chapter 1

Summary: Issues and Options

Chapter 1

Table

Figures

Chapter 1

Summary: Issues and Options

The genetic alteration of plants, animals, and micro-organisms has been an important part of agriculture for centuries. It has also been an integral part of the alcoholic beverage industry since the invention of beer and wine; and for the past century, a mainstay of segments of the pharmaceutical and chemical industries.

However, only in the last 20 years have powerful new genetic technologies been developed that greatly increase the ability to manipulate the inherited characteristics of plants, animals, and micro-organisms. One consequence is the increasing reliance the pharmaceutical and chemical industries are placing on biotechnology. Micro-organisms are being used to manufacture substances that have previously been extracted from natural sources. Animal and plant breeders are using the new techniques to help clarify basic questions about biological functions, and to improve the speed and efficiency of the technologies they already use. Other industries–from food processing and pollution control to mining and oil recovery—are considering the use of genetic engineering to increase productivity and cut costs.

Genetic technologies will have a broad impact on the future. They may contribute to filling some of the most fundamental needs of mankind–from health care to supplies of food and energy. At the same time, they arouse concerns about their potential effects on the environment and the risks to health involved in basic and applied scientific research and development (R&D). Because genetic technologies are already being applied, it is appropriate to begin considering their potential consequences.

Congressional concern with applied genetics dates back to 1976, when 30 Representatives requested an assessment of recombinant DNA (rDNA) technology. Support for the broader study reported here came in letters to the Office of Technology Assessment from the then Senate Committee on Human Resources and the House Committee on Interstate and Foreign Commerce, Subcommittee on Health and the Environment. In addition specific subtopics are of interest to other committees, notably those having jurisdiction over science and technology and those concerned with patents.

This report describes the potentials and problems of applying the new genetic technologies to a range of major industries. It emphasizes the present state of the art because that is what defines the basis for the future applications. It then makes some estimates of economic, environmental, and institutional impacts—where, when, and how some technologies might be applied and what some of the results might be. The report closes with the possible roles that Government, industry, and the public might play in determining the future of applied genetics.

The term ***applied genetics,*** as used in this report, refers to two groups of technologies:

- ***Classical genetics***—natural mating methods for the selective breeding of organisms for desired characteristics–e. g., breeding cows for increased milk production. The pool of genes available for selection is comprised of those that cause natural differences among individuals in a population and those obtained by mutation.
- ***Molecular genetics*** includes the technologies of genetic engineering that involve the directed manipulation of the genetic material itself. These technologies—such as rDNA and the chemical synthesis of genes —can increase the size of the gene pool for any one organism by making available genetic traits from many different populations. Molecular genetics also includes technologies in which manipulation occurs at a level higher than that of the gene—at the cellular level, e.g., cell fusion and in vitro fertilization.

Significant applications of molecular genetics to micro-organisms, such as the efforts to manufacture human insulin, are already underway in several industries. Most of these applications

depend on fermentation—a technology in which substances produced by micro-organisms can be obtained in large quantities. Applications to plants and animals, which are biologically more complex and more difficult to manipulate successfully, will take longer to develop.

Biotechnology

Biotechnology-the use of living organisms or their components in industrial processes—is possible because micro-organisms naturally produce countless substances during their lives. Some of these substances have proved commercially valuable. A number of different industries have learned to use micro-organisms as natural factories, cultivating populations of the best producers under conditions designed to enhance their abilities.

Applied genetics can play a major role in improving the speed, efficiency, and productivity of these biological systems. It permits the manipulation, or engineering, of the micro-organisms' genetic material to produce the desired characteristics. Genetic engineering is not in itself an industry, but a technique used at the laboratory level that allows the researcher to modify the hereditary apparatus of the cell. The population of altered identical cells that grows from the first changed micro-organism is, in turn, used for various industrial processes. (See figure 1.)

The first major commercial effects of the application of genetic engineering will be in the pharmaceutical, chemical, and food processing industries. Potential commercial applications of value to the mining, oil recovery, and pollution control industries—which may desire to use manipulated micro-organisms in the open environment —are stll somewhat speculative.

The pharmaceutical industry

FINDINGS

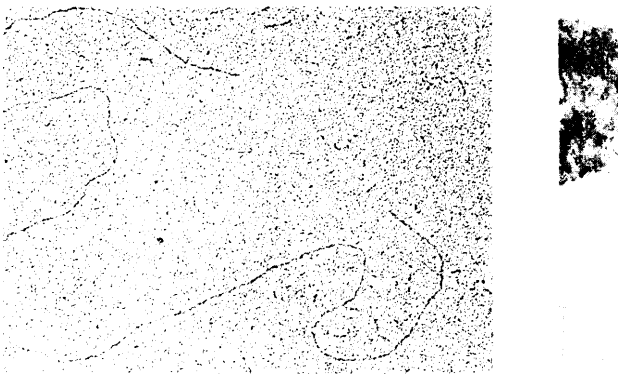
The pharmaceutical industry has been the first to take advantage of the potentials of applied molecular genetics. Ultimately, it will probably benefit more than any other, with the largest percentage of its products depending on advances in genetic technologies. Already, micro-organisms have been engineered to produce human insulin, interferon, growth hormone, urokinase (for the treatment of blood clots), thymosin-a **1** (for controlling the immune response), and somatostatin (a brain hormone). (See figure 2.)

The products most likely to be affected by genetic engineering in the next **10** to 20 years are nonprotein compounds like most antibiotics, and protein compounds such as enzymes and antibodies, and many hormones and vaccines. Improvements can be made both in the products and in the processes by which they are produced. Process costs may be lowered and even entirely new products developed.

The most advanced applications today are in the field of hormones. While certain hormones have already proved useful, the testing of others has been hindered by their scarcity and high cost. Of 48 human hormones that have been identified so far as possible candidates for production by genetically engineered micro-organisms, only 10 are used in current medical practice. The other 38 are not, partly because they have been available in such limited quantities that tests of their therapeutic value have not been possible.

Genetic technologies also open up new approaches for vaccine development for such intractable parasitic and viral diseases as amebic dysentery, trachoma, hepatitis, and malaria. At present, the vaccine most likely to be produced is for foot-and-mouth disease in animals. However, should any one of the vaccines for human diseases become available, the social, economic, and political consequences of a decrease in morbidity and mortality would be significant. Many of these diseases are particularly prevalent in less industrialized countries; the developments of vaccines for them may profoundly affect the lives of tens of millions of people.

Figure 1.— Recombinant DNA: The Technique of Recombining Genes From One Species With Those From Another



Electron micrograph of the DNA, which is the plasmid SPO1 from *Bacillus subtilis.* This plasm id which has been sliced open is used for recombinant DNA research in this bacterial host

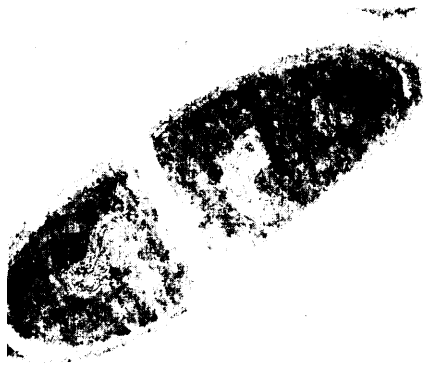
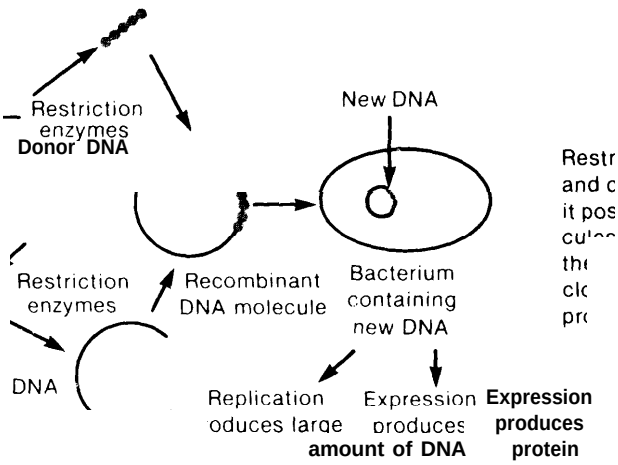


Photo credits; Professor F. A. Eiserling, UCLA Molecular Biology Institute

Electron micrograph of *Bacillus subtilis* in the process of cell division. The twisted mass in the center of each daughter cell is the genetic material, DNA



Restriction enzymes recognize certain sites along the DNA and can chemically cut the DNA at those sites. This makes it possible to remove selected genes from donor DNA molecules and insert them into plasmid DNA molecules to form the recombinant DNA. This recombinant DNA can then be cloned in its bacterial host and large amounts of a desired protein can be produced.

