SPACE AND BIOTECHNOLOGY: AN INDUSTRY PROFILE

Preface

This research was conducted under the auspices of the Research Institute for Computing and Information Systems by Richard S. Johnston, David J. Norton, and Baldwin H. Tom, at the Center for Space and Advanced Technology, Arlington, Virginia. Dr. Peter C. Bishop, Director of the Space Business Research Center at the University of Houston-Clear Lake, served as RICIS technical representative.

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The views and conclusions contained in this report are those of the author and should not be interpreted as representative of the official policies, either express or implied, of NASA or the United States Government.

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National Aeronautics and Space
Administration
Lyndon B. Johnson Space Center
Houston, Texas 77058

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I. EXECUTIVE SUMMARY

This report presents the results of a study conducted by the Center for Space and Advanced Technology (CSAT) for NASA-JSC. The objectives were to determine the interests and attitudes of the U.S. biotechnology industry toward space biotechnology and to prepare a concise review of the current activities of the biotechnology industry.

In order to accomplish these objectives, two primary actions were taken. First, a questionnaire was designed, reviewed and distributed to U.S. biotechnology companies. Second, reviews of the various biotechnology fields were prepared in several aspects of the industry (Biotechnology Business, Agriculture, Medicine and Veterinary Medicine). For each review, leading figures in the field were asked to prepare a brief review pointing out key trends and current industry technical problems. The result is a readable narrative of the biotechnology industry which will provide space scientists and engineers valuable clues as to where the space environment can be explored to advance the U.S. biotechnology industry.

The questionnaire was designed for a two-tiered response system. The first tier dealt with the industry's level of awareness of basic space program activities and interest in pursuing space biotechnology. The second tier was more comprehensive and dealt with a wider range of capabilities and attitudes toward space biotechnology.

To enhance the overall study, the primary study team assembled an advisory group consisting of individuals on the front lines of both research and business development. This group helped design the questionnaire and suggested additional industry contacts. Individuals in the advisory group and certain other specific experts were also asked to prepare review articles on various phases of the industry.

According to the Arthur Young High Technology Group report, "Biotech '88: Into the Marketplace," the U.S. biotechnology industry has a universe of over 900 corporations and is still growing at 10% per year. Of these 900, approximately 400 companies can truly be identified as primarily involved in biotechnology. The gross expenditure for this industry is some $17 billion, while revenues are about $13 billion or a net loss of $4 billion. One reason why expenses are so heavy is that biotechnology is research driven. Approximately 27% of all expenses are for R&D with an additional 26% spent to acquire technology through purchase. This 53% compares with the normal industry range of 2-7%.

Thus the industry is very dynamic and is continually seeking competitive advantages. This is the environment which the questionnaire on space biotechnology penetrated. Two hundred and four U.S. firms were selected out of the biotechnology universe representing a broad array of size and product orientation. Roughly one third of those responding had research budgets below $10 million, one-third $10-100 million and one-third over $100 million.

Some 21% of those surveyed responded to the first tier, while 10% responded to the second tier--the more detailed part. Of the respondents, 83% felt that space research for space-based processes was of value to the biotechnology industry. Further, 54% would like to participate in space biotechnology through workshops, user groups, and cooperative research programs. Another important response was that 69% felt that the Space Station would provide support for the U.S. biotechnology industry.

When asked what type of information was needed to encourage their participation, the following answers were most frequently provided:

- a bibliography of publications providing results of past space biotechnology research and details of the space environment relative to space biotechnology.
- a compendium of space biotechnology resources available
- cost and time information for planning experiments
- evidence of tangible benefits of space biotechnology

The overall impression gathered from the questionnaire, the biotechnology review articles, and telephone interviews is that the biotechnology industry is a rapidly growing field which is research and development oriented. Remarkable applications for improved plants and animals have been developed in recent years to complement past progress in the pharmaceutical area. Research, however, is costly and difficult to sustain for any private enterprise, and, therefore, most are scrambling for funds and new ideas to increase their competitive edge. Thus, the possibility of NASA, private industry, and university cooperative research in these areas is attractive.

While there is considerable interest in space biotechnology, the industry is not well informed of the space environment or applicable space biological research. As was identified in the questionnaire, it will be important to provide the industry with basic materials and workshops on space and its potential for biotechnology. Conversely, stronger lines of communication for NASA must also be established so that they understand the needs of the biotechnology industry.

II. INTRODUCTION

The objective of this study was the development of a U.S. biotechnology industry profile which describes the industry's technology needs, outlines trends in research and technology which may benefit from space research, and determines corporate interest in space biotechnology research. A major segment of the U.S. biotechnology industry has been surveyed in this study. Two hundred and four U.S. biotechnology companies were requested to complete a biotechnology questionnaire. Two mailings and selected telephone follow-up were made. Twenty three percent of the companies responded by completing the questionnaire. This report provides an overview of the biotechnology field and summarizes the results of the study with recommendations for future NASA activities.

The Center for Space and Advanced Technology, under a subcontract to the University of Houston at Clear Lake, is developing a long-range strategic plan to assist NASA in structuring a program to promote the utilization of the Space Station for commercial purposes. This plan will assist NASA management in developing a combination of policies, objectives and programs that will ensure that United States corporations have the opportunity to fully exploit the potentials of commercial space enterprises. Industries which may be interested in space biotechnology are being asked their perception of the space station and their interest in research in the microgravity environment.

A. Biotechnology Overview

In the past 15 years, dramatic new developments in the ability to select and manipulate genetic material have generated interest in the medical, agricultural, and industrial uses of living organisms and their products. A major technology revolution is occurring in the United States and in foreign countries. Biotechnology is having a major impact on traditional American industry as a continuous stream of novel technologies create new business opportunities. Biotechnology represents a breakthrough on a par with that of computers and micro electronics. It is a field that is projected to expand from current levels of $750 million per year to $40 billion per year by the year 2000. The report, "Commercial Biotechnology, an International Analysis," published in 1984 by the Office of Technology Assessment, gives the following description:

> Biotechnology, broadly defined, includes any technique that uses living organisms (or parts of organisms) to make or modify products, to improve plants, or to develop microorganisms for specific uses. Biological processes and organisms have been used with great success throughout history and have become increasingly sophisticated over the years. Since the dawn of civilization, people have deliberately selected organisms that improved agriculture, animal husbandry, baking and brewing. More recently, a better understanding of genetics has led to more effective

application of traditional genetics in such areas as antibiotics and chemical production. The novel techniques used in biotechnology are extremely powerful because they allow a large amount of control over biological systems.

Recombinant DNA (rDNA) technology, one of the new techniques, allows direct manipulation of the genetic material of individual cells. The ability to direct which genes are used by cells permits more control over the production of biological molecules than every before. Recombinant DNA technology can be used in a wide variety of industrial sectors to develop microorganisms that produce new products, existing products more efficiently, or large quantities of otherwise scarce products. This technology can be used to develop bacteria that degrade industrial wastes or new strains of agriculturally important plants. Cell fusion (the artificial joining of cells) combines the desirable characteristics of different types of cells into one cell. This technique has been used to incorporate in one cell, the traits of immortality and rapid proliferation from cancer cells with the ability to produce useful antibodies from specialized cells of the immune system. The cell line resulting from such a fusion, known as a hybridoma, produces large quantities of monoclonal antibodies (MABs), so called because they have been produced by the progeny, or clone, of a single hybridoma cell. MABs are demonstrating great potential in the diagnosis and treatment of disease and in the purification of proteins. The commercial success of specific industrial applications of rDNA and cell fusion techniques will hinge on bioprocess engineering.

Bioprocess technology, though not a novel genetic technique, is the application of biological methods of production to large-scale industrial use. Many industrial biological syntheses at present are carried out in single batches, with small amounts of products being recovered from large quantities of cellular components, nutrients, waste products, and water. Recent improvements in techniques for immobilizing cells or enzymes and in bioreactor designs, for example, are helping to increase production and facilitate recovery of many substances. Additionally, new genetic techniques can aid in the design of more efficient bioreactors, sensors and recovery systems. In the next decade, competitive advantage in areas related to biotechnology may depend as much on developments in bioprocessing engineering as on innovation in genetics, immunology and other areas of basic science.

The same technologies that yield commercial products will also provide new research tools. The new genetic technologies described above have ignited an explosion of fundamental knowledge. The widespread use of rDNA and cell fusion techniques in the investigation of a wide variety of biological phenomena in plants, animals, microorganisms, and viruses highlights the impact of these technologies on basic science research and the advances in fundamental knowledge that they make possible. This new knowledge in return, may reveal new commercial applications.

The industrial applications of biotechnology in the next ten years are likely to occur in pharmaceuticals, veterinary sciences and agriculture, and specialty chemicals. Subsequent chapters in this report will provide field survey reports on the application in medicine, agriculture, and veterinary biotechnology. In the pharmaceutical field, biotechnology is being used for the production of proteins such as insulin and interferon; antibiotics for treating patients; diagnostics; and vaccines for bacterial and viral parasitic diseases. In veterinary medicine products are being developed similar to those being developed in the pharmaceutical industry with animal vaccines of great economic significance. In the specialty chemicals and food additives area, possible applications include improvements in existing bioprocesses, such as the production of amino acids, vitamins and steroid compounds. Biotechnology may provide single or shorter production steps than those complex multi-step production processes currently used. In plant agriculture, some important traits of plants, including stress-resistance and pest-resistance appear to be rather simple genetically, and it may be possible to transfer these traits to important crop species in the next few years. Other traits such as increased growth rate and increased photosynthetic ability are genetically more complex and it is likely to take years to develop and field test plants with these new traits. Environmental applications of biotechnology include mineral leaching and metal concentration, pollution control, toxic waste degradation, and enhanced oil recovery.

