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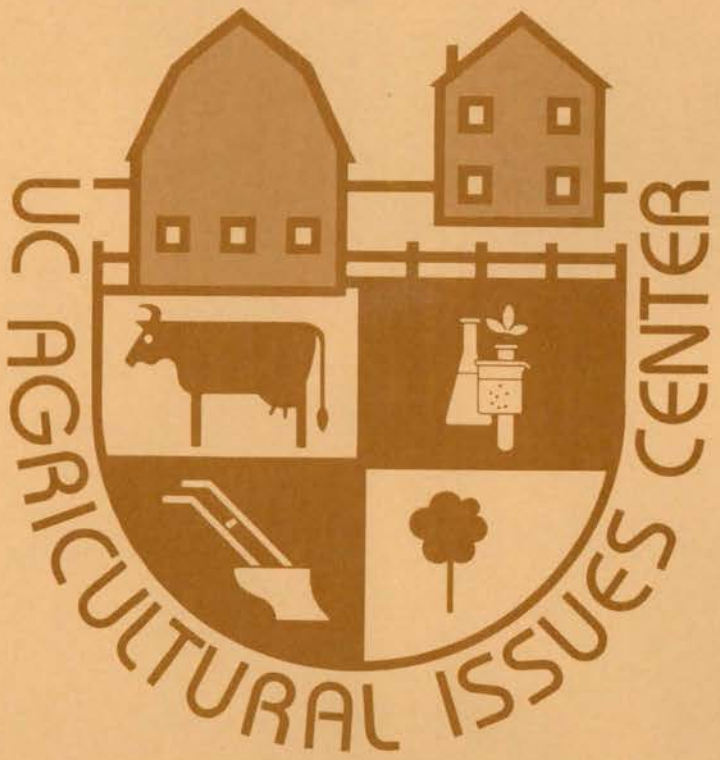

Agricultural Issues Center
University of California
Davis, CA 95616

University of California
Department of Agricultural Economics, UC Davis
and
Agricultural Issues Center

AGRICULTURAL BIOTECHNOLOGY RESEARCH: AN OVERVIEW

by

Luanne Lohr, Harold O. Carter, and Samuel H. Logan[1]

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[1]The authors are respectively, a graduate research assistant and Professors of Agricultural Economics at the University of California, Davis.

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1. INTRODUCTION

Significant technological advances have marked agricultural production throughout history. These new technologies have lowered production costs, increased yield and quality of agricultural products, and changed the structure of the industry. The current generation of improvements lies mostly within the realm of biotechnology. Biotechnology is a field of activity defined as "the application of scientific and engineering principles to the processing of materials by biological agents to provide goods and services" (Bull, Holt and Lilly, 1982).

Expenditures in 1985 by the U.S. Department of Agriculture for biotechnology research totalled $75.1 million (Phillips, 1985). Estimates of budgeted and actual expenditures on research and commercialization of biotechnology by private firms ranges from $180 million (Phillips, 1985) to $2 billion (Cape, 1984).

An example of potential returns from biotechnological genetic improvement is found in the case of Zea diploperennis, an ancient wild relative of corn. The potential lies in transferring genes from this perennial variety to the standard annual varieties. One University of California researcher estimated potential savings to farmers from not having to buy seed and prepare croplands every year at $4.4 billion annually worldwide (Witt, 1985).

An era of biotechnological innovation has begun with the expansion of basic and applied research in such areas as genetic engineering for

agriculture. Basic research may be defined as "inner-directed" towards the development of primary scientific structure and knowledge, while applied research may be viewed as "outer-directed" towards relationships outside the world of primary scientific knowledge (Carter and Oreskes, 1984). In many instances, this distinction blurs when basic research results are directly useful in commercial applications.

This report describes some of the current research in agricultural biotechnology in the United States and in other countries. An all-inclusive effort is beyond the scope of this paper, but examples from many fields of agriculture are given. A discussion of roles played by universities, corporations, and governments is also provided.

The paper is drawn from current sources on biotechnology research. A two-volume compilation of papers from the proceedings of meetings called Biotech '84 held in Europe and the United States provides information on legal, institutional, and economic aspects of biotechnology research, as well as scientific reports. The periodical Practical Biotechnology, a monthly publication, reports changes in the industry and the research progress of specific biotechnology firms. Biotechnological advances made by international agricultural research centers are discussed in Biotechnology in International Agricultural Research, the proceedings of a conference held at the International Rice Research Institute in the Phillipines in 1984. Reports by the U.S. Office of Technology Assessment and the National Research Council of the National Academy of Sciences provide explanations of the technical aspects of biotechnology research as well as examples of recent

accomplishments in the field. Many other valuable publications and reports exist, but for the reader who wishes a good introduction with a minimal bibliography, these works and others cited in the reference section represent a useful background.

Section 2 provides an overview of the process of research development and production of biotechnology. The "actors" in the system and the methods of funding are discussed. Section 3 gives detailed examples of biotechnology in basic research and in plant, animal and related agricultural research. Section 4 summarizes directions for social science research on biotechnological advances.

2. RESEARCH, DEVELOPMENT, AND PRODUCTION

Section 2.1 describes the processes involved in the evolution of a biotechnology from an idea to an application to a commercially viable product. The motivations and roles of the agents of these processes are discussed. Section 2.2 outlines funding aspects of biotechnology research and development. Problems arising from differing outlooks of the actors in the biotechnology transfer process are delineated in Section 2.3.

2.1 Biotechnology Transfer

Biotechnology transfer may be described by three processes: research, development, and production. Research involves the formation of a basic concept in biotechnology and the preliminary work which creates a tangible result of the ideas. Development refers to the process by which basic research is transformed into practical applications. Production is the manufacturing process which makes the biotechnology available on a commercial level.

As an example, a concept such as genetic control of nitrogen fixation might be a subject of research. This could be developed into a process for fixing nitrogen in cereals or other nonlegumes. Production of the genetic material needed for commercialization of the process might then be undertaken.

The three main agents in this biotechnology transfer process are universities, corporations, and governments. The roles they play in the biotechnology industry are often overlapping. A simplified diagram of the processes each performs is given in Figure 1.

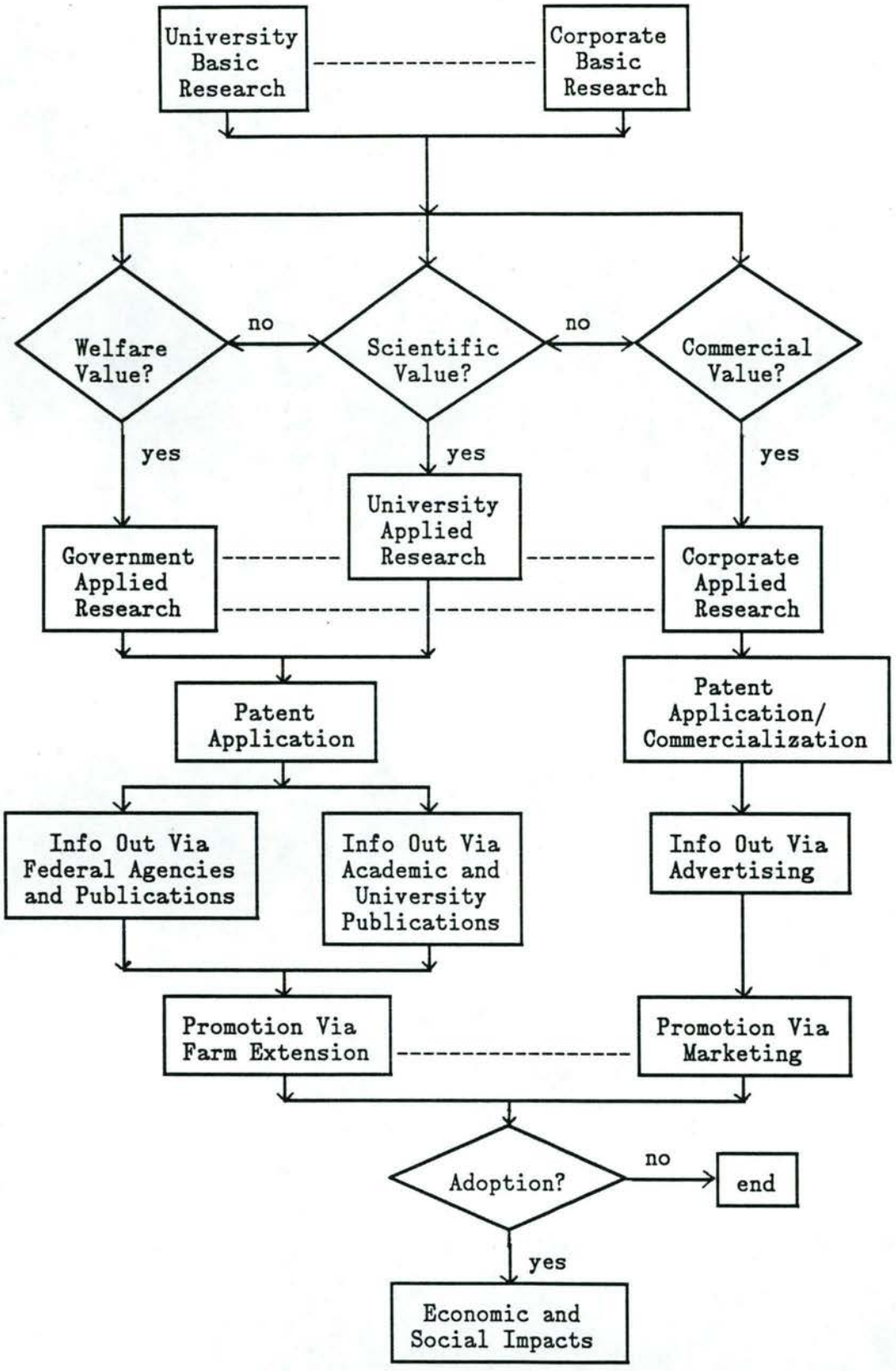

FIGURE 1. Flow Diagram of Agricultural Biotechnology Transfer Process

Basic research forms the groundwork for applications. Usually, this work is funded by federal governments and performed by universities or research institutes. However, private industry is involved in biotechnology basic research to some extent, either directly or through funding of university groups to promote innovation (Committee on Biotechnology, 1984). Success at this stage may be judged by the gains in understanding of genetic processes and the analysis of biotechnology from conceptual to concrete examples.

Results of basic research are usually carried forward into applied research, which may be performed by any of the three entities. Each of these agents has objectives which guide the decision of whether to pursue applied research. Figure 1 shows the primary motivations usually ascribed to each entity. Governments, and the international consortiums they fund, may ask whether the basic research has social value, such as whether third world food supplies may be increased as a result of an application of this research. Universities typically pursue research which has scientific value, whether it will result in widespread applications or not. Corporations base their applied research decisions on the potential commercial value of results.

Clearly, a single biotechnological innovation may meet all three criteria at once. For example, nitrogen fixation in nonlegumes is worth pursuing from social, academic, and commercial standpoints. Additionally, cooperation among the three agents may provide more than one reason for pursuing applied research. For instance, university basic and applied research may be performed under contract to a private

corporation or in conjunction with research by private firms, so that both academic and commercial potential are of interest. Federal agencies such as the U.S. Department of Agriculture may work with research departments in the land grant university system to develop biotechnology which has social, academic and commercial value (Committee on Biotechnology, 1984). In other countries, government and corporate cooperative efforts are being established which are socially and commercially motivated (Practical Biotechnology, March 1983).

Both universities and federal organizations tend to disseminate their research findings as results become available. Although monetary gain is not usually a primary motivation for undertaking research, patent applications are often made to insure that the inventor and/or the sponsoring university or government receive royalties due them. Academic and university extension publications and government documents usually serve as sources of information about new developments. These sources are available to the general public at low cost. Farm extension programs are utilized to introduce and promote the proper use of the product or process. For biotechnological developments, the clientele for farm extension programs is expected to include industrialists, financiers, and venture capitalists, as well as farm operators (Committee on Biotechnology, 1984).

Corporations typically restrict access to their research results for proprietary reasons. They attempt to protect the potential returns to applied biotechnology by patenting processes and registering plant or animal innovations. At this stage, there may be greater reliance on

farm extension programs to help determine the most acceptable form, process or practice for marketing biotechnology products (Committee on Biotechnology, 1984). Construction and operation of large-scale facilities for production of biotechnology commodities may begin in anticipation of future sales. Information is then disseminated through advertising, often in trade publications. Promotion of the biotechnology occurs through the marketing chain, which may include sales representatives who visit farms and farm supply outlets to demonstrate the correct use of the process or product.

