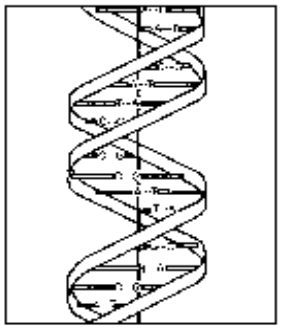
Introduction 1

Practical application of federally funded research depends on transferring technology to industry, whose laboratories translate intellectual property into commercial products that benefit the economy and society. This is often, but not always, accomplished through the patenting and licensing of research results (31). Unless guaranteed some measure of market exclusivity via intellectual property protection, most companies are reluctant to invest the millions of dollars and time required to develop and fine tune inventions from federally funded research (1,33,79).

Today, the United States enjoys the economic benefits of an industrial biotechnology sector unmatched worldwide. This success stems from, in part, U.S. patent law and the success of federal technology transfer of biomedical research over the past 15 years (84,85). More recently, scientists around the world have undertaken an estimated 15-year, $3 billion initiative—referred to as the Human Genome Project—to identify and map the components of biological inheritance, called genes (box 1-1). As with other biomedical research, expectations exist that federal technology transfer of human genome research will play a key role in companies' development of new genetic diagnostic and therapeutic products (75,48,17).



This background paper first reviews the development of federal technology transfer legislation and regulations, generally. It discusses the mechanisms and policies of the federal entities responsible for funding the Human Genome Project: the National Institutes of Health (NIH) of the U.S. Department of Health and Human Services and the U.S. Department of Energy (DOE). It examines the role and influence of this matrix on commercialization of life sciences and human genome research funded extramu-

BOX 1-1: The Human Genome Project

In humans, as in essentially all forms of life, deoxyribonucleic acid (DNA) contains the entire genetic blueprint for an individual Currently, scientists in the United States and abroad have committed to revealing the details of this blueprint, or genome. In 1985, the Human Genome Project emerged as an ambitious effort to identify the location and composition of the 50,000 to 100,000 human genes (the fundamental units of inheritance) (16) The project has been undertaken with the expectation that enhanced knowledge about genetic disorders, increased understanding of gene-environment interactions, and improved genetic diagnoses can advance therapies for the 5,000 or so currently recognized human genetic conditions, a premise supported by the fact that even prior to formal launching of the project, advances in medical genetics were instrumental in the development of new therapeutic approaches (16,20,62,84).

Progress in understanding human genetics can aid drug development by defining specific subpopulations of patients, thus simplifying the process of ascertaining the efficacy of new drugs Another promising treatment strategy the Human Genome Project might accelerate is gene therapy--deliberately introducing genes into human cells to compensate for aberrant genes that cause genetic disease In the future, DNA itself could serve as a therapeutic agent (87,88).

Still, molecular genetics research constitutes only one of many approaches to alleviate disease (77) Following the trail down to the DNA sequence cannot even fully explain many classical genetic diseases, and clearly genetic factors are just a part of most major diseases. The attraction of the Human Genome Project and genetic approaches to disease, however, is that molecular technologies are so powerful. Most major diseases have been studied for decades. Those more readily explained by traditional approaches have yielded, molecular biology offers a strategy to crack those that have not.

SOURCE Office of Technology Assessment, 1995

rally and intramurally by NIH and DOE. And finally, it reports data from three OTA surveys on: academic research institutions' experiences since enactment of federal laws to enhance technology transfer; industry's experience with collaborative arrangements involving NIH or DOE; and the extent to which partnerships with industry are of benefit-as measured by publications, citations, and patents—to NIH intramural scientists. International technology transfer-either the transfer of technology across borders or the practices of other countries—is beyond the scope of this background paper.

HISTORICAL PERSPECTIVE

Following World War II, the federal government became the major source of funding for research and development (R&D) in the United States. Today, federal agencies fund nearly half of the nation's R&D, largely to meet public objectives such as national defense, space exploration, improved health, greater food production, and energy conservation. Recently, however, some in industry and government have advocated that the federal government undertake the additional responsibility of supporting the U.S. scientific and technical enterprise to promote economic competitiveness (39).

The notion that the federal government should play a direct and active role in stimulating R&D as it relates to economic growth first came under scrutiny through President Kennedy's Science Advisory Committee's recommendations regarding industrial innovation (8). Subsequent administrations elaborated on these recommendations: President Nixon's Council of Economic Advisors encouraged active partnerships between the public and private sectors in research and technological innovation, and President Carter's Domestic Policy Review explored what steps the federal

government should take to encourage industrial innovation (56). These broad appeals for an activist role of government in stimulating R&D eventually evolved into current technology transfer policies.