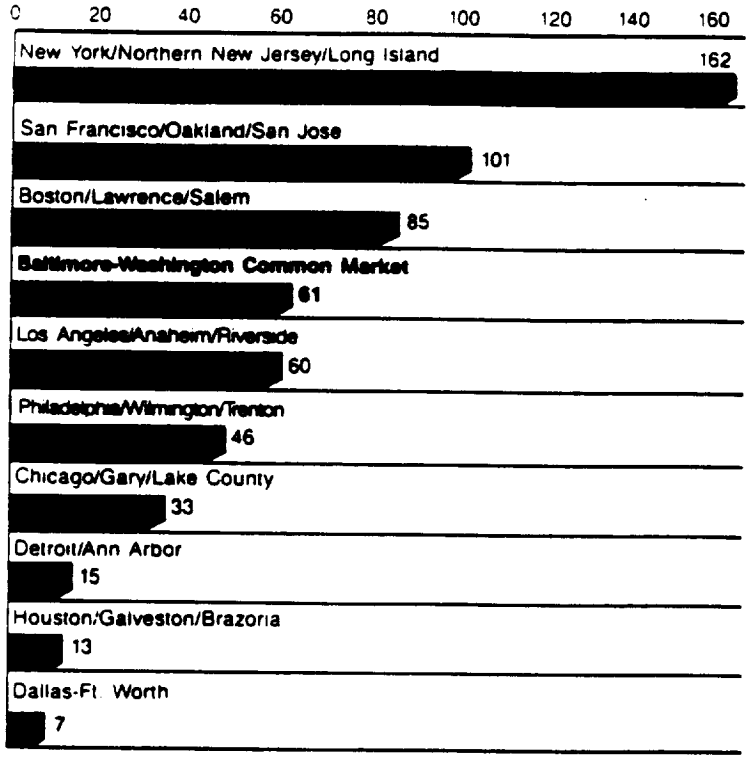
Commodity chemicals, which are now produced from petroleum feedstocks, could be produced biologically from biomass feedstocks such as cornstarch and lignocellulose. In the area of bioelectronics, biotechnology could be used to develop improved biosensors or new conducting devices called biochips. Sensors that use enzymes for detecting specific substances are available now. However their use is limited by the narrow range of substances they detect and by their temperature instability. Biotechnology could be instrumental in the development of more versatile sensors that use enzymes or MABs. Better sensors would be especially useful in the control of industrial bioprocesses. Biotechnology may also make it possible to construct devices that use proteins as a framework for molecules that act as semiconductors. The anticipated advantages of these biochips are their small size, reliability, and the potential for self assembly. The production of biochips is one of the most distant applications of biotechnology.

B. Locations of U.S. Biotechnology Companies

The highest density of biotechnology firms in the U.S. is in the San Francisco Bay and Boston areas around the excellent universities in these areas. Other concentrations include: Seattle, Los Angeles, and the eastern seaboard from Connecticut to Virginia. The Carolinas, Georgia, Florida and Texas have a lesser density of biotechnology firms. Figure 1 shows the number of biotechnology firms by major Certified Metropolitan Statistical Areas (CMSA) for 1987. In the report-figure vs. the explaining-figure, the Northeast is not included.

This chart was prepared by The Baltimore - Washington Common Market, using data from "Biotech '88: Into the Marketplace," Arthur Young High Technology Group. The survey universe was 1,054 firms, with the remaining 471 distributed across the U.S. The Southwest is lagging behind the rest of the country.

Figure 1: Number of Biotechnology Firms by Major CMSA — 1987



C. Research and Development in Biotechnology

The Congressional Office of Technology Assessment has recently compiled a report on the rapid progress of the biotechnology industry. This report surveyed some 349 companies; large and small. The reported R & D spending for 1987 was broken down into research areas comparing small biotechnology firms with large firms with biotechnology interests.

Overall, in 1987 some $2 billion were spent on biotechnology by the private sector. Table 1 outlines the various categories of research spending for the biotechnology industry, while Table 2 outlines Federally Funded Biotechnology Research for 1985.

TABLE 1: R & D Spending by Biotechnology Companies

Where the Money Is Being Spent

The private sector spent about $2 billion on biotechnology research and development in 1987. The number of companies involved in each primary research segment is in parentheses; dollar values are in millions.

Research Area	Biotech Companies*		Other Large Companies*	
Drugs	$252	(63)	$208	(14)
Diagnostics	216	(52)	88	(6)
Chemicals	84	(20)	168	(11)
Plant agriculture	96	(24)	104	(7)
Animal agriculture	72	(19)	64	(4)
Specialized chemicals	144	(34)	32	(2)
Waste disposal/treatment	12	(3)	16	(1)
Equipment	48	(12)	16	(1)
Cell culture	24	(5)	16	(1)
Diversified/other	264	(44)	88	(6)
Total:	1,200	(296)	800	(53)

*From a sampling of 349 companies. The biotech companies spend at least 60 percent of their research and development on biotechnology; the large companies spend at least 20 percent.

Source: Office of Technology Assessment

The New York Times/ July 13, 1988

TABLE 2: Federally Funded Biotechnology Research (1985)

	Total R&D	Biotech Research
Agricultural Research Service	469.7	24.5
Cooperative State Research	284.3	48.4
Environmental Protection Agency	320.4	1.5
FDA	82.0	2.6
National Institute of Health	4824.4	1849.5
NSF	1345.6	81.6
	7325.4	2005.1
	$7.3 B	$2.0 B

III. STUDY PLAN

The purpose of this study was to develop a biotechnology industry profile which describes current industrial technology needs, identifies trends in research and technology which might benefit from space research, and determines corporate interest in space biotechnology research.

A. Study Objectives

1. To determine industry's understanding and expectations about NASA's plans for conducting biotechnology and space biology research in the Space Station.

2. To determine industry's perception about NASA activities to encourage and assist private enterprise in space.

3. To determine what type of information would be useful to biotechnology corporations to assist them in becoming active participants in the commercial utilization of space.

4. To assess the biotechnology corporate understanding of the space environment, sciences, and technology.

5. To determine the sensitivities of biotechnology companies about entering into collaborative relationships with NASA, universities, and other biotechnology companies.

6. To determine if any company funds are currently being committed to space related biotechnology research.

7. To assess the key trends and future events which might impact industry's decision to enter into space related research activities, and the type of ground and flight research needed to fulfill critical biotechnology needs to stimulate industrial participation in the Space Station Program.

For the purposes of this study, Biotechnology covers the following areas:

- Bioprocessing
- Cell/Tissue Culture
- Enzymology
- Fermentation
- Hybridoma (Cell Fusion)
- Large Scale Purification
- Process Monitoring and Control
- Purification/Separation
- Recombinant DNA
- Sequencing
- Synthesis

B. General Description of Study Plan

Methodology: The study plan was developed to utilize an industry questionnaire (see Appendix A). Initially, plans were made to make limited visits to selected biotechnology companies. Plans for these

visits were deleted from the program. Funding limitations precluded the desired number of visits and it was felt that a well designed questionnaire should produce the information needed. It was decided that telephone calls would be made as a substitute for the corporate visits. Ten percent of those companies who did not respond to the first mailing were called to answer questions and to encourage completion of the written questionnaire. To assist in the development of uniform information, a telephone check list was developed. Several of the company executives indicated that their company did not take part in this type of study, nor did they complete these types of questionnaires. Two companies indicated that they would complete the questionnaire as a result of the telephone conversation. One company executive stated that his technical staff did not feel that the space environment could help with their research programs. Another company officer indicated that he had a problem understanding how the space environment related to his technical problems, although this individual was aware of the McDonnell Douglas electrophoresis flight experiments and the attempts to grow crystals in space. Several people indicated an interest in the final report. Many companies had administrative or secretarial personnel return the telephone calls. It was obvious from these telephone calls that the executives of biotechnology companies were extremely busy and did not have time to let discussion of space biotechnology interfere with their business.

A program management plan and schedule were developed to implement this study. Payload Systems, Inc. was subcontracted as a study team member to conduct a preliminary analysis of industry R & D in space related biotechnology corporations. Results of the Payload Systems, Inc. effort were submitted to NASA in March 1988. The University of Houston Clear Lake provided biotechnology literature surveys. Results from this effort are included in the bibliography (Appendix B). The study schedule was established at the start of the project. The final schedule lists the scheduled date and the actual completion dates. This schedule was reviewed with the NASA technical monitor during study review meetings. The completion of this final report was delayed to include more technical information and a bibliography.

C. Organization

A Study Management Team was established to plan the study program, develop a questionnaire, conduct a telephone survey, organize an industry workshop, and prepare the final report. Members of the Study Management Team were:

Biotechnology Study Manager: Richard S. Johnston, Senior Advisor
Center for Space and Advanced Technology

Project Director: Peter C. Bishop, Ph.D.
University of Houston-Clear Lake

Study Manager: Michael J. Svegliato
NASA/Johnson Space Center

Technical Advisor: David J. Norton, Ph.D., Director, STAR Center Houston Area Research Center

Technical Advisor: Baldwin H. Tom, Ph.D., Associate Director, Bioprocessing Center, UT Health Science Center at Houston (Present address: American Leadership Forum)

An Advisory Panel was established to provide professional review of the overall study. Specific responsibilities included: review industrial questionnaire, assist in industry survey and mailing list, provide personal contacts, and review final report. Members of the Advisory Panel were:

Saul Kit, Ph.D., Biochemical Virology, Baylor College of Medicine
Robb Moses, M.D., Department of Cell Biology, Baylor College of Medicine
Robert Stone, M.D., Institute of Biosciences and Technology, TAMU
Peter Ulrich, Biosciences Corporation of Texas

D. List of Companies

A mailing list of companies for distribution of the questionnaire (Appendix C) was made from two primary sources:

1) Sixth Annual GEN Guide to Biotechnology Companies, November/December 1987, Genetic Engineering News, 1651 Third Avenue, New York, NY 10128. This listing is an annual publication of Genetic Engineering News. It provides a listing of 522 companies in 24 countries. The listing provides information including Chief Executive Officer, Research Officer, principal technologies and major products. Only the U.S. company listings were used in this study (Appendix C). Data on companies surveyed is in Appendix D.

2) Payload Systems, Inc. Study: This study provided a preliminary analysis and overview on the U.S. biotechnology industry's research trends and gave an initial mailing list for the biotechnology study questionnaire (Appendix A). An executive summary of the Payloads Systems, Inc., "Analysis of Industry R & D in Space-Related Biotechnology", is incuded in this report in Section V: HISTORICAL PERSPECTIVES: SPACE BIOTECHNOLOGY RESEARCH.

E. Questionnaire

A two part questionnaire was prepared and reviewed by the Advisory Panel in December 1987 (Appendix A). The study questionnaire and planned schedule were approved by the NASA-Johnson Space Center study manager on December 30, 1987. A listing of over 200 U.S. biotechnology companies was developed from the Payload Systems report and other sources (Appendix C). This listing was reviewed with the Advisory Panel and NASA. Efforts were made to develop a list of key technical personnel within as many companies as possible. Members of the panel made suggestions for this key personnel list. To increase the industry responses, two mailings were made. The first on March 25, 1988 and the second on April 11, 1988. Telephone follow-up calls were made during the month of April using a check list. Summary data from the questionnaires was entered onto a computer by the staff at the Houston Area Research Center. Data from the questionnaire is contained in Section IV of this report. An industry workshop may be held in the Fall of 1988 to review the study results and to discuss future activities in space biotechnology.

