions is the National Technology Transfer Center (NTTC) in Wheeling, West Virginia. At the direction of Congress, NASA initiated in April 1991 a five-year development program to establish the NTTC as a national resource for Federal technology transfer. The NTTC's principal mission is to assist all Federal agencies in executing the technology transfer mandate as a means of enhancing U.S. competitiveness. Via the alignment of six Regional Technology Transfer Centers (RTTCs) and six FLC regions, the NTTC is currently designing key capabilities and services to act as a national clearinghouse for federal technology transfer in an effort to link federal agencies and laboratories with U.S. firms and industries. The RTTCs provide "value-added services" to meet the technology needs of individual businesses and industrial clients, including information services, technical services and commercialization services. Of greatest interest to potential licensees, the NTTC will provide computerized searches of federal technology databases and other technology sources. This service is expected to be available in October 1992. (See Table 5—Access to the National Technology Transfer Center).

6. Accessing Federal Technology

The way a particular company approaches laboratory offices of technology transfer will influence its probability of success in locating and acquiring a useful technology. The three most common approaches are as follows:

- What do you have? This is often the approach of entrepreneurs seeking a technology that provides an opportunity to start a business. The lack of specificity of this type of request makes for a difficult response

due to the volume of available technology. As a result, the probability of success is low.

- Submission of lengthy and detailed technology listings. Generally, larger companies employ this method. As the laboratory's technology transfer office is able to match up their facility's capabilities and available patent and copyright portfolios with the company's expressed interests, this approach is usually more successful than the one preceding. The laboratory finds it helpful if the requester prioritizes their list since neither the company nor the laboratory has the resources to explore more than a few match-ups in any finite time period.
- Submission of a single, well-defined capability or technology of interest. This approach is used by companies of all sizes, but most often by small and medium-sized firms. It has the highest probability of success.

The overall federal laboratory system experience indicates that the degree of request specificity and accuracy in the company's defined technological needs correlate to the laboratory's response time and probability of success in locating a useful technology.

When requesting laboratory information or assistance, there is a simple, highly effective, three-step protocol a company can follow to articulate its need so that a federal laboratory can respond most effectively. Experience dictates that written submissions are the best way to provide this information to the laboratory, as copies can be circulated to individuals best qualified to respond with appropriate action. In any written request, a company should:

1. State the business opportunity the technology will support.
2. State the technology/technologies believed to be needed.
3. State the problems the company hopes to solve with the sought technology.

Should the company or laboratory feel the need to protect proprietary information, a confidentiality agreement can be executed.

Assuming a visit to the laboratory takes place as a result of such written requests, the care taken by the company to articulate its needs according to such protocol may prove very beneficial. Detailed, in-depth information from the company permits laboratory personnel to provide approaches or technologies that are unknown to the requester. As a result, a value-added experience and superior opportunity may be obtained by the company.

Another means of enhancing a subsequent company visit is to understand that federal technology exists in two major forms—intellectual property, and capabilities and know-how.

[a] Intellectual Property

A laboratory's inventory of intellectual property available for licensing will reside in patents pending, patents issued, patents maintained and, in the case of GOCO laboratories, copyrighted software.

Federal laboratories commonly license technology in the patent pending stage. Due to the costs incurred when obtaining and maintaining patents, it is common practice for the technology transfer and licensing offices in the federal system to select for transfer only those patent disclosures or software perceived to have obvious commercial potential. Such technology will then be advertised to attract a potential licensee. Companies expressing a desire to license such technology are then often required to sign a proprietary information agreement before being permitted to review the patent application. After the licensee has been identified, the application will then be submitted to the U.S. Patent and Trademark Office (PTO). Thereafter, negotiations begin. Finally, provisions will be made in the terms of the license should the patent not issue.

Patents are also routinely filed to protect a potentially useful technology whether or not a licensee has been identified. In such cases, a laboratory will include the issued patent in its data base. Afterward, the laboratory may choose to advertise its availability through a variety of outreach mechanisms.

The laboratory intellectual property arsenal also includes existing patents or "patents maintained." The term, "patents maintained" denotes those for which at least one PTO maintenance payment has been made. This first payment is made between three and three and a half years after the patent is issued. Although maintained, it is unlikely that these maturing patents will be advertised by the laboratory of origin or its sponsoring agency, To access such patents, a company will have to actively seek them. Since many inventions are made before their time, it is quite possible there is commercial value in this portfolio of existing patents.

Upon request, a copy of a laboratory's patent portfolio can be obtained directly from the laboratory of origin or its sponsoring agency. Moreover, a patent, once issued, can be licensed from either the laboratory of origin or its sponsoring agency. There are exceptions, however, i.e., the GOCO laboratories in which the contractor may have taken title to certain patents.

Because of the tendency to patent only technology with easily recognized commercial potential and other resource limitations existing in the ORTA's, a company seeking federal technology solely in the forms of patents or copyrights may be limiting itself to a minute fraction of the opportunities actually available to it.

[b] Capabilities and Know-How

The vast body of technology in the federal laboratory system resides in the form of the capabilities and know-how of its people. The existence of this capability and know-how, in a general sense, can be identified from the less formal outreach mechanisms of transfer cited earlier, i.e., articles, seminars, conference agendas, etc.

Upon recognizing that a specific federal laboratory possesses a capability of company interest, it is advisable to contact the ORTA office at the laboratory in question and employ the previously cited three-step protocol to articulate the company's need. Such action will effectively enlist the support and assistance of the ORTA to explore the full range of laboratory capabilities and know-how in the company's field of interest. Many times this results in the company's identifying valuable technology which might otherwise have gone unnoticed. Furthermore, company interest often leads to the filing of a patent application. This same approach applies to copyrights available in the GOCO system. Since the company may have identified as commercially valuable a technology that would otherwise have gone unnoticed then, in the GOCO system, at least, the availability of the technology would not have to be advertised. The company could acquire an exclusive license for its use. This contingency is provided for in the National Competitiveness Technology Transfer Act of 1989. *National Competitiveness Technology Transfer Act of 1989*, 15 U.S.C. §§ 3701–3710 (1989).

A transfer mechanism of increasing importance for acquiring technology in the form of capabilities and know-how is the CRADA. When the technology is in such an early research stage, there is no actual intellectual property. Furthermore, significant development is still required. CRADAs include provisions to license the resulting intellectual property. Therefore, CRADAs are becoming an important form of contractual technology transfer mechanism between companies, universities, and federal laboratories. The provisions of CRADAs apply equally to both GOGO and GOCO laboratories and routinely contain clauses for licensing intellectual property developed in the course of the agreement. It is common for a CRADA to result in a license.

In its 1992 Handbook of Fundamentals for Federal Laboratory Consortium Representatives, the Consortium provides the following excellent summary of the CRADA. Federal Laboratory Consortium, *Handbook of Fundamentals for Federal Laboratory Consortium Representatives*, 992 at 7–8:

> In 1986, The Federal Technology Transfer Act of 1986, PL 99-502 pertaining to GOGO laboratories and 1989 The National Competitiveness Technology Transfer Act of 1989, PL 101-189, pertaining to GOCO laboratories, legislation was enacted as part of the Stevenson-Wydler Technology Innovation Act to enable federal laboratories to enter into cooperative research and development agreements (CRDAs) [also known as CRADAs] with private businesses and other entities. Since then, over 1000 CRDAs have been signed based on this authority. CRDAs provide the means to leverage R&D efforts and to create teams for solving technological and industrial problems. Through CRDA's companies or groups of companies can work with one or more federal laboratories to pool resources and share risks in developing technologies. The CRDA is a useful R&D relationship when the transfer of technology and subsequent transfer of rights are expected to be important to the collaborating party.
>
> CRDAs are potentially very flexible. There are many benefits. These are instances when companies have entered into CRDAs with federal software developers and have made such significant contributions or changes to the software, that the company has been able to copyright the product resulting from the CRDA effort.