Generically speaking, technology transfer is the process by which research results are developed and applied in another area, organization, or commercial sector. However, the term has different meanings in different contexts. It can refer to the legal and administrative process by which the transfer of legal rights--such as the assignment of a patent to a contractor or the licensing of a government-owned patent to a company-is achieved. Or, it can refer to the informal movement of information, knowledge, and skill from a federal laboratory to the private sector through person to person contact or collaboration. One of the most crucial aspects of technology transfer is the use of research to derive a new commercial product or process.

Although the substance of current federal technology transfer has roots in the 1960s, the concept of technology transfer as a federal activity is not new (67). The federal government has laws and policies encouraging innovation, dating back to the Patent Act of 1790 (69). The U.S. Department of Agriculture (USDA) has been transferring technology for over a century, beginning with the establishment of the land grant colleges under the 1882 Merrill Act. The Hatch Act of 1887 created agricultural research stations separate from university systems. The goals of both laws were to improve agricultural productivity through direct education of farmers by providing them with the latest research results and intervening in farming practices to increase yield. Thus, Congress had public interest and commercial motivations (46).

Policymakers in both the executive and legislative branches have favored domestic technology transfer, but never with as much enthusiasm as in the 1980s. During this period, concern grew about the ability of U.S. business to compete in international markets. One sentiment pervaded discussions in Congress, the executive branch, and industry: American "know how''--often generated via public funding-was being transferred

with increasing frequency to foreign nations, only to return to the United States as commercial products (67). Furthermore, few of the inventions for which the U.S. Patent and Trademark Office (PTO) granted the federal government patents each year were ever licensed for commercial use (61). At the same time, U.S. industry was increasingly aware that other nations were challenging its long held position of technological supremacy and that its competitive edge in many sectors was in jeopardy (39,66). A consensus that competitiveness was linked to innovation and that research and technology transfer played a critical role in the nation's ability to compete led some in industry to express increased interest in creating and strengthening its own connections with the scientific community (39).

Congress focused on scientific research conducted in academic laboratories as a key place to improve U.S. technology transfer. University research tended to be more open than research conducted in government laboratories because many federal facilities were created to develop defense technologies and therefore barred unfettered public access. Additionally, because of national security concerns, significant legal barriers had been enacted specifically to prevent technology transfer.

rity concerns, significant legal barriers had been enacted specifically to prevent technology transfer.

In contrast, during the 1970s, policymakers and scholars almost uniformly viewed universities as the fount from which new scientific and technological breakthroughs would improve the U.S. economy. University-industry partnerships were touted as the vehicle through which sustained economic development could be achieved (32,47). Thus, during this decade, new relationships between universities and industry emerged, involving such activities as industrial support of academic research, opportunities for academic consulting, research collaborations, research consortia, shared equipment use, publications, and conferences (68,32). In the 1980s, attention also began to focus on drawing resources of commercial potential out of federal laboratories.

TECHNOLOGY TRANSFER LEGISLATION

Several laws enacted over the past 15 years encourage technology transfer of results from federally funded research. Early legislation focused on technology transfer of research funded by the government but undertaken at universities and academic research institutions. Other laws arose exclusively from concern about the state of technology transfer to industry from research conducted at U.S. government laboratories.

In particular, three technology transfer laws enacted in the 1980s fundamentally shape today's practices and policies:

- **The Bayh-Dole Act of 1980** (Public Law 96-517) allowed private parties to retain patent rights via a "title in contractor" policy—meaning small businesses and nonprofit organizations, including universities, could retain intellectual property rights to results from federally funded federal research. Prior to Bayh-Dole, such a policy was implemented on an agency-by-agency basis. Amendments to the Act in 1984 brought research contracts with universities that operate DOE's national laboratories within the scope of the title in contractor policy, provided statutory authority for the government to dispose of patent rights to contractors, and made the U.S. Department of Commerce (DOC) the lead federal agency for technology transfer policy.
- **The Stevenson-Wydler Act of 1980** (Public Law 96-480) required that federal agencies administering research establish an Office of Research and Technology Applications (ORTA) at all government-operated or contractor-operated laboratories with an annual budget greater than $20 million. The Act also provided general guidance for the efforts that the government should take to encourage technology transfer. While acknowledging its value, the legislation provided no means to enforce the requirement for ORTAs. Moreover, Congress withheld much of the funding for the program.
- **The Federal Technology Transfer Act of 1986** (FTTA; Public Law 99-502) amended Stevenson-Wydler; it had become apparent that little technology transfer from federal laboratories was occurring. FTTA shifted the emphasis in federal policy from one permitting technology transfer to one requiring that agencies act vigorously in working with industry to commercialize federally funded research. FTTA's signature feature is the authority of agencies to negotiate Cooperative Research and Development Agreements (CRADAs) and include exclusive licensing terms with CRADA partners—i.e., CRADAs are the administrative and legal mechanism through which commercialization of research performed at federal facilities may be achieved. FTTA also contained provisions specifying federal researchers' rights to royalties and rights to pursue a patent should an agency decline to pursue one.