IV. QUESTIONNAIRE RESULTS

A. Summary of Data from Questionnaire

The questionnaire was initially mailed to some 204 corporate officers representing a wide range of biotechnology firms in the United States. This mailing was repeated after a three week interval to those firms which had not responded to the first mailing. The total response from both mailings was 46 or 23 percent.

This percentage is relatively high, especially considering the intensity of effort at most biotechnology firms trying to create successful enterprises. This indicates that despite the financial pressure on these firms, there is a high level of interest in space and its possibility for obtaining new knowledge which might provide a competitive advantage.

The questionnaire was designed in two parts. The first part was the front page and was largely designed with short-answer questions to encourage participation. All responders filled in this portion of the survey except one. The second part was longer and delved into more subjective aspects of their business and their attitudes regarding collaboration with NASA and others. Thirty five percent (35%) of the respondents filled out the entire questionnaire.

B. Analysis of Information

PART I.

Q 1. Who are you?

The respondents were drawn from the upper ranks of each corporation. Some 92% listed titles of President, Vice President, Director or Manager. The balance were research scientists or market analysts for their corporations.

Q 2. Are you familiar with NASA's Space Programs?

	Knowledgeable	Some Knowledge	Not Familiar
a) Space Shuttle	46%	50%	2%
b) Space Station	24	63	11
c) Space Bio & Biotech	11	74	13
d) Commercial Programs	7	59	33

The results show that there is general awareness of the Space Shuttle and the Space Station but considerably less knowledge about the commercial programs and the biological and biotechnological aspects of NASA's activities. Only 7% felt that they were knowledgeable about the commercial programs. Further, two-thirds checked at least one box requesting additional information concerning these programs. The most frequent request was for information regarding biological and commercial programs.

Q 3. Are you familiar with the Space Environment?

	Knowledgeable	Some Knowledge	Not Familiar
a. Microgravity	22%	63%	13%
b. Vacuum	24	59	13
c. Space Radiation	13	50	33

The question shows that there is a great deal less understanding of the value of the space environment than the general aspects of the major space programs. Seventy-six percent indicate only some knowledge or no knowledge of microgravity. This aspect of the space environment is likely to be the key asset in space biotechnology.

Q 4. Is there value in space research for the Biotech Industry?

	Yes	No
a. Space Research for Space-based Processes	83%	13%
b. Space Research for Earth-based Processes	74	22
c. Commercial Biotechnology Use of Space	59	37
d. Overall Space Biotechnology	63	30

Overall this question implies a substantial belief that there is value in space based research for the biotechnology industry. By a ratio of six to one, respondents believed that research in space for space based processes was of value to the industry. To a lesser, but still significant degree, research in space for earth based processes was held to be of value. It was less clear that there would be value in space based commercial uses. Overall by a two to one margin, space biotechnology was considered to be of real value to the industry.

Q 5. Would you like to participate in Space Biotechnology?

Yes 54% No 46% If yes, indicate possible interests:

a. Workshops	33%
b. User Group for Space Biotechnology	20
c. Cooperative Research with NASA	33
d. Cooperative Research with Univesities	20
e. Other	7

PART II.

Q 9. Major Corporate Technologies

There was a wide array of technologies listed under this question. However, several appeared quite frequently. Those included:

- rDNA
- Monoclonal Antibodies
- Cell and Tissue Culture
- Immuno assays (immunology)
- Vaccines and pharmaceuticals

Q 10. Major Products

Again, this question brought out a long list of products and services provided by these firms. For the smaller firms, many times the technologies listed above are the products and services of the corporation. For the larger firms, many technologies come together to form a family of products. Thus for a small firm, cell sorting is the technology and the product. For a larger firm, immunology and monoclonal antibodies may lead to important antigens and even pharmaceuticals.

Q 11. Is your Company a part of any existing joint venture?

Some 37% indicated that they were a part of joint ventures. Several indicated that there were too many to list while others were not involved.

Q 12. Company Resources

A very even distribution of companies responded. Thirty one percent indicated that their research budgets were in excess of $100 million. Twenty percent had research budgets between $10 and $100 million, while 37% had budgets less than $10 million. Interestingly, none of the respondents indicated any current budget devoted to space biotechnology efforts.

Q 13. Company understanding of U.S. Commercial Space Programs.

	Aware	Not Aware
a) McDonnell-Douglas Electrophoresis	49%	49%
b) 3M Protein Crystal Studies	31	69
c) Space Industries Inc. - Industrial Space Facility	27	73

To a large degree, the biotechnology industry is not aware of the related programs and opportunities for space biotechnology.

Q 14. Do you envision that the Space Station will provide support for the Biotechnology Industry? Yes 69% No 28%

The industry believes that the space station will support biotechnology.

Q 15. What are the most difficult technologies facing the industry?

From the listing of technology difficulties the following were most often mentioned: (frequencey ordered)

- Scale and reproducibility
- Separation and purification of cell products and biologicals
- Cell biology-control and gene expression
- Clinical studies

Q 16. What type of information or scientific data is needed to encourage participation?

In this case, there was a very clear voice as to what was needed: (frequency ordered)

- A bibliography or publications on:
  - -past experience in space biotech
  - -space environment including microgravity
- Resources available for space biotechnology
- Cost information
- Evidence of tangible benefits (a success)

Q 17. What are the key trends and future events which may impact space biotechnology?

The answers to this question are not well focused and it is difficult to summarize the results. The most consistent answer with respect to industry was that a clear demonstration of success in the field would stimulate a great deal of interest.

Q 18. Suggested areas of research for NASA to pursue.

- Cloning efficiency in microgravity
- Tissue culture growth in microgravity
- Separation in microgravity
- Cell productivity in space
- Freeze drying

Q 19. Would you consider forming a joint venture to pursue Biotechnology in space?

Fifty-seven percent indicated that they would consider forming a joint venture in space.

Q 21. Would you be willing to attend a workshop in Houston to review this questionnaire and space biotechnology?

Fifty-seven percent indicated that they would be willing to attend a workshop.

C. General Comments

It is clear from these results that the industry needs information before it can make informed decisions about space biotechnology. Except for the pharmaceutical field, the biotechnology industry is a young one striving to use new technologies and discoveries in business. In this very competitive industry, things change rapidly. As such, they are not generally aware of commercial space opportunities or the existing work going on in NASA. There is, however, a prediposition to believe that the Space Station and the civil space program will be a resource for biotechnology in America.

The U.S. biotechnology industry already participates in joint ventures and appears willing to participate in cooperative activities with NASA and universities especially if the intellectual property issues can be worked out to provide a competitive advantage.

V. HISTORICAL PERSPECTIVES: SPACE BIOTECHNOLOGY RESEARCH

Payload Systems, Inc.

This review focuses on studies conducted aboard United States spacecraft and is presented to provide a background showing the limited biotechnology experiments flown to date. This perspective serves not only to illustrate that few studies are available but also to underscore our understanding that the planning for future experimentation will require design input from both NASA and the biotechnology practitioners. With the limited availability of space-based experimentation, we must optimize each future flight opportunity, and target studies not possible on Earth, and/or those of near term economic benefit.

Space-based Biological Research

- Manned space flights for over 25 years.
- Biological payloads begun in the 1960's.
- Manned Skylab experiments (1972-1974): Biological and biotechnology experiments, including studies on antigen-antibodies and cell culture growth.
- Space shuttle and space lab studies (from 1981). Focus on bioprocessing, life sciences, and materials sciences.

Recent Space-based Biotechnology Research

- Bioseparations using electrophoresis, potential use in isolation of rare cells.
- Protein crystallization, potential use in pharmaceuticals and electronics.
- Cell physiology, potential in exploiting cell product synthesis. Prelude to space bioreactor use.

Bioseparations

The most ambitious efforts to exploit microgravity for molecular purification are the electrophoresis studies. In 1971, a zonal electrophoresis experiment was flown aboard Apollo 14. The study revealed a significant problem in separation process by the dominance of electroosmotic flow in space. This separation technology was re-flown on Apollo 16, Apollo-Soyuz, and STS-3. During Skylab flights, isotachophoresis experiments with hemoglobin, red cells, and ferritin were performed. The first flight using free-flow electrophoresis hardware took place in 1982 on STS-3. Subsequently, industry took an increased interest in the concept. McDonnell Douglas Aeronautics and Astronautics Corporation (MDAC) developed a continuous flow electrophoresis system (CFES) for experimental use in the middeck of the space shuttle. The equipment has been tested on seven flights, resulting in the demonstration that up to 700 times more protein per unit time could be run through the CFES than was possible on Earth. The purification factor of four achieved on Earth with a mixture of

proteins was maintained in the microgravity experiments. A production run attempted in the last flight in 1985 produced significant amounts of the hormone, erythropoietin, an important drug for stimulating blood cell formation. However, the product was contaminated by bacterial endotoxin. Future flights will be needed to develop measures to overcome the contamination problem.

One area which might be exploited to advantage in microgravity is the use of CFES for the isolation of rare cells from large cell populations. The isolation of the growth hormone producing cells from the pituitary, or the insulin producing cells from the pancreas, might be worthwhile candidates. The cell or subcellular organelle focus for microgravity separation should be seriously considered, since the focus on the microgravity purification of proteins is now difficult to justify. There is presently rapid development of large-scale, high purity separation techniques for proteins by the research and development communities. In addition, genetically engineered protein production is further diminishing the drive to seek microgravity protein production.

The USSR has also been operating electrophoresis devices on the Salyut space station. The system, named Kashtan, incorporates one separation chamber of 1.2 m and can hold up to 70 ml. The experiments have demonstrated improvements in throughput of several orders of magnitude over ground-based equipment, with efficiency factors between 10-15. USSR collaborative activities are taking place with France (free-flow electrophoresis) and Germany (molecular sieve electrophoresis). The Soviets have offered space on their MIR space station for commercial processing of materials.

Protein Crystallization

The knowledge of the structure of certain proteins can lead to the rational design of drugs and the creation of analogs for antiviral, chemotherapy, immunosuppressive, neurological, and hormonal applications. Any technique that will enhance the definition of protein structures is of considerable interest to the pharmaceutical, biotechnological, and agricultural communities. X-ray crystallography is a powerful method for determining the three-dimensional structures of complicated biological molecules. Crystallographic studies of proteins and nucleic acids have played key roles in establishing the structural foundations of molecular biology. More recently, crystallographic studies of biological macromolecules have become of considerable interest to the biotechnology industry, as promising tools in protein engineering and drug design.[1] Crystallography, to be effective, requires that relatively large crystals be grown in order to have sufficient amounts of the same material to use in determining molecular structure. The growth of such crystals occurs when the molecules are stabilized and allowed to spontaneously assemble by weak molecular interactions. In the presence of a gravitational field, such weak interactions are overwhelmed by stronger macroscopic influences, such as convection and sedimentation forces.