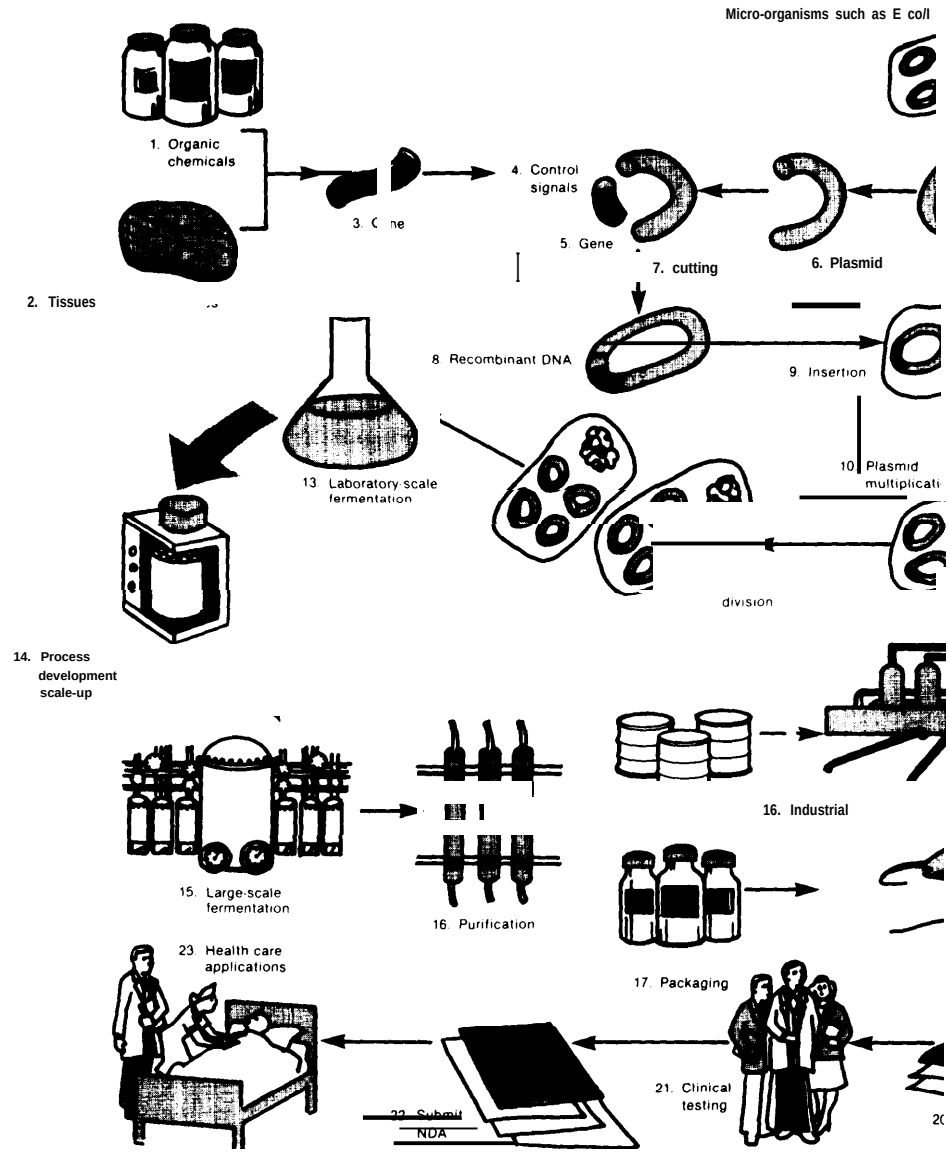
SOURCE: Office of Technology Assessment.

For some pharmaceutical products, biotechnology will compete with chemical synthesis and extraction from human and animal organs. Assessing the relative worth of each method must be done on a case-by-case basis. But for other products, genetic engineering offers the only method known that can ensure a plentiful supply; in some instances, it has no competition.

By making a pharmaceutical available, genetic engineering may have two types of effects:

- Drugs that already have medical promise will be available in ample amounts for clinical testing. Interferon, for example, can be tested for its efficacy in cancer and viral therapy, and human growth hormone can be evaluated for its ability to heal wounds.
- Other pharmacologically active substances for which no apparent use now exists will be available in sufficient quantities and at low enough cost to enable researchers to explore new uses. As a result, the potential for totally new therapies exists. Regulatory proteins, for example, which are an entire

Figure 2.-The Product Development Process



The development process begins by obtaining DNA either through organic synthesis (1) or derived from biological sources such as tissues (2). The DNA obtained from one or both sources is tailored to form the basic "gene" (3) which contains the genetic information to "code" for a desired product, such as human interferon or human insulin. Control signals (4) containing instructions are added to this gene (5). Circular DNA molecules called plasmids (6) are isolated from micro-organisms such as *E. coli;* cut open (7) and spliced back(8) together with genes and control signals to form "recombinant DNA" molecules. These molecules are then introduced into a host cell (9).

Each plasmid is copied many times in a cell (10). Each cell then translates the information contained in these plasmids into the desired product, a process called "expression" (11). Cells divide (12) and pass on to their offspring the same genetic information contained in the parent cell.

Fermentation of large populations of genetically engineered micro-organisms is first done in shaker flasks (13), and then in small fermenters (14) to determine growth conditions, and eventually in larger fermentation tanks (15). Cellular extract obtained from the fermentation process is then separated, purified (16), and packaged (17) either for industrial use (18) or health care applications.

Health care products are first tested in animal studies (19) to demonstrate a product's pharmacological activity and safety, in the United States, an investigational new drug application (20) is submitted to begin human clinical trials to establish safety and efficacy. Following clinical testing (21), a new drug application (NDA) (22) is fried with the Food and Drug Administration (FDA). When the NDA has been reviewed and approved by the FDA the product maybe marketed in the United States (23).

SOURCE: Genentech, Inc.

class of molecules that control gene activity, are present in the body in only minute quantities. Now, for the first time, they can be recognized, isolated, characterized, and produced in quantity.

The mere availability of a pharmacologically active substance does not ensure its adoption in medical practice. Even if it is shown to have therapeutic usefulness, it may not succeed in the marketplace.

The difficulty in predicting the economic impact is exemplified by interferon. If it is found to be broadly effective against both viral diseases and cancers, sales would be in the tens of billions of dollars annually. If its clinical effectiveness is found to be only against one or two viruses, sales would be significantly lower.

At the very least, even if there are no immediate medical uses for compounds produced by genetic engineering, their indirect impact on medical research is assured. For the first time, almost any biological phenomenon of medical interest can be explored ***at the cellular level.*** These molecules are valuable tools for understanding the anatomy and functions of cells. The knowledge gained may lead to the development of new therapies or preventive measures for diseases.

The chemical industry

FINDINGS

The chemical industry's primary raw material, petroleum, is now in limited supply. Coal is one appealing alternative; another is biomass, a renewable resource composed of plant and animal material.

Biomass has been transformed by fermentation into organic chemicals like citric acid, ethanol, and amino acids for decades. Other organic chemicals such as acetone, butanol, and fumaric acid were at one time made by fermentation until chemical production methods, combined with cheap oil and gas, proved to be more economical. In theory, most any industrial organic chemical can be produced by a biological process.

Commercial fermentation using genetically engineered micro-organisms offers several advantages over current chemical production techniques.

- ***The use of renewable resources:*** starches, sugars, cellulose, and other components of biomass can serve as the raw material for synthesizing organic chemicals. With proper agricultural management, biomass can assure a continuous renewable supply for the industry.
- ***The use of physically milder conditions:*** chemical processes often require high temperatures and extreme pressures. These conditions are energy intensive and pose a hazard in case of accidents. Biological processes operate under milder conditions, which are compatible with living systems.
- ***One-step production methods:*** micro-organisms can carry out several steps in a synthetic process, eliminating the need for intermediate steps of separation and purification.
- ***Decreased pollution:*** **because biological** processes are highly specific in the reactions they catalyze, they offer control over the products formed and decrease undesirable side-products. As a result, they produce fewer pollutants that require management and disposal,

The impact of this technology will cut across the entire spectrum of chemical groups: plastics and resin materials, flavors and perfumes materials, synthetic rubber, medicinal chemicals, pesticides, and the primary products from petroleum that serve as the raw materials for the synthesis of organic chemicals. Nevertheless, the specific products that will be affected in each group can only be chosen on a case-by-case basis, with the applicability of genetics depending on a variety of factors. Crude estimates of the expected economic impacts are in the billions of dollars per year for dozens of chemicals within 20 years.

INDUSTRY AND MANPOWER IMPACTS

Although genetic engineering will develop new techniques for synthesizing many substances, the direct displacement of any current industry seems doubtful. Genetic engineering should be considered simply another industrial tool. Industries will probably use genetic

engineering to maintain their positions in their respective markets. This is already illustrated by the variety of companies in the pharmaceutical, chemical, and energy industries that have invested in or contracted with genetic engineering firms. Some large companies are already developing inhouse genetic engineering research capabilities.

Any predictions of the number of workers that will be required in the production phase of biotechnology will depend on the expected volume of chemicals that will be produced. At present, this figure is unknown. An estimated $15 billion worth of chemicals maybe manufactured by biological processes. This will employ approximately 30,000 to 75,000 workers for supervision, services, and production. Whether this will represent a net loss or gain in the number of jobs is difficult to predict since new jobs in biotechnology will probably displace some of those in traditional chemical production.