Id. The latter refers to GOGO laboratories.

Law establishes the following conditions for a CRDA:

> 1. Collaboration involves the expenditure of federal funds and the use of federal personnel, services, facilities, equipment, intellectual property or other resources. However, no federal funds may flow to the CRDA partner.
>
> 2. Non-federal contributions include funds, personnel, services, facilities, equipment, intellectual property or other resources.
>
> 3. Special consideration is given to small businesses and consortia involving small businesses.
>
> 4. Preference is given to businesses that are located in the United States and undertake to manufacture substantially in the United States products that embody inventions developed under the CRDA or are produced using inventions developed under the CRDA.
>
> 5. The United States Government always retains a nonexclusive or nontransferable, irrevocable, and paid-up license to practice any inventions developed under a CRDA for governmental purposes.
>
> 6. The federal laboratory may in advance grant or agree to grant to a collaborating party exclusive patent licenses or assignments for all laboratory employee inventions made under the CRDA.
>
> 7. Federal laboratories may protect from public access commercially valuable information produced under CRDAs by both federal and non-federal participants for up to five years as negotiated for each CRDA; trade secret or commercially valuable information that is privileged or confidential information which is obtained in the conduct of research or as a result of activities under a CRDA from a non-federal participant will not be disclosed.
>
> As more experience is gained with CRDAs, federal departments and agencies are developing general policy guidelines. For instance, IR&D [Institutional Research and Development] funds may be used as a CRDA contribution in the case of DOD and NASA contractors providing the costs would have been allowable as IR&D had there been no CRDA.

Id.

The CRADA activities of the various federal agencies has increased significantly in recent years. A corresponding increase in CRADA-related licensing should eventually follow. (See Table 8, a listing for the CRADA activities of the various federal agencies.)

7. Federal Laboratory Licensing Considerations

When it comes to licensing and pricing, the details of the deal will vary between GOGO and GOCO facilities. Both facilities, however, will provide this information in advance, including copies of model agreements.

Patent licensing practices of GOGO facilities are authorized by various statutes, including the Stevenson-Wydler and Bayh-Dole Acts of 1980. 15 U.S.C. § 3701–3714; 35 U.S.C. §§ 200–212; *See also* 37 C.F.R. § 404 for regulations governing patent licenses. Inventions available for licensing are those covered by patent or an application for same in either the United States or foreign countries, the title to which has been assigned or vested in the U.S. Government. The custody of a federally-owned invention can be transferred to another federal agency for licensing, i.e., the National Technical Information Service (NTIS) of the U.S. Department of Commerce. NTIS licenses technology for a number of federal agencies. (See Table 6.)

In general, government regulations applicable to GOGOs reflect a preference for non-exclusive licensing. Exclusive licenses that promote successful commercial development can be granted, however, when various criteria are met. Such criteria may vary and should be obtained from the appropriate licensing office. Moreover, applicants for an exclusive license must submit a detailed justification that addresses the specific criteria. The notice for each proposed exclusive license (other than those that result from a CRADA) is published in the Federal Register and, as required by 37 C.F.R. § 404.11, seek public comment within ninety days. Should a valid objection to the exclusive license be received, the license may not be granted. In such instance, appeal by either the proposed licensee or the objecting party is also provided for.

GOCO laboratories, most of which are in the DOE, have within their contracts the right, subject to various provisions, to take title to inventions made at their facility. Licensing is normally conducted at the GOCO laboratory that gave rise to the technology. (See Table 2 for a list of the GOCO laboratory technology transfer offices.) GOCO laboratory licensing offices further differ from their GOGO counterparts in that they are not required to publish in the Federal Register an intent to grant an exclusive license.

Licensing practices of GOGO and GOCO laboratories commonly include both small business preference and U.S. preference. The U.S. preference requirement is found in both the Federal Technology Transfer Act of 1986 and the National Competitiveness Technology Transfer Act of 1989. 15 U.S.C. §§ 3701–3714 (1986); 15 U.S.C. §§ 3701–3710 (1989). It mandates that potential licensees agree that products embodying the invention or that are produced through use of the invention will be manufactured substantially in the United States if such products are to be sold domestically. Licenses can be granted to U.S.-based subsidiaries of foreign-owned companies which meet this criterion.

The terms and conditions of exclusive and non-exclusive licenses negotiated for federal intellectual property reflect general industry practice. Normally a business plan is required of the potential licensee. The plan is used to validate the company as a credible recipient of federal technology, to establish due diligence provisions, and to serve as the basis for negotiations concerning royalties and other provisions. The business plan may also serve as the basis of selection of the party to be awarded a license should there be competition among multiple companies for a specific technology.

The license is generally acknowledged as the first step in a long-term relationship between organizations. The mutual benefit of both parties is a desired outcome. Once negotiations for the license begins, the same considerations pertain as would normally occur in industry. A few of these considerations, with particular relevance to federal licensing, appear below.

As mentioned earlier, the stage of the technology's development at the time of licensing is important as this determines the magnitude of investment by the licensee to develop a market-ready product or process. Market size and the number of potential licensees are also important. Since many federal technologies are leading edge, resulting products or processes are often directed to small, highly specialized niche markets, a situation incapable of supporting multiple licensees. Conversely, this leading edge characteristic can provide incremental or revolutionary opportunities in large existing markets. The breadth and early stage of development of many federal technologies provide opportunities for innovative companies to define advantageous, unique fields of use. Offsetting resource contributions from the company to the laboratory in the form of specialized equipment used or loaned, knowledge, software documentation and maintenance, etc., are additional benefits to be taken into account. Again, technology transfer in the form of continuing support from the licensor to the licensee, during the term of the license, should be provided to enhance these benefits.

8. Pricing Considerations

The pricing of federal technology is reflected in the royalty structure of the license. The nature and range of royalties negotiated by federal licensing offices are similar to those in the private sector. A comprehensive and quite useful guide to such royalties is provided in *Busi-*

ness Strategy and Factors Affecting Royalty Rates: Results of a Survey, LICENSING LAW AND BUSINESS REPORT (Vol. 13, No. 6, March–April 1991).

Patent royalties include up-front, minimum and running elements. Recovery of the costs of patenting and licensing is up-front and documented for the licensee. Up-front, non-exclusive royalties may range from $2000–$50,000. Exclusive licenses are commonly in the $25,000–$200,000 range. Furthermore, minimum royalties are highly variable, subject to many considerations. Running royalties, however, are often tied to sales volume and expressed as a percentage of net sales, i.e., a fraction of 1 percent to as much as 15 percent in rare cases. The federal licensing office may choose, at its discretion, to delay the receipt of running royalties because of small business preference considerations. For small and start-up companies, this avoids staving them for cash during a critical growth period. Fair return to U.S. taxpayers is assured by agreement for a higher percentage of net sales later when the company is financially healthy.

Royalty ranges and conditions for patented or copyrighted software are generally similar to those for all other patents. Running royalties are commonly in the 5 percent to 15 percent range but may be higher because of special considerations. These include the extent of documentation, maintenance, and service to be provided by the licensor.

DOE GOCO laboratories are required to submit software to the agency's Energy and Sciences and Technology Software Center in Oak Ridge, Tennessee. For licensed software, these submission requirements apply in diminished form and will be a factor in setting the royalty structure.