Many techniques are used in protein crystallography. These are well described in McPherson's paper.[2] According to McPherson, the crystallization of proteins is actually more art than science. Among the most popular microgravity techniques is the hanging drop [1,3] method, in which a drop of a few microliters of a solution of protein, buffer and salt (or often polyethylene glycol) is hung and left to equilibrate. During the associated evaporation of the solution, the protein concentration is increased causing the protein to precipitate to form crystals. This technique is very sensitive to the crystallization parameters: concentration of the constituents of the solution, pH, and temperature. Growing a successful crystal often requires experimenting with the crystallization parameters. In any case, the process of crystallization is especially slow and is often measured in terms of weeks.

The hanging drop technique has been used in flight in the western world mainly by two teams. Littke's team [3,4] has carried out many flights including Spacelab missions (1, D-1 and planned for D-2 and IML-1) and rocket missions on the TEXUS program. They have carried out these studies with the proteins lysozyme and beta-galactosidase, and have observed increased rate of growth and larger crystals when compared to proteins crystallized on the ground. A U.S. team headed by Bugg [1,5] has also flown hanging drop experiments on STS-51D, 61C, 51F, and 61F. They used lysozome, human serum, albumin, human C-reactive protein, and concanavalin. Both teams have experienced crystal growth ranging from 22 times (beta-galactosidase) to 1000 times (lysozyme) the volume of those produced on the ground (under the same conditions).

A study carried out by the Harvard Business School in May 1985 indicated that pharmaceutical firms would be willing to pay between one and two hundred thousand dollars (U.S.) to have a protein crystallized in microgravity. This economic potential is driving firms in the U.S. (Instrumentation Technology Associates, McDonnell Douglas) and in Europe (Matra and Intospace) to develop private protein crystallization hardware. Such systems are aimed at carrying out their operations in an autonomous, or at least in a semi-autonomous fashion, aboard spacecraft with their own re-entry capability.

Bioreactors

The culture of mammalian cells in bioreactors is used in the biotechnology industry for the production of hormones, enzymes, viral vaccines, antigens, antibodies, and cells. Because of gravity, the content of the bioreactor must be mixed in order to obtain a good distribution of nutrients, oxygen, temperature, and pH. This mixing creates a harsh hydrodynamic shear environment detrimental to fragile mammalian cells. If not mixed properly, the cells tend to congregate and by zone sedimentation fall to the bottom of the bioreactor. Further, the requirements for oxygenation creates foaming in the bioreactor which also damages cells.[6] The above factors contribute to limiting the concentration and density of the bioreactor broth. The

concentration and density of the solution are directly linked to the optimal performance of bioreactors; the higher the density, the more cost effective is the bioreactor run.

In microgravity, zone sedimentation disappears which should reduce the aggregation of cells. Only gentle mixing is required to distribute the nutrients and oxygen. These factors permit higher concentrations and densities to be achieved. Additionally, since the cells do not need to maintain the same surface forces that they require in higher gravity, they can divert more energy sources for growth and differentiation [6,7] and hopefully increase products. It is anticipated that the driver for a space bioreactor will be the clear need for labile materials to be purified by a subsequent space process, e.g., electrophoresis. The first space bioreactor was developed by the Johnson Space Flight Center under the guidance of Morrison.[8] In support of these developments of a space bioreactor, NASA has taken an aggressive stance, funding several university research teams to study reactor vessel fluid dynamics, shear conditions, cell stress proteins, and cell metabolism in reactors. Further, in addition to the current NASA bioreactor,[8a] a rotating culture vessel (clinostat) is under development for study as a 1-G counterpart to the space bioreactor.

Cell Physiology

Work related to the culture of cells in microgravity has been carried out on rocket flights as well as on Spacelab 3 and more recently on Spacelab D-1.[9] It is on this last mission that the most extensive and fascinating work was carried out, demonstrating a significant improvement in the productivity and differentiation characteristics of a variety of cells. This supports some of the work carried out by Hymer[10] at the Center for Cell Research at Penn State University on rat pituitary and by a French-Soviet team on parameciums.

The pattern of increased (altered) cell activity may be a consequence of microgravity due to the decreased cell interactions (contacts) when cells are freely suspended. One set of results from the D1 mission should raise concerns. The study demonstrated that human lymphocytes have a negligible response to mitogenic stimulants in culture. Further, cells tested from the astronauts exhibited a 50% reduction in response over the ground base controls. If bacteria/infectious agents have enhanced activity and the lymphocyte cells which provide our immunity are suppressed, we must be concerned about the potential consequences in the health of space travelers. Future microgravity experiments are needed to further define these preliminary conclusions. These cell studies may indeed lead to an understanding of the mechanisms by which cells control production of hormones and other cell products. With this knowledge, control of enhanced, sustained secretion of product by cells is possible.

Conclusions

The United States, along with its research partners, has performed a variety of space studies related to the growth of cells, production of cellular products, purification of biologics, and the production of protein crystals.[11,12] Future experiments for microgravity need to be carefully identified and designed to provide maximal return of information. The desire to consider a space biotechnology research focus is understandable, since the United States has the research base for both space and biotechnology areas which are unparalleled in the world. However, marrying the two areas will require that practitioners from both disciplines work together to identify the critical needs and capabilities of each. Most importantly, this effort will need the strong direction of leaders with vision. This report has been written with these underlying considerations.

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VI. REVIEWS OF BIOTECHNOLOGY INDUSTRY

The survey identified a clear and immediate need--the need for biotechnologists to understand the space program and its environment. Nevertheless, if the space biotechnology effort is to move forward, driven by biotechnology industry demands, space engineers and technologists, in turn, must understand what is required in the biotechnology fields and respond to those specific needs. Thus, biotechnologists need to describe to NASA the future directions of their field and the present technologies.

To broaden this report to NASA, biotechnology specialists have reviewed their fields and identified production limitations in the agricultural, medical, and veterinary biotechnology areas. The first report highlights the economic significance of the biotechnology field. Written by the Arthur Young High Technology Group, this report offers insight into the important product areas for biotechnology. The goal of this series of reports is to educate and stimulate development of new ideas for research and development, of new collaborations, and of new applications for the resources of outer space.

A. Biotechnology Business
Mr. John James, Arthur Young High Technology Group

Introduction

The products of biotechnology are moving into the marketplace, some of them highly publicized, others filling their niches successfully without fanfare. At different stages in different market segments, the process has been rougher than expected, but the industry is learning from each success and temporary barrier.

Progress Towards the Marketplace

Biotechnology products are not yet reaching the marketplace routinely, but the experience curve pitched upward in 1987. The rate of product introduction differs considerably across the various markets. Some human therapeutics, long under the approval process of the Food and Drug Administration, have just begun to reach the markets for which they were intended. Others expected to reach the market in 1988-89 are of the nature of "flagship products," taken by investors and the general public as symbols of the industry. Their commercialization is being closely followed and their market performance will be regarded by some as leading indicators for the industry as a whole.

Diagnostics are already and will continue to be more plentiful in the marketplace and should cumulatively make an enormous contribution to medical progress. However, because diagnostic products support medical decision-making and do not directly work "miracle cures" they are unlikely to draw the publicity attending certain therapeutics. The exception to this generalization has been in AIDS diagnostics which are of urgent interest to the community and a major element in the biotechnology industry's work on the disease.

Biotechnology applications in agriculture have been less glamorous and, for the moment, lag behind. However, it is being remedied at every level--in the universities that train plant and animal scientists, in industry itself, and in Government, which is responsible both for regulatory matters and for considerable funding of new research. The slower start says nothing about the prospects for the future. Biotechnology will have enormous impacts on agriculture, improving crop yields, developing crops for harsh environments and promoting healthier, more productive herds. World hunger is a serious challenge; biotechnology is an important part of the answer.

Unique and Not Wholly Unique

The biotechnology industry is not unique from start to finish in its commercialization process, as many people believe. It shares the obligation to submit certain products for regulatory testing with the pharmaceutical industry and with chemical companies that manufacture pesticides and herbicides. It also shares with these industries the possibility of occasional disappointments or delays owing to regulatory requirements. It shares scientific complexity at the R & D stage with the pharmaceutical, chemical and electronics industries. It

shares obligations in manufacturing with the food processing and other industries. It is perhaps closer to the universities than any other industry, from which have come many key personnel and product development programs. However, this university connection is not unique; for example, the recent flurry of interest in superconductivity originated in an industry lab but quickly extended to university researchers.

All of this said, the biotechnology industry is unique and rightfully defends its uniqueness. Some of the major biotechnology companies with a therapeutic focus intend to become vertically integrated biopharmaceutical companies--that unobtrusive prefix speaking to the continued uniqueness of the enterprise. Pharmaceutical firms are likely to evolve into biopharmaceutical firms in the 1990's. The biotechnology industry may, in effect, acquire the pharmaceutical industry in technological terms if not financial and not vice versa, as some analysts have predicted.

Organization for the Long Term

Vertical integration is much in the minds of biotechnology executives at the present stage of industry development. In business terms, vertical integration means wholeness, completeness, independence, maturity and it is, as a consequence, the noble idea of many biotechnology companies. Their goal is to evolve into fully integrated companies with R&D, manufacturing, regulatory management, and marketing and sales functions available in strength, in house. However, some of us (at Arthur Young) have begun to question this ideal in its practical application. Certain biotechnology companies should and will become vertically integrated; others will do well to take a look at that strategic goal in relation to their real strengths, current and anticipated.

Vertical integration is not the only route to profitability and a mature organizational profile. A number of different models are emerging in the industry, from R&D houses with sound commercial futures to vertically integrated, fledgling biopharmaceutical firms--and everything in between. Strategic partnerships with firms that have complementary strengths are likely to be a permanent part of the biotechnology industry's commercialization strategy. This does not necessarily spell second class status for those that choose other paths; the industry is likely to consist of many different organizational configurations.

Emerging Issues

Patents, competition, pricing, managing the regulatory process, product liability insurance, and key people are among the issues that will increasingly engage the industry attention.

The patent issue may well be paramount at the moment because it impinges on everything the biotechnology companies do. Patents contribute to the definition of market niches and can severely narrow

or close the gateways to those niches. Biotechnology companies that have targeted the same market niches and have developed reasonably parallel products, at great cost, may find themselves drawn into a turf battle at the gateways.