Despite availability of information about biotechnology innovations and their use, there is no guarantee of farm adoption of the process or product. Usually, commercialization by corporations is undertaken only after an innovation is assigned a high probability of customer acceptance through market studies. However, several factors can work against adoption. The timing of the introduction may be poor, or the cost-reducing or output-increasing potential overrated.

2.2 Funding Biotechnology Transfer

Funding of basic research is primarily conducted by federal governments. Typically, basic research has aspects of a public good, providing utility for all segments of society in the form of scientific information, with the property of being nonexclusive. Although private corporations do undertake basic research, the lack of a direct market for the results and the expense and financial risk involved tend to lessen this possibility. Private firms may develop relations with universities to promote basic research with commercial potential. Basic

research performed by firms is often undertaken at the behest of governments, who provide the funding for such projects.

Applied research is commonly funded by both public and private sector groups. Governments may fund university, institute, and corporate research. Corporations may fund university research or engage in joint ventures with other private groups.

2.2.1 Government Support

The levels of funding and official encouragement for agricultural biotechnology provided by federal governments vary. Data on exact expenditures by country are not available. However, reports prepared by federal agencies often give some clue as to the extent of support.

An example of differing commitments in the European Economic Community (EEC) is provided in Table 1. Expenditures of each country in the general field of biotechnology in 1982 are reported in millions of e.u.a (European units of account). These amounts are then compared to the total EEC budget of 502.1 million eua for agricultural research in 1980.

The United Kingdom spent the most on biotechnology (35.0 million e.u.a.), while Belgium spent the least (5.0 million e.u.a.). For two countries, Italy and the Netherlands, no expenditures were made in 1982, but spending was proposed for the future. The total funding for biotechnology in 1982 was about 91.0 million e.u.a. Funds are not only spent on basic research, but on education (France), formation of biotechnology centers (Federal Republic of Germany, France and the United Kingdom), promotion of industrial ventures (France and the United Kingdom), and foundation studies (Federal Republic of Germany).

TABLE 1. WESTERN EUROPEAN PUBLIC SECTOR SPENDING ON BIOTECHNOLOGY AND BIOTECHNOLOGY-RELATED AGRICULTURAL FIELDS

Country	Expenditure[a]	Percentage of 1980 EEC Total Agricultural Research Budget[b]
Belgium	5.0	1.0
Federal Republic Germany	22.0	4.4
France	29.0	5.8
Italy	20.0[c]	4.0[c]
Netherlands	28.0[c]	5.6[c]
United Kingdom	35.0	7.0
Total	91.0[d]	18.2[d]

[a]Million European units of account (e.u.a.) 1982.

[b]Total spending in 1980 in the European Economic Community, excluding Denmark, for research in biotechnology-related agricultural areas is as follows: general agricultural research (126.4 M eua), domestic medical animal products (168.3 M eua), crops and wine (303.3 M eua), food, drink and tobacco (4.1 M eua). The total expenditures in this area were 502.1 M eua.

[c]Proposed in five-year plans.

[d]Excludes Italy and the Netherlands.

SOURCE: "Wise Words But No Action in Brussels," Practical Biotechnology, v.3, no. 1, March 1983, pp. 9-13

The comparison of expenditures in 1982 with the total agricultural budget in 1980 must be viewed with some caution. The obvious discrepancy in units and the fact that in some cases, perhaps none of the biotechnology expenditures for a country are applied to agricultural research prevent conclusive discussion. However, these numbers do provide some sense of the upper limit that agricultural biotechnology could achieve. If all existing biotechnology expenditures had been devoted to agricultural research, the highest expenditure by any country would have been 7.0 percent (United Kingdom) of the total agricultural research budget in the EEC. Total biotechnology spending would have been 18.2 percent of the total EEC agricultural research budget for 1980. Allowing for inflation, these percentages are even smaller.

The United States has demonstrated the greatest commitment to basic biotechnology research of competitor countries in western Europe and Japan. Recent data for agricultural biotechnology expenditures in the United States were made available by the U. S. Department of Agriculture (USDA) and cited by Phillips (1985). The past and current expenditures for fiscal years 1983 through 1985 are delineated in Table 2.

Increases in funding have occurred in most areas over the 1983 to 1985 time period. The greatest increases have been in Agriculture Research Service (ARS) commodity conversion and delivery (2400 percent), Cooperative State Research Service (CSRS) special research grants (112.5 percent) and competitive research grants (255.4 percent), and Forest Service intramural grants (150 percent). ARS funding for plant productivity and animal productivity biotechnology research has increased 69.5 percent and

TABLE 2. AGRICULTURAL BIOTECHNOLOGY RESEARCH FUNDING IN THE UNITED STATES

Area of Research	Funding (10^6 current $) FY1983	FY1984	FY1985	1985 Funding As Percentage of 1985 Total
Agriculture Research Service (ARS)				
Plant productivity	5.9	6.9	10.0	13.3
Animal productivity	6.6	6.8	8.8	11.8
Soil and water conservation	1.0	1.1	0.2	0.3
Commodity conversion and delivery	0.3	0.6	7.2	9.6
Human nutrition	a	a	0.1	0.1
Cooperative State Research Service (CSRS)				
Hatch Act	8.9	9.1	12.2	16.3
Special research grants	1.6	3.5	3.4	4.5
Competitive research grants	8.3	9.0	29.5	39.4
All other CSRS	1.0	1.0	1.0	1.3
Forest Service				
Intramural	0.4	1.1	1.0	1.3
Competitive grants	a	a	1.6	2.1
Total	34.0	39.1	75.0	100.0

[a]Negligible.

SOURCE: Phillips, Michael J., "Enhancing Competitiveness: Research and Technology in Agriculture," Draft for Symposium on Competing in the World Marketplace: The Challenge for American Agriculture, Kansas City, Missouri, October 31 - November 1, 1985, p. 13.

33.3 percent, respectively, over the same period. Total biotechnology funding by the USDA was $75.0 million in 1985, approximately 120 percent higher than in 1983.

Plant productivity accounted for 13.3 percent of total 1985 USDA biotechnology research funding, while animal productivity accounted for 11.8 percent. The largest percentage (39.4 percent) of total biotechnology research funding was allocated to CSRS competitive research grants. Often these funds are made available to universities or institutes for basic and applied research projects.

Additionally, support is obtained by scientists of state agricultural experiment stations from the National Institutes of Health (NIH) and the National Science Foundation (NSF). Grants from these groups may be directed towards biotechnology research. Total biotechnology support obtained from the NIH was $33,051,701 in 1982, while the NSF contributed $24,371,579 in the same year (Committee on Biotechnology, 1984). The total amount provided by these federal agencies was equal to three times the 1984 level of funding by the USDA competitive grants program.

Other countries which have a strong commitment to basic biotechnology research include West Germany, the United Kingdom, and Switzerland (Phillips, 1985). The presence of trained biologists, immunologists, microbiologists, biochemists, entymologists, and other life scientists in these countries and the United States contributes to the emphasis on basic science, and indicates that such emphasis will continue (Phillips, 1985).

Governments also fund corporate and generic applied research in biotechnology. Japan has assumed the lead in this approach, and has coordinated efforts among Mitsubishi Corporation, Sumitomo Corporation, and Mitsui and Company, Ltd. - three of the biggest corporations in the country - in recombinant DNA research (Cape, 1984). As with the semiconductor industry, government support in biotechnology is devoted to the mobilization of resources for large-scale commercialization. This allocation increases the probability that Japan will eventually hold the largest market share in biotechnology products, as envisioned by Japan's Ministry of International Trade and Investment (Cape, 1984).

Other governments which have a strong commitment to applied research are France, West Germany and the United Kingdom, though none is likely to approach Japan's success (Phillips, 1985). The United Kingdom is fostering commercial development of biotechnology partially to prevent foreign exploitation of domestic innovations, as occurred with monoclonal antibodies. In this case, basic research supported by the United Kingdom was adopted and developed for commercial profit in other countries.

In West Germany, there has been impetus for cooperative agreements with other governments, including Japan, Sweden, the United Kingdom, and the United States to reduce the costs of applied support. France has indicated a plan to assume 10 percent of the world biotechnology business by 1990, but lacks trained research personnel and coordination between universities and industry (Cape, 1984). This deficiency can be overcome by academic and industrial exchanges with other countries, a

policy actively pursued by France. The Flemish Development Agency of Belgium formed Plant Genetic Systems NV as a venture jointly funded by two Belgian firms, one U.S. firm, and one Swedish firm (Practical Biotechnology, March 1983).

Governments have contributed to formation of private companies to conduct applied research and commercialization, as has been the case for Celltech and Agricultural Genetics Company, Ltd. of Great Britain and Transgene of France (Phillips, 1985; Practical Biotechnology, August 1983).

Internationally, there has been much cooperative work toward biotechnological development for specific crops as is performed at the International Rice Research Institute located in the Phillipines, and the International Maize and Wheat Improvement Center in Mexico. There are ten such facilities throughout the world at which biotechnology research may be conducted (Consultative Group on International Agricultural Research, 1985). Additionally, the United Nations has established the International Centre for Genetic Engineering and Biotechnology to research specific crops of importance to the world economy and Third World consumption.

2.2.2 Corporate Support

Private biotechnology research companies have flourished more in the United States than in any other country because of the availability of venture capital and the cultural bias toward entrepreneurial activities (Cape, 1984). Since 1976, more than 100 new biotechnology firms (NBFs) have been started with private venture capital (Phillips, 1985).

Limited partnerships, over-the-counter stocks, and the existence of approximately 600 venture capital firms provide access to funds for new firms (Phillips, 1985; Cape, 1984; Gallagher and Beaumont, 1984).

Established firms in the United States also have developed biotechnology research and commercialization capabilities. Tax structures which encourage research and development - low capital gains tax rates, research and development tax credits, etc. - have stimulated growth of biotechnology research among established firms (Phillips, 1985). For the larger diversified companies, self-financing is possible. Monsanto Chemical Company has directed more than $30 million of its agricultural research budget to biotechnology research (Phillips, 1985). Many of these companies were already in the pharmaceutical, chemical, fertilizer, plant, and animal agriculture industries.

One tabulation concluded that 100 U.S. biotechnology companies employed more than 7,100 people and budgeted $546 million in 1984 for research and commercialization. Inclusion of large, diversified corporations raises the budgeted level to over $2 billion (Cape, 1984). Another survey indicated that 1984 private sector expenditures on agricultural research totaled approximately $95 million, excluding NBFs. Total expenditures for all biotechnology research in 1984 were likely between $180 million and $280 million for all firms (Phillips, 1985). Worldwide, 350 firms ranging from large multinationals to small venture capital companies entered the biotechnology field in the five years following 1977 (Wittwer, 1983).

Western European nations tend to emphasize government involvement and joint cooperation with other nations as mentioned in Section 2.2.1. In some nations, such as France, private industry has not exhibited the enthusiasm of the federal government, and expenditures by private firms remain low (Cape, 1984). In other countries, the private sector has assumed a major share of the funding burden. West German private concerns spend about $90 million per year to the government's $40 million for biotechnology research and development (Cape, 1984).

Where private sector developments have occurred, they have been spurred by large established companies, rather than NBFs (Phillips, 1985). Imperial Chemical Industries in Great Britain is famous for the development of a continuous fermentation process, single cell proteins, and biotechnologically produced polymers. In West Germany, multinational companies utilize the structure of their subsidiaries and international cooperative agreements to supplement research capabilities, rather than funding joint ventures with small biotechnology companies (Cape, 1984).

After the United States, Japan has the most funding available for companies developing biotechnology. This funding is derived from the government, low-interest loans from banks which are major shareholders, and occasionally, from wealthy individual investors (Phillips, 1985).

There are over 150 companies in Japan involved in developing applications for biotechnology. These companies spend over $217 million per year on research and development (Cape, 1984). Corporations are the primary researchers in Japan, due to the mainly educational role of

universities. The lack of basic research is not as much of a problem as it would seem due to the ability to obtain and adapt results of such research from other countries.

A prominent role in Japanese biotechnology is played by six multinational companies, or trading companies - Mitsubishi Corporation, Mitsui and Company, Ltd., Marubeni Corporation, C. Itoh and Company, Ltd., Sumitomo Corporation and Nissho Iwai Corporation. These companies have traditionally been leaders in gathering international biotechnology information and establishing contacts between companies and institutions for biotechnology research and commercialization. The information-gathering role is very important, as Japan lacks the structure and trained personnel necessary for a strong basic research effort upon which commercialization is based (Cape, 1984).