Food processing industry

FINDINGS

Genetics in the food processing industry can be used in two ways: to design micro-organisms that transform inedible biomass into food for human consumption or into feed for animals; and to design organisms that aid in food processing, either by acting directly on the food itself or by providing materials which can be added to food.

The use of genetics to design organisms with desired properties for food processing is an established practice. Fermented foods and beverages have been made by selected strains of mutant organisms (e.g., yeasts) for centuries. Only recently, however, have molecular technologies opened up new possibilities. In particular, large-scale availability of enzymes will play an increasing role in food processing.

The applications of molecular genetics are likely to appear in the food processing industry in piecemeal fashion:

- Inedible biomass, human and animal wastes, and even various industrial effluents are now being transformed into edible micro-organisms high in protein content (called single-cell protein or SCP). Its present cost of production in the United States is relatively high, and it must compete with cheaper sources of protein such as soybeans and fishmeal, among others.
- Isolated successes can be anticipated for the production of such food additives as fructose (a sugar) and the synthetic sweetener aspartame, and for improvements in SCP production.

An industrywide impact is not expected in the near future because of several major conflicting factors:

- The basic knowledge of the genetic characteristics that could improve food has not been adequately developed.
- The food processing industry is conservative in its expenditures for R&D to improve processes. Generally, only one-third to one-half as much is allocated for this purpose as in technologically intensive industries.
- Products made by new microbial sources must satisfy the Food and **Drug Administration's** (FDA) safety regulations, which include undergoing tests to prove lack of harmful effects. It may be possible to reduce the amount of required testing by transferring the desired gene into micro-organisms that already meet FDA standards.

The use of genetically engineered micro-organisms in the environment

FINDINGS

Genetically engineered micro-organisms are being designed now to perform in three areas (aside from agricultural uses) that require their large-scale release into the environment:

- **mineral leaching and recovery,**
- **enhanced oil recovery, and**
- **pollution control.**

All of these are characterized by:

- **the use of large volumes of micro-organisms,**

decreased control over the behavior and fate of the micro-organisms,

sil the possibility of ecological disruption, and
/e less development in basic R&D (and more speculation-) than in the industries in which micro-organisms are used in a controlled environment.

MINERAL LEACHING AND RECOVERY

Bacteria have been used to leach metals, such as uranium and copper, from low-grade ores. Although there is reason to believe leaching ability is under genetic control in these organisms, practically nothing is known about the precise mechanisms involved. Therefore, the application of genetic technologies in this area remains speculative. Progress has been slow in obtaining more information, partly because very little research has been conducted.

In addition to leaching, micro-organisms can be used to recover valuable metals or eliminate polluting metals from dilute solutions such as industrial waste streams. The process makes use of the ability of micro-organisms to bind metals to their surfaces and then concentrate them internally.

The economic competitiveness of biological methods is still unproved, but genetic modifications have been attempted only recently. The cost of producing the micro-organisms has been a major consideration. If it can be reduced, the approach might be useful.

ENHANCED OIL RECOVERY

Many methods have been tried in efforts to remove oil from the ground when natural expulsive forces alone are no longer effective. Injecting chemicals into a reservoir has, in many cases, aided recovery by changing the oil's flow characteristics.

Micro-organisms can produce the necessary chemicals that help to increase flow. Theoretically, they can also be grown in the wells themselves, producing those same chemicals in situ. The currently favored chemical, xanthan, is far from ideal for increasing flow. Genetic engineering should be able to produce chemicals with more useful characteristics.

The current research approach, funded by the Department of Energy (DOE) and independently by various oil companies, is a two-phase process to find micro-organisms that can function in an oil reservoir environment, and then to improve their characteristics genetically.

The genetic alteration of micro-organisms to produce chemicals useful for enhanced oil recovery has been more successful than the alteration of micro-organisms that may be used in situ. However, rDNA technology has not been applied to either case. All attempts have employed artificially induced or naturally occurring mutations.

POLLUTION CONTROL

Many micro-organisms can consume various kinds of pollutants, changing them into relatively harmless materials before they die. These micro-organisms always have had a role in "natural" pollution control: nevertheless, cities have resisted adding microbes to their sewerage systems. Although the Environmental Protection Agency (EPA) has not recommended addition of bacteria to municipal sewerage systems, it suggests that they might be useful in smaller installations and for specific problems in large systems. In major marine spills, the bacteria, yeast, and fungi already present in the water participate in degradation. The usefulness of added microbes has not been demonstrated.

Nevertheless, in 1978, the estimated market of biological products for pollution control was $2 million to $4 million per year, divided among some 20 companies; the potential market was estimated to be as much as $20 million per year.

To date, genetically engineered strains have not been applied to pollution problems. Restricting factors include the problems of liability in the event of health, economic, or environmental damage; the contention that added organisms are not likely to be a significant improvement; and the assumption that selling microbes rather than products or processes is not likely to be profitable.

Convincing evidence that microbes could remove or degrade an intractable pollutant would encourage their application. In the meantime, however, these restrictions have acted to inhibit the research necessary to produce marked improvements.

CONSTRAINTS IN USING GENETIC ENGINEERING TECHNOLOGIES IN OPEN ENVIRONMENTS

The genetic data base for the potentially useful micro-organisms is lacking. Only the simplest methods of mutation and selection for desirable properties have been used thus far. These are the only avenues for improvement until more is learned about the genetic mechanisms.

Even when the scientific knowledge is available, two other obstacles to the use of genetically engineered micro-organisms will remain. The first is the need to develop engineered systems on a scale large enough to exploit their biological activity. This will necessitate a continual dialog among microbial geneticists, geologists, chemists, and engineers; an interdisciplinary approach is required that recognizes the needs and limitations of each discipline.

The second obstacle is ecological. Introducing large numbers of genetically engineered micro-organisms into the environment might lead to ecological disruption or detrimental effects on human health, and raise questions of legal liability.

Issue and Options—Biotechnology

ISSUE: How can the Federal Government promote advances in biotechnology and genetic engineering?

The United States is a leader in applying genetic engineering and biotechnology to industry. One reason is the long-standing commitment by the Federal Government to the funding of basic biological research; several decades of support for some of the most esoteric basic research has unexpectedly provided the foundation for a highly useful technology. A second is the availability of venture capital, which has allowed the formation of small, innovative companies that can build on the basic research.

The chief argument for Government subsidization for R&D in biotechnology and genetic engineering is that Federal help is needed in areas such as general (generic) research or highly speculative investigations ***not*** now being developed by industry. The argument ***against*** the need for this support is that industry will develop everything of commercial value on its own.

A look at what industry is now attempting indicates that sufficient investment capital is available to pursue specific manufacturing objectives. Some high-risk areas, however, that might be of interest to society, such as pollution control, may justify promotion by the Government, while other, such as enhanced oil recovery might might not be profitable soon enough to attract investment by industry.

OPTIONS:

A. Congress could allocate funds specifically for genetic engineering and biotechnology R&Din the budget of appropriate agencies.

Congress could promote two types of programs in biotechnology: those with long-range payoffs (basic research), and those that industry is not willing to undertake but that might be in the national interest.

B. Congress could establish a separate Institute of Biotechnology as a funding agency.

The merits of a separate institute lie in the possibility of coordinating a wide range of efforts, all related to biotechnology. On the other hand, biotechnology and genetic engineering cover such a broad range of disciplines that a new funding agency would overlap the mandates of existing agencies. Furthermore, the creation of yet another agency carries with it all the disadvantages of increased bureaucracy and competition for funds at the agency level.

C. ***Congress could establish research centers in universities to foster interdisciplinary approaches to biotechnology. In addition, a program of grants could be offered to train scientists in biological engineering.***

The successful use of biological techniques in industry depends on a multidisciplinary approach involving biochemists, geneticists, microbiologists, process engineers, and chemists.

Little is now being done publicly or privately to develop the expertise necessary.

D. Congress could use tax incentives to stimulate biotechnology.

The tax laws could be used to stimulate biotechnology by expanding the supply of capital for small, high-risk firms, which are generally considered more innovative than established firms because of their willingness to undertake the risks of innovation. In addition to focusing on the supply of capital, tax policy could attempt to directly increase the profitability of potential growth companies.

A tax incentive could also be directed' at increasing R&D expenditures. It has been suggested that companies be permitted to take tax credits: 1) on a certain percentage of their R&D expenses; and 2) on contributions to universities for research.

E. Congress could improve the conditions under which U.S. companies collaborate with academic scientists and make use of the technology developed in universities, which has been wholly or partly supported by tax funds.

Developments in genetic engineering have kindled interest in this option. Under legislation that has recently passed both Houses of Congress, small businesses and universities may retain title to inventions developed under federally funded research. Currently, some Federal agencies award contractors these exclusive rights, while others insist on the nonexclusive licensing of inventions.