9. Results of Federal Licensing

Table 6 provides a summary of federal patent and licensing activities for fiscal years 1981–90. The GAO/RCED report notes that, "according to Air Force, Army and Navy patent attorneys, their principal objective in patenting inventions has been to protect the U.S. Department of Defense's procurement programs from a patent infringement lawsuit by another organization that might subsequently make and patent an invention used in a defense weapons systems." 1991 GAO/RCED Rep. at 16. Note, however, that while the Air Force, Army and Navy filed 49 percent of the patent applications and received 57 percent of the patents issued to agencies and laboratories surveyed before fiscal years 1981 and 1990, they granted only 8 percent of the licenses. *Id.*

The report further stated:

> The federal agencies and contractor-operated laboratories surveyed have modestly increased the average number of patent licenses granted per year from 130 licenses per year between fiscal years 1987 and 1990. The agencies and laboratories also increased the percentage of licenses requiring royalty payments from less than 50 percent of the licenses granted in the early 1980s to 95 percent of the licenses granted in fiscal year 1990. This increase in federal patent licensing activity primarily reflects implementation of provisions in (1) the Patent and Trademark Amendments of 1980, which allow federal agencies to grant exclusive licenses; (2) 1984 amendments to the Patent and Trademark Amendments of 1980, which allow nonprofit organizations that operate Energy's contractor-operated laboratories, with few exceptions, to retain title to federally funded inventions they make; and (3) the Federal Technology Transfer Act of 1986, which allows federal inventors and laboratories to share in any royalty and other income earned on licensed patents.

Id.

Over the past ten years numerous changes in federal patent licensing have occurred. These changes, as listed in the GAO/RCED report, indicate that:

> [T]he percentage of exclusive licenses granted by the agencies and laboratories surveyed increased from only 6 percent of 173 licenses granted in fiscal year 1981 to 32 percent of 114 licenses granted in fiscal year 1986 to 41 percent of 191 licenses granted in fiscal year 1990. Federal patent licensing officials said that businesses generally seek an exclusive license to protect their investment in developing an invention into a commercial product.

Id.

Moreover, during fiscal year 1987, DOE approved modifications to the contracts for several of its contractor-operated laboratories that generally enable the contractors to retain title to and license inventions that they develop. *Id.* In the six years before this change took effect, DOE issued an average of nineteen licenses per year. *Id.* Since fiscal year 1987, DOE and its contractor-operated laboratories have issued an average of sixty-two licenses per year. *Id.*

In response to the royalty-sharing provisions of the Federal Technology Transfer Act, several agencies that formerly relied on NTIS to negotiate royalty-bearing licenses have expanded their own patenting and licensing activities. Between fiscal years 1981 and 1990, NTIS granted 310 licenses for NIH and other Health and Human Services patents, ninety-three licenses for Agriculture patents, twenty licenses for NIST and other Commerce patents, and two licenses for EPA patents. *Id.* Agriculture and EPA have begun to negotiate royalty-bearing licenses. *Id.* Similarly, in recent years NIH and NIST have filed more patent applications and while continuing to use NTIS, are assuming more control over the licensing decisions. *Id.*

Licensing of Defense inventions had minimal importance until the last two years, when Defense began to incorporate technology transfer into its mission in response to the Federal Technology Transfer Act of 1986. *Id.* 15 U.S.C. §§ 3701–3714 (1986). In fiscal years 1989

and 1990, the Air Force, Army, and Navy granted sixteen licenses per year and received $190,000 in license income per year. *Id.* During the five preceding fiscal years, they granted eight licenses per year and received only $31,000 per year in license income. *Id.*

The federal agencies and contractor-operated laboratories surveyed also increased their patent licensing income from $348,000 in fiscal year 1981 to $5 million in 1986 and $9.4 million in 1990. *Id.* Nonexclusive licenses that NTIS granted for two inventions made at NIH (a hepatitis B vaccine and an Acquired Immune Deficiency Syndrome test kit,) earned $22.6 million or 60 percent of the $37.5 million received from fiscal year 1981 through fiscal year 1990. *Id.* Furthermore, DOE contractor-operated laboratories have earned $4.8 million since they began licensing inventions in fiscal year 1987. *Id.*

The percentage of total licenses granted (269) to patent applications (1758) is 15.3 percent in 1991 vs. 9.04 percent (1416 licenses, 15,659 applications) in 1981–90. (See Table 8 for a listing of federal patent and licensing activities.) The recent increase in the ratio of licenses to applications may reflect both increased licensing activity and the practice of applying for a patent application after a potential licensee has been identified. In 1991 alone, 269 licenses were granted, 18.9 percent of the 1416 total in the decade of 1981–90. 1991 also reflects the trend toward granting more exclusive licenses on the part of a majority of the agencies. However, DOE and Health and Human Services, while increasing their licensing significantly in 1991, continued to grant a greater number of nonexclusive relative to exclusive licenses in 1991. These agencies have also become the two most active in federal licensing. Licensing income has also increased significantly in 1991 relative to the 1981–90 period, with the caveat shown in Table 7 for Health and Human Services.

Table 8 lists active CRADAs by federal agencies. Collection of this data began in 1987 and is provided since many of these agreements will result in future licenses for the industrial partners. Overall in 1991, 731 CRADAs were signed between companies and federal laboratories. Remember that the DOE-GOCO laboratories were not authorized to negotiate and conduct CRADAs until passage of the National Competitiveness Technology Transfer Act in November 1989. The majority of agencies exhibit increases in the number of active CRADAs. Agriculture is the clear leader with 177 CRADA's with Health and Human Services in second place with 144, and Energy just beginning to show its potential.

The steadily increasing patenting, licensing, and CRADA activity in recent years indicates that companies are responding to the government's invitation to acquire federal technology to improve their competitive position in world markets.

Table 1. Government Agency Initial Contacts for Technology Transfer and Licensing*

Agency	Contact	Tel. Number
Agriculture	W. Tallent	202/447-3973
Commerce	J. Paugh	202/377-8100
NIST**	D. Edgerly	301/975-4500
NTIS***	D. Johnson	703/487-4805
Defense	D. Appler	703/274-7913
Air Force	C. Chatlynne	703/695-3891
Army	C. Lanham	301/394-4210
Navy	R. Culpepper	703/696-4448
Energy	Ms. C. Langenfeld	202/586-3873
ESTSC+	M. Fomwall	615/576-1264
Environmental Protection Agency	L. Fradkin	513/569-7781
Health and Human Services	R. Adler	301/496-0750
Interior	D. Ralston	202/634-4857
NASA++	L. Ault.	703/557-5598
Transportation	J. Hohl	202/366-4978
Veterans' Affairs	L. Lorei	202/535-7159

* Courtesy Department of Commerce

** National Institute of Standards and Technology

*** National Technical Information Service

\+ Energy Sciences and Technology Software Center

++ National Aeronautics and Space Administration

Table 2. Energy's Government Owned, Contractor Operated (GOCO) Laboratories,* Technology Transfer Office Contacts**

Laboratory or Location	Operating Contractor	Phone Number**
Armas Laboratory	Iowa State Univ.	515/294-2635
Argonne Nat'l. Lab.	Univ. of Chicago	708/252-5361
Brookhaven Nat'l. Lab.	Associated Universities, Inc.	516/282-7338
Fermi Nat'l Accelerator Lab.	University Research Association, Inc.	708/840-3333
Idaho Nat'l Engineering Lab.	EG&G Idaho, Inc.	208/526-1571
Lawrence Berkeley National Laboratory	University of California	510/486-6502
Lawrence Livermore National Laboratory	University of California	415/422-6416
Los Alamos National Laboratory	University of California	505/667-3839
Oak Ridge National Laboratory	Martin Marietta Energy Systems, Inc.	615/574-4552
Pacific Northwest Laboratory	Battelle Memorial Institute	509/375-2789

Princeton Plasma Physics Laboratory	Princeton University	609/243-3009
Sandia National Laboratories	AT&T Technologies, Inc.	505/845-9407
Solar Energy Research Institute	Midwest Research Institute	303/231-7115
Stanford Unsar Accelerator Center	Stanford University	415/926-2213
Savannah River Laboratory	Westinghouse Savannah River Co.	803/725-3020

* from GAO/RCED-91-80, Federal Patent Licensing Activities, p. 15.