Competition is a fast-emerging issue. The origin of biotechnology in university research and the continuing connection of biotechnology companies with research groups in universities and other not-for-profit institutions has, until recently, helped to disguise the fact that biotechnology companies are commercial enterprises approaching a competitive marketplace. In addition, investors have had confidence in the industry and helped to finance it through public equity participations and limited partnerships. The return on investment they now expect can only be won in the competitive arena. Biotechnology companies will not lose the scientific vision and business acumen that have sustained them so far, but they will be increasingly pitted in competition with each other and with major established companies. Partners are a competitive weapon, but not the only one. Marketing expertise, manufacturing efficiency, pricing strategies, and other mainstream business skills will play their part.

Pricing is likely to emerge as an issue when some of the flagship products reach the marketplace. The advantage of patent protection allowing a freer hand to recoup high product development costs more quickly, may be offset to some degree by other factors. Therapeutic dosages priced at $1,000 or more may be priced down both by competition or public disfavor.

The regulatory process has recently emerged as a controversial issue. The natural assumption that a good product will make good progress through the regulatory process has been shaken not only in the therapeutic area but in agri-tech as well. Regulatory decision criteria have shown themselves to be complex and demanding - not without reason - and the management of the regulatory process has visibly become an indispensable skill.

Access to highly qualified people has been and remains a necessity for the industry. Biotechnology has proven its ability to attract outstanding professionals in science, medicine, and management, but companies inevitably compete against each other for the same people. Key people are considered by biotechnology companies to be a leading competitive advantage. Senior biotechnology officials tend to be a breed apart with business skills, entrepreneurial spirit, and scientific knowledge in roughly equal measures. Such men and women will always be a scarce resource.

The abiding issue in the industry is to stay on course - to maintain a high level of sophisticated R & D to finance product development creatively and to reach the marketplace with profitable innovative products in which the industry as a whole can take pride. The industry has acquired a strong public presence, considerably more so this year than in the past. If the recent trends continue and the industry's major stakeholders maintain faith in the promise it holds, it will remain in the public spotlight for many years to come.

B. Agricultural Biotechnology

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Agricultural biotechnology from the plant science perspective is a broad, complex field, and there is considerable overlap of technique and technology into areas properly termed industrial biotechnology and chemical engineering. It is, moreover, a rapidly moving field. It is to be expected that by the time this document has been read, there will be other, new developments.

It is beyond the scope of this overview to enter into a detailed discussion of the techniques that are used. The purpose here is to provide a framework that can be used by the nonbiologist, technical manager in thinking about agricultural biotechnology concepts and approaches in his or her program planning. As a general and arbitrary but defensible classification, we subdivide agricultural biotechnology into three major categories: microbial products and techniques, crop improvement, and plant products or chemicals obtained by non-traditional methodology. We will highlight the main approaches representing the state of the art in these areas and provide a few recent and specific examples of each.

Microbiological Methodology and Products

Microbiological methods are the basis for much of what is known as genetic engineering and are applied in exploitation of wide variety of cell systems in chemical engineering and industrial microbiology. However, there are specific uses to which microbial systems are put for support of agriculture. The primary emphasis here is upon the development of crop management approaches which are environmentally benign in comparison with pesticides, herbicides, fertilizers, and crop or soil conditioners now in common use.

For perhaps 20 years, a natural bacterial pathogen of insects, Bacillus thuringiensis, has been used as an insecticide in control of Lepidopteran insect pests. This method has involved the production of Bacillus thuringiensis in fermentor-culture and the spray application of stabilized spore suspensions onto crops. With the advent of molecular genetics methodology, however, there have been renewed efforts in radically improving the insecticidal properties of the Bacilli cells themselves, through the development of advanced techniques in the screening for improved bacterial strains. Ecogen Inc., of Langhorne, Pennsylvania, and the US Department of Agriculture at Beltsville are pioneers in this area. Even more radically, the plant itself is being rendered less susceptible by insertion of genes for toxic bacterial protein. Several companies including Monsanto, Rohm and Haas, and Advanced Genetic Sciences Inc. of Oakland, California are experimentally producing such transformed plants.

It has long been known that some soils are more beneficial to crops than other soils. This is related, in part, to the physical chemistry of the soil. However, a significant portion of it has been found to be related to microbial populations. There has been a significant effort to select or develop and encourage specific

organisms which can enhance productivity. For example, Biotechnica International in Cambridge, Massachusetts, is testing genetically altered Rhizobium, a symbiotic nitrogen fixing bacterium, for inoculation into legumes which are the natural hosts of these bacteria.

It is also known that certain bacteria and fungi tend to antagonize one another; that there is a balance of these organisms in the soil. Recently there has been an effort in development of bacterial fungicides and in the selection and genetic engineering of bacteria which can be introduced into the soil or onto plants to antagonize certain phytopathogenic fungi. Ecogen, Inc. is producing a preparation of Pseudomonas (trade name, Daggar G) aimed at control of disease-causing soil fungi.

A special case which has been very much in the news recently because of the opposition of environmental groups is the recent experiments with Frostban by Advanced Genetic Sciences Inc. This preparation consists of a culture of Pseudomonas syringae which has been altered by recombinant DNA techniques to remove the gene responsible for the ice nucleation compounds found in plant leaf bacteria. These bacteria, when inoculated onto plants, are able to crowd out the populations of unmodified (ice nucleating) bacteria and thus impart freezing resistance to the plant leaves.

Crop/Plant Improvement

Efforts in selection or breeding for improvement of crop plants have been ongoing for thousands of years. Molecular genetic technology approaches have been built on an already large experience and genetic base. Despite their relative newness, they have already, in many cases, produced quite spectacular results even when compared to the very substantial improvements obtained by more conventional methods.

Pest resistance has naturally been one objective that has been pursued with considerable vigor. A number of efforts are being considered in which molecular genetic techniques are being used to insert genes into plants; it is hoped that these genes will stimulate the production of various compounds which will result in increased resistance to pests. In addition to insertion of the gene for B. thuringiensis toxin, efforts are underway to insert other genes enhancing plant resistance, such as a gene for toxin tolerance. For example, the US Department of Agriculture, ARS, in Beltsville, Maryland, is using protoplast fusion techniques to introduce the genes for Leptine, an insect repellent compound found in a specific wild potato, into domestic potato plants in order to provide resistance to the Colorado potato beetle.

Herbicides are used in production of all of the major crops. No herbicide is specific for weeds alone, and a significant cultural cost in modern crop production is associated with the efforts to avoid herbicide contact with the crop plants as well as with losses due directly to inadvertent herb contact with the crop. A recent approach which has been the subject of heavy investment by various chemical

companies and that is gaining wide attention, is the development of crop plants which are resistant to the commonly used herbicides. The most prominent of these are the experiments in insertion of genes for resistance to RoundUp (a widely used and extremely efficient nonselective herbicide) being pursued by **Monsanto**. Experiments along the same lines are being conducted by E. I. **Dupont** for resistance to sulfonyl urea herbicide.

The improvement of quality or the alteration of particular crop plant products is of considerable interest, and there have been major efforts over the years aimed at improvement by conventional methods. Currently, a number of efforts use molecular genetic techniques to improve various use qualities of the major food crops. For example, **Biotechnica International** is producing alfalfa strains with increased protein content. **The American Soybean Association** has begun to manipulate the oil composition of soybeans. **Calgene Inc.**, of Davis, California, has developed the marker genes and techniques for genetically transforming canola, or oil seed rape, for modification of oil composition. **Sungene Technologies Corp.**, of Palo Alto, California, has achieved similar capabilities for producing high oleic acid sunflower oil for the food frying industry. The efforts in product improvement are as diverse as the products. For example, **DNA Plant Technology** of Cinnaminson, New Jersey, has developed a new variety of high-solids tomato to be used specifically in tomato paste production.

Conventional methods of crop production have served well in the long search for increased crop productivity. Classical plant selection and breeding and the improvement of cultivation techniques, the use of herbicides, growth regulators, and fertilizer application, and the precise manipulation of water and other stresses have resulted in very large increases in productivity. There is, however, considerable interest in utilization of the new technologies for improving productivity. This takes the form of improvements in resistance to environmental stresses as well as improvements in the general reactions which govern productivity. For example, E. I. **Dupont** is experimenting with insertion of genes for higher rates of photosynthesis with the assumption that productivity is gained at a single point. However, there is a major problem here in that productivity, as such, is not subject to simple genetic manipulation in the way that resistance to herbicides and pests or the increases of quality or quantity of specific products are improved. All of the processes of productivity are governed by many genetic factors interacting in extremely complex ways. Thus, we are faced with the problem of knowing much more about how to change the plant than we understand about what precisely needs to be changed. There is a clear need for a systems approach to the improvement of productivity in plants.

A somewhat different aspect of the plant improvement technology is in the use of biotechnology as the tool for effecting the various transformations desired. Plant tissue culture and cell culture which derive from the techniques of microbiology are the primary tools. They are used, not only for the genetic transfer, but in the

propagation and proliferation of the genetically altered materials. It is worth noting that the protocol for each plant species or strain is usually different, and each, at the moment, must be worked out through trial and error. While reports of somewhat spectacular successes are constantly appearing, the relative number of plants that can be transformed is quite small compared to the number needed. Individual successes should not be taken as indications that large problems are solved.

The task of merely introducing new DNA into a plant cell still has no very satisfactory solution. The fact that a plant has a rigid cell wall has greatly restricted the insertion of genetic material. The evolving solutions that have been brought to bear on this problem include preparation of plant protoplasts and development of methods aimed at inducing plant protoplasts to fuse. More positive but laborious techniques involve the direct injection of foreign DNA containing the desired genetic material into the plant cells or protoplasts. The latest approaches include the use of lasers to open holes in the plant cells in the presence of concentrated DNA solutions and the use of explosive charges to blast particles containing the DNA into and through the plant cells.

The effectiveness of any of these techniques in producing a useful plant then relies upon the capability for regenerating whole plants from the single cells (somatic embryogensis) and upon subsequent testing of these regenerated plants for the presence of the desired traits. All of this must be laboriously accomplished for each plant species or strain at a time. Multiplication of such transformed plants to commercially useful numbers will then rely either upon the production of seeds or resorting to cell or tissue culture techniques again to propagate the improved genetic material with concomitant mass expenditures of energy and labor. Here is a specific major need for technological improvements in automation in every stage, ranging from genetic transformation through the multiplication and preparation of propagation material for field use.

Plant Products and Chemicals

For thousands of years, useful chemical products have been extracted from plants collected from the wild or grown in conventional agricultural systems. These "secondary products" of plants are still of great economic importance. Roughly 70% of the drugs, pharmaceuticals, flavorings, and perfumes are either extracted directly from plants or processed from plant products. More are synthesized from models provided by plant chemicals. There are still a great many potentially useful plant chemicals to be discovered, and there has been recent growing interest in initiating new concerted searches for such chemicals.