F. Congress could mandate support for specific research tasks such as pollution control using microbes.

Microbes may be useful in degrading intractable wastes and pollutants. Current research, however, is limited to isolating organisms from natural sources or from mutated cultures. More elaborate efforts, involving rDNA techniques or other forms of microbial genetic exchange, will require additional funding.

G. ***Most efforts could be left to industry and each Government agency allowed to develop programs in the fields of genetic engineering and biotechnology as it sees fit.***

Generic research will probably not be undertaken by any one company. Leaving all R&D in industry's hands would still produce major commercial successes, but does not ensure the development of needed basic general knowledge or the undertaking of high-risk projects.

Agriculture

The complexity of plants and animals presents a greater challenge to advances in applied genetics than that posed by micro-organisms. Nevertheless, the successful genetic manipulation of microbes has encouraged researchers in the agricultural sciences. The new tools will be used to complement, but not replace, the well-established practices of plant and animal breeding.

The applications of genetics to plants

FINDINGS

It is impossible to exactly determine the extent to which applied genetics has directly contributed to increases in plant yield because of simultaneous improvements in farm management, pest control, and cropping techniques using herbicides, irrigation, and fertilizers. Nevertheless, the impacts of breeding technologies have been extensive.

The plant breeder's approach is determined for the most part by the particular biological factors of the crop being bred. The new genetic technologies potentially offer ***additional*** tools to allow development of new varieties and even species of plants by circumventing current biological barriers to the exchange of genetic material.

Technologies developed for classical plant breeding and those of the new genetics should not be viewed as being competitive; they are both tools for effectively manipulating genetic

information. One new technology -e.g., protoplasm fusion, or the artificial fusion of two cells– allows breeders to overcome incompatibility between plants. But the plant that may result still must be selected, regenerated, and evaluated under field conditions to ensure that the genetic change is stable and that the attributes of the new variety meet commercial requirements.

In theory, the new technologies will expand the capability of breeders to exchange genetic information by overcoming natural breeding barriers. To date, however, they have not had a widespread impact on the agricultural industry.

As a note of caution, it must be emphasized that no plant can possess every desirable trait. There will always have to be some tradeoff; often quality for quantity, such as increased protein content but decreased yield.

NEW GENETIC TECHNOLOGIES FOR PLANT BREEDING

The new technologies fall into two categories: those involving genetic transformations through cell fusion and those involving the insertion or modification of genetic information through the cloning of DNA and its vectors. Techniques are available for manipulating organs, tissues, cells, or protoplasts in culture; for regenerating plants; and for testing the genetic basis of novel traits. So far these techniques are routine only in a few species.

The approach to exploiting molecular biology for plant breeding is similar in some respects to the genetic manipulation of micro-organisms. However, there is one major conceptual dif-

A plantlet of loblolly pine grown in Weyerhaeuser Co.'s tissue culture laboratory. The next step in this procedure is to transfer the plantlet from its sterile and humid environment to the soil

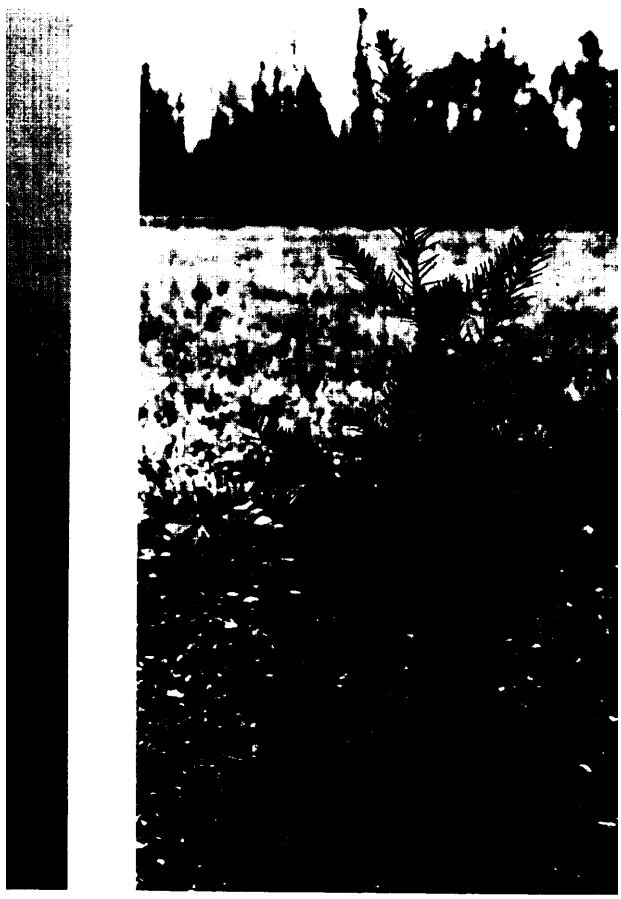


Photo credits: Weyerhaeuser Co.

A young Douglas fir tree propagated 4 years ago from a small piece of seedling leaf tissue. Three years ago this was at the test-tube stage seen in the loblolly pine photograph

ference. In micro-organisms, the changes made on the cellular level are the goals of the manipulation. With crops, changes made on the cellular level are meaningless unless they can be reproduced in the entire plant as well. There- fore, unless single cells in culture can be selected and **grown into mature plants and the desired traits expressed in the mature plant– procedures which at this time have had limited success—the benefits of genetic engineering will not be widely felt in plant breeding.**

Moderate success has been achieved for growing cells in tissue culture into mature plants. Tissue culture programs of commercial significance in the United States include the asparagus, citrus fruits, pineapples, and strawberries. Breeders have had little success, however, in regenerating mature plants of wide agronomic importance) such as corn and wheat.

Some success can be claimed for engineering changes to alter genetic makeup. Both the stable integration of genetic material into a cell and the fusion of genetically different cells are still largely experimental techniques. Technical breakthroughs have come on a species-by-species basis, but key discoveries are not often applicable to all plants. Initial results suggest that agronomically important traits, such as disease resistance, can be transferred from one species to another. Limited success has also been shown in attempts to create totally new species by fusing cells from different genera. Attempts to find both suitable vectors and genes for transferring one plant genes to another are only now beginning to show promise.

CONSTRAINTS ON USING MOLECULAR GENETICS FOR PLANT IMPROVEMENTS

Molecular engineering has been impeded by a lack of answers to basic questions in molecular biology and plant physiology owing to insufficient research. Federal funding for plant molecular genetics in agriculture has come primarily from the U.S. Department of Agriculture (USDA) and the National Science Foundation (NSF). In USDA, research support is channeled primarily through the flexible competitive grants program (fiscal year 1980 budget of **$15** million) for the support of new research directions in plant biology. The total support for the plant sciences from NSF is approximately $25 million, only **$1** million of which is specifically designated for plant genetics.

The shortage of a trained workforce is a significant constraint. Only a few universities have expertise in both plants and molecular biology. In addition, there are only a few people who have the ability to work with modern molecular techniques related to whole plant problems. As a result, a business firm could easily develop a capability in this area exceeding that at any individual U.S. university. However, the building of industrial laboratories and subsequent hiring from the universities could easily deplete the expertise at the university level. With the recent investment activity by many bioengineering firms, this trend has already begun; in the long-run it could have serious consequences for the quality and quantity of university research.

GENETIC VARIABILITY, CROP VULNERABILITY, AND THE STORAGE OF GERMPLASM

Successful plant breeding is based on the availability of genetically diverse plants for the insertion of new genes into plants. The number of these plants has been diminishing for a variety of reasons. However, the rate and extent of this trend is unknown; the data simply do not exist. Therefore, it is essential to have an adequate scientific understanding of how much genetic loss has taken place and how much germplasm (the total genetic variability available to a species) is needed. Neither of these questions can be answered completely at this time.

Even if-genetic needs can be adequately identified, there is disagreement about the quantity of germplasm to collect. Furthermore, the extent to which the new genetic technologies will affect genetic variability, vulnerability, or the storage technologies of germplasm has not been determined. As a result, it is currently difficult, if not impossible, to state how much effort should be expended by the National Germplasm System to collect, maintain, and test new gene resources (in this case as seed).

Finally, even if an adequate level of genetic variability can be assessed, the real problem of vulnerability—the practice of planting only a

single variety—must be dealt with at an institutional or social level. Even if no genetic technologies existed, farmers would still select only one or a few "best" varieties for planting.

Issues and Options—Plants

ISSUE: Should an assessment be conducted to determine how much diversity in plant germplasm needs to be maintained?

An understanding of how much germplasm should be protected and maintained would make the management of genetic resources simpler.

OPTIONS:

A. Congress could commission a study of how much genetic variability is necessary or desirable to meet present and future needs.

A comprehensive evaluation of the National Germplasm System's requirements for collecting, evaluating, maintaining, and distributing genetic resources for plant breeding and research could serve as a baseline for a further assessment.

B. Congress could commission a study on the need for international cooperation to manage and preserve genetic resources both in natural ecosystems and in repositories.

This investigation could include an evaluation of the rate at which genetic diversity is being lost from natural and agricultural systems along with an estimate of the effects this loss will have.