Recently, the trading companies described above have begun providing investment funds and expertise for biotechnology ventures, primarily at the urging of the government and the mass media in Japan (Itoh, 1984). The trading companies maintain agential, shared, and joint ventures with both domestic and foreign biotechnology businesses as indicated in Table 3. The foreign affiliations include some with British and American companies.

TABLE 3. BIOTECHNOLOGY BUSINESS AFFILIATIONS OF SIX MAJOR JAPANESE TRADING COMPANIES

Company	Domestic Affiliations	Foreign Affiliations
C. Itoh & Co., Ltd.		Integrated Genetics[a,b,c]
		Repligen[a,b]
Marubeni Corp.		Adler[d]
Mitsubishi Corp.	Plantech Research Institute[a]	Battelle[b]
	Japan Maize Products[a]	Frontenack/EV4[d]
		TA Associates/ADVENTS[d]
Mitsui & Co., Ltd.	Nippon Zeon Co., Ltd.[b]	Genentech[b]
	Mitsui Toatsu Chemicals[a]	Gentronix[b]
	Mistui Petrochemicals[a]	
Nissho Iwai Corp.	Fuji Seito[a,c]	Monotech Lab[b]
		University Genetics[b]
		Twyford Plant Lab[b,c]
		Specialty Grain[a]
Sumitomo Corp.	Japan Immuno-monitor[a]	Celltech[b]

[a]Shared venture.

[b]Agential relationship.

[c]Joint venture.

[d]Investment relationship.

SOURCE: Itoh, Toshio, 1984, "The Features of Biotechnology in Japan," Biotech 84 Europe, World Biotech Report 1984, vol. 1: Europe, Pinner, U.K.: Online Publications, Ltd., p.28.

2.3 Barriers to Biotechnology Transfer

The three-pronged process of biotechnology transfer - research, development, and production - is performed by universities and corporations. As mentioned, universities primarily perform the basic research, while both groups develop these results into commercializable forms. Corporations tend to be more efficient in this phase. Production for commercial use is almost strictly performed by corporations, who have facilities and resources available for large-scale operations. Unfortunately, the disjointedness of this three-stage technology transfer process creates some gaps in biotechnology transfer.

Problems in biotechnology transfer may arise in interactions among the three agents. Corporate-university conflicts arise at the research and development levels. Government-corporate and government-university interactions can create difficulties primarily at the testing stage of the research process. Public interest groups may generate other barriers to biotechnology transfer.

Vaughan (1984) outlined several areas where problems arise between corporations and universities. One problem is communication. Academic research interests and results may have no relevance to industrial problems being considered. Industrialists may be unaware of research being conducted in the academic sector, so that solutions may already exist to industrial problems. Further, expectations of the potential commercialization of research results may differ between industrialists and academics. Poor communication can result in unnecessary hostility between the two groups.

Another area of potential conflict between universities and corporations is that of priorities. As described in section 2.1, universities often promote the concept of academic freedom, that is, of researching what is of scientific interest, rather than what may be of commercial interest. The industrialist may view universities as national research institutions which should be generating research applicable to social and industrial problems (Vaughan, 1984).

In the United States, the incompatibility of these views is emphasized by the conflict between the desire of academics to publish research results versus the desire of industrialists to maintain secrecy of processes or products until patents are obtained. The difference in motivations between these groups may be explained by their purposes - universities exist to disseminate knowledge while corporations exist to make profits. This difference was institutionalized in the land-grant university system for which federal mandate requires that research results be made freely available to anyone desiring access (Phillips, 1985).

The magnitude of these conflicts differs by country. In Japan, traditional university-corporate ties have been close, and government policy encourages an even closer relationship (Phillips, 1985). Communication between academia and industry is also stressed in western European nations.

Some coordination, either through research funding and direction by corporations or paybacks to universities in exchange for not publishing results, would facilitate technology transfer in the United States

(Vaughan, 1984). The right to patent biotechnology discoveries within the land-grant system has created the proprietary rights desired by private firms, but has raised questions about the legitimacy of public funding for research which confers exclusive benefits to the developers (Phillips, 1985).

Barriers to biotechnology research and development also can be erected by governments through health, safety, and environmental regulations (Phillips, 1985). Testing and marketing of applied research results are particularly affected. Fear of unleashing new strains of bacteria, viruses, and even crops on the environment motivates strong restrictions on field testing. Public backlash by ecology groups has twice postponed testing of a frost-inhibiting bacteria to be tested on potatoes and strawberries in Northern California (Practical Biotechnology, October 1983; Sacramento Bee, 1985). The U.S. Occupational Safety and Health Administration regulates workplace hazards, which includes research and field testing of new biotechnology products insofar as they generate such dangers (Korwek, 1984).

Various agencies have mandates or specific regulations which affect marketing of biotechnology products (Korwek, 1984). Section 5 of the Toxic Substances Control Act empowers the U.S. Environmental Protection Agency to regulate commercial production of all new chemicals, among which recombinant DNA substances may be included. The U.S. Food and Drug Administration and the U.S. Department of Agriculture have the widest jurisdiction with respect to new products for human and animal use or consumption. Both have extensive premarket clearance authority

for drugs, biologics, *in vitro* diagnostics, foods and food additives, depending on the legal class to which these products are assigned.

Ease of entry into the U.S. market is based on the "newness" of the product (Korwek, 1984). Products which are already subject to regulation typically do not require premarket clearance. It is unclear whether new methods of manufacture, e.g., biotechnological derivations, will constitute grounds for premarket clearance, whether the product composition changes or not. There are substantial industry-wide implications for a policy statement in this area.

The United States is more restrictive than western Europe in product introduction for pharmaceuticals and animal drugs, but less so than Japan. It is to be expected that biotechnological product introduction will take less time in Europe than in other developed countries. Environmental regulations restricting testing are less well-defined in Europe and Japan than in the United States (Phillips, 1985).

Future coordination of the research, development, and production of biotechnological innovations will depend on government, corporate, and academic interactions. These in turn are governed by cultural and legal aspects of nations, and funding sources. The level and allocation of government and corporate funding, and the regulatory environment in the United States and in other countries will have considerable bearing on future directions for biotechnological research.

3. BIOTECHNOLOGY RESEARCH AREAS

Tables 4 through 9 provide samples of basic and applied biotechnology agricultural research being conducted by universities, corporations, and governments. Section 3.1 discusses basic research, while Section 3.2 describes applied research.

3.1 Basic Agricultural Research

The basic research projects listed in Table 4 all relate to plants. Basic research in animal biotechnology is closely related to human biotechnology research, since many of the expected results from basic research on animals will have applications for humans, and since animals typically serve as test cases for humans. The overlap in applications makes it difficult to separate biotechnology research performed on animals for agricultural purposes from that performed for human health purposes. Therefore, basic research on animals is not included here.

Basic research in plant biotechnology may be divided into two basic groups - gene transfer and somatic cell genetics. These areas are thoroughly described by the National Research Council's Board on Agriculture [NRC] (1984). The majority of this discussion is derived from that text.

Gene transfer involves insertion of single or multiple genes into plants to achieve desired traits which are governed by those genes. Vectors are the bodies used to ferry foreign DNA to plant genomes. Ti (tumor-inducing) plasmids are popular vectors. Nine researchers of vectors are listed, with two performing research on virus and pollen vectors.

TABLE 4. A SAMPLE OF BASIC RESEARCH IN AGRICULTURAL BIOTECHNOLOGY

BASIC TECHNIQUES (DNA transfer, protoplast fusion, tissue culture)

University

University of California, Davis, C. Meredith. Tissue culture.

University of California, Riverside, J. W. Einset and T. Murashige. Ti plasmid vector.

Cornell University, J. Shine. Pollen vectors in tomato and tobacco.

University of Florida, D. Pring. Basic DNA structure.

University of Illinois, J. M. Widholm. Cauliflower mosaic virus vector.

Israel Weizmann Institute, M. Edelman. Chloroplast regulatory protein.

Massachusetts General Hospital, M. Goodman. Vectors.

Michigan State University, P. Carlson. Tissue culture.

University of Minnesota, R. L. Phillips. Vectors.

University of Missouri, D. J. Merlo. Vectors.

North Carolina State University, C. S. Levings. Genetics of maize.

Purdue University, P. Hasegawa. Tissue culture.

University of Washington, A. Bendich. Vectors.

Washington University, V. Walbot. Tissue culture.

Wayne State University, A. Siegel. Vectors.

University of Wisconsin, J. D. Kemp. Vectors.

SOURCES: CRIS USDA. Electronic data search conducted at University of California, Davis in December, 1985. Searched under keywords Biotechnolog..., Biotechnolog... and Economic, and Biotechnolog... and Cost.

Murray, Dennis J., and Patrick J. O'Connor, 1983. A Guide to Corporate-Sponsored University Research in Biotechnology. Millbrook, NY: Genetic Sciences International. pp. 267-275, 278-279, 288-291.

Practical Biotechnology. Various years and issues.

General procedures for controlling gene activity have been developed which have great potential for applications. One of these is antisense technology. This technology takes advantage of the two-part structure of DNA bases, referred to as "plus and minus" or "fence and antifence". Normally, messages are read from one strand in the gene to another strand to communicate the genetic information specific to that gene. Antisense technology combines the plus strand from one gene with the minus strand from another gene to prevent the normal joining of strands from the same gene. This also prevents the genetic information from being communicated properly within the host gene. Artificial antisense ribonucleic acid (RNA) can be inserted into genes to perform this function. One application for this technology is the blocking of normal virus functions when antisense RNA is introduced to virus genes (Valentine, 1986).

Another new procedure likely to have widespread effects on basic research is the transfer of plant genes to microbes. The viability of bacteria as hosts for plant genes provides a cheap medium for experimentation with plant genes. In addition, the ability to study plant genes in bacteria speeds up the process by permitting isolation of specific genes so that other plant genes do not interfere with the results. The isolation of single genes or multiple genes which control the desired traits is an important area of gene transfer research. Stress resistance and yield appear to be factors which are controlled by more than one gene. Some types of herbicide resistance are controlled by a single gene. Identification of these relationships is the first step to their transfer (Valentine, 1986).

Related to gene transfer is research on selective expression, that is, switching on and off the expression of particular traits. This prevents desired traits from appearing in the wrong part of the plant or at the wrong phase of growth. Use of a microbial host for this type of research can increase efficiency and improve creativity in experimentation.

The other main area of basic plant biotechnology research is somatic cell genetics, in which regeneration of plants from single cells or groups of cells is the objective. There are three areas of somatic cell genetic research - cell cultures, protoplast fusion, and somaclonal variation.

Tissue culture techniques include regeneration from callus (a clump of plant tissue made up of integrated cells), cell-suspension, and protoplast culture. Callus regeneration proceeds from a shoot or other clump of plant tissue. This process is very reliable and is used for many horticultural crops, such as orchids. Cell-suspension techniques agitate callus in solution to break it into single cells. Regeneration may then proceed from a single cell. This procedure has been successful for potatoes, tobacco, and corn, but has not worked with cereals and legumes. Protoplast culture is the most difficult process of the three types. In this case, regeneration is attempted from single cells which have had their outer walls removed.

Mass propagation can proceed directly from individual cells or cell clumps through this regenerative process. This procedure may result in nearly identical plants if all the parent cells are from the same plant,

in contrast with the comparatively nonuniform results of cross-pollination and traditional plant breeding of whole plants. Speed and relative cost make regenerative mass propagation desirable.

Tissue culture and mass propagation may be of substantial importance in selecting and breeding varieties with desired yield or other traits. Table 5 lists plants which are propagated through tissue culture. There are 50 agricultural and horticultural plants, three pharmaceutical plants, and five silvicultural plants which use this method. Other strains of these crops and different species may eventually be reproduced by this technique.

Mass production using tissue culture techniques has been possible with alfalfa, strawberries, asparagus, oil palms, pineapples, and potatoes, but major agronomic crops such as wheat, oats, and barley have yet to be regenerated (Office of Technology Assessment [OTA], 1982). Research in the U.K. in this area has focused on wheat, barley, oilseed rape, potato, and sugar beet crops (Jones et al., 1984). This method accounts for important breeding variation for beets, brussel sprouts, cauliflower, tomatoes, citrus, bananas, chrysanthemums, carnations, African violets, foliage plants, and ferns (OTA, 1982).

Protoplast fusion is the joining of different plants, whether the same or different species, to achieve new hybrids with desirable characteristics. Some minor successes have been observed with this procedure, but the process lacks specificity in obtaining desirable traits without simultaneously transmitting undesirable ones.