In spite of our dependence upon natural plant products, many of these so-called secondary plant products are in very short supply, and an enormous effort has to be expended to get them. In some cases plants are not available because they come from endangered native habitats in developing countries. In other cases, cartels control their production and import. In other cases, very large quantities of

plant materials must be processed to obtain tiny quantities. There is thus a growing need for development of sources of such chemicals, sources which are more reliable and which are not subject to limits on production or on quality. In effect, the need is for transition from agricultural and wild gathering methodologies to a biotechnology for optimized, stable manufacture of products which are, in some cases, of strategic importance. There is a major need for the development of this technology in terms of biochemical and automated techniques. This first requires screening for novel plant chemicals and subsequent production of plant materials in bulk amount in cell culture systems.

Concluding Remarks

This discussion has related primarily to the genetic technology of plant systems and the manipulation in various ways for the improvement of the plant and its products or of the production system. The discussion has been simplified for the sake of brevity. The reader should not be led by this to believe that the technology is simple. There are some cautions that should be given special note. First, it is generally considered by plant scientists that the plant is genetically over-built compared to animal systems and is likely to be a much more difficult system to manipulate. A number of very interesting successes have been seen. Compared to the needs and the possible range of manipulations, however, these may be considered relatively superficial. Moreover, none of the advances of the genetic technologies noted have yet reached full commercial realization for a number of technical reasons related to the complexities mentioned above.

One hears the occasional comment by non-biological managers having minimal or no biological training, that it appears that plant biologists in general cannot give them many new ideas about what may be done with plant systems. The plain fact of the matter is that the new ideas are not easy to come by and wouldn't be recognized unless they were potentially extremely valuable; any plant scientist who had such a good idea would naturally be quite reticent about discussing such things with anyone.

It should be noted, with emphasis, that one of the major limitations on bringing a great deal of plant biotechnology to the market place is the lack of availability of conventional engineering technology rather than of genetic engineering technology. Most of the manipulations required in producing genetic materials and in processing these plant materials for use in the field are extremely labor intensive. There is a major need for automation and for development of mechanical technology for carrying such material through the various stages and particularly into the mass production end of the process. This problem has received very little attention, even in a cursory manner.

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C. Human Biotechnology

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Introduction

Human biotechnology is entering several new arenas. We can now determine the presence or absence of disease states, in some instances, for which we do not have an understanding of the molecular basis of the disease, instrumentation has allowed improved monitoring of body functions, and biochemical synthesis allows the development of targeted drugs.

Current Status

Recombinant DNA--The overwhelming factor in current medical advances is recombinant DNA methodology. Nowhere is this more clearly manifest than in the field of human genetics. Cloning, restriction endonuclease mapping, and sequencing of human genes allows the diagnosis in some instances of diseases which have remained a riddle at the biochemical level. One example is the Lesch-Nyhan disease. This disease is the result of an abnormal purine metabolism and produces severe mental retardation, failure to thrive, and self-mutilation. We have an understanding of the biochemical basis for Lesch-Nyhan disease, but recent accomplishments including cloning the gene for this x-linked disease affords the opportunity for pre-natal diagnosis. Duschenne Muscular Dystrophy represents a recent triumph of "reverse genetics." By the isolation and identification of the gene for this x-linked muscular dystrophy which is invariably fatal by the end of the third decade, the protein product, dystrophin, involved in the disease process has just been isolated.[1] Thus recombinant DNA technology has allowed for the identification of individuals who are affected and has led to new understanding at the biochemical level. While the two diseases mentioned are x-linked, cystic fibrosis is an autosomal recessive disease, the most common in Caucasian populations. The gene itself has not been isolated and characterized, but very close markers have been isolated allowing prenatal diagnosis and identification of affected individuals when adequate family studies are available. Huntington's disease, a severe central nervous system degenerative disorder with onset in the fourth decade or even later, is an autosomal dominant disease. We now have closely linked markers allowing identification of affected individuals for this disease.[2] Thus, although we lack an understanding of the molecular basis of the disease, we are able to make a prenatal diagnosis.

From the standpoint of therapy, gene replacement will be eagerly awaited. Presently this is beyond the grasp of medicine, but it is possible to establish gene transfer in animals creating "transgenic" animals.

Another area in which recombinant DNA technology promises forward leaps is that of tumor identification and staging. This is a science which extends back well over 100 years and which was formerly limited to surface markers or chromosomal markers in tumors. We are now beginning to discover the first of what will doubtless be many DNA markers which are important for prognosis and treatment in individual tumor types.

A third arena in which recombinant DNA technology serves modern medicine is the production of bio-active molecules. This list includes hormones, drugs, and cellular products. With the human population increase in the world, it has simply been impossible to meet demand with natural products. An excellent example of this is growth hormone which has been cloned and has been released to the market within the last year. The drive to produce the recombinant human growth hormone was accelerated because it was found that some of the natural product was contaminated with a slow virus which gave rise to neuro- degenerative disorders in individuals who had received the growth hormone treatment.[3] The recent unlimited availability of growth hormone will offer clinical relief to individuals who might not have qualified under the former strict guidelines. Additional categories of products which are being produced include the interleukins and interferon. These drugs are active in certain disease processes in improving the quality of life or survival.[5] Thus the productive capabilities of recombinant DNA technology offer totally new levels of attack on diseases.

Instrumentation--In the area of instrumentation, much has been accomplished in the last two decades in miniaturization and sensitivity. Examples of this are endoscopy procedures and the development of intrauterine fetoscopy. Although technically demanding, fetoscopy is now routinely available in several large U.S. medical centers. Coupled with other advances in instrumentation such as improved resolution by the non-invasive imaging technique of ultrasound in real time, the accurate positioning of the invasive procedures has allowed improved safety and comfort for the patient. At the same time, the development of modern external monitoring devices for blood pressure and heart rate have given medicine the opportunity to monitor patients with duration or specificity not available previously.

In the area of cytogenetics, development of semi-automated scanning for chromosome preparations has achieved a practical application. This means it is now possible to avoid such dependence on skilled labor.

Where is human biotechnology going?

Recombinant DNA technology will continue to be a major contributor to human biotechnology for the foreseeable future. This technology will require the continued co-development of computer systems to allow the storing and comparison of nucleic acid sequences in even more accessible and friendly formats.

Science is committed to sequencing the human genome. This is an effort which is somewhat comparable in scope to the moon shot effort of NASA. The estimates for the total sequencing have run in the 10 to 15-year range with a variety of estimates for total cost.[4] While this is an actively debated current topic, we can anticipate that it is reasonable for the time needed to be cut by a factor of 3 with the development of new DNA sequencing techniques and improvement of collating and storing of data in computers.

There will be continued improvement in instrumentation. The goals of instrumentation improvement will be miniaturization and non-invasiveness. Magnetic resonance imaging, which has just become available within the last two years, promises to displace the computerized tomography X-ray approach which has been developed and brought to such a usefulness over the last 10 year. Magnetic resonance imaging allows the clinician to obtain information regarding the functionality of body tissues as well as a static picture to be interpreted.

Drugs under development will give previously unimagined control against the formation of thrombosis and clotting; we will probably see the first active intervention in cardiovascular accidents (strokes); there will be third generation drugs for the control of lipid and cholesterol levels in the individual; there are on the horizon new cardio-active drugs, and chemotherapy for cancer will enter a new phase of usefulness within the next 3 to 4 years.

What are the technical roadblocks?

The technical roadblocks which can be identified readily at this stage include improved software for nucleic acid sequences, acquisition and retrieval, as well as comparison. Decreased invasiveness of instrumentation will remain a persistent goal. The avoidance of pain in testing and treatment will become a primary goal of medicine over the next decade.

Socio-political roadblocks will increase with regard to environmental considerations in using animals for testing and using isotopes in man. An area of development of medicine which will probably require increased attention over the next two decades will be the area of the human psyche. In particular, I anticipate that the management of stress in patients will be a very fruitful area as medicine becomes more and more mechanized. The patient consequently has a new type of stress during diagnosis and treatment. In addition, the application of the new technologies poses major problems for society: Should candidates for a job be drug-tested? Should candidates for a job have polymorphic DNA testing to indicate risk for diseases which are common in society such as diabetes, heart disease and stroke? Can an employer refuse to hire an individual on the basis of such results? Should the recombinant DNA technology be used to diagnose "silent" diseases in the individual with the incumbent psychological risk this implies?

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D. Animal Health/Veterinary Medicine

Saul Kit, Ph.D., Biochemical Virology, Baylor College of Medicine

Analysts have estimated that by 1995, 30% of the animal health market will consist of biotechnology-derived products and services, as compared with only 4.8% of the total agribusiness market ($2.3 billion out of $47.9 billion). Currently, over 100 biotechnology companies in the U.S.A. are engaged in research and development on animal health projects. This strong emphasis on animal health biotechnology is not surprising, considering that animals provide humans with food, clothing, recreation, sport, and power. Animals are also human companions. Hence, animal health is inextricably connected to human health. Animals must be healthy to assure our food supply and the other items listed. On the economic side, outbreaks of animal diseases may bankrupt farmers and ranchers. Animals and humans are subject to common diseases, that is, zoonoses such as rabies and influenza. Therefore, barriers to animal diseases also interrupt or terminate human epidemics. Finally, research into the natural diseases of animals provides important parallels and models for analogous studies on human diseases. Drug experiments which cannot be performed on humans may be carried out expeditiously on animals. The results of these studies can then be applied to human therapeutics.

Animal health biotechnology encompasses the diagnosis, treatment, and prevention of animal disease and the improvement of livestock productivity. In 1986, there were 120 test kits available for use by veterinarians and farmers for infectious disease diagnosis, for the determination of the sex of fetuses, and for facilitating fertility. Examples of the diagnostic kits are those for livestock diseases such as bovine brucellosis, bovine leukosis, and bovine diarrhea, and those for diseases of companion animals such as canine heartworm and feline leukemia. Most of the diagnostic kits employ monoclonal antibodies to detect the antigens of the disease-causing parasites, bacteria, and viruses. Monoclonal antibodies have also been used to measure fertility hormones in blood and milk, for example, in pregnancy testing in mares. In addition, Y-chromosome DNA probing is being used in combination with embryo cloning to provide cattle of a pre-selected sex.

In 1983, Genecol 99, the first veterinary therapeutic, was introduced in Canada by **Molecular Genetics, Inc.** The product is a mouse monoclonal antibody for treatment of diarrhea (scours) caused by E. coli in calves. **American Cyanamid** is treating cows for bovine mastitis with a pathogen-specific protein cloned and expressed in Bacillus hosts. Interferons and interleukins are other therapeutic products of biotechnology utilized for animal health.