C. ***Congress could commission a study on how to develop an early warning system to recognize the potential vulnerability of crops.***

Where high genetic uniformity still exists, proposals could be suggested to reduce any risks due to uniformity. Alternatively, the avenues by which private seed companies could be encouraged to increase the levels of genetic diversity could be investigated.

ISSUE: What are the most appropriate approaches in overcoming the various technical constraints that limit the success of molecular genetics for plant improvement?

Although genetic information has been transferred by vectors and protoplasm fusion, DNA transformations of commercial value have not yet been performed. Molecular engineering has been impeded by the lack of vectors that can transfer novel genetic material into plants, by insufficient knowledge about which genes would be useful for breeding purposes, and by a lack of understanding of the incompatibility of chromosomes from diverse sources. Another impediment has been the lack of researchers from a variety of disciplines.

OPTIONS:

A. The level of funding could be increased for plant molecular genetics research supported by NSF and USDA.

B. Research units devoted to plant molecular genetics could be established under the auspices of the National Institutes of Health (NIH), with emphasis on potential pharmaceuticals derived from plants.

C. An institute for plant molecular genetics could be established under the Science and Education Administration at USDA that would include multidisciplinary teams to consider both basic research questions and direct applications of the technology to commercial needs and practices.

The discoveries of molecular plant genetics will be used in conjunction with traditional breeding programs. Hence, each of the three options could require additional appropriations for agricultural research.

Advances in reproductive biology and their effects on animal improvement

FINDINGS

Much improvement can be made in the germplasm of all major farm animal species using existing technology. The expanded use of artificial insemination (AI) with stored frozen sperm, especially in beef cattle, would benefit both producers and consumers. New techniques for synchronizing estrus should encourage the wider use of **AI. Various manipulations of embryos will find limited use in producing breeding stocks, and sex selection and twinning techniques should be available for limited applications within the next 10 to 20 years.**

The most important technology in reproductive physiology will continue to be AI. Due in part to genetic improvement, the average milk yield of cows in the United States has more than doubled in the past 30 years, while the total number of milk cows has been reduced by more than half. AI along with improved management and the availability and use of accurate progeny records on breeding stock have caused this great increase. (See figure 3.)

The improvement lags behind what is theoretically possible. In practice, the observed increase is about 100 lb of milk per cow per year, while a hypothetical breeding program using AI would result in a yearly gain of 220 lb of milk per cow. The biological limits to this rate of gain are not known.

In comparison with dairy cattle, the beef cattle industry has not applied AI technology widely. Only 3 to 5 percent of U.S. beef is artificially inseminated, compared to 60 percent of the dairy herd. This low rate for beef cattle can be explained by several factors, including management techniques (range v. confined housing) and the conflicting objectives of individual breeders, ranchers, breed associations, and commercial farmers.

The national calf crop—calves alive at weaning as a fraction of the total number of cows exposed to breeding each year—is only 65 to 81 percent. An improvement of only a few percentage points through AI would result in savings of hundreds of millions of dollars to producers and consumers.

Coupled with a technology for estrus-cycle regulation, the use of AI could be expanded for both dairy and beef breeding. Embryo transfer technology, already well-developed but still costly, can be used to produce valuable breeding stock. Sexing technology, which is not yet perfected, would be of enormous benefit to the beef industry because bulls grow faster than heifers.

In the case of animals other than cows:

- Expanded use of AI for swine production will be encouraged by the strong trend to confinement housing, although the poor ability of boar sperm to withstand freezing will continue to be a handicap.
- The benefits of applied genetics have not been realized in sheep production because neither **AI nor performance testing has** been used. As long as the use of AI continues to be limited by the inability to freeze semen and by a lack of agents on the market for synchronizing estrus, no rapid major gains can be expected.
- Increasing interest in goats in the United States and the demand for goat products throughout the world, should encourage attention to the genetic gains that the use of AI and other technologies make possible.
- Poultry breeders will continue to concentrate on improved egg production, growth rate, feed efficiency, and reduced body fat and diseases. The use of frozen semen should increase as will the use of AI and dwarf broiler breeders.
- Genetics applied to production of fish, mollusks, and crustaceans in either natural environments or manmade culture systems is only at the rudimentary stage.

Breeders must have reliable information about the genetic value of the germplasm they are considering introducing. Since farmers do not have the resources to collect and process data on the performance of animals other than those in their own herds, they must turn to outside sources. The National Cooperative Dairy Herd Improvement Program (NCDHIP) is a mod-

Figure 3.-The Way the Reproductive Technologies Interrelate

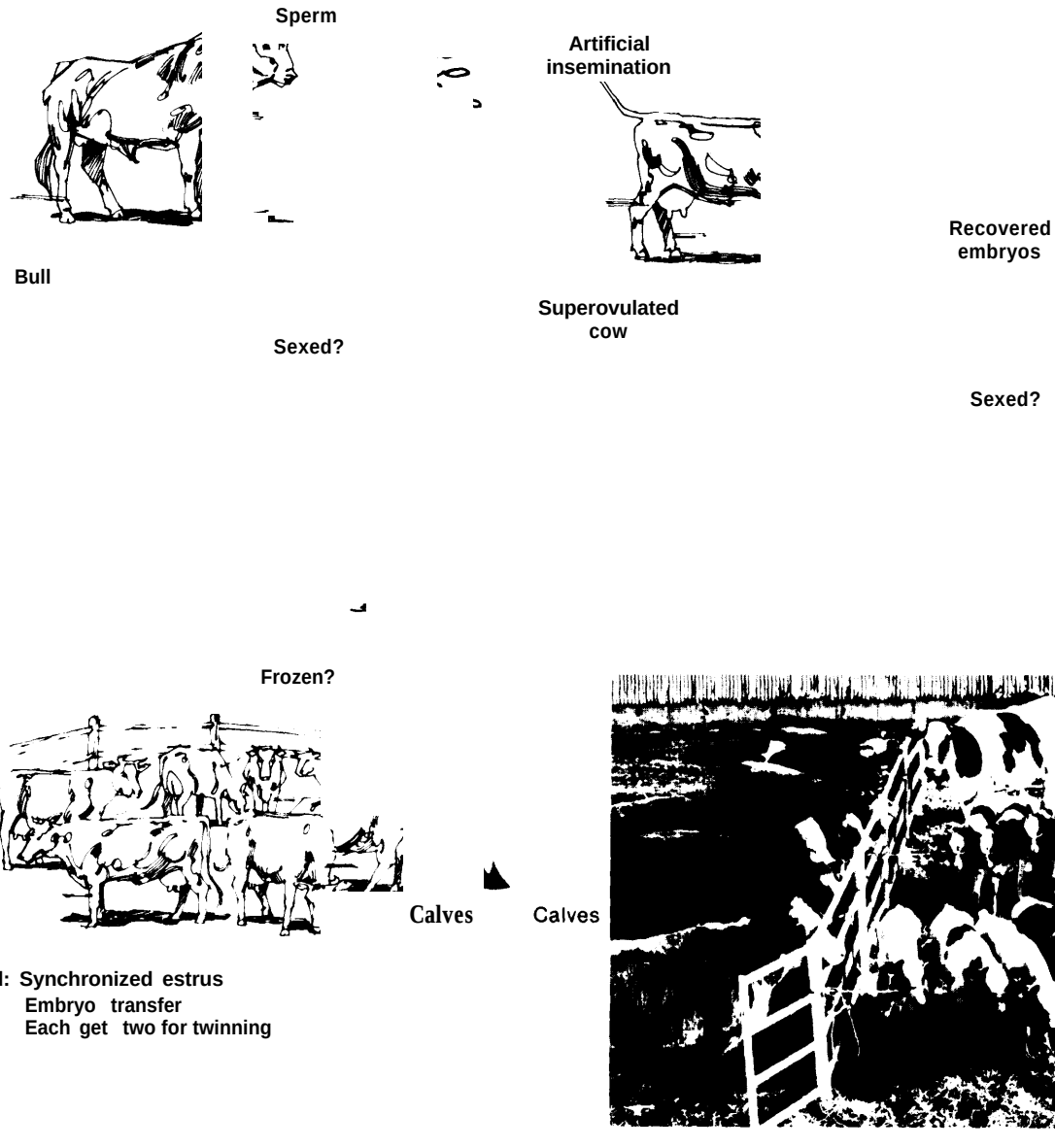


Photo Credit: Science

These 10 calves from Colorado State University were the result of superovulation, in vitro culture, and transfer to the surrogate mother cows on the left. The genetic mother of *all* 10 calves is at upper right

SOURCE: Office of Technology Assessment.

el information system and could be adapted to other species.

Selection—deciding which animals to mate —is the breeder's most basic tool. When going outside his herd to purchase new germplasm, the breeder needs impartial information about the quality of the available germplasm. NCDHIP had recorded **2.8 million of the 10.8 million U.S. dairy cattle in 1979. In 1978, cows enrolled in the official plans of NCDHIP outproduced cows not enrolled by 5,000 lb of milk per cow, representing 52 percent** more milk per lactation.