TABLE 5. PLANTS PROPAGATED THROUGH TISSUE CULTURE FOR PRODUCTION OR BREEDING

VEGETABLE CROPS

Asparagus
Beets
Brussels sprouts
Caluiflower
Eggplant
Onion
Spinach
Sweet potato
Tomato

FRUIT AND NUT TREES

Almond
Apple
Banana
Coffee
Date
Grapefruit
Lemon
Olive
Orange
Peach

FRUIT AND BERRIES

Blackberry
Grape
Pineapple
Strawberry

FOLIAGE

Silver vase
Begonia
Cryptanthus
Dieffenbachia
Dracaena
Fiddleleaf
Pointsettia
Weeping fig
Rubber plant

FLOWERS

African violet
Anthruium
Chrysanthemum
Gerbera daisy
Gloxinia
Petunia
Rose
Orchid

FERNS

Australian tree fern
Boston fern
Maidenhair fern
Rabbitsfoot fern
Staghorn fern
Sword fern

BULBS

Lily
Daylily
Easter lily
Hyacinth

PHARMACEUTICAL

Atropa
Ginseng
Pyrethium

FOREST TREES

Douglas fir
Pine
Quaking aspen
Redwood
Rubber tree

SOURCE: Office of Technology Assessment, 1982. Genetic Technology - A New Frontier. Boulder, CO: Westview Press. p.141.

Somaclonal variation occurs when there is differentiation of numerous plants with different characteristics from the same parent tissue clump. This technique means plants with remarkable genetic diversity can be derived from the same parent. The use of tissue culture techniques to encourage somaclonal variation speeds recognition of desirable mutations, such as disease resistance in various species, since so many mutations may be observed in a single generation of plants. Once recognized, the processes of isolation and transfer of these traits may be begun.

Most of the research reported in Table 4 is being performed by universities. As indicated in Section 2.1, this is typical for basic research projects. However, often applied research includes aspects of basic research, as specific groundwork must be available as a foundation to applications. Several examples are provided in the next section.

3.2 Applied Agricultural Research

Tables 6 through 9 outline a variety of applications of basic plant and animal biotechnology research. Each table outlines a sample of the university, corporate, and government efforts being conducted in several areas of application. Miscellaneous corporate biotechnology research is provided in the last sections of these tables. These sections represent companies which have been identified as performing some plant- or animal-related biotechnology research, but for which specific information is not available.

Applied plant research is discussed in Section 3.2.1. Applied animal research is described in Section 3.2.2. Other agriculture-related biotechnology research is outlined in Section 3.2.3.

3.2.1 Applied Plant Research

Applications of basic plant research described in Section 3.1 may be subdivided into five categories - (1) disease and herbicide resistance in plants, (2) crop improvement, (3) plant growth enhancement and environmental tolerance, (4) crop pest control, and (5) tree improvement. Miscellaneous, or general plant biotechnology applications include several of these categories. University, corporate, and government research in these areas is outlined in Table 6.

3.2.1.1 Disease and Herbicide Resistance

Disease and herbicide resistance in plants is controlled by genetic composition. Research in this area has attempted to isolate and transfer these genes across varieties within species, and across species. Although plant breeding for this application has been carried out for more than 100 years, the results have been largely random, with little understanding of the underlying genetic factors which permit the transfer of characteristics (National Research Council [NRC], 1985).

Successes in gene transfer have frequently come through the more standard breeding processes, such as the atrazine-resistant strains of oilseed rape and summer turnip rape produced through backcrosses with resistant weeds in the same botanical family (NRC, 1984; National Academy of Engineering, 1984). Cytoplasm transfers from weed donors into host protoplast are expected to produce an atrazine-resistant potato within a few years (NRC, 1984).

TABLE 6. A SAMPLE OF APPLIED PLANT BIOTECHNOLOGY RESEARCH RELATED TO AGRICULTURE

DISEASE AND HERBICIDE RESISTANCE IN PLANTS

University

University of California, Davis, R. Michelmore. Disease resistance in lettuce.

University of California, Davis, L. Rappaport. Fungal resistance in celery.

University of California, Davis, J. N. Rutger. Herbicide resistance in rice.

University of California, Davis, M. Saltveit. Russet spot resistance in lettuce.

University of California, Riverside, N. Keen. Resistance in soybeans.

Cornell University, O. C. Yoder. Fungi disease resistance.

Israel Weizmann Institute, M. Edelman. Herbicide resistance.

University of Kentucky, J. Kuc. Plant immunization.

Oklahoma State University, E. E. Sebesta. Disease resistance in wheat.

University of Oregon, D. I. Mills. Disease resistance in legumes.

University of Wisconsin, R. S. Hanson. Disease resistance.

Corporate

Allelix, Ontario, Canada. Resistance in potatoes (through cell fusion).

Agrigenetics Corp., Denver, CO and Madison, WI. Disease resistance in cereals and legumes..

Asgrow Seed Co., U.S. Disease resistance.

Calgene, Davis, CA. Herbicide resistance.

DeKalb-Pfizer Genetics, U.S. Herbicide resistance in corn.

DuPont Co. Experiment Station, Wilmington, DE. Resistance to disease, herbicides, and insects.

International Plant Research Institute, San Carlos, CA. Disease resistance in wheat.

Koppers/ DNA Plant Technology Corp., U.S. Diagnostic kits for plant diseases of citrus and turf grasses.

Nippon Shinayaku, Kyoto, Japan. Herbs with worm-repellent seeds.

Phytogen Inc., Pasadena, CA. Disease resistance.

CROP IMPROVEMENT

University

University of California, Davis, A. B. Bennett. Tomato.

University of California, Davis, C. Meredith. Grape.

University of California, Davis, C. F. Quiros. Celery, cool season crops.

University of Guelph, Ontario Agricultural College, K. J. Kasha. Barley.

Iowa State University, P. A. Peterson. Maize.

Kansas State University, J. Shepard. Potatoes.

University of Minnesota, B. G. Gengnebach, and J. L. Geadelmann. Maize.

Purdue University, B. A. Larkins. Cereals and legumes.

University of Wisconsin, O. Nelson. Maize.

Corporate

Advanced Genetic Sciences, Greenwich, CT. Potatoes, asparagus, strawberries.

Agricultural Genetics Co., Ltd, U.K. Plant breeding.

Asahi Chemical Industry, Ltd./ Hitachi Ltd., Japan. Rice, soybeans, other cereals.

Campbell Soup Company, U.S. Tomatoes.

Cetus, Madison, WI. Crop improvement.

DeKalb-Pfizer Genetics, DeKalb, IL. Corn, sorghum.

DNA Plant Technology Corp., Cinnaminson, NJ. Tomatoes.

Frito-Lay Inc., Dallas, TX. Potatoes.

Kikkoman, Japan. Seed biotechnology.

Kirin Brewery, Japan. Seed biotechnology.

Life Sciences Inc., St. Petersburg, FL. Bulbs, seeds.

Mitsubishi, Japan. Seed biotechnology.

Mitsui Toatsu Chemicals Inc./ Kirin Brewery Ltd., Japan. Carrots and eggplant.

Mogen International, Leiden, Holland. Agronomic crops.

Molecular Genetics, Inc., Minnetonka, MN. Corn, cereals, sorghum.

Native Plants, Salt Lake City, UT. Agronomic crops and microorganisms.

Sungene Technologies Corp., San Francisco, CA. Crop varieties.

Twyford Labs, Glastonbury, U.K. Crop improvement.

Government

International Centre for Genetic Engineering and Biotechnology, U.N. Rice.

Consultative Group for International Agricultural Research, F.A.O., U.N. (13 nonprofit international research institutes). Rice, potatoes, maize, legumes, wheat.

PLANT GROWTH ENHANCEMENT AND ENVIRONMENTAL TOLERANCE

University

University of Arizona, G. Tollin and R. Jensen. Photosynthesis.

University of California, Berkeley, W. C. Taylor. Photosynthesis.

University of California, Berkeley, S. Lindow. Frost prevention bacteria.

University of California, Davis, K. J. Bradford. Influences on plant growth hormones.

University of California, Davis, M. Matthews. Water stress in grape leaves.

University of California, Davis, C. Meredith. Genetic resistance to mineral stresses.

University of California, Davis, R. Valentine. Nitrogen fixation, osmotic stress tolerance.

University of California, Davis, J. Yoder. Genetic resistance to disease, salt, and cold in tomatos.

University of California, Riverside, I. P. Ting. Nitrogen fixation.

University of California, San Diego, S. H. Howell. Photosynthesis.

University of California, San Diego, D. Helinski. Nitrogen fixation.

University of Chicago, R. Haselkorn. Nitrogen fixation.

Cornell University (Boyce Thompson Institute), A. Szalay. Nitrogen fixation.

Cornell University, M. Alexander, V. Gracen, and E. Earle. Nitrogen fixation.

Harvard University, L. Bogorad. Photosynthesis.

Harvard University, F. M. Ausubel. Nitrogen fixation.

University of Indiana, H. Gest. Nitrogen fixation.

Iowa State University, A. G. Atherly. Nitrogen fixation.

Kansas State University, L. C. Davis. Nitrogen fixation.

University of Maryland, S. O. Kung. Photosynthesis.

University of Michigan, R. Helling. Photosynthesis.

Michigan State University, C. P. Wolk and K. Schubert. Nitrogen fixation.

University of Missouri, J. D. Wall. Nitrogen fixation.

University of North Carolina, G. H. Elkan. Nitrogen fixation.

Temple University, R. E. Goldberg. Nitrogen fixation.

University of Utah, J. Y. Takemoto. Photosynthesis.

University of Wisconsin, W. Brill. Nitrogen fixation.

Corporate

Advanced Genetic Sciences, U.S. Frost protection bacteria.

Agricultural Genetics Co., Ltd., U.K. Microbial innoculants.

Calgene, Davis, CA. Genetic engineering for nutrient efficiency, stress-salt tolerance.

Cetus Corp., Berkeley, CA, Nitrogen fixation, inoculants.

Ciba-Geigy, Research Triangle Park, NC. Plant-bacterial interactions.

DuPont Co. Experiment Station, Wilmington, DE. Growth regulation.

International Plant Research Institute, San Carlos, CA. Stress resistance in wheat.

Native Plants Inc., Salt Lake City, UT. Stress tolerance.

New Plant Products, Cambridge, U.K. Rhizobium innoculants.

Ortho Research Center, Richmond, CA. Plant growth enhancers.

Phytogen Inc., Pasadena, CA. Photosynthesis.

R and A Plant/Soils Inc., Pasco, WA. Microbial soil inoculants.

Government

Indian Agricultural Research Institute, New Delhi, India. Blue-green algae biofertilizer for rice.

CROP PEST CONTROL

University

University of California, Davis, P. Baumann. Biological control of pea aphid.

Cornell University, W. Roelofs. Insect control.

University of Idaho, L. A. Bulla. Microbial insecticides.

University of Idaho, L. K. Miller. Viral insecticides.

University of Massachusetts, C. Ying. Gypsy moth control.

North Carolina State University, R. L. Mott. Fusiform rust on pine and oak trees.

Texas A&M University, M. Summers. Viral insecticides.

Corporate

Agricultural Genetics Company, Ltd., U.K. Biological control products.

Bayer, U.S. Biotech insecticides, fungicides, and herbicides.

Biogen, U.K. Biodegradable herbicides.

Biotechnology General Corp., Tel-Aviv, Israel. Fungi to protect plants from microorganisms.

Ciba-Geigy, Research Triangle Park, NC. Crop protection chemicals.

DuPont Co. Experiment Station, Wilmington, DE. Crop protection chemicals.

Genentech, Inc., U.S. Agricultural pest control.

Ortho Research Center, Richmond, California. Agricultural pest control.

Zoecon Corp., Palo Alto, CA. Pest control.

Government

Hokkaido National Agricultural Experiment Station, Japan. Vaccine against cucumber mosaic virus for tomatoes, pimentos, and melons.

Microbial Resources Ltd., U.K. Bacterial, fungal, and viral pesticides.

TREE IMPROVEMENT

University

University of California, Davis, A. M. Dandekar. Fruit and nut trees.

University of California, Davis, D. J. Durzan. Silviculture and pomology species.

Corporate

[6~Calgene, Pacific, U.S. Tree improvement.

Genetics Lab, U.S. Fruit tree grafting.

Native Plants, Salt Lake City, UT. Tree improvement.

Oji Paper Co., Kameyama, Japan. Cell fusion for tree improvement.

Simpson Timber Co., Seattle, WA. Tissue culturing for controlled breeding of Coastal redwood.

Weyerhaeuser Co., Centralia, WA. Tissue culturing for Douglas fir.