** Contacts derived from Technology '91, DOE/ER-0531P DE9200 4573, pp. 139-157.

Table 3. Technology Transfer Laws Since 1980

- Stevenson-Wydler Technology Innovation Act of 1980 (PL96-480). 15 U.S.C. § 3701-3714.
- Bayh-Dole Act of 1980 (PL96-517). 35 U.S.C. §§ 200-212.
- Federal Technology Transfer Act of 1986 (PL99-502). 15 U.S.C. §§ 3701-3714.
- Technology Competitiveness Act of 1988 (PL100-418).
- National Competitiveness Technology Transfer Act of 1989 (PL101-189). 15 U.S.C. § 2701-3710, as amended.
- American Technology Pre-Eminence Act of 1992 (PL101-245).

Table 4. Federal Laboratory Consortium Contracts

Administrator's Office
Dela Barre & Assoc.
Sequim, WA
206/683-1005

FLC Locator
Dr. A. Cowan
Sequim, WA
206/683-1005

Regional Contacts

Far West
Ms. Di Johnson
San Diego, CA
619/553-2101

Midwest
Dr. P. Betten
Argonne, IL
706/252-5361

Mid Continent
Mr. A. Norris
Jefferson, AZ
501/543-7516

Southeast
Mr. H. Wright
Knoxville, TN
615/632-6435

Northeast
Mr. A. Lupinetti
Atlantic City, NJ
609/484-6689

Mid Atlantic
Dr. R. Rein
Washington, D.C.
202/767-3744

Washington, DC Rep.
Dr. B. Berger
Washington, DC
202/331-4220

* *See* Dela Barre & Assoc., *Technology Transfer And The FLC*, March 1991).

Table 5. National Technology Transfer Center Contacts

Headquarters
Mr. L. Rivers
Wheeling, WV
304/243-2455

Far West
Mr. R. Stark
Los Angeles, CA
213/743-6132

Mid-West
Dr. J. Ray
Cleveland, OH
216/734-0094

Mid-Continent
Mr. G. Sera
College Station, TX
409/845-0538

Northeast
Dr. W. Gasko
Westborough, MA
508/870-0042

Mid-Atlantic
Ms. L. Hummel
Pittsburgh, PA
412/648-7000

Southeast
Mr. J. Thornton
Alachua, FL
904/462-3913

Table 6. Federal Patent and Licensing Activities for Fiscal Years 1981–1990
(Dollars in thousands)

Agency	Patent applications	Patents issued	License Granted: Nonexclusive	License Granted: Exclusive	License Income
Agriculture	506	421	166	26	$148
Commerce					
NIST*	86	53	0	0	0
NTIS*	0	0	259	194	30,226
Defense	7,742	6,371	64	46	682
Energy**	4,411	2,405	239	122	5,629
Environmental Protection Agency	20	11	0	1	3
Health and Human Services	986	266	0	0	0
Interior	215	187	32	0	0
NASA	1,559	1,276	136	65	652
National Science Foundation	0	0	0	0	0
Tennessee Valley Authority	117	68	85	1	174
Transportation*	22	18	0	0	0
Veterans Affairs*	5	***	0	0	0
Total	15,669	11,075	981	455	$37,514

* NTIS licenses patents for several federal agencies including Agriculture, Commerce, the National Security Agency in Defense, EPA, Interior, the Public Health Service in Health and Human Services and Veterans Affairs. About $36 million, or 96 percent of NTIS' licensing revenue was earned from nonexclusive licenses, including $22.6 million from AIDS test lot and Hepatitis B vaccine licenses.

** Includes data from sixteen contractor-operated laboratories on patent applications filed, licenses granted, and license income. Data on patents issued to the laboratories were not available.

*** Date not available.

Source: GAO compilation of agency data.

Table 7. Federal Patent and Licensing Activities for Fiscal Year 1991*

Agency**	Patent applications	Non-exclusive	Exclusive	Total	License Income***
Agriculture	110	3	26	29	$863
Commerce	18	2	0	2	26
Defense					
Airforce	N/A	N/A	N/A	N/A	39
Army	274	3	14	17	96
Navy	467	6	9	15	130
Energy	397	96	29	125	3,193
Environmental Protection Agency	8	0	2	2	74
Health and Human Services	261	53	16	69	13,384****
Interior	21	0	5	5	58
NASA	201	1	4	5	292
Transportation	1	0	0	0	—
Veterans Affairs	N/A	0	0	0	—
TOTAL	1758	164	105	269	18,155

* Derived from Tables 3, 4 and 5, of the Second Biennial Report of the Federal Technology Transfer Act of 1986, prepared by the Department of Commerce for Release in the Summer of 1992.

** Agencies using Federal Technology Transfer Act of 1986. These provisions did not apply to Energy until late 1989.

*** Licensing income shown in thousands of dollars.

**** Includes nonrecurring funds from settlements of disputes over distribution of royalties from Aids test kits.

Table 8. Active CRADAs by Federal Agency*

Agency	Fiscal Years 1987	1988	1989	1990	1991
Agriculture	9	51	98	128	177
Commerce	0	9	44	82	115
Defense:					
Air Force	0	2	7	13	26
Army	2	9	32	80	115
Navy	0	0	2	20	52
Energy**					
Environmental Protection Agency	0	0	2	11	31
Health and Human Services	22	28	89	110	144
Interior	0	0	1	12	11
Transportation	0	0	0	1	9
Veterans Affairs	0	0	1	2	8
TOTALS	33	99	276	460	731

* 2nd Diennual Report of The Federal Technology Transfer Act of 1986, Department of Commerce, Summer 1992.

** The majority of DOE laboratories were not covered under the FITA until 1989.

PERSPECTIVES ON TECHNOLOGICAL COMPETITIVENESS

By Harvey Drucker

Argonne and I, for various reasons, are generally interested in technology transfer and specifically interested in the development of commercial technology from basic and applied research in biology and medicine.

One of my responsibilities at Argonne probably accounts for my generic interest. I have Lab-wide responsibility for Technology Transfer; that is, the conversion of discoveries made through tax-supported research into commercial products or services which benefit the general public. Technology transfer has been recognized by our primary research sponsor (The Department of Energy); by congress, and increasingly, by industry, as a key element in the nation's efforts to improve its technological competitiveness.

As for my specific interest, as associate director for Energy and Environmental Science and Technology, the Argonne Center for Mechanistic Biology falls within my purview. We have a very active group developing methods for genomic sequencing based on DNA hybridization; we will be running what I consider the principal user facility for structural biology in the United States sometime in 1996 (the Structural Biology Center at the Advanced Photon Source) and are in process of developing a computational biology group which we hope will provide the paradigms; the software and hardware for converting complex biological data into simple chemical and medical technology.

Anyone who reads the newspaper or looks at television broadcasts has to be aware that the nation is in economic trouble. Politicians -- from the President to County Commissioners -- either wring their hands or claim victory based upon tenths of percent changes in employment; GNP: balance of payments.

Joblessness makes good copy when there isn't a beached whale or a middling quality murder to report. In fact, however, the headline and the vote values reflect an underlying weakness in the American Economy.

It started a decade ago when we lost our market dominance in what were then called the basic industries -- like steel and automobiles. First we lost in international markets. Then we lost in our own home markets.

Next we fell behind in the high tech markets, like consumer electronics and computers.

Underlying this loss of markets was a destructive cycle in which weakened financial position led to lower investment in research and development which led to further loss of market which led to further financial weakness. This cycle was aggravated by a decade of takeover sharks threatening leverage buy out; corporations taking poison pills, and a corporate focus foreshortened down to the next quarterly dividend. Add to this ferment a work force no longer at the definitive edge in literacy and mathematics; and basic industrial technologies that require less hands but greater training. Throw in laws and regulations on environment and the workplace that are not universal and you have the makings of a very bad brew.