No comparable information system exists for other types of livestock. Beef bulls, for example, continue to be sold to a large extent on the basis of pedigrees, but with relatively little objective information on their genetic merit. Data on dairy goats in the United States became available through NCDHIP for the first time in late 1980. No nationwide information systems exist for other species, although pork production in the United States would greatly benefit from a national swine testing program.

The more esoteric methods of genetic manipulation will probably have little impact on the production of animals or animal products within the next 10 years. other in vitro manipulations, such as cloning, cell fusion, the production of chimeras, and the use of rDNA techniques, will continue to be of intense interest, especially for research purposes. It is less likely, however, that they will have widespread practical effects on farm production in this century.

Each technique requires more research and refinement. Until specific genes of farm animals can be identified and located, no direct gene manipulation will be practicable. In addition this will be difficult because most traits of importance are due to multiple genes.

Issue and Options—Animals

ISSUE: How can the Federal Government improve the germplasm of major farm animal species?

OPTIONS:

A. Programs like the NCDHIP could have increased governmental participation and funding. The efforts of the Beef Cattle Improvement Federation to standardize procedures could receive active support, and a similar information system for swine could be established.

The fastest and least expensive way to upgrade breeding stock in the United States is through effective use of information. Computer technology, along with a network of local representatives for data collecting, can provide the individual farmer or breeder with accurate information on the available germplasm so that he can make his own breeding decisions.

This option implies that the Federal Government would play such a role in new programs, and expand its role in existing ones.

B. Federal funding could be increased for basic research in total animal improvement.

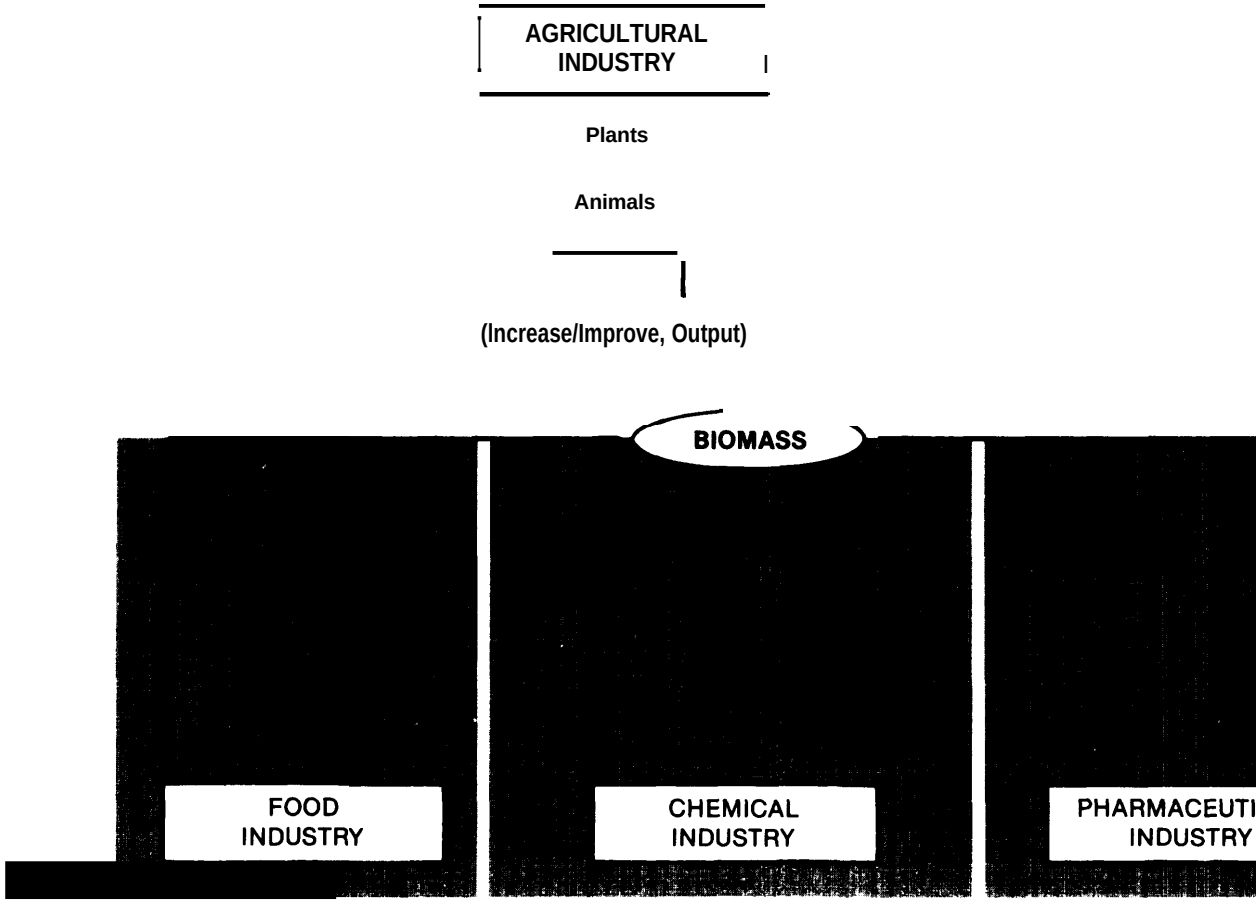
This option, in contrast to option A, assumes that it is necessary to maintain or expand basic R&D to generate new knowledge that can be applied to the production of improved animals and animal products.

* * *

The wide variety of applications for genetic engineering is summarized in figure 4. Genetics can be used to improve or increase the quality and output of plants and animals for direct use by man. Alternatively, materials can be extracted from plants and animals for use in food, chemical, and pharmaceutical industries.

Biological materials can also be converted to useful products. In this process, genetic engineering can be used to develop micro-organisms that will carry out the conversions. Therefore, genetic manipulation cannot only provide more or better biological raw materials but can also aid in their conversion to useful products.

Figure 4.—Applications of Genetics



SOURCE: Office of Technology Assessment.

Institutions and society

Regulation of genetic engineering

FINDINGS

No evidence exists that any unexpectedly harmful genetically engineered organism has been created. Yet few experts believe that molecular genetic techniques are totally without risk to health and the environment. Information that has proved useful in assessing the risks from these techniques has come from three sources: experiments designed specifically to test the consequences of working with rDNA, experiments designed for other purposes but relevant to levant and scientific meetings and workshops.

A program of risk assessment was established at NIH in 1979 to conduct experiments and collate relevant information. It assesses one form of genetic engineering, rDNA. On the basis of these data, conjectured, inadvertent risk is generally regarded as less likely today than originally suspected. Risk due to the manipulation of genes from organisms known to be hazardous is considered to be more realistic. Therefore, microbiological safety precautions that are

appropriate to the use of the micro-organisms serving as the source of DNA are required. Nevertheless, it has not been demonstrated that combining those genes in the form of rDNA is any more hazardous than the original source of the DNA.

Perceptions of the nature, magnitude, and acceptability of the risk differ. In addition, public concern has been expressed about possible long-range impacts of genetic engineering. In this context, the problem facing the policymaker is how to address the risk in a way that accommodates the perceptions and values of those who bear it.

The NIH Guidelines for Research Involving Recombinant DNA Molecules and existing Federal laws appear adequate in most cases to deal with the risks to health and the environment presented by genetic engineering. However, the Guidelines are not legally binding on industry, and no single statute or combination will clearly cover all foreseeable commercial applications of genetic engineering.

The Guidelines are a flexible evolving oversight mechanism that combines technical expertise with public participation. They cover the most widely used and possibly risky molecular genetic technique–rDNA–prohibiting experiments using dangerous toxins or pathogens and setting containment standards for other potentially hazardous experiments. Although compliance is mandatory only for those receiving NIH funds, other Federal agencies follow them, and industry has proclaimed voluntary compliance. Rare cases of noncompliance have occurred in universities but have not posed risks to health or the environment. As scientists have learned more about rDNA and molecular genetics, the restrictions have been progressively and substantially relaxed to the point where 85 percent of the experiments can now be done at the lowest containment levels, and virtually all monitoring for compliance now rests with approximately 200 local self-regulatory committees called institutional biosafety committees (IRCs). (See table 1.)

Under the Guidelines, NIH serves an important oversight role by sponsoring risk assessment programs, certifying new host-vector systems, serving as an information clearinghouse, and coordinating Federal and local activities. Limitations in NIH's oversight are that: it lacks legal authority over industry; its procedures for advising industry on large-scale projects have not incorporated sufficient expertise on large-scale fermentation technology; its monitoring for either compliance or consistent application of the Guidelines by individuals or institutions is virtually nonexistent; and it has not systematically evaluated other techniques, such as cell fusion, that might present risks.