Government

United States Forest Service (with Calgene), U.S. Tree improvement.

MISCELLANEOUS PLANT BIOTECHNOLOGY

Corporate

Agra-Cetus, U.S.

Allied Chemical Corp., U.S.

American Cyanamid Co., U.S.

ARCO Plant Cell Research Institute, U.S.

Biotechnica International, Inc., U.S.

Centaur Genetics Corp., U.S.

Crop Genetics International, U.S.

Dow Chemical Co., U.S.

Ecogen, U.S.

Eli Lily and Co., U.S.

Enzo Biochem, Inc., U.S.

General Foods Corp., U.S.

Genetics Institute, U.S.

Genetics International, Inc., U.S.

W. R. Grace and Co., U.S.

Ingene, U.S.

International Genetic Engineering, Inc., Santa Monica, CA.

International Genetic Sciences Partnership, U.S.

International Minerals and Chemical Corp., U.S.

Martin Marietta, U.S.

Miller Brewing Co., U.S.

Multivac, Inc., U.S.

Nabisco, Inc., U.S.

Neogen Corp., U.S.

Pfizer, Inc., U.S.

Phyto-Tech Lab, U.S.

Pioneer Hybrid International Corp., U.S.

Plant Genetics, Inc., U.S.

Rohm and Haas, U.S.

Sandoz, Inc., U.S.

Shering-Plough Corp., U.S.

A.E. Staley Manufacturing Co., U.S.

Standard Oil of Indiana, U.S.

Standard Oil of Ohio, U.S.

Stauffer Chemical Co., U.S.

Universal Foods Corp., U.S.

The Upjohn Co., U.S.

Worne Biotechnology, Inc., U.S.

Xenogen, Inc., U.S.

SOURCES: CRIS USDA. Electronic data search conducted at University of California, Davis in December, 1985. Searched under keywords Biotechnolog..., Biotechnolog... and Economic, and Biotechnolog... and Cost.

Lohr, L., 1986. Results of UCD Biotechnology Survey Undertaken October 1985. University of California, Davis. Department of Agricultural Economics. Unpublished.

Murray, Dennis J., and Patrick J. O'Connor, 1983. A Guide to Corporate-Sponsored University Research in Biotechnology. Millbrook, NY: Genetic Sciences International. pp. 267-275, 278-279, 288-291.

Office of Technology Assessment, 1982. Genetic Technology - A New Frontier. Boulder, CO: Westview Press. pp. 307-308.

Phillips, Michael J., 1985. "Enhancing Competitiveness: Research and Technology in Agriculture." Draft for Symposiumm on Competing in the World Marketplace: The Challenge for American Agriculture held in Kansas City, Missouri on October 31 - November 1. pp. 16-18.

Practical Biotechnology. Various years and issues.

Wittwer, Sylvan H., 1983. "Epilogue: The New Agriculture: A View of the Twenty-first Century," in Agriculture in the Twenty-First Century, John W. Rosenblum, ed., New York: John Wiley and Sons, p.353.

The first successful artificially transplanted gene may be GlyphoTol, which protects crops implanted with it from the effects of the herbicide Roundup (and other glyphosate-based herbicides). Gene insertion into tobacco plants has been partially successful, and forest trees and soybeans tested have shown even better results. Calgene of Davis, California, who is experimenting with the gene, claims that herbicide-resistant tomatoes should be on the market by 1988, followed by cotton in 1989, soybeans in 1990 or 1991, and corn by 1991 or 1992 (Britton, 1986). Turf grass may also receive the gene, allowing gardeners to destroy unwanted weeds while preserving the grass.

Disease resistance is also of great importance in applied plant biotechnology. Virus-free plants are commonly obtained by culturing and heat treating the meristem of plants maintained through standard asexual propagation. Over 134 potato cultures as well as strawberries, sweet potatoes, citrus, freesias, irises, rhubarbs, gooseberries, lilies, hops, gladiolus, geraniums, and chrysanthemums have been made virus-free as a result of this method (OTA, 1982). In vitro clonal propagation has produced disease-free cassava and potato cultivars, enhancing plant health and yield (Roca, 1985).

Disease resistance may be developed by gene-splicing techniques. Although positive results have been obtained for tobacco resistance to Fusarium wilt fungus, yield reductions have accompanied the enhancement (NRC, 1984). Researchers at the University of California at Davis expect to isolate in two to three years a gene for resistance to downy mildew in lettuce, although practical introduction into lettuce is not expected for more than 10 years (Britton, 1986).

Acquired resistance, in which the host plant is innoculated with with an avirulent strain of bacterial, fungal, or viral pathogen, is a possible solution to plant disease. Injections with several strains may identify those mutants for which acquired resistance does not occur in the host plant. Comparison with active strains can lead to information about the reaction process between pathogen and host. Such studies are currently being conducted for stem rot and wilt in potatoes, tobacco, ginger, tomatoes, and bananas (NRC, 1985). One bacteria strain, Agrobacterium radiobacter, is used commercially for the prevention of crown gall disease (Lisanksy, 1984).

Fungi may be used to control plant diseases. The most promising results have been observed from strains of Trichoderma which attack other fungi. Commercially available products include one sold in the U.K. for silver-leaf disease of plums, one sold in France for control of dry bubble disease in mushrooms, one to be introduced in France for control of botrytis on grapes (Lisanksy, 1984).

3.2.1.2 Crop Improvement

This category refers primarily to yield or quality enhancement of specific crops, rather than to disease or herbicide resistance of the plants. Examples include attempts to increase protein in grains, produce tomatoes with more solids, and produce larger or more flavorful fruits. These improvements are possible only with successes in breeding techniques for characteristic isolation and transfer. Three desirable aspects of breeding programs which are enhanced by biotechnological techniques are haploidy, somaclonal variation, and mutant isolation.

Ploidy is a method which alters the number of chromosomes in plants. Since chromosomes are inherited in sets, increases in ploidy results in gains in full sets of chromosomes. This polyploidy results in increases in plant size, and larger flowers, fruit, and seeds. Domestic strawberries bred in this manner have four times the chromosomes of wild strawberries, and have much fleshier fruit (OTA,1982).

Haploidy increases selection efficiency and speed of incorporation of new genes after genetic recombination. Haploids methods use half the genetic materials of normal plant breeding techniques (Iwanaga, 1985). Plants are raised from pollen, rather than seed in this technique. Improved varieties of rice, wheat, maize, rubber, and sugarcane with high yield, good grain quality, early maturity, and cold resistance have been developed through anther culture (Chopra, 1985). Other methods such as chromosome elimination (barley), alien species crosses (wheat, potato), and genetic induction (maize) have proven successful in haploidy (Inter-Center Seminar on IARC, 1985).

Somaclonal variation (genetic variability) is displayed in many species which are regenerated from tissue culture techniques. Greater somaclonal variation is desirable since it increases the chances for production of desirable characteristics and genetic diversity. Wide variation has been observed in maize, rice, wheat, potato, sugarcane, alfalfa, tomato, and lettuce (Scowcroft et al., 1985; Jones et al., 1984).

Mutant isolation is the process of selecting mutant strains of crops with desirable traits for genetic study and transfer. In vitro

techniques permit a more efficient selection process than field screening for these plants (Inter-Center Seminar on IARC, 1985).

Genetic material transfers and wide crosses are used to provide intervarietal improvements in crops based on the genetically diverse characteristics derived from somaclonal variation and mutant isolation. Embryo cultures have been used to produce tomatoes with high yields, contemporaneous ripening, high sugar content, and disease resistance and to produce diverse genetic material for primary triticale breeding (Ancora, 1985). Calgene of Davis, California, is attempting to alter the profile of oil produced by oilseed rape and sunflowers, to enable the plants to manufacture cocoa butter, jojoba, and other exotic oils through genetic manipulation (Britton, 1986).

Horticultural advances have provided plants with many new characteristics. NPI, Inc. of Salt Lake City has used tissue culture to create long-stemmed roses which bloom before they have many roots, so that single roses may be grown in small pots of soil. The product, which may be planted in a garden after the bloom fades, is already commercially available (Britton, 1986). Crinkly-leaved versions of common shrubs have been developed by Calgene of Davis, California from a particular method of gene movement and restructuring rather than a specific gene. The same company has isolated genes for the color blue in flowers and expects to market blue roses, carnations and chrysanthemums by 1990 (Britton, 1986).

There are two major constraints to crop improvement through these methods. First, many important traits are determined by several genes,

which must be isolated and recombined. Second, it is unclear how much genetic variation for improvement exists in nature. If plants themselves do not display the characteristics of interest, the genetic basis for these characteristics cannot be uncovered. This genetic homogeneity may make substantially higher yields impossible (OTA, 1982).

3.2.1.3 Growth Enhancement and Environmental Tolerance

This section refers to biotechnology designed to enhance the health of the entire plant, and its ability to withstand environmental stresses. Experimentation in this field identifies mechanisms of plant metabolism and environmental response and attempts to transfer desirable traits among varieties and species.

Plant growth enhancement has focused on plant metabolism (photosynthesis and hormone reactions), and interaction with other organisms (nitrogen fixation). These areas share with basic research the characteristics of very long lead times to application and reliance on fundamental plant science principles. Improvements in these areas may substantially alter the nature of crop varieties in existence. As shown in Table 6, most research in these areas is performed by universities.

Physiochemical stresses such as drought, heat, cold, salt, and toxic ions have immediate adverse yield consequences. The economic gains from development of resistance are immediate. Consequently, much of the research in this area is being performed by private corporations.

In photosynthesis, light energy is gathered by plants and used to convert carbon dioxide into sugars for plant food and produce oxygen.

Photosynthetic efficiency differs between C_3 plants such as wheat, rice, and seed legumes, and C_4 plants such as corn, with C_4 being more efficient (NRC, 1985). One proposed method for enhanced growth is to improve the photosynthetic efficiency per leaf by some genetic engineering technique to transfer C_4 characteristics to C_3 plants. This method has debatable applicability due to the multigene nature of the characteristics of interest (Jensen, 1983).

Three other methods of improving photosynthetic efficiency are optimization of the plant canopy structure (plant leaf arrangement) as a light-absorbing system, optimization of the partition and use of assimilates (the segregation of photosynthates into starches and sugars and the subsequent usage in plant parts) and lengthening the duration of leaves to increase photosynthetic duration (Cramer, 1985). Improvement in the accumulation of photosynthate in desired plant parts is an effective way to improve crop yields. One crop plant undergoing experimentation in this area is the soybean, which mobilizes a high percentage of its nitrogen from other plant parts to deposition in seed. Total crop yield may be increased if vegetative growth is increased so that more nitrogen from the roots, stems, nodules, and leaves is available for transport to the seeds (NRC, 1985).

Photosynthate is accumulated as either sugar or starch in plants, with species such as wheat, barley, and spinach accumulating more sucrose than starch, while such plants as peanuts, soybeans, and tobacco accumulate more starch than sugar (NRC, 1985). The ability to control such partitioning would enhance control of the makeup and quantity of

crop harvests. Repartitioning of wheat, rice, maize, sorghum, and soybean has successfully increased grain yield (Jain, 1985).

A method for increasing duration of photosynthetic activity during seed fill in corn is being used successfully by a hybrid seed company. Longer photosynthesis during this period is achieved by introducing varieties whose leaves senesce (or fall off) later in the maturation cycle. This process is often referred to as a "stay green" or "delayed leaf senescence" characteristic. The result is higher photosynthate accumulation (Huffaker, 1986).

Plant development regulators include five identified classes of plant hormones and two photomorphogenic pigment systems. Two difficulties in research in this area are the low concentrations at which hormones are active, and the simultaneity of effects on several hormones which are active at one time (NRC, 1985). Regulators are typically used to neutralize biological or environmental stress or to promote a physiological activity which produces enhanced growth or yield (Stutte, 1983).

Applications of hormones may be made in different concentrations and to different parts of whole plants to achieve growth inhibition or stimulation. Flowering plants can be produced at any season by manipulating the natural photoperiod through phytochrome applications. Auxins and ethylene precursors induce flowering in certain species. Gibbererllins are used in the brewing industry to improve barley malting and in the agricultural industry to stimulate the growth of seedless grapes. Ethylene, abscisic acid, and indoleacetic acid are applied to

encourage ripening of fruit, defoliate cotton for harvesting, increase sucrose production in sugarcane, stimulate latex yields in rubber trees, and prevent sprouting of potatoes in storage (NRC, 1985; Stutte, 1983).