Last year, the National Science Board reported that American spending for research and development has started to fall for the first time since the 1970s. At the same time, foreign rivals have increased their investments in research.

Annual national expenditures for research and development fell from $154.3 billion in 1989 to $151.6 billion in 1990. Preliminary analysis indicates that the 1991 and 1992 totals might be down even further.

At the same time Japan has now equaled or surpassed the United States as the world's top patron of industrial research and development according to the Competitiveness Policy Council created by Congress. It might be worth recalling that Japan's R&D budget overwhelmingly addresses civilian research, thus causing an even greater disparity in terms of potential market impact for their dollars versus ours.

There are many reasons for this loss of competitive position. But one which is the target of heavy public attention and heavy criticism is our traditionally poor integration between publicly-funded R and D and privately-funded R and D. We look especially sad compared to the Japanese, where such integration is part of the political and economic culture.

We have not had close collaboration between research universities, national laboratories, research hospitals and corporations. Historically we haven't needed it.

For most of the modern era, our publicly-funded R and D centers were the acknowledged world's champions in basic research. Corporations were acknowledged world champions in industrial applications. The traditional theory seemed to be working: that the discoveries would be made in the public sector and trickle down through some intellectual flow of gravity to industry and the public. This is still true to some extent in medical R and D -- pharmacology, machinery; prosthesis.

Unfortunately, we held on to our belief in that philosophy long after our loss in world markets indicated that it wasn't working well enough. Meanwhile, decades of separation between federal labs, universities, and corporations had fostered psychological and legal barriers between them.

Three distinct species of elitism worked against that collaboration.

Most industrial research organizations were permeated with the suspicion that solutions that did not come from the in-house organization probably were of questionable validity in terms of ultimate market application. Many universities let traditional concern for academic freedom interfere with the role they could play in industrial support. Research hospitals tended to limit their collaboration with their related universities. And national laboratories were slow giving up their self image as free-standing centers of scientific and technological expertise. Federally funded researchers were to put new technologies on the shelf and let customers pick and choose; not to consider potential applications of inventions and pursue customers.

In addition, an array of legal hurdles had been raised.

One was the uniquely American set of anti-trust laws and attitudes. It blocked research collaboration of many kinds. It made corporate research and legal executives chary of involvement with publicly-funded R and D. We had no creatures like Mitsubishi Shoji; trading companies that could cross technological lines easily and bring semiconductors to watches; ceramics to scissors. Further, in our recent history, we have -- at least for civilian purposes -- not mixed government and industry well. One has the distinct sense that an adversarial relationship exists between government and industry.

Another was the apparently logical prohibition in federal government against granting to one company the exclusive rights to discovery that had been paid for by everyone's tax money. The only flaw was that no company would invest the money needed to convert a scientific discovery into a market-ready product unless their proprietary rights were protected. The result was that in saying the discovery belonged to everyone, we ended up having it exploited by no one.

Congressmen and federal administrators had this mortal fear of government technology making someone rich. What if -- perish the thought -- federally funded technology resulted in a Xerox or a Polaroid? If we give invention to everyone, it lowers the chance that anyone will become disgustingly wealthy.

But times are changing. We may be entering an era where the transmission of knowledge to the private sector is a blessed event -- especially if it creates jobs for Americans, and even if it should provide a few minor country estates.

What are some of these changes?

Well, for one thing, agencies like the Department of Energy have done a U-turn in attitude about proprietary rights. Corporations now can protect resources invested to develop a discovery made at a national laboratory.

One of the newest and best mechanisms to accomplish this is a program of cooperative research and development agreements, or CRADAs. Under these agreements, Argonne and the corporation provide an investment of resources (most of the time co-equal) in an approved project. The company retains proprietary rights and has its information protected.

For example, Argonne is currently negotiating more than 70 CRADAs. We have some thirty of them signed. They include:

- Baxter Health Care — blood
- Notre Dame — bugs to eat contamination in soil
- Caterpillar — inspection of ceramic-coated engine parts
- Allied Signal — ceramic erosion in engines and petrochemical pumps.

Another example of a change is one pioneered by Argonne. We fostered the organization of the Midwest Plant Biotechnology Consortium with 16 midwestern universities and 35 agri-business corporations.

We originally called a meeting of this group at which industrial representatives specified major problems that could be solved with scientific research. The universities and Argonne chose those they believed they had a capability to solve. A series of partnerships was formed with the corporations and grants focused on each problem were awarded based upon relevance to application and technical excellence.

Since 1988, we have averaged about $4 million per year to fund such research. In 1992, a new activity involving bulk chemical production through biotechnology was funded at about this same level.

A traditional area of cooperation with non-Argonne researchers has been in our "user facilities." These are giant research machines that are too expensive to put into every campus or industrial park. Instead, the nation has the national laboratories build and operate them. But they are open to use by researchers from industry, hospitals, universities or other national labs.

Currently, Argonne is building what we believe will be the most effective user facility that the nation has ever constructed. It is a $456 million accelerator called the Advanced Photon Source. It will generate the world's most brilliant X-rays for materials research.

More than 300 scientists and engineers will perform as many as 100 different experiments at one time on the machine.

These X-ray beams, 10,000 times brighter than those at existing X-ray sources, will reveal the atomic and molecular structure to improve America's competitiveness in such areas as steels, medicine, semi-conductors, polymers, pharmaceuticals and catalysts. The APS has attracted more industry participation in its planning stages than any previous basic research facility built in this country.

One demonstration of its value to industry is the creation of a consortium by 13 pharmaceutical companies to build and operate its own beam lines at the Advanced Photon Source. We have started a precursor of our Structural Biology Center at the National Synchrotron Light Source at Brookhaven National Lab, and this same group of companies are purchasing time at this facility.

Another indicator is that both Japan and Europe are rushing forward to put up their own version of this powerful X-ray source to support their science and industry.

I can offer another Argonne example which must have the trust-busters rolling over in their graves. It is the current Battery Research Program conducted by the Department of Energy. The bulk of that research funding will go to a collaboration with the Big Three auto makers called the United States Advanced Battery Consortium or USABC. The industry will match funds with the national laboratories and their associated institutions to develop better batteries, better vehicles and especially, concepts which will, and I quote, "take the automobile out of the environment equation."

Recently General Motors on its own conducted what it called a "garage sale." The national labs were invited to bring in all their good ideas through displays, literature and personal representatives. G.M. research teams engaged in intensive "shopping" at this pioneering bazaar.

We have also chartered ARCH, or the Argonne-University of Chicago Development Corporation, to foster commercialization of scientific discoveries made at the university and Laboratory. It negotiates with corporations to license inventions and patents, to set up joint ventures or to establish new companies.

But enabling legislation, and pioneering mechanisms for tech transfer are not enough. As I mentioned earlier, a major barrier to effective collaboration has been the differences that exist between the cultures of the parties to these partnerships.

To collaborate effectively, it is essential that each of us get to know the strengths and peculiarities of the other kinds of institutions.

A university researcher who disdains constant concern with market response is bound to have trouble working with an industrial research partner. A corporate researcher with no tolerance for federal bureaucracy has a hard row to hoe to work cooperatively with a national lab. And an Argonne researcher who is unaware of university sensitivity to dominance by big federal institutions probably is going to strike out in his dealing with his research and development partners from such institutions.

What might all of this mean for those interested in the human genome and/ or in the development of commercial technologies from genomic research. First, the good news:

Per my comments, there are now contractual instruments and technology transfer models that, with a little bit of work, should be adaptable to new private sector ventures in biology .

Second, These instruments and models are being used. Companies are getting exclusive rights to intellectual property and information is being held proprietary.

Third, there is a change in attitude on the part of the federal labs, their sponsors, and their technical staff. They are looking to make deals.

A few words on the other side of the coin.