Federal laws on health and environment will cover most commercial applications of genetic engineering. Products such as drugs, chemicals, and foods can be regulated by existing laws. However, uncertainty exists about the regulation of either production methods using engineered micro-organisms or their intentional release into the environment, when the risk has not been clearly demonstrated. While a broad interpretation of certain statutes, such as the Occupational Safety and Health Act and the Toxic Substances Control Act, might cover these

Table I.—Containment Recommended by the National institutes of Health

Biological—Any combination of vector and host must be chosen to minimize both the survival of the system outside of the laboratory and the transmission of the vector to nonlaboratory hosts. There are three levels of biological containment:	
[illegible]	**Requires the use of *Escherichia coli K12* or other weakened strains of micro-organisms that are less able to live outside the laboratory.**
[illegible]	**Requires the use of specially engineered strains that are especially sensitive to ultraviolet light, detergents, and the absence of certain uncommon chemical compounds.**
[illegible]	**No organism has yet been developed that can qualify as HV3.**
Physical—Special laboratories (P1-P4)	
[illegible]	**Good laboratory procedures, trained personnel, wastes decontaminated**
[illegible]	**Biohazards sign, no public access, autoclave in building, hand-washing facility**
[illegible]	**Negative pressure, filters in vacuum line, class II safety cabinets**
[illegible]	**Monolithic construction, air locks, all air decontaminated, autoclave in room, all experiments in class III safety cabinets (glove box), shower room**

SOURCE: Office of Technology Assessment.

situations, regulatory actions based on such interpretations could be challenged in court. In any evident those agencies that could have substantial regulatory authority over commercial genetic engineering have not yet officially acted to assert that authority.

Issue and Options—Regulation

ISSUE: How could Congress address the risks presented by genetic engineering?

OPTIONS:

A. Congress could maintain the status quo by letting NIH and the regulatory agencies set the Federal policy.

Congress might determine that legislation to remedy the limitations in current Federal oversight would result in unnecessary and burdensome regulation. No known harm to health or the environment has occurred under current regulation. Also the agencies generally have the legal authority and expertise to adapt to most new problems posed by genetic engineering.

The disadvantages are the lack of a centralized, uniform Federal response to the problem, and the possibility that risks associated with commercial applications will not be adequately addressed. Conflicting or redundant regulations of different agencies would result in unnecessary burdens on those regulated.

B. Congress could require that the Federal Interagency Advisory Committee on Recombinant DNA Research prepare a comprehensive report on its members' collective authority to regulate rDNA and on their regulatory intentions.

The Industrial Practices Subcommittee of this Committee has been studying agency authority over commercial rDNA activities. Presently, there is little official guidance on regulatory requirements for companies that may soon market products made by rDNA methods. A congressionally mandated report would ensure full consideration of these issues by the agencies and expedite the process. On the other hand, the agencies are studying the situation, which must be done before they can act. Also, it is often easier and more efficient to act on each case as it arises, rather than on a hypothetical basis before the fact.

C. Congress could require that all recombinant DNA activity be monitored for a limited number of years.

This represents a "wait and see" position by Congress and the middle ground between the status quo and full regulation. It recognizes and balances the following factors: 1) the absence of demonstrated harm to human health or the environment from genetic engineering; 2) the continuing concern that genetic engineering presents risks; 3) the lack of sufficient knowledge and experience from which to make a final judgment; 4) the existence of an oversight mechanism that seems to be working well, but that has clear limitations with respect to commercial activities; 5) the virtual abolition of Federal monitoring of rDNA activities by recent amendments to the Guidelines; and 6) the expected increase in commercial genetic engineering.

This option would provide a data base that could be used for: 1) determining the effectiveness of voluntary compliance with the Guidelines by industry, and mandatory compliance by Federal grantees; 2) determining the quality and consistency of the local self-regulatory actions; 3) continuing a formal risk assessment program; 4) identifying vague or conflicting provisions of the Guidelines for revision; 5) identifying emerging trends or problems; and 6) tracing any long-term adverse impacts on health or the environment to their sources.

The obvious disadvantage of this option would be the required paperwork and effort by scientists, universities, corporations, and the Federal Government.

D. Congress could make the NIH Guidelines applicable to all rDNA work done in the United States.

This option would eliminate any concern about the effectiveness of voluntary compliance with the Guidelines, and it has the advantage of

using an existing oversight mechanism. The major changes that would have to be made in the area of enforcement. Present penalties for noncompliance—suspension or termination of research funds-are obviously inapplicable to industry. In addition, procedures for monitoring compliance would have to be strengthened.

The main disadvantage of this option is that NIH is not a regulatory agency. Since NIH has traditionally viewed its mission as promoting biomedical research, it would have a conflict of interest between regulation and promotion. One of the regulatory agencies could be given the authority to enforce the Guidelines.

E. Congress could require an environmental impact statement and agency approval before any genetically engineered organism is intentionally released into the environment.

There have been numerous cases where an animal or plant species has been introduced into a new environment and has spread in an uncontrolled and undesirable fashion. Yet in pollution control, mineral leaching, and enhanced oil recovery, it might be desirable to release large numbers of engineered micro-organisms into the environment.

The Guidelines currently prohibit deliberate release of any organism containing rDNA without approval of NIH. One disadvantage of this prohibition is that it lacks the force of law. Another is that approval may be granted on a finding that the release would present "no significant risk to health or the environment;" a tougher or more specific standard may be desirable.

A required study of the possible consequences of releasing a genetically engineered organism would be an important step in ensuring safety. An impact statement could be filed before permission is granted to release the organism. However, companies and individuals might be discouraged from developing useful organisms if this process became too burdensome and costly.

F. Congress could pass legislation regulating all types and phases of genetic engineering from research through commercial production.

This option would deal comprehensively and directly with the risks of novel molecular genetic techniques. A specific statute would eliminate the uncertainties over the extent to which present law covers particular applications of genetic engineering and any concerns about the effectiveness of voluntary compliance with the Guidelines. Alternatively, the legislation could take the form of amending existing laws to clarify their applicability to genetic engineering.

Other molecular genetic techniques, while not as widely used and effective as rDNA, raise similar concerns. Of the current techniques, cell fusion is the prime candidate for being treated like rDNA in any regulatory framework. No risk assessment of this technique has been done, and no Federal oversight exists.

The principal argument against this option is that the current system appears to be working fairly well, and the limited risks of the techniques may not warrant the significantly increased regulatory burden that would result from such legislation.

G. ***Congress could require NIH to rescind the Guidelines.***

Deregulation would have the advantage of allowing money and personnel currently involved in implementing the Guidelines at the Federal and local levels to be used for other purposes.

There are several reasons for retaining the Guidelines. Sufficient scientific concern exists for the Guidelines to prohibit certain experiments and to require containment for others. Most experiments can be done at the lowest, least burdensome containment levels. NIH is serving an important role as a centralized oversight and information coordinating body, and the system has been flexible enough in the past to liberalize the restrictions as evidence indicated lower risk than originally thought.

H. Congress could consider the need for regulating work with all hazardous micro-organisms and viruses, whether or not they are genetically engineered.

It was not within the scope of this study to examine this issue, but it is an emerging one that Congress may wish to consider.

76-565 0 - 81 - 3

Patenting living organisms

On June 16, 1980, in a 5-to-4 decision, the Supreme Court ruled that a human-made micro-organism was patentable under Federal patent statutes. The decision while hailed by some as assuring this country's technological future was at the same time denounced by others as creating Aldous Huxley's Brave New World. It will do neither.

FINDINGS

1. ***Meaning and Scope of the*** Decision.—The decision held that a patent could not be denied on a genetically engineered micro-organism that otherwise met the legal requirements for patentability solely because it was alive. It was based on the Court's interpretation of a provision of the patent law which states that a patent may be granted on ". . . any new and useful . . . manufacture, or composition of matter. . . ." **(35 U.S.C. $101)**

It is uncertain whether the case will serve as a legal precedent for patenting more complex organisms. Such organisms, however, will probably not meet other legal prerequisites to patentability that were not at issue here. In any event, fears that the case would be legal precedent sometime in the distant future for patenting human beings are unfounded because the 13th amendment to the Constitution absolutely prohibits ownership of humans.

2. *Impact on the Biotechnology Industry.—The* decision is not crucial to the development of the industry. It will stimulate innovation by encouraging the dissemination of technical information that otherwise would have been maintained as trade secrets because patents are public documents that fully describe the inventions. In addition, the ability to patent genetically engineered micro-organisms will reduce the risks and uncertainties facing individual companies in the commercial development of those organisms and their products, but only to a limited degree because reasonably effective alternatives exist. These are: 1) maintaining the organisms as trade secrets; 2) patenting microbiological processes and their products; and 3) patenting inanimate components of micro-organisms, such as genetically engineered plasmids.

3. ***Impact on the Patent Law and the Patent and Trademark*** Office.— Because of the complexity, reproducibility, and mutability of living organisms, the decision may cause some problems for a body of law designed more for inanimate objects than for living organisms. It raises questions about the proper interpretation and application of the patent law requirements of novelty, nonobviousness, and enablement. In addition, it raises questions about how broad the scope of patent coverage on important micro-organisms should be, and about the continuing need for two statutes, the Plant Patent Act of 1930 and the Plant Variety Protection Act of 1970. These uncertainties could result in increased litigation, making it more difficult and costly for owners of patents on living organisms to enforce their rights.