Nitrogen metabolism is essential to plant growth and development and is commonly the limiting factor in plant productivity. Fixed nitrogen is assimulated into organic nitrogen compounds in the plant. Three major lines of research on nitrogen fixation are maximization of efficiency of currently important symbiotic associations with crop plants, development of new nitrogen fixation catalysts, extension of biological nitrogen-fixing capabilities to crop plants which currently rely on commercial fertilizers (Burgess, 1983).

Although both free-living and symbiotic microorganisms fix nitrogen, it is the latter type which is of major importance to agriculture. Symbiotic organisms attach to a host and provide it with biologically fixed nitrogen. Rhizobium (associated with legumes), Azolla and Anabaena (associated with rice), and Frankia (associated with alder trees) are some of the better-known nitrogen-fixing microorganisms (Burgess, 1983). Development of superior nitrogen-fixing strains has occurred in laboratories, but little documented field improvement has been noted (NRC, 1985).

Transfer of genes for nitrogen fixation to nonleguminous plants such as corn would be of major economic significance. As yet, lack of detailed molecular information and inability of these plants to supply necessary energy and nitrogenase protection limit the extension of Rhizobium hosts (NRC, 1985; Burgess, 1983).

Nitrogen fixation is dependent on the photosynthetic process, and the efficiency of this process is in turn dependent on the physiochemical stresses to which the plant is exposed (NRC, 1985). Stress in the form of drought, low or high temperatures, salinity, and excessive ion concentrations adversely affect plant metabolism and yield.

Adaptions to environmental stresses are observed in wild plants, such as mangrove trees, which grow in saltwater, cacti, which grow in desert environments, plants which survive in tundras or on stripmined soil with high ion levels (NRC, 1985). Comparison of crops with these wild species may help identify certain stress-tolerance mechanisms.

Tolerance for salt, acid, and aluminum at the cellular level has been elicited through tissue culture techniques. Successful varieties of salt-tolerant oats and rice have been developed by the Tissue Culture for Crops Project at Colorado State University and are commercially available (Nabors and Dykes, 1985). The Project is also working toward development of similar traits in wheat and pearl millet.

Another approach to enhancing stress tolerance involves the application of materials to plants, rather than genetic alteration of the plants themselves. The most prominent example is 'Ice Minus' (Frostban is the commercial name) developed by Advanced Genetics Sciences, Inc., of Oakland, California. This product was developed with a single-gene splice of Pseudomonas syringae which stripped the bacteria of its ice-crystalizing properties (Magagnini, 1985). Although the product was to be tested on potatoes and strawberries, legal problems have stalled testing (Business Week, 1985; Magnini, 1985).

3.2.1.4 Crop Pest Control

Crop pest control methods include genetic alteration of plants to improve pest-resistance, genetic alteration of pests to make them less viable, improved agricultural pesticides, and development of biological controls of pests (Battenfield and Haynes, 1983). Some of these techniques have been practiced for many years. However, the advent of biotechnology has enhanced the ability to improve these systems. Plants may be bred for nonpreference (where a plant is unattractive to insect pests), antibiosis (where a plant is actually harmful to pests), and tolerance (where a plant suffers little damage from pest populations).

Host plant resistance is typically isolated in resistant cultivars, then bred into other varieties. Single-gene resistance is most commonly identified and transferred. Pest-resistance bred from wild species often results in yield reductions, so that limited numbers of resistant species with small yield reductions were commercially accepted. These include Hessian fly-resistant wheat, European corn borer-resistant corn, and cereal leaf beetle-resistant wheat (Battenfield and Haynes, 1983).

Other successes have resulted from breeding plants which avoid peak insect seasons at maturity. An example is cotton in Texas, which develops before boll weevil larvae develop in the boll (Battenfield and Haynes, 1983). Trap crops may be grown which stimulate the hatching of eggs, but do not support insect growth, such as is accomplished with nematodes (NRC, 1985).

Genetic alteration of pests focuses on insect neurobiology, which controls growth, development, homeostasis, and reproduction. Hormone

manipulation of four identified neurohormones can permit alteration of cardiac and flight muscle action, lipid synthesis, and pheromone production, so that flight, metamorphosis, and reproduction may be disrupted (NRC, 1985).

Other hormones with potential use for alteration of biological functions include bursicon (which causes skeleton hardening), diuretic hormone (which controls water and salt balance), and egg development neurotropic hormone (which determines secretion of eggs in female mosquitoes) (NRC, 1985). Modification of the normal function of the insect nervous system through manipulation of these genetic controls can be a longterm solution to adaptation of insects to pesticides.

Another pest alteration technique is disruption of normal reproduction by introduction of sterile insects or insects with susceptibility to certain chemicals or environments. Sterile insect release methods have been successful against screwworms, fruit flies, codling moths, and medflies (Battenfield and Haynes, 1983). A strain of blowflies was developed which was resistant to the pesticide dieldrin, but could not overwinter. After spraying with dieldrin, the insect population shifted toward the winter-susceptible variety, so that the advent of winter drastically reduced the remaining blowflies (Battenfield and Haynes, 1983).

Chemical control of pests has been established as a mainstay of modern agriculture. In the past, pesticides were discovered using synthesis and screening of thousands of chemicals until effective ones were found (NRC. 1985). Insect adaptation to such pesticides has been

rapid in some cases, so that discovery efforts which focus on knowledge about insect biology are favored. Concern for environmental degradation has led to interest in chemicals which are less toxic to the environment. Development of more specialized compounds could be expensive for chemical companies from the standpoint of research costs and the limited demand which can be expected (Battenfield and Haynes, 1983). Nevertheless, many of the companies listed in Table 6 under miscellaneous plant biotechnology are large agrochemical and drug companies who are heavily involved in such research.

The biological control of crop pests has received a great deal of attention as more is discovered about insect-pathogen relationships and about insect biology in general. Microorganic pathogens can be used to control pest populations. An example is the use of Bacillus thuringiensis bacterium which is lethal to the caterpillar stage of many insects through disruption of digestion (NRC, 1985). Other bacteria with potential include B.sphaericus (toxic to mosquitoes), B. moritae (harmful to flies), and B. popilliae and B. lentimorbus (Japanese beetle pathogens) (Lisanksy, 1984). Monsanto Agricultural Company of St. Louis hopes to test and market microbes that kill pests which attack corn roots (Britton, 1986).

Fungi may be used to infect insects via the gut, mouthparts, and cuticle, remaining on the insect and sporalating after the insect's death to infect other pests for considerable periods. The drawback to their use is that most fungi have a restricted range of suitable environmental conditions. Several fungi with proven effectiveness are

Verticillium lecanii (available in the United Kingdom for control of aphids and whitefly), Hirsutella thompsonii (effective in restrictive environments against citrus and coconut mite), Metarhizium anisopliae (available in Brazil for control of spittlebug), Beauveria bassiana (available in the Soviet Union for control of Colorado potato beetle), Nomuraea rileyi (useful against caterpillars on soybeans), Entomophthora spp. (excellent against aphids and other insects) (Lisanksy, 1984).

Viruses can be very effective against insects, but are difficult to produce and may be destroyed by ultraviolet radiation in sunlight. One commercially available virus in the U.K. is Virox, which affects Pine sawfly. Research is being done on the Codling moth granulosis virus, the Pine beauty moth virus, and others (Lisanksy, 1984).

Insect predators of harmful pests may be released to control pest populations. Plant Genetics, Inc. of Davis, California has developed gelatin capsules stuffed with nematodes which kill army worms and cutworms. The capsules can be embedded in the soil where the nematodes are then released (Britton, 1986).

Biological controls and genetic resistance are expected to have a major role in the future control of crop pests. The reliance on specific data on interactions among pests, pathogens, and crops implies a need for more basic research in this area.

3.2.1.5 Tree Improvement

Much of the research on crop improvement, and disease and pest resistance applies to tree improvement. Although much research is being conducted in this area, there were not many general results found

outside the specific forestry literature. Research interest in mass production and trait identification through tissue culturing is high.

A project by Weyerhauser Co. of Centralia, Washington was begun in 1970 to develop a mass propagation technology for Douglas fir through tissue culturing (OTA, 1982). Weyerhauser has encountered a typical problem of woody species in that results generally take more than one year to obtain. This project has involved a heavy investment in basic research for the company, as plant physiology of an extremely intricate species must be understood before propagation techniques can be devised. Most private companies are not willing to participate in such research due to the high costs and long term payback period.

A program to develop a mass production system of redwoods has been a project of Simpson Timber Co. of Seattle, Washington for several years (OTA, 1982). Two methods of selection have been devised. One involves cloning from rootings developed from the uppermost branches of elite trees. The other technique clones seed through tissue culture of needles. Implementation of these systems may soon occur, but final research results are not expected for 10 to 15 years.

Genetic engineering techniques described previously may be used to improve the quality of tree products, such as fruit, nuts, and timber, and to improve the general health of the tree. These are the province of corporations such as those listed in Table 6.

3.2.2 Applied Animal Research

Table 7 describes three specific areas of applied animal research - animal breeding, vaccines and disease prevention, and milk and meat

production. Miscellaneous animal biotechnology includes components of these areas as well as projects which have applications for nonagricultural animals and humans. The following sections outline these categories of animal research.

3.2.2.1 Animal Breeding

Reproductive capacity improvement research has long been of interest to the livestock industry (Ford, 1983). Breeding with artificial insemination (AI) attempted to acquire desired traits in livestock, but lacked the precision for isolating genes (OTA, 1982). More recent efforts focus on four objectives: (1) improvement of male fertility, (2) gamete and embryo mainpulation, (3) increase in number of offspring per female in the breeding population, and (4) reduction in generation intervals (Ford, 1983). Currently available breeding technologies are outlined in Table 8. These techniques are explained in the remainder of this section.

Previously, improved male fertility was difficult to evaluate, relying on conception rate statistics of bred females for data. An effective means of assessing male fertility has been devised, so taht determination of fertility levels is possible (Ford, 1983).

Several technologies relate to improvement of male fertility. Sperm storage preserves semen in a frozen state at -196^{o}C for an indefinite time. This procedure makes transporting and screening sperm easier (OTA, 1982).

Artificial insemination, or manual placement of sperm into the uterus is a highly developed technique practices on many species. Average conception rates upon first insemination are only 50 percent,

TABLE 7. A SAMPLE OF APPLIED ANIMAL BIOTECHNOLOGY RESEARCH RELATED TO AGRICULTURE

ANIMAL BREEDING

University

University of California, Davis, G. Anderson. Cloning of genetically superior animals.

University of California, Davis, C. C. Calvert. Genetic manipulation for improved growth.

University of California, Davis, G. P. Moberg. Stress resistance in farm animals for reduced reproductive failure.

University of California, San Francisco, W. L. Miller. Cloning of bovine prolactin gene.

Colorado State University, P. Elsden, G. Seidel, T. Williams. Cattle embryo removal for transplant.

University of Illinois, C. N. Graves. Improved embryogenesis in cattle.

University of Minnesota, A. Hunter. Cattle cloning.

Ohio State University, T. E. Wagner. Mammalian gene transfer.

University of South Carolina, P. A. Sandifer. Artificial insemination in prawns.

Corporate

International Embryos. Animal breeding and embryo transfer.

VACCINES AND DISEASE PREVENTION IN ANIMALS

University

University of California, Davis, P. Baumann. Biological control of disease-carrying mosquitos.

University of California, Davis, M. Privalsky. Avian leulosis viruses.

University of California, Davis, K. Radke. Retroviruses and induced malignancy in domestic food animals.

Cornell University, S. E. Bloom. Genetic manipulation of poultry embryos for disease resistance.

University of Florida, J. F. Butler. Animal parasites in livestock.

Mississippi State University, E. M. Huddleston. Herd health management, new drugs and biologicals, and procedures for animal health.

Virginia Polytechnic Institute, R. C. Bates. Structure of canine parvovirus DNA.

Corporate

Agra-Cetus, U.S. Animal health care.

Biogen, U.K. Foot and mouth vaccine.

Ciba-Geigy, Research Triangle Park, NC. Animal health care.

Genentech, Inc., U.S. Foot and mouth vaccine.

Molecular Genetics, Minneapolis, MN. Veterinary products.

Neogen Corp., East Lansing, MI. Animal disease control.

RIBI Immunochem Research, Inc. Antitumor agent for cattle and horses.

Government

Houghton Poultry Research Station, Cambridge, U.K. Infectious bronchitis vaccine for chickens.

National Institute of Animal Health and Ministry of Agriculture, Forestry, and Fisheries, U.K. Antibodies for swine cholera virus.

MILK AND MEAT PRODUCTION

University

University of California, Davis, R. L. Baldwin. Bovine growth hormone.