Prior to the development of recombinant DNA techniques, protein hormones such as bovine and porcine somatotrophins could only be obtained by purification from pituitary glands. They were therefore only available in small quantities and were very expensive. Now such compounds are available from recombinant organisms in quantities

sufficient to treat large animals commercially. For example, recombinant DNA-derived somatotrophins have been used to increase the growth of pigs, to increase the proportion of lean meat to fat, and to increase milk yield in dairy cows.

One of the most important future uses of biotechnology in animal health is that of the production of transgenic animals. The first model experiment along these lines was carried out by Ralph Brinster, who produced a transgenic mouse expressing the rat growth hormone gene. Since that time, transgenic rabbits, sheep, and pigs have been produced. Super salmon are being engineered in Japan by injecting cloned salmon growth hormone into the cytoplasm of uncleaved fertilized salmon eggs. Production of transgenic animals opens up the possibility of introducing extra copies of genes coding for desirable traits--for example, to improve muscle growth, milk, egg, and fiber production. Another possibility is the use of transgenic animals as expression systems for desirable proteins. Simons and co-workers in Edinburgh, Scotland, have generated transgenic mice carrying the sheep milk protein, beta lactoglobulin (BLG), and shown that, in such mice, BLG is specifically and abundantly made in the mammary gland during lactation. These findings suggest that the manipulation of milk composition by gene transfer has considerable potential for the improvement of dairy animals. One may also fantasize transgenic domestic sheep which produce vicuna or alpaca wool.

Among the most fruitful applications of biotechnology to animal health are the development of many novel genetically engineered vaccines. These include subunit vaccines, modified-live virus vaccines, and live subunit virus vaccines.

Subunit vaccines incorporate only a part of the pathogen and are therefore non-infective. This approach was used in a vaccine launched by **Intervet International** in April of 1982 to protect calves and pigs from enteric colibacilosis. Their vaccine, Nobi-vac LT K88, consisted of copies of genes for adhesion factors inserted into multicopy *E. coli* plasmid, thereby allowing for large-scale antigen production.

Modified-live virus vaccines consist of replicating viruses with genetically engineered deletions in virulence factors to enhance their safety. Unlike conventional live-virus vaccines, genetically engineered deletion mutants cannot revert to virulence. The first recombinant DNA-derived modified-live virus vaccine to be licensed for manufacture and sale was developed by Drs. Saul and Malon Kit of the Baylor College of Medicine and **NovaGene, Inc.** The U.S.D.A. licensed OMNIVAC in 1986 after extensive field tests demonstrated that OMNIVAC could be used safely in pregnant sows in all stages of gestation and in newborn piglets to prevent the deadly swine disease called Aujesky's disease (mad-itch; pseudorabies). In the OMNIVAC vaccine, a virulence gene which encodes the enzyme thymidine kinase was permanently deleted so that there was no danger of the vaccine accidentally causing central nervous system disease or abortion. More than a million doses of OMNIVAC have been used on U.S. farms over the last 2 years without any complaints from the users. Analogs of

modified-live virus vaccines for cattle and equine diseases have also been developed by Drs. Kit. In addition, second generation vaccines have been produced and licensed. OMNIMARK, for example, consists of OMNIVAC further modified by the detection of a gene which encodes a major virus surface protein, called GIII. Pigs infected with field strains of pseudorabies virus always develop antibodies to gIII.

However, pigs vaccinated with OMNIMARK, which lacks the gene for gIII, do not develop gIII antibodies and, hence, can be differentiated from field strain-infected animals by simple blood tests. This development has opened the possibility for eradicating pseudorabies disease and is also beneficial to the farmer in that pigs protected by vaccination can be shipped to other locations. Previously, shipment of vaccinated pigs was restricted because blood tests were not available to distinguish vaccinated from infected animals. Vaccinated animals gave a positive blood test for pseudorabies virus. Hence, the possibility could not be excluded that the vaccinated animal was already harboring a latent virulent virus which might endanger a herd.

One of the most important uses of modified-live virus vaccines is that of engineering live subunit vaccines. Live subunit vaccines utilize modified-live viruses as vectors to amplify and deliver subunit immunogens from heterologous microorganisms to the vaccinated animal. At the present time, the most popular live subunit vaccine utilizes Jenner's smallpox vaccine virus, Vaccinia, as a vector. Hybrid Vaccinia vaccine viruses expressing several different foreign proteins have been engineered and tested in the laboratory. However, none has yet been approved for manufacture and sale by the United States or foreign governments. The first recombinant Vaccinia vaccine to undergo open field testing contains the antigens that are required for protection against rabies. The first field trial of the Vaccinia-rabies hybrid virus is being managed by the Belgium Fund for Research Against Rabies in a joint program with the Wistar Institute of Philadelphia, PA; Transgene, France's biotechnology research and development firm; and Institute Rhone-Merieux of Lyon, France. In November of 1987, foxes inhabiting a wooded military reservation in southern Belgium were vaccinated orally by sowing their territory with succulent chicken heads containing capsules of the hybrid Vaccinia-rabies vaccinia. The military enclave was chosen for the field release test because the area was closed to civilians and domestic animals and was rich in wildlife, much of it rabid. The managers of the trial are tracking the fate of their vaccine-seeded chicken heads, which are marked by tetracycline fluorescent label, traceable in the bones of animals that take the bait. Preliminary results indicate that the foxes on this enclave did take the bait.

The Wistar Institute has also requested permission to test the hybrid Vaccinia-rabies vaccine in wildlife on uninhabited islands off the coasts of Virginia and the Carolinas.

Vaccinia virus is only one of the many viruses that are being used as vectors for live subunit vaccines. The strategy adapted by NovaGene, Inc. of Houston, Texas employs the U.S.D.A. approved OMNIVAC

pseudorabies virus as a vector so that swine would be immunized against Aujeszky's disease and, likewise, a second microbial disease. Similarly, infectious bovine rhinotracheitis virus is being used both to immunize against this important bovine disease and to serve as a vector for the immunogens of other bovine microbes.

Large scale protein purification and sequencing devices would greatly facilitate the production of sub-unit vaccines and of virus reagents for diagnosis. Yet, the most critical need for small biotechnology firms is adequate and sustained funding to benefit from the economies of scale.

The largest of the new biotechnology companies are capitalized at about 25-50 million dollars. However, most of the new biotechnology companies have been founded by entrepreneurs with minimal capitalization. Although these small companies are likely to develop the most innovative products and to be efficient and cost effective, they are often on shaky grounds economically. Therefore, the strategy adopted by many small companies is that of forming alliances with universities, research institutions, government laboratories (like NASA), and the grant multinational corporations. The highest priority must be given by small biotechnology companies to obtain funding to maintain an essential cadre of trained personnel for a 5- to 10-year period, at which time their cash flow may increase for essential capital equipment and facilities for long-term growth and expansion. Long-term low interest government loans, governmental partnerships with small companies, or seeding grants represent imaginative ways to enhance the chances of success of the small biotechnology companies and to increase local jobs.

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8. "Transgenic 'Super' Salmon Sought." Newswatch. September 21, 1987. Page 8.

VII. RECOMMENDATIONS FOR FOLLOW-UP

The survey shows that biotechnology companies recognize the value of research and development. As an industry, they are very much involved in the process and understand that there is potential value in space biotechnology research. On the whole, industry executives are not well informed about the microgravity environment and the results of previous space biotechnology studies. A need exists to provide basic information about the space environment and the past work in this field.

Some 83% indicated that space based research would be valuable to the biotechnology industry. Over 50% of the companies indicated that they would be willing to participate in space biotechnology. Roughly one third indicated that they would want to participate in workshops and cooperative research activities with NASA. These statistics indicate that there is interest in space biotechnology which could complement NASA's own space biotechnology and human performance needs in connection with a permanent presence in space.

The results of this industry profile, together with the key contacts established during the course of this study provide the basis to develop a U.S. Space Biotechnology Institute (SBI). Such a group could be patterned after the GEOSAT Working Group which was developed in the mid 1970's in the earth resources field.

The functions of the Space Biotechnology Institute could include the following:

1. Develop for NASA a plan for communication with and development of understanding of the U.S. biotechnology industry and the university based research programs.

2. Create and operate a NASA-Industry-University working/users group.

3. Conduct workshops and conferences for information exchange and develop educational materials for industry.

4. Develop new simplified mechanisms for NASA/Industry working agreements, contracts, MOU, JEA, etc.

5. Establish the requirements for the development of biotechnology research facilities which could be used in cooperative ground and space flight research and development.

6. Identify research opportunities, evaluate research proposals, and coordinate ongoing research efforts.

7. Support NASA in the integration of experiments and applications.

VIII. APPENDICES

APPENDIX A

INDUSTRY QUESTIONNAIRE

BACKGROUND INFORMATION FOR SPACE BIOTECHNOLOGY QUESTIONNAIRE

1. Definitions: BIOTECHNOLOGY for the purposes of this study covers the following areas:

   Bioprocessing
   Cell/Tissue Culture
   Enzymology
   Fermentation
   Hybridoma/Cell Fusion
   Large Scale Purification
   Process Monitoring Control
   Purification/Separation
   Recombinant DNA
   Sequencing
   Synthesis

2. Study Objectives:

   A. To determine industry's understanding and expectations about NASA's plans for conducting biotechnology and space biology research in the Space Station.

   B. To determine industry's perception about NASA activities to encourage and assist private enterprise in space.

   C. Determine what type of information would be useful to biotechnology corporations to assist them in becoming active participants in the commercial utilization of space.

   D. What is the biotechnology corporate understanding of space sciences and technology? What is their understanding of the space environment?

   E. What are the sensitivities of biotechnology companies about entering into collaborative relationships with NASA, universities, and other biotechnology companies?

   F. Are there company funds currently being committed to space related biotechnology research?

   G. What are the key trends and future events which might impact industry's decision to enter into space related research activities? What type of ground and flight research is needed to fulfill critical biotechnology needs to stimulate industrial participation in the space station program?

FACT SHEET - BACKGROUND INFORMATION

Space-related Biological Research

1. Manned space flights for over 25 years.
2. Biological payloads began in the 1960's.
3. Manned skylab experiments (1972-1974): Biological and biotechnology experiments, including studies on antigen-antibodies and cell culture growth.
4. Space shuttle and space lab studies (from 1981). Focus on bioprocessing, life sciences, and materials sciences.