There is a growing federal bureaucracy involved in technology transfer. Office upon office seems to be involved in issues like conflict of interest, foreign preference, dissemination of profits. If anything can destroy technology transfer; especially to small businesses with infinite legal budgets, this is it.

Second, federal labs now have no specific pots of money for codevelopment of technologies. Work that departs from proposed effort requires a separate dispensation. Good ideas thus can be stalled or stopped while an agency waits for the next fiscal year or Congress considers budgets.

Third, the message on technology transfer is not a monolith. Different institutions and their scientists are accepting or rejecting work with industry based upon their histories, their interpretations of law; their perception of the sponsor's attitude.

Overall, however, especially in areas where research is far ahead of development like the human genome, things are looking good. We invite you to Argonne, Los Alamos, Oak Ridge and the other brethren. You just might find something interesting.

THE HUMAN GENOME PROJECT AND THE DOWNSIDE OF FEDERAL TECHNOLOGY TRANSFER

Christopher J. Harnett(1)

Introduction -- Technology Transfer at NIH

In adopting a technology transfer policy largely dictated by the Federal Technology Transfer Act of 1986(2) ("FTTA"), the National Institutes of Health ("NIH") has increasingly encouraged collaborations between its researchers and private industry. Indeed, under the FTTA, technology transfer is regarded as an essential part of a researcher's job description, and promotion and positive job performance evaluation are contingent upon successful technology transfer efforts.(3) The FTTA also provides financial incentives for government scientists to transfer technology to the private sector.(4)

By signing the FTTA into law, the Reagan administration sought to increase the return on the nation's

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(1) Mr. Harnett is an associate with the law firm of Fish & Neave in New York. The views expressed in this article are those of the author and do not reflect or suggest the views of Fish & Neave or any of its clients.

(2) The Federal Technology Transfer Act of 1986, Pub.L. No. 99-502, 100 Stat. 1785 (codified at 15 U.S.C. § 3710 (1986)).

(3) Id., at 15 U.S.C. § 3710(a)

(4) 1992 PHS Technology Transfer Directory, NIH/ADAMHA/CDC/FDA, Office of Technology Transfer, National Institutes Of Health Bethesda, Maryland.

research and development investment by generating new products and processes and by enhancing international competitiveness.(5) Furthermore, the Reagan administration predicted that the FTTA would be viewed in retrospect as "one of the seminal developments in the history of federal efforts to put technology to work for the taxpayers who paid for it" even though the Act challenged "long held views on the proper role of Federal laboratories and scientists".(6)

Since the implementation of the FTTA, NIH/industry collaborations have flourished. The NIH reports that, as of July 1992, its researchers were actively involved in 87 separate Cooperative Research and Development Agreements (CRADAs) with collaborating companies.(7) According to NIH, CRADAs are instrumental in achieving the FTTA's objective of assisting "universities and the private sector in broadening our national technological base by moving new knowledge from the research laboratory into the development of new products and processes."(8)

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(5) R. Mosbocher, The Federal Technology Transfer Act 1986: The First Three Years, Report To The President And The Congress From The Secretary Of Commerce, July 1989.

(6) Id. at 2.

(7) See, supra, note 4.

(8) NIH/ADAMHA/CDC Policy Statement On Cooperative Research and Development Agreements And Intellectual Property Licensing, NIH Office of Technology Transfer, Bethesda, Md.

While promoting introduction of new products and enhancing American competitiveness through commercialization of federally-funded biomedical research are legitimate public policy goals, commentators have noted that there is a distinct downside to the technology transfer policies embodied by the FTTA. For example, as implemented by NIH, the provisions of the FTTA inappropriately influence the direction of biomedical research. By placing an inordinate premium on research with immediately apparent commercial rewards, the FTTA policies tend to skew the direction of research decidedly away from basic scientific investigation. Over the long run, the FTTA policies threaten to adversely affect the continued vitality of the federal biomedical research establishment.(9) Furthermore, mandatory collaboration between federal researchers and private industry may have a corrupting effect on NIH research by magnifying the potential for conflicts of interest and restricted dissemination of information among scientists.(10)

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(9) See, Harnett, "Federal Technology Transfer: Should We Build Subarus in Bethesda?", 1 RISK - Issues In Health & Safety 313 [Fall 1990].

(10) See, e.g., Bass, "Privately Funded Research May Breed Conflicts", United Press Intn'l, June 13, 1989; Booth, "NIH Scientists Agonize Over Technology Transfer", 243 Science 20, 21 (January 6, 1989); Culliton, "NIH, Inc.: The CRADA Boom", 245 Science 1036 (September 8, 1989).

The foregoing problems associated with the FTTA's policies are evident in current NIH research initiatives, including the Human Genome Project. Indeed, the recent controversial NIH decision to file applications seeking patent protection for more than 2,700 partial complementary DNA ("cDNA") fragments has been met with warnings that pursuing such patents will have a negative impact on the international cooperation and open communication between genome scientists necessary for the prompt and successful completion of the Human Genome Project.(11) Critics also note the potential for conflicts of interest(12) and distortions in the conduct of basic biomedical research(13) as a result of the NIH patenting decision.

Analysis of the NIH cDNA patenting decision reveals yet another problem: the existence of patent rights to the partial cDNA fragments, and any attempts by NIH to license those rights, may significantly impede development of related products. This potential impediment to product development will be discussed in detail below.

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(11) See, e.g., Leslie Roberts, "Genome Patent Fight Erupts," 254 Science 184 (October 11, 1991).

(12) See, e.g., Christopher Anderson, "Genome Project Goes Commercial," 259 Science 300 (January 15, 1993).

(13) See, Statement of the National Institutes of Health Department of Energy Subcommittee for Interagency Coordination of Human Genome Research, January 3, 1992.

Using the NIH decision to pursue the cDNA patents as a case study, this article will argue that the NIH decision reflects an inappropriate merger of NIH interests with the interests of the private biotechnology industry. Because the FTTA mandates collaborations between federal scientists and private industry, it is inevitable that NIH will confuse its proper technology transfer goals with the commercialization interests of private sector collaborators. NIH justifies its controversial patenting decision as an attempt to provide an incentive for private industry to commercially develop products related to the partial cDNA fragments. That decision may, therefore, be viewed as a natural and predictable outgrowth of federal technology transfer policies. However, implementation of such policies may impede development of related products, thereby subverting one of the primary objectives of the FTTA. In light of this potentially paradoxical result, NIH should reexamine its implementation of FTTA policies.

NIH's cDNA Patent Applications

As noted above, NIH has been widely criticized for filing applications in June 1991 and February 1992 seeking patent protection for partial cDNA sequences identified by Dr. Craig Venter, then a genome project researcher working at the National Institute of Neurological Disorders and Stroke. Those patent applications are directed to, inter

alia, approximately 2,700 expressed sequence tags (ESTs) that were isolated from commercially available and custom-made cDNA libraries. ESTs are short cDNA sequences, about 150-400 base pairs in length that correspond to the coding sequence of an expressed gene.(14) The ESTs described in the Venter applications correspond to individual genes expressed in the human brain.

Using conventional techniques, ESTs can serve as a starting point to fully sequence corresponding expressed genes. While ESTs indicate that a gene exists and is expressed, they do not shed light on the biological activity or function of that gene.

Both Venter patent applications claim the 2,700 expressed sequence tags, the full length genes corresponding to the ESTs, and miscellaneous antisense oligonucleotides

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(14) By way of simplified relevant background, individual genes comprise: regulatory regions including a promoter that directs expression of the gene; a coding region that can code for a polypeptide; and a termination signal. Gene expression proceeds from DNA to messenger RNA (mRNA) to a polypeptide. mRNA can be converted to double stranded cDNA in a two step process by reverse transcriptase and a DNA polymerase.