University of California, Davis, E. Bandman. Chicken muscular development.

University of California, Davis, E. Chang. Arthropod growth hormone for lobster culturing.

University of California, Davis, T. Richardson. Dairy cow engineering for nutritionally superior milk.

Cornell University, D. Bauman. Bovine growth hormone.

Cornell University, R. Gorewitt. Control of milk production.

Cornell University, S. E. Bloom. Chicken growth hormone.

Michigan State University. Bovine growth hormone clones.

Corporate

American Cyanamide, U.S. Bovine growth hormone.

AMGen, CA. Chicken growth hormone.

Biogen, U.K. Bovine growth hormone.

Biotechnology General Corp., Tel-Aviv, Israel. Bovine growth hormone.

Monsanto, U.S. Bovine growth hormone.

Upjohn, U.S. Bovine growth hormone.

MISCELLANEOUS ANIMAL BIOTECHNOLOGY

University

University of Georgia, T. J. Kerr. Cattle feed from peanut shells.

Corporate

Ambico, U.S.

American Cyanamid Co., U.S.

American Qualex, U.S.

Animal Vaccine Research Corp., U.S.

Antibodies, Inc., U.S.

Applied Genetics, Inc., U.S.

Atlanta Antibodies, U.S.

Bethesda Research Laboratories, Inc., U.S.

Bio-con, Inc., U.S.

Biotechnica International, Inc., U.S.

California Biotechnology, Inc., U.S.

Cambridge Bioscience Corp., U.S.

Centaur Genetics Corp., U.S.

Chiron Corp., U.S.

Diamond Laboratories, U.S.

Diamond Shamrock Corp., U.S.

Dow Chemical Co., U.S.

Enzo Biochem, Inc., U.S.

Genetic Replication Technologies, Inc., U.S.

Genetics International, Inc., U.S.

Genex Corp., U.S.

W. R. Grace and Co., U.S.

Hem Research, U.S.

Indiana BioLab, U.S.

International Genetic Sciences Partnership, U.S.

International Minerals and Chemical Corp., U.S.

Lederie Laboratories, U.S.

The Liposome Co., Inc., U.S.

Liposome Technology, Inc., U.S.

Merck and Co., Inc., U.S.

Miles Laboratories, Inc., U.S.

Monoclonal Antibodies, Inc., U.S.

Multivac, Inc., U.S.

Neogen Corp., U.S.

Norden Laboratories, U.S.

Pfizer, Inc., U.S.

Repligen Corp., U.S.

Salk Institute Biotechnology/Industrial Associates, Inc., U.S.

Sandoz, Inc., U.S.

Shering-Plough Corp., U.S.

SDS Biotech Corp., U.S.

SmithKline Beckman, U.S.

A.E. Staley Manufacturing Co., U.S.

Synbiotex Corp., U.S.

Synergen, U.S.

Syngene Products and Research, Inc., U.S.

Syuntex Corp., U.S.

Syntro Corp., U.S.

Unigene Laboratories, Inc., U.S.

The Upjohn Co., U.S.

Worne Biotechnology, Inc., U.S.

Zoecon Corp., U.S.

SOURCES: CRIS USDA. Electronic data search conducted at University of California, Davis in December, 1985. Searched under keywords Biotechnolog..., Biotechnolog... and Economic, and Biotechnolog... and Cost.

Lohr, L., 1986. Results of UCD Biotechnology Survey Undertaken October 1985. University of California, Davis. Department of Agricultural Economics. Unpublished.

Murray, Dennis J., and Patrick J. O'Connor, 1983. A Guide to Corporate-Sponsored University Research in Biotechnology. Millbrook, NY: Genetic Sciences International. pp. 267-275, 278-279, 288-291.

Phillips, Michael J., 1985. "Enhancing Competitiveness: Research and Technology in Agriculture." Draft for Symposiumm on Competing in the World Marketplace: The Challenge for American Agriculture held in Kansas City, Missouri on October 31 - November 1. pp. 16-18.

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Wittwer, Sylvan H., 1983, "Epilogue: The New Agriculture: A View of the Twenty-first Century," in Agriculture in the Twenty-first Century, John W. Rosenblum, ed., New York: John Wiley and Sons, p. 353.

and depend on a variety of factors related to the procedure. Although estrus detection in large herds may be a problem, there is a marked cost reduction for AI versus keeping live sires, and an enhanced ability to control diseases (OTA, 1982).

Estrous synchronization using drug treatments improves the success rate of AI with larger herds, and reduces management inputs (Ford, 1983). This technique also raises the measured success of male animal fertility.

Other factors important to male fertility are related to the presence of sexual aggressiveness of males and the environmental influences around the animal. Detection of these influences leads to management practices to improve fertility. One example is maintenance of boars in air-conditioned rooms during hot summer days, due to the fertility decreases after exposure to elevated temperatures (Ford, 1983).

Gamete (sperm and egg) and blastocyst (cell mass formed and growing from the egg-sperm union) manipulation techniques have recently become more widespread. Karyotyping is the technique of removing cells from the embryos to identify the sex of the unborn. No reliable method for identifying and segregating male-producing from female-producing sperm currently exists (OTA, 1982).

Superovulation, in which hormones are used to stimulate the release of more than one ova during ovulation, is a gamete manipulation biotechnology. Embryo recovery is used to collect fertilized ova for storage or transfer to maintain the lineage of animals with desired

TABLE 8. CURRENTLY AVAILABLE ANIMAL BREEDING BIOTECHNOLOGIES

Technology	Species
Sperm storage	Cattle, horses, swine, sheep, goats, poultry
Artificial insemination	Cattle, horses, swine, sheep, goats, poultry
Estrus synchronization	Dairy cattle (heifers), beef cattle, sheep
Superovulation	Cattle, swine, sheep, goats
Embryo recovery (surgical)	Cattle, horses, swine, sheep, goats
(nonsurgical)	Cattle, horses
Embryo transfer (surgical)	Cattle, horses, swine, sheep, goats
(nonsurgical)	Cattle, horses
Embryo storage (short term)	Cattle
(long term)	Cattle, sheep, goats
Twinning	Cattle

SOURCE: Office of Technology Assessment, 1982, Genetic Technology - A New Frontier, Boulder, CO: Westview Press, pp. 183-190, 309-314.

traits. For some species surgical techniques are used, which increase cost and may be limited by the formation of scar tissue (OTA, 1982).

Embryo transfer is a manipulation technique which enables greater numbers of offspring to be obtained from a single female. Transfer techniques may be surgical or nonsurgical. Under this procedure, there is potential for twinning. Cost-effectiveness of producing twins must be weighed against increased costs of the procedure, especially where surgery is required (OTA, 1982). This method has been increasingly popular for use with cattle. Predictions are that embryo transfer will account for 500,000 pregnancies in cattle in 1990 (Ford, 1983).

Long and short term embryo storage increases the advantages of embryo transfer procedures and lowers the cost of transporting animal germplasm, although it is not always successful. This procedure, like sperm storage, permits higher quality genetic material to be maintained at a reduced cost. With storage, the fertilized ova do not have to be transferred immediately, permitting farmers more options for breeding females (OTA, 1982).

Other procedures which could potentially increase the number of offspring per female are pregnancy diagnosis for culling, improvement in neonatal survival rates, and improved eggshell quality in poultry (Ford, 1983). Potential techniques without proven success include cloning, cell fusion, parthogenesis, and gene transfer, all of which can increase homogeneity of offspring while increasing the numbers available from a single female (OTA, 1982).

Reduction in generation intervals could greatly improve reproduction capacity. Earlier ages for first breeding of females are being recommended. Shortening the post-partum interval and improving estrus detection should also result in a decreased generation interval (Ford, 1983).

It is likely that most animal breeding techniques will complement, rather than replace each other. For example, 10,000 offspring may be produced by one bull in a year using AI, while embryo transfer might produce 15 offspring from one cow in one year (NRC, 1985).

Usage of the techniques varies by industry. In the beef cattle industry, only 4 percent of the U.S. beef cows are artificially inseminated. However, 70 percent of the nation's dairy cows receive this treatment (NRC, 1985).

Several observations on these technologies are in order. First, they are at different stages of research and development. Second, the usefulness of each varies by species. Finally, the technologies interrelate, and in some cases, follow a set sequence, such as embryo recovery, transfer, and storage (OTA, 1982). These points indicate that usefulness and cost of the techniques may vary widely, and further research is needed to obtain optimal results.

The unproven technologies of cloning, cell fusion, gene transfer, and mixing of cells from different embryos may be used to generate standard animals with new, desirable characteristics, or even to originate new animals (chimera). An example of a new animal formed this way is the sheep-goat chimera, which represents an embryonic cross of

cells from two species (NRC, 1985). These practices are not expected to be of commercial use for at least 20 more years (OTA, 1982).

3.2.2.2 Vaccines and Disease Prevention

There is considerable overlap in applied research in vaccines and disease prevention for animals and for humans. Drugs and treatments developed for human use are usually tested on animals. Most of the corporations listed under the category of miscellaneous animal biotechnology in Table 7 are drug and chemical companies which provide commercial applications of biotechnology to both animals and humans.

Drug and treatment developments for a variety of animal pests and diseases are based on both traditional and untraditional methods. Vaccines are based on disease viruses treated to destroy infectivity, but with the antigenic features left intact to produce an immune response. An older method of vaccine preparation uses live attenuated (low virulence) viruses which are capable of replication (Rowlands, 1984). These methods are inadequate for some infectious disease, such as bovine viral diarrhea, and in some cases contribute to the spread of diseases (NRC, 1985).

Several new approaches to vaccine preparation are possible. One method relies on the expression of viral antigens in prokaryotes. Transformed bacteria are able to replicate viral proteins along with their own DNA. Up to 20 percent of total bacterial proteins may be represented by desired proteins. This method has proven very successful for production of the VP1 protein of foot and mouth disease virus, but limited results have been obtained for other viruses (Rowlands, 1984).

This method utilizes only subunit vaccines, so that only the critical part of the virus necessary to stimulate antibody production and not the genetic material is transferred (NRC, 1985).

Another technique is the expression of viral antigens in eukaryotes. The production of hepatitis B surface antigen protein may be accomplished in yeast. Yeast derived particles are similar to natural immunogens in their ability to protect chimpanzees from infection. Other virus antigens may be cultivated in this manner (Rowlands, 1984).

Synthetic antigen production has been successful for foot and mouth vaccine. Manipulation of nucleic acids can result in creation of viable low virulence mutants of more dangerous viruses. Each of these methods shows potential for future development (Rowlands, 1984).

Permission has been given to Biologics Corporation for marketing of a vaccine against pseudorabies produced from genetic alteration of the virus (Sacramento Bee, 1986). Protests similar to the situation with testing of "ice-minus" on strawberries are being made based on the uncertainty of the effects of the vaccine on humans who may be exposed. This vaccine represents the first genetically altered product to be used commercially in agriculture and is available in the Midwest and South. Future vaccines will be made available in this manner, first undergoing licensing by the U. S. Department of Agriculture.

Disease resistance may also be bred into animals. One class of genes which controls the expression of the immune response is the major histocompatibility complex (MHC) (NRC, 1985). A family of genes on a single chromosome codes for MHC. Two MHC-related diseases are Marek's

disease (a blood cancer in chickens) and scrapie (a central nervous system disease in sheep). Different breeds of these animals have varying levels of resistance to the diseases due to MHC expression. Animals displaying high resistance may be bred to improve the overall resistance of herds and flocks.

Another group of genes controlling immune response expression are lymphokines (NRC, 1985). These hormones act as mediators which facilitate immune response. Interferon is one of the best known examples. It is being tested as a preventative measure for bovine respiratory disease. These hormones may be used to offset stress-related endemic diseases caused by alterations in immunological competence during animal shipment, weaning, and other stressful activities.

A class of genes which codes for antibodies directs the synthesis of an antibody to foreign molecules by rearranging the DNA in the immune cell (NRC, 1985). Ongoing studies are being conducted on antibodies for livestock viral diseases such as bluetongue, malignant catarrhal fever, bovine leukemia, scrapie, pseudorabies, African swine fever, Marek's disease, and avian inluenza and leudosis. Similar work is being done on bacterial diseases such as mastitis, rickettsial diseases such as anaplasmosis, and parasitic diseases such as babesiosis.

Vaccines are typically not helpful against disease-causing parasites due to the ability of parasites to alter or mask their antigens so that antibodies cannot recognize them. Genetic alteration of microbial agents can cause them to be destructive to the disease-carrying insects.