The impact on the Patent and Trademark Office is not expected to be significant in the next few years. Although the number of patent applications on micro-organisms have almost doubled during 1980, the approximately 200 pending applications represent less than 0.2 percent of those processed each year by the Office. While the number of such applications is expected to increase in the next few years because of of the decision and developments in the field, the Office should be able to accommodate the increase. A few additional examiners may be needed. ,

4. *Impact on Academic* Research.—Because the decision may encourage academic scientists to commercialize the results of their research, it may inhibit the free exchange of information, but only if scientists rely on trade secrecy rather than patents to protect their inventions from competitors in the marketplace. In this respect, it is not clear how molecular biology differs from other research fields with commercial potential.

Issue and Options—Patenting Living Organisms

ISSUE: To what extent could Congress provide for or prohibit the patent ing of living organisms?

OPTIONS:

The Supreme Court stated that it was undertaking only the narrow task of determining whether or not Congress, in enacting the patent statutes, had intended a manmade micro-organism to be excluded from patentability solely because it was alive. Moreover, the opinion specifically invited Congress to overrule the decision if it disagreed with the Court's interpretation. Congress can act to resolve the questions left unanswered by the Court, overrule the decision, or develop a comprehensive statutory approach. Most importantly, Congress can draw lines; it can decide which organisms, if any, should be patentable.

A. Congress could maintain the status quo.

Congress could choose not to address the issue of patentability and allow the law to be developed by the courts. The advantage of this option is that issues will be addressed as they arise, in the context of a tangible, nonhypothetical case.

There are two disadvantages to this option: a uniform body of law may take time to develop; and the Federal judiciary is not designed to take sufficient account of the broader political and social interests involved.

B. Congress could pass legislation ***dealing with the specific legal issues raised by the Court's decision.***

Many of the legal questions are so broad and varied that they do not readily lend themselves to statutory resolution, The precise meaning of the requirements for novelty, nonobviousness, and enablement as applied to biological inventions will be most readily developed on a case-by-case basis by the Patent Office and the Federal courts. On the other hand, some questions are fairly narrow and well-defined; thus, they could be better resolved by statute. The most important question is whether there is a continuing need for the two plant protection acts that grant ownership rights to plant breeders who develop new and distinct varieties of plants.

C. ***Congress could mandate a study of the Plant Patent Act of 1930 and the Plant Variety Protection Act*** of 1970.

These Acts could serve as models for studying the broader, long-term potential impacts of patenting living organisms. Such a study would be timely not only because of the Court's decision, but also because of allegations that the Acts have encouraged the planting of uniform varieties, loss of genetic diversity, and increased concentration in the plant breeding industry.

D. Congress could prohibit patents either on any living organism or on organisms other than those already subject to the plant protection Acts.

By prohibiting patents on any living organisms, Congress would be accepting the arguments of those who consider ownership rights in living organisms to be immoral, or who are concerned about other potentially adverse impacts of such patents, A total prohibition would slow but not stop the development of molecular genetic techniques and the biotechnology industry because there are severa] good alternatives for maintaining exclusive control of biological inventions. Development would be slowed primarily because information that might otherwise become public would be withheld as trade secrets. A major consequence would be that desirable products would take longer to reach the market.

Alternatively, Congress could overrule the Supreme Court's decision by amending the patent law to prohibit patents on organisms other than the plants covered by the two statutes mentioned in option C. This would demonstrate congressional intent that living organisms could be patented only by specific statute.

E. Congress could pass a comprehensive law covering any or all organisms (except humans).

This option recognizes that Congress can draw lines where it sees fit in this area. It could specifically limit patenting to micro-organisms,

or it could encourage the breeding of agriculturally important animals by granting patent rights to breeders of new and distinct breeds. In the interest of comprehensiveness and uniformity, one statute could cover plants and all other organisms that Congress desires to be patentable.

Genetics and society

FINDINGS

Continued advances in science and technology are beginning to provide choices that strain human value systems in areas where previously no choice was possible. Existing ethical and moral systems do not provide clear guidelines and directions for those choices. New programs, both in public institutions and in the popular media, have been established to explore the relationships among science, technology, society, and value systems, but more work needs to be done.

Genetics-and other areas of the biological sciences—have in common a much closer relationship to certain ethical questions than do most advances in the physical sciences or engineering. The increasing control over the characteristics of organisms and the potential for altering inheritance in a directed fashion raise again questions about the relationship of humans to each other and to other living things. People respond in different ways to this potential; some see it (like many predecessor developments in science) as a challenging opportunity, others as a threat, and still others respond with vague unease. Although many people cannot articulate fully the basis for their concern, ethical, moral, and religious reasons are often cited.

The public's increasing concern about the advance of science and impacts of technology has led to demands for greater participation in decisions concerned with scientific and technological issues, not only in the United States but throughout the world. The demands imply new challenges to systems of representative government. In every Western country, new mechanisms have been devised for increasing citizen participation.

The public has already become involved in decisionmaking with regard to genetics. As the science develops, additional issues in which the public will demand involvement can be anticipated for the years ahead. The question then becomes one of how best to involve the public in decisionmaking.

Issues and Options—Genetics and Society

Issue: How should the public be involved in determining policy related to new applications of genetics?

Because public demands for involvement are unlikely to diminish, ways to accommodate these demands must be considered.

OPTIONS:

A. Congress could specify that public opinion must be sought in formulating all major policies concerning new applications of genetics, including decisions on the funding of specific research projects. A "Public Participation Statement" could be mandated for all such decisions.

B. Congress could maintain the status quo, allowing the public to participate only when it decides to do so on its own initiative.

If option A were followed, there would be no cause for claiming that public involvement was inadequate (as occurred after the first set of Guidelines for Recombinant DNA Research was promulgated). Option A poses certain problems: How to identify a major policy and at what stage public involvement would be required. Should it take place only when technological development and application are imminent, or at the basic research stage?

Option B would be less cumbersome to effect. It would permit the establishment of ad hoc mechanisms when necessary.

ISSUE: How can the level of public knowledge concerning genetics and its potential be raised?

There are some educators who believe that **too little** time is spent on genetics within the **traditional educational** system. outside the traditional school system, a number of sources may contribute to increased public understanding of science and the relationship between science and society.

Efforts to increase public understanding should, of course, be combined with carefully designed evaluation programs so that the effectiveness of a program can be assessed.

OPTIONS:

A. ***Programs could be developed to increase public understanding of science and the relationship between science, technology, and society.***

Public understanding of science in today's world is essential, **and there is concern about the adequacy** of the **public's knwledge.**

B. programs could be established to monitor the level of ***public understanding of genetics and*** of ***science in general, and to determine whether public concern with decisionmaking in science and technology is increasing.***

Selecting this option would indicate that there is need for additional information, and that Congress is interested in involving the public indeveloping science policy.

C. ***The copyright laws could be amended to permit schools to videotape television programs for educational purposes.***

Under current copyright law, videotaping television programs as they are being broadcast may infringe on the rights of the program's owner, generally its producer. The legal status of such tapes is presently the subject of litigation.

In favor of this option, it should be noted that many of the programs are made at least in part with public funds. Removing the copyright constraint on schools would make these programs more available for another public good, education. On the other hand, this option could have significant economic consequences to the copyright owner, whose market is often limited to educational institutions.

ISSUE: Should Congress begin preparing now to resolve issues that have not yet aroused much public debate but which may in the future?

As scientific understanding of genetics and the ability to manipulate inherited characteristics develops, society may face some difficult questions that could involve tradeoffs between individual freedom and the needs of society. This will be increasingly the case as genetic technologies are applied to humans. Developments are occurring rapidly. Recombinant DNA technology was developed in the 1970's. In the spring of 1980, investigators succeeded in the first gene replacement in mammals; in the fall of ***1980,*** the first gene substitution in humans was attempted.

Although this study was restricted to nonhuman applications, many people assume from these and other examples that what can be done with lower animals can be done with humans and will be. Therefore, some action might be taken to better prepare society for decisions on the application of genetic technologies to humans.

OPTIONS:

A. A commission could be established to identify central issues, the probable time frame for application of ***various genetic technologies to humans, and the probable effects on society, and to suggest courses of action. The commission might also consider the related area of how participatory democracy might be combined with representative democracy in decisionmaking.***

B. The life of the President Commission could be extended for the study of Ethical problems in Medicine and Biomedical and Behavioral Research, for the purpose of addressing these issues.

This 1 l-member ‘Commission was established in November 1978 and terminates on December 31, 1982. It could be asked to broaden its coverage to additional areas. This would require that the life span of the commission be extended and additional funds be appropriated.

A potential disadvantage to using the existing commission to address societal issues associated with genetic engineering is that a number of issues already exist, and more are likely to arise in the years ahead. Yet there are also other issues in medicine and biomedical and behavioral research not associated with genetic engineering that also need review. Whether all these issues can be addressed by one commission should be considered. Comments from the existing commission would assist in deciding the most appropriate course of action.