The coding regions of genes may be discontinuous: coding sequences known as exons may alternate with non-coding regions known as introns. The mRNA includes exons but does not include introns. A full length cDNA, therefore, is a double stranded DNA copy of a mRNA that contains all of the exons of a gene. ESTs such as those described in the Venter applications are partial cDNA sequences that can be used to identify the full-length cDNA "clone" of an expressed gene.

and triple helix probes. The June 1991 application also claims proteins coded by the genes.

Critics of the NIH patent decision argue that because Venter's ESTs do not teach the biological activity of the gene, attempts to obtain broad patent protection based on those ESTs are premature and inappropriate. For example, Nobel laureate Paul Berg commented that "patenting bits and pieces of sequence that are meaningless functionally ... makes a mockery of what most people feel is the right way to do the Genome Project."(15)

NIH, however, has justified its decision to file patent applications as an effort to promote the public good and to fulfill NIH's statutory technology transfer obligations and objectives.(16) Reid G. Adler, Director of

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(15) Leslie Roberts, "NIH Gene Patents, Round Two", 255 Science 912 (February 21, 1992). Even more strident were the comments of another Nobel laureate, James Watson, who expressed horror over NIH's attempt to obtain patent protection for Venter's ESTs because, in Watson's view, using commonly available automated sequencing machines "virtually any monkey" could identify ESTs. See, supra, note 11.

(16) Remarks of Dr. Bernadine Healy at the Fourth Annual PHS Technology Transfer Forum, November 14, 1991. Dr. Healy commented that "NIH has a record of utilizing the patent system in a socially responsible way. When NIH does move into the patent arena it is with the public good as a driving force and not because scientists want to get rich." Dr. Healy also noted that "the real concern" would be if a big pharmaceutical company got all of the gene patents. Developments since November 1991 demonstrate that the NIH decision to pursue partial cDNA sequence patent did not preclude private concerns from following suit. For example, Incyte Pharmaceuticals Inc., of Palo Alto, California is

(continued...)

the NIH Office of Technology Transfer, reported that the decision was motivated by a desire to protect Venter's invention "early enough to give meaningful patent protection to companies that might seek a license from NIH."(17) Indeed, NIH's efforts to license the Venter invention commenced within months of filing the first application.(18)

Moreover, NIH was concerned that publishing Venter's discoveries and data without first filing patent applications might render obvious and unpatentable future discoveries such as the elucidation of whole genes corresponding to Venter's ESTs.(19) NIH feared that the potential loss of patentability for future discoveries would create a disincentive for companies to perform the subsequent research necessary to bring valuable products to market.(20)(21)

(16)(...continued)
reportedly planning to file patent applications for as many as 100,000 cDNA sequences a year. See, Anderson, supra, note 12.

(17) See, supra, note 11 at 185.

(18) Id.

(19) A thorough discussion of the merits of this concern is beyond the scope of this article. For a discussion of this topic, see, e.g., Reid G. Adler, "Genome Research: Fulfilling The Public's Expectations For Knowledge And Commercialization," 257 Science 908 (August 14, 1992); Rebecca S. Eisenberg, "Genes, Patents, And Product Development," 257 Science 903 (August 14, 1992).

(20) See, supra, note 11.

(21) Testimony of Dr. J. Craig Venter before the Senate
(continued...)

The NIH justification for filing the Venter patent applications is troublesome because it suggests that NIH actions are driven by the commercial concerns of its private sector collaborators. As a public institution with its primary mission "to conduct biomedical ... research that will lead to the better health of the American people"(22), it seems inappropriate for NIH to predicate major policy decisions on the desire to insure the existence of meaningful licenses for its private sector collaborators, and to preserve the existence of future exclusive rights for those collaborators(23). The troublesome nature of the NIH cDNA patent decision extends beyond philosophical concerns about the proper role of the NIH vis a vis private industry -- there are practical implications as well. Because of the undeveloped nature of the Venter technology, there is little likelihood that NIH patenting and subsequent licencing efforts will effectively advance the commercial development of related products. In fact, as will be discussed below, the existence of any patent or licensing

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(21)(...continued)
Judiciary Subcommittee on Patents, Copyrights and Trademarks, September 22, 1992.

(22) See, supra, note 4.

(23) See, Association of Biotechnology Companies Statement on NIH Patent Filing for the Human Genome Project (Association of Biotechnology Companies, Washington, D.C., May 1992): "Whether future patent claims are obtainable ... is not the concern of the NIH, which should not become engaged in schemes designed to ensure future exclusivity."

rights is likely to impede commercial development of clinically useful products and processes related to Venter's discoveries.

Possible Scope of Patent Protection

NIH's ability to license the Venter technology depends, in large measure, on the scope of the claims, if any, that are eventually allowed by the Patent Office. In its initial response to the Venter applications, the Patent Office reportedly(24) rejected the NIH claims because they did not satisfy the three fundamental requirements for patentability -- novelty, utility and non-obviousness.(25) The NIH was expected to file a response to the initial Patent Office rejection by February, and a final decision of the Patent Office would then be expected in late 1993 or early 1994.

Because Venter's partial cDNA sequences do nothing to elucidate the biological activity of the genes, the issue of patentable utility with respect to the Venter disclosure has drawn considerable attention from commentators.(26) NIH argues that the Venter invention has patentable utility

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(24) See, Leslie Roberts, "Rumors Fly Over Rejection of NIH Claim," 257 Science 1855 (September 25, 1992).

(25) See, 35 U.S.C. §§ 101, 102 and 103.

(26) See, e.g., Thomas D. Kiley, "Patents on Random Complementary DNA Fragments?," 257 Science 915 (August 14, 1992).

because the disclosed partial cDNA sequences can be used: 1) as polymerase chain reaction (PCR) primers; 2) to isolate the coding sequence of cDNAs; 3) to isolate complete genes; 4) to determine the position of genes on the human chromosome; 5) to produce antisense oligonucleotides and triple helix probes; and 6) in forensic applications.(27)

While the utility requirement is typically considered a low hurdle to patentability,(28) the United States Supreme Court has held that the utility requirement is not satisfied if an invention is useful only in research.(29) If, therefore, the Patent Office believes that Venter's sequences are useful merely as a means for making discoveries, the claims may be rejected for lack of utility.(30) Moreover, the Patent Office has, on occasion, applied unusually stringent utility standards to promote what it considers to be public policy objectives.(31)

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(27) Patent application of Craig Venter, "Sequences Characteristic of Human Gene Transcription Product." A partially redacted version of this patent application is publicly available through the NIH Office of Technology Transfer.

(28) See, e.g., Stiftung v. Renishaw PLC, 945 F.2d 1173 (Fed. Cir. 1991); Envirotech Corp. v. Al George, Inc., 730 F.2d 753 (Fed. Cir. 1984).

(29) Brenner v. Manson, 383 U.S. 519 (1966).

(30) Id. at 383 U.S. 536, "But a patent is not a hunting license. It is not a reward for the search, but a compensation for its successful conclusion."

(31) The Patent Office has recently adopted an informal

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Considering the high-profile and controversial nature of the present case, the Patent Office may again be inclined to apply stringently the utility standard.

As noted above, the claims of both Venter patent applications encompass much more than the disclosed ESTs. The specifications of the Venter applications describe, in detail, procedures for identifying and sequencing the ESTs, procedures for identifying the sequence of a gene using an EST as a starting point, and procedures for accomplishing gene expression. The Venter disclosure, however, does not identify the full length sequence of previously unknown genes, identify the polypeptides coded by those genes, or teach the biological activity of those genes or polypeptides. As such, there is considerable doubt that Venter will be entitled to claims directed to full length genes or polypeptides coded by those genes.(32) Indeed, recent case law suggests that, even assuming the novelty, utility and nonobviousness standards are satisfied, Venter would not be entitled to claims that extend much beyond the

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(31)(...continued)
"policy" under which claims directed to treatment of HIV infection are rejected for lack of utility where the claimed effectiveness is supported only by in vitro data. See, e.g., In re Balzarini, 21 USPQ2d 1892 (B.P.A.I. 1991); A similar "policy" relating to anti-cancer compounds in the 1970s was brought to an end by In re Jolles, 628 F.2d 1322 (C.C.P.A. 1980).