Appendix A describes these laws in greater detail, as well as two additional laws enacted by Congress to enhance and facilitate domestic technology transfer: the Omnibus Trade and Competitiveness Act of 1988 (Public Law 100-418)

der the jurisdiction of federal laws, regulations, and policies not explicitly designed for oversight of technology transfer processes. Hence, antitrust laws, tax laws, and other policies and initiatives that can affect technology transfer also are briefly outlined in appendix A.

CONTEXT OF THIS BACKGROUND PAPER

As mentioned earlier, technology transfer of biomedical research has enjoyed visible and commercial success. Molecular biological research and the industrial sector it spawned—biotechnology—are established sources of innovation in pharmaceutical R&D, contributing both production technologies and research tools. Biotechnology is likely to be the principal scientific driving force for the discovery of new drugs as we enter the 21st century, and the impact of biotechnology (including genetic technologies), on the discovery of new therapeutic entities is difficult to overestimate (87).

With the launch of the Human Genome Project in the late 1980s, there was little expectation that results from genome research would not follow a similar path of technology transfer from university and federal facilities to commercial development. Nevertheless, in 1991, technology transfer of human genome research became the subject of intense scrutiny by researchers, universities, industry, and policymakers.

Until summer 1991, as scientific advances in human genetic research incrementally progressed, researchers, universities, and biotechnology companies filed and received a range of human DNA sequence patents on genes and their products—for diagnostic, therapeutic, or research purposes. In June 1991, however, many felt this

Aerial *view of the National Institutes of Health campus in Bethesda, Maryland.*

orderly process, or at least one perceived as orderly, was altered when NIH sought intellectual property protection on more than 6,000 short sequences of human DNA that, by the nature of their isolation method, coded for putative human genes and therefore human proteins, but were themselves incomplete gene sequences.

A swift, and predominantly negative, outcry followed the public disclosure of NIH's maneuver (4,5,6,20,30), which was defended as being required by federal technology transfer laws (1 ,44). That is, the filing of the NIH patent applications was justified, in part, as an attempt by the federal government to ensure that the public investment's in biomedical research-in this case at a federal laboratory-was optimized by seeking intellectual property protection that would be attractive to investment by potential industrial partners.[1]

Thus, OTA sought to examine the impact of technology transfer laws on life sciences research, in particular research funded by the two entities responsible for funding the Human Genome Proj-

[1] In fall 1992, NIH Announced that the U.S. Patent and Trademark Office (PTO) had rejected NIH's applications (as it does for most first applications, which tend to seek the broadest possible scope of coverage.) PTO held the NIH applications lacked novelty, utility, and were obvious. NIH responded to PTO's initial rejection in February 1993, modifying the claims, but the PTO examiner again rejected the applications. A year later in February 1994, facing a deadline to appeal the rejection to the Board of Patent Appeals and Interferences (a review body within PTO) or the Federal courts, NIH withdrew all applications. Nevertheless, their legacy challenged conventional drinking about strategies for seeking patents on human DNA sequences, spotlighted the role of Federal technology transfer in biotechnological innovation, and underscored the perception of the pivotal impact that molecular medicine will play in ameliorating disease.

Thus, OTA sought to examine the impact of technology transfer laws on life sciences research, in particular research funded by the two entities responsible for funding the Human Genome Project—NIH and DOE. What have been universities' experiences since enactment of Bayh-Dole, Stevenson-Wydler, and FTTA? Does industry view collaborative arrangements involving NIH or DOE as one where benefits outweigh risks? And, what has been the impact on federal scientists—NIH researchers, in particular—of evolving federal technology transfer policies? The following chapters analyze these issues in light of data gathered through OTA surveys, interviews, and a 1994 workshop of a wide range of companies involved in genome-related research.