An example is the attempt to adapt Bacillus thuringiensis, a bacterium which contains toxins lethal to mosquitoes and black flies, to environments where these insects breed (NRC, 1985).

Detection of diseases is important to timely and appropriate treatment. Development of antibody reagents to detect diseases at an early stage is part of the research in antibodies. Monoclonal antibodies and DNA manipulation can be used to identify diseases. Diagnostic reagents do not yet exist for many diseases, such as malignant catarrhal fever, fatal herpesvirus in cattle and sheep, and scrapie, meaning that effective control is not yet possible (NRC, 1985).

Monoclonal antibodies have also been used effectively as a therapeutic agent against bovine diarrhea (NRC, 1985). This usage is particularly useful for neonatal pigs and calves which suffer the effects of this disease.

Combination of these techniques into animal disease control strategies has evolved into programs such as the development of the preconditioning feeder-cattle program. This program consists of performing a number of procedures for health enhancement on feeder cattle prior to their sale. The usual practices are vaccination against respiratory diseases and other diseases, louse and grub treatment, deworming, castration, and dehorning (Sorensen, 1983). This "well-treatment" approach will greatly benefit from biotechnological advances in disease identification and treatment.

The livestock integrated pest management program helps identify and biologically control harmful livestock pests (Sorensen, 1983). In

California, this program has been aimed at filth flies associated with animal confinement operations. A feedlot operation in Nebraska developed a program to control rodents and flies, and in Louisiana, mosquito control for steer protection was targeted. This type of integration of biological control methods with management techniques is expected to be an effective disease-control practice.

3.2.2.3 Milk and Meat Production

Breeding improvements as outlined in Section 3.2.2.1 have been utilized to select for animals with greater milk and meat production capacity. Also, hormonal treatments of animals have been instituted to increase muscle mass in livestock for enhanced meat production. The most celebrated example is that of the bovine growth hormone (bgh).

Dairy cattle breeding superiority has been enhanced by the existence and operation of the National Cooperative Dairy Herd Improvement Program (NCDHIP) over the last 50 years (OTA, 1982). This program collects, analyzes, and disseminates information on the performance of dairy cattle, allowing farmers to maximize the effectiveness of techniques such as artificial insemination. Cows enrolled in the Official Dairy Recordkeeping Plans in the NCDHIP have outproduced cows not enrolled by 52 percent (OTA, 1982).

Dairy breeding tends to be one of the easier manipulations to perform, since traits such as milk yield and fat content may be isolated for selection. Beef cattle display no such overwhelming trait to emphasize in genetic improvement. Growth rate and carcass quality are possibilities, since these may be measured in both sexes of beef cattle,

whereas milk production may be assessed only in female dairy cattle (OTA, 1982). Pork breeding programs have resulted in leaner, higher quality pork, as well as improved growth rates, feed efficiencies, carcass merit, and litter size (OTA, 1982). Poultry breeding has continued to increase growth rate of broilers by 4 percent per year. It is expected that by the 1990s, birds will reach 4.4 pounds in 5 weeks (OTA, 1982).

Although it has been known for decades that naturally-occurring bgh can increase milk yields in dairy cattle, inability to produce highly purified material in large batches restricted the commercial application of bgh (Practical Biotechnology, March 1984). Recent scientific studies have indicated that bgh affects metabolism in the cow to give an elevated protein content in tissue and higher milk production (Baldwin, 1986).

Study results have demonstrated yield increases of 10 percent to 40 percent over the biological capacity of the individual cow (Kalter et al., 1984). Twice-daily injections (or, in the future, implants) and increased feed requirements are the main direct costs associated with use of the hormone. In the short term studies conducted thus far, no serious side effects have been observed. Several companies have shown interest in commercializing bgh, as indicated in Table 7.

3.2.3 Agriculture-Related Research

Table 9 lists some of the applied research in fields which are related to agriculture, such as food processing and energy production. The following sections describe some of the work being conducted in these areas.

3.2.3.1 Food Processing

Use of genetics in food processing is useful in two ways : 1) to design microoganisms that transform inedible biomass into food for human consumption or for animal feed, and to design organisms that aid in food processing. Microorganisms have been used to stabilize, flavor, color, and modify food properties, and to control spoilage. Trends in this usage are expected to continue as new developments occur.

The construction of single-cell proteins (SCP) which can be converted into animal or human food has incurred greater interest, but costs of production remain higher than for some competing protein sources such as soybeans (OTA, 1982). Current commercial production of SCP is primarily from cane and beet molasses, but other materials such as petroleum-based hydrocarbons, methane or methanol, and carbohydrates from sawdust, meatpacking wastes, straw, and seed husks have been tested (OTA, 1982).

Use of whey (a byproduct of cheese production) may prove to be the most easily accessible source of fermentable materials for SCP production (Feillet, 1984). The Welsh Bio-Isolates company developed a technology for this type of production, and was planning a joint venture with a dairy for a full scale plant to increase production over the 40 ton per year limit of its trial plant (Practical Biotechnology, February 1983).

Yeasts used in baking, brewing, and winemaking have great commercial significance, but hybridizations of yeast strains used in these activities have been difficult to reproduce (OTA, 1982).

TABLE 9. A SAMPLE OF APPLIED RESEARCH IN AGRICULTURALLY-RELATED BIOTECHNOLOGY

FOOD PROCESSING

University

University of California, Davis, R. Dewey. Improvement of yeast for wine fermentation, development of one-step fermentation process.

University of California, Davis, M. J. Lewis. Improvement of yeast used as a coloring agent in animal feed.

University of California, Davis, M. O'Mahoney. Sensory mechansims of human taste.

University of California, Davis, C. Shoemaker. Properties of suspension systems which relate to processing conditions.

University of California, Davis, J. R. Whitaker. Improvement of nutritional and functional properties of food proteins.

Cornell University, J. E. Kinsella. Separation of proteins from microbial sources.

Massachusetts Institute of Technology, N. Solomon, A. Demain, S. A. Goldblith, and A. J. Sinskey.

North Carolina State University, T. R. Klaenhammer. Enzymes and starter cultures.

North Carolina State University, J. Scandalios. Single-cell protein.

University of Virginia, E. L. Gaden.

Corporate

Bio-Isolates, Wales, U.K. Protein from whey.

Corning Glass/ Kroger, U.S. Edible protein from cheese whey.

Kubota Ltd./ Meiji Milk Products Ltd. Lactic acid bacteria.

Sturge Enzymes, U.K. Lactase enzymes in dairy products.

ENERGY, ALCOHOL, AND BIOGAS PRODUCTION

University

University of Arizona, T. Peoples. Euphorbia as a fuel source.

Arizona State University, J. L. Kuester. Biomass hydrocarbon fuels.

University of California, Davis, R. Sacks. Euphorbia.

University of California, Davis, D. D. Ruy. Biomass energy from winery wastes.

Colorado State University, R. W. Hansen. Biomass fuel.

Colorado State University, J. C. Linden. Alternative liquid fuels.

Cornell University, W. J. Jewell. Agricultural residue alcohol.

University of Illinois, E. D. Rodda. Alcohol and biogas.

Lehigh University, A. E. Humphrey. Ethanol

Massachusetts Institute of Technology, . J. Sinskey. Xylose fermentation for biomass ethanol.

Purdue University, M. Chang. Gasoline from biomass ethanol.

Rutgers University, T. Chase, and D. E. Eveleigh. Biomass ethanol.

South Dakota State University, T. L. Dobbs. Biomass alcohol.

Texas A&M University, R. J. Newton, and C. G. Coble. Biomass fuels.

Texas Tech University, J. P. Goodin. Biomass fuels.

Government

Eastern Regional Research Laboratory, Illinois. Manure-crop residue methane.

International Centre for Genetic Engineering and Biotechnology, U.N. Biomass energy.

U. S. Meat Animal Research Center, Clay Center, Nebraska. Animal-crop residue methane.

SOURCES: CRIS USDA. Electronic data search conducted at University of California, Davis in December, 1985. Searched under keywords Biotechnolog..., Biotechnolog... and Economic, and Biotechnolog... and Cost.

Lohr, L., 1986. Results of UCD Biotechnology Survey Undertaken October, 1985. University of California, Davis. Department of Agricultural Economics. Unpublished.

Murray, Dennis J., and Patrick J. O'Connor, 1983. A Guide to Corporate-Sponsored University Research in Biotechnology. Millbrook, NY: Genetic Sciences International. pp. 267-275, 278-279, 288-291.

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Enzymes produced by fermentation techniques and by extraction from natural tissues are widely used. In the food processing industry, enzymes are used to process starches and to convert sugars, such as pullulanase, which breaks down the polysaccharide pullulan to maltose for use in jams and jellies. Other examples are glucose isomerase, invertase, and amylase which have made the production of high fructose corn sweeteners profitable (OTA, 1982). The use of genetic engineering can make possible production in larger quantities of existing enzymes, such as rennet as well as synthesizing new products, such as aspartame (Wittwer, 1983).

3.2.3.2 Energy, Alcohol, and Biogas Production

As shown in Table 8, many universities are conducting research into biomass fuels and alcohol. The production of chemicals from biomass (starch, sucrose, and cellulose) through biotechnological fermentation processes may someday rival that of production from petroelum and gas (Feillet, 1984). Organic acids, solvents, alcohols, and polyols may be produced in this manner. Improvements in crop yields will result in an abundance of biomass for conversion. The main obstacles to commercialization appears to be extraction and purification costs, water content of biomass, and low concentration of products in fermentation broth (Feillet, 1984).

In general, commercial interest in biomass fuels has dropped with the stabilization of lower oil prices. Several previously planned ethanol plants have been cancelled (Practical Biotechnology, February 1983). However, interest in on-farm anaerobic digestors and combustors,

and industrial boilers fueled by biomass wastes remains high in some areas, such as California, where large-scale food production generates large quantities of wastes.

4. AREAS FOR SOCIAL SCIENCE RESEARCH

The nature of biotechnology research is diverse and its influence is pervasive. Besides the agricultural applications described in this paper, there is an overwhelming body of research in pharmaceuticals, basic medical research, and even environmental engineering. The brief overview in this paper is intended only as a starting point for social scientists interested in agricultural biotechnology.

Studies in the economics of biotechnology and behavioral models of technology adoption and interaction among corporations, universities and governments are beginning to assume prominence. The impacts of the innovations discussed in this paper and those on the threshold of development promise to be greater than for any previous agricultural development. This is due to the rapidity of development and magnitude of yield or quality alteration possible from a single biotechnological innovation, and to the potential for widespread and immediate adoption of approved technologies.

A good example of the impact of a biotechnological development is the bovine growth hormone described in Section 3.2.2.3, which may increase milk production by 10 percent to 40 percent <u>per cow</u> at a time when the United States is facing the largest excess dairy production in history and the USDA is encouraging retirement of dairy producers through stock sales. Farmers are virtually forced into technology adoption to remain competitive in the market. Despite widespread adoption, it is unlikely that all current dairies will survive. There

will likely be many fewer dairy farmers, each with slightly larger herds as they gain market share from dairies going out of business. The net result could be a drastically reduced dairy industry. Moreover, industries which provide inputs to the dairy sector may also be severely affected.

The level of interest in the bovine growth hormone is high. At present there are 26 U.S. universities, three USDA research centers, and six foreign universities conducting and/or financing research on bgh (Rosenberg, 1986).

In general, predicted impacts from agricultural biotechnology developments include lower prices for consumers and gains to early adopters of innovations. Utilization of inputs may shift among existing or new inputs, may shift to different quality inputs, or may remain constant while production levels increase. Land inputs in particular may be affected as higher per-acre yields are made possible. The structure of agriculture may be altered as some developments may favor larger firms while others, such as 'ice-minus' will reduce risk of farming certain crops for all producers. Environmental conditions may also be affected by widespread adoption of biotechnological developments (Committee on Biotechnology, 1984).

Biotechnological developments may have unforeseen global effects. Innovations in human health-related biotechnology may increase demand for food products by improving overall health of individuals and by increasing life spans. Agricultural biotechnology research aimed at crops widely used in underdeveloped countries offers hope for reducing

the cost of food and increasing food supplies in deficit areas (Committee on Biotechnology, 1984).

The manner in which the public and the private sector respond to biotechnological developments should be shaped not only by the production impacts of the innovations, but also by the economic and social impacts. Study of these problems may require analysis with new techniques. At a minimum, dynamic analysis should be used to capture the crucial time component involved in biotechnological advances - the development of a magnitude of change in a few years which previously took generations to achieve. As revision of existing models and development of new models to project the impacts of these changes occurs, policymakers will be better equipped to make decisions which wisely utilize biotechnological innovations.

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