(32) See, e.g., Rebecca S. Eisenberg, "Genes, Patents, and Product Development," 257 Science 903 (August 14, 1992).

specifically disclosed ESTs.(33) Thus, it appears that even if NIH can prevail on the issue of utility, the scope of the claims that may be allowed are likely to be substantially narrower than the claims filed in Venter's applications.

Possible Licensing Consequences

Federal patent laws in effect since 1980 have permitted and encouraged licensing of government owned patent rights.(34) Under the FTTA, federal laboratories can agree to grant intellectual property rights in advance to collaborators who are party to a CRADA.(35) The NIH technology transfer policy relies heavily on the patent system, and in its general licensing policy, NIH states that, "Congress and the President have chosen to utilize the patent system as the primary mechanism for transferring Government inventions to the private sector."(36) Indeed, NIH officials have suggested that patent protection for the cDNA sequences is necessary to induce potential licensees to commit the time and financial resources to develop

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(33) See, e.g., Fiers v. Revel, 984 F.2d 1164 (Fed.Cir. 1993); see also Amgen Inc. v. Chugai Pharmaceutical Co., 927 F.2d 1200 (Fed.Cir. 1991)

(34) See, Government Patent Policy Act of 1980, P.L. 96-517, 94 Stat. 3015 (codified at 35 U.S.C. § 200-212 (1990)).

(35) See, supra, note 4 at 307, 309.

(36) See, supra, note 4 at 309.

commercially viable products derived from the NIH's cDNA discoveries.(37)

Federal statutes directed to technology licensing balance the need for exclusivity to induce commercial development against the possible adverse consequences of an unnecessary monopoly. Consequently, NIH licensing policies, in most circumstances, favor non-exclusive licenses over exclusive licenses.(38) However, consistent with a fundamental principle of the patent system(39), NIH is willing to "grant exclusive commercialization licenses under their patent or other intellectual property rights in cases where substantial additional risks, time and costs must be undertaken by a licensee prior to commercialization."(40)

Federal law, however, permits a federal agency to license its inventions on an exclusive basis only if it is determined that: 1) the public interest is served by the

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(37) Testimony of Dr. Bernadine Healy before the Senate Judiciary Subcommittee on Patents, Trademarks and Copyrights, September 22, 1992.

(38) See, supra, note 4 at p. 310.

(39) See Loctite Corp. v. Ultraseal Ltd., 781 F.2d 861 (Fed. Cir. 1985), "The patent system, which is rooted in the United States Constitution serves a very positive function in our system of competition, i.e., 'the encouragement of investment based risk.'" (citations omitted); U.S. Const. Art 1. Sec. 8, Cl. 8: "The Congress shall have power ... to promote the progress of science and useful arts, by securing for limited times to authors and inventors exclusive right to their respective writings and discoveries."

(40) See, supra, note 4.

exclusive license in light of the prospective licensee's plans and ability to promote the public's utilization of the invention; 2) the practical development of the invention has not or is not likely to be expeditiously achieved under a non-exclusive license; 3) the exclusive license is required to attract capital and stimulate interest needed to develop the invention; and 4) the proposed scope of the exclusive license is not broader than is necessary to accomplish development of the invention.(41) Moreover, NIH reserves the right to revoke an exclusive license if the licensee fails to make reasonable progress in developing the invention or if the licensee cannot satisfy unmet public health needs.(42)

Attempts by NIH to license any patent that may issue from the Venter applications will be problematic. As discussed above, the claims of such a patent are likely to be narrow. One commentator has suggested that claims limited to the specifically disclosed ESTs and their equivalents may not be "broad enough to offer effective protection to firms seeking to bring related products to market...."(43) The private sector, therefore, may not be interested in licensing the Venter technology, either

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(41) 35 U.S.C. § 209(c)(1); see also 37 C.F.R. § 404.7.

(42) See, supra, note 4 at 311.

(43) See, supra, note 32.

exclusively or non-exclusively. As such, the NIH patent protection will do nothing to advance the development of commercial products or processes and may indeed hinder such developments by contributing to the "thicket of patent rights that firms must negotiate their way past before they can get products on the market."(44)

On the other hand, if NIH is somehow entitled to broader patent coverage (or if private sector participants are nonetheless interested in licensing a narrow NIH patent), then NIH must determine whether an exclusive or non-exclusive license is appropriate. Because the vast majority of the 2,700 genes corresponding to Venter's EST's are not likely to be immediately significant for clinical applications, the Venter patent applications clearly present a situation where substantial (and risky) expenditures of time and money are necessary before any commercially viable product may be marketed. Therefore, potential licensees may not be inclined to expend resources without an exclusive license.

As discussed above, the technology disclosed and claimed in the Venter applications is not well developed and encompasses vast subject matter -- Venter's claims may

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(44) Id. at 904. See also, Leslie Roberts, "Scientists Voice Their Opposition," 256 Science 1273 (May 29, 1992). Michael Roth, a patent attorney at Pioneer Hybrid comments that the NIH patent approach "does not build a road to further advances, it just builds a toll booth along the way."

theoretically "read on" approximately 5% of all expressed human genes. An exclusive license to use Venter's EST's would, therefore, provide an extreme disincentive for non-licensees to investigate the biological significance of the 2,700 expressed genes and polypeptides corresponding to Venter's partial cDNA sequences. Such a disincentive may result in a "meta-monopoly" whereby a single entity would acquire de facto dominion over the eventual identification of 2,700 genes, their gene products and methods of exploiting their biological activity. Such a meta-monopoly may run afoul of the patent licensing laws(45) and would do nothing to promote development of useful products.(46) Exclusivity over Venter's discoveries may bring about a result decried by the Supreme Court in Brenner v. Manson:

> Such a patent may confer power to block off whole areas of scientific development, without compensating development to the public. The basic quid pro quo contemplated by the Constitution and the Congress for granting a patent monopoly is the benefit derived by the public from an invention with substantial utility. Unless and until a process is developed to this point--where specific benefit exists in currently available form--there is insufficient justification for

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(45) 35 U.S.C. § 209

(46) Craig Venter himself states that "The patent system wasn't designed to give me and a small group of people ownership of half the genome." See, supra, Roberts at note 44.

> permitting an applicant to engross what may prove to be a broad field.(47)

Thus, either exclusive or non-exclusive licensing schemes for any patents issuing from the NIH applications may stand in the way of ultimately developing clinically useful products related to Venter's ESTs. NIH should, therefore, seriously consider dedicating the Venter technology to the public as a means to ensure widespread access to that technology and to best eliminate impediments to the ultimate development of clinically significant products.

Conclusion

The NIH decision to seek patent protection for Dr. Venter's substantially undeveloped discoveries demonstrates that NIH's technology transfer activities are driven by the commercial objectives of its private sector collaborators. Merger of NIH and private sector objectives is an inevitable consequence of the NIH's implementation of the FTTA. Such a merger threatens to shift the focus of NIH research, compromise the objectivity of that research and, in certain circumstances, impede the ultimate introduction of products ultimately developed from NIH research. Therefore, NIH policies such as the cDNA patent decision

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(47) See, supra, note 29 at 534-535.

that overzealously promote private commercial interests should be reconsidered.

This author believes that the progress of science and the interests of the public are best served by maintaining NIH as an objective research institution rather than a vehicle for advancing the commercial interests of private biomedical research concerns. The biotechnology industry does not need NIH to protect its commercial interests -- those interests are adequately protected by numerous individual private companies and by their lobbying groups. The public, however, does need NIH to continue to perform high-level objective research in order to preserve the United States' status as the world leader in biomedical sciences.