Space Attributes

1. High vacuum (up to 10-14 torrs).
2. Infinite heat sink
3. Extreme temperature gradients.
4. Microgravity

   In orbit, the centrifugal force balances the gravitational force so that the mass of a satellite exists in a state of apparent zero gravity. The term microgravity has been coined to suggest the relatively small effect of gravity which can be obtained in orbit. It has been taught that a fundamental property of a liquid was that it would conform to the shape of the vessel which contained it. This is not true in microgravity because weak forces called surface tension and adhesion become dominant. Liquid may form a single large drop in the center or it may adhere in a thin layer over the container's inner surface or in one of many almost random combinations. Without external body forces the familiar role of convection (the rising of lighter fluids and their replacement by heavier ones) is absent. This has real implications in any process involving the need for a high, uniform temperature. The absence of convection and the ability to process materials at uniform temperature in a contaminant-free environment permits the formation of crystals, the size and purity of which are impossible to create on earth. These microgravity phenomena have important implications for the electronics and pharmaceutical industries. As such, the opportunity to experiment in space is valuable in the knowledge it might reveal. Once discovered, it may be possible to reproduce these substances on earth in production quantities.

Recent Space-based Biotechnology Research

1. Bioseperations, using electrophoresis, potential use in isolation of rare cells.
2. Protein crystallization, potential use in pharmaceuticals and electronics.
3. Cell physiology, potential in exploiting cell product synthesis.

Useful Readings

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Mr. Peter G. Ulrich, Biosciences Corporation of Texas
Dr. Saul Kit, Baylor College of Medicine
Mr. Al Scheid, President, Houston Biotechnology, Inc.

SPACE BIOTECHNOLOGY QUESTIONNAIRE

PART I

The NASA biotechnology program is being developed to provide U.S. corporations a window in the development of space biotechnology research and new technologies which can aid progressive companies. Additionally, these programs will help U.S. biotechnology corporations maintain their competitive positions with Japanese and European firms which are aggressively developing space biotechnology. Opportunities exist for U.S. corporations to participate in NASA funding.

1. **WHO ARE YOU?**

   Name: _____

   Title: _____

   Firm: _____

   Address: _____

   _____

   Telephone Number: (____) _____

2. **ARE YOU FAMILIAR WITH NASA's SPACE PROGRAMS?**

	Knowledgeable	Some Knowledge	Not Familiar
a) Space Shuttle	[ ]	[ ]	[ ]
b) Space Station	[ ]	[ ]	[ ]
c) Space Biology and Biotechnology	[ ]	[ ]	[ ]
d) Commercial Programs	[ ]	[ ]	[ ]

   I would like more information on the above: a[ ] b[ ] c[ ] d[ ]

3. **ARE YOU FAMILIAR WITH THE SPACE ENVIRONMENT?**

	Knowledgeable	Some Knowledge	Not Familiar
a) Low gravity (microgravity)	[ ]	[ ]	[ ]
b) Low pressure (vacuum)	[ ]	[ ]	[ ]
c) Space Radiation	[ ]	[ ]	[ ]

   I would like more information on the above: a[ ] b[ ] c[ ]

4. **DO YOU PERCEIVE VALUE IN SPACE RESEARCH FOR THE BIOTECHNOLOGY INDUSTRY?**

	Yes	No
a) Research in space for space-based processes	[ ]	[ ]
b) Research in space to understand earth processes	[ ]	[ ]
c) Commercial biotechnology use of space	[ ]	[ ]
d) Overall Space Biotechnology	[ ]	[ ]

5. **WOULD YOU LIKE TO PARTICIPATE IN SPACE BIOTECHNOLOGY?** Yes [ ] No [ ]

   If yes, indicate possible interests below:

   a) Workshops (space environment, space biotech opportunities, etc. [ ]
   b) User group for Space Biotechnology [ ]
   c) Cooperative Research Programs with NASA [ ]
   d) Cooperative Research Programs with Universities [ ]
   e) Other _____ [ ]

6. **IF YOU FEEL THAT YOUR FIRM WOULD BE INTERESTED IN SPACE BIOTECHNOLOGY, PLEASE FILL IN THE REMAINDER OF THIS QUESTIONNAIRE. OTHERWISE, PLEASE FOLD AND PLACE IN ENVELOPE PROVIDED AND MAIL TODAY. THANKS FOR YOUR PARTICIPATION.**

PART II

In this section we would like to understand your sensitivities to participation in Space Biotechnology and to get your ideas on directions NASA might take. The information acquired will be kept confidential and will not be attributable to your organization.

7. VP/Director of Research: _____

8. VP/Director Corporate Development: _____

9. Major Corporate Technologies: _____

_____

_____

_____

10. Major Products: _____

_____

_____

_____

11. Is your company a part of any existing Joint Ventures and/or Consortiums?
Yes [ ] No [ ]
List: _____

_____

_____

_____

_____

_____

12. Company Resources:
Number of Research Staff Members: _____
Research Budget: Over $100 Million [ ]
$10 to 100 Million [ ]
Under $10 Million [ ]
% Space Related Biotech _____

13. Company understanding of U.S. Corporate Programs in Space Commercialization:

	Aware	Not Aware
McDonnell Douglas-Electrophoresis	[ ]	[ ]
3M Corporation-Protein Crystal Studies	[ ]	[ ]
Space Industries-Industrial Space Facility	[ ]	[ ]

14. Do you envision that the Space Station Program will provide support to the Biotechnology field? Yes [ ] No [ ]
How? _____

_____

_____

_____

15. Technology Information: What are the most difficult technologies facing the biotechnology industry? (For example: separation of product, scale up of production, etc.) List in order of importance.

16. What type of information or scientific data would you suggest is needed from NASA by Biotechnology industries to encourage participation in space research activities?

17. What are the key trends and future events which may impact the biotechnology industry's decision to enter into space related activities?

Industry:

Government:

Competition (International):

Other:

18. Could you suggest research areas that NASA should pursue which would be of benefit to the U.S. Biotechnology Industry?

19. Would you consider the formation of a joint venture to pursue Biotech research in space?
    Yes [ ] No [ ]
20. Do you have any other suggestions on how to broaden the US industries participation and interest in trying to exploit the uses of the space environment by the Biotech community?
    Yes [ ] No [ ]
    COMMENTS _____

21. Would you be willing to attend a Spring 1988 Workshop in Houston to review the findings of this questionnaire and to review Space Biotechnology?
    Yes [ ] No [ ]

22. Finally, any other suggestions or comments you might have? _____

APPENDIX B

BIOTECHNOLOGY BIBLIOGRAPHY

Current Assessment of Biotechnology

A Bibliography

The last major public study on biotechnology was the 1984 OTA study listed below. Since that study reviewed the status of biotechnology to that point, most of the references here are to studies between 1984 and 1988.

General

Commercial Biotechnology: An International Analysis.
January 1984 SuDoc #Y3.T22/2:C73/7 612 pg.
RESEARCH ORGANIZATION: Office of Technology Assessment
PUBLISHER: U.S. Government Printing Office North Capital and H St., NW
Washington DC 20402
United States of America
TELEPHONE: (202)275-2051

Assesses competitive position of U.S. with respect to Japan, United Kingdom, Switzerland, France, and Federal Republic of Germany in commercial development of new biotechnology. Discusses uses in pharmaceuticals, agriculture, chemistry, energy production, and bioelectronics. Identifies U.S. biotechnology companies; and U.S. and foreign companies involved in joint ventures. Shows distribution of foreign and domestic sales of top 20 U.S. and foreign pharmaceutical companies, 1981; number of new products by country of origin, 1961-1980, 1981, 1982, 1983; and pharmaceutical research and development expenditures by country, 1964, 1973, 1978.

Biotechnology : status and perspectives
Daniel I.C. Wang
Wang, Daniel I-chyau, 1936-
Corporate Source: American Institute of Chemical Engineers.; Meeting (1986 : Miami Beach, Fla.)
New York : American Institute of Chemical Engineers, 1988.
Publication Date(s): 1988
ISBN: 0816904375
LC Call No.: TP248.2.W36 1988 Dewey Call No.: 660/.6

EVALUATING THE MAINTENANCE AND EFFECTS OF GENETICALLY ENGINEERED MICROORGANISMS.
SAYLER G S; HARRIS C; PETTIGREW C; PACIA D; BREEN A; SIROTKIN K M
DEP. MICROBIOLOGY AND GRADUATE PROGRAM IN ECOLOGY, UNIV. TENNESSEE, KNOXVILLE, TENN. 37996.
DEVELOPMENTS IN INDUSTRIAL MICROBIOLOGY, P.135-150, 1987.
Pierce, G. (Ed.). Developments in Industrial Microbiology, Vol. 27; Symposia of the Forty-second General Meeting of the Society for Industrial Microbiology, Boston, Massachusetts, USA, Aug. 4-9, 1985.

Space Business Research Center

x+183p.+++Elsevier Science Publishers: Amsterdam, Netherlands (dist. in the USA and Canada by Elsevier Science Publishing Co. Inc.: New York, New York, USA). Illus. ISBN 0-444-80870-1
Language: ENGLISH

A CRITICAL EVALUATION OF MICROBIAL PRODUCT FORMATION IN BIOLOGICAL PROCESSES.

RITTMANN B E; BAE W; NAMKUNG E; LU C-J
DEP. CIVIL ENGINEERING, UNIV. ILL. URBANA-CHAMPAIGN, URBANA, ILL. 61801,U.S.A.
WATER SCIENCE AND TECHNOLOGY, VOL.19, NO.3-4, P.517-528, 1987.
Thirteenth Biennial Conference of the International Association on Water Pollution Research and Control, Part 2, Rio de Janeiro, Brazil, August 17-22, 1986. WATER SCI TECHNOL
Language: ENGLISH

PB87-141362/XAB

Competition and the Role of Technology: An Assessment of the Biotechnology/Agribusiness Industry

Sakura, D. ; Wheat, D. ; Berkley, P. ; Reardon, M. ; Bondaryk, R. Industrial Research Inst., Inc., New York.
Corp. Source Codes: 044789000
Sponsor: Little (Arthur D.), Inc., Cambridge, MA.; Economic Development Administration, Washington, DC.
Apr 85 163p
See also PB87-141396. Prepared in cooperation with Little (Arthur D.), Inc., Cambridge, MA. Sponsored by Economic Development Administration, Washington, DC.
Languages: English
NTIS Prices: PC A08 Journal Announcement: GRAI8706
Country of Publication: United States
Contract No.: EDA-RED-803-G-83-5; EDA-99-7-13611
The objective of the study was to identify technology development areas in the agribusiness industry which would maintain or increase the international competitive position of the United States. Biotechnology was emphasized since this new developing technology offered the greatest potential for technical areas benefiting from accelerated development. The study covers animal health products and nutritional ingredients, animal and plant breeding including the seed industry, and agricultural chemicals including fertilizers and pesticides. The study concluded that the United States is the technical leader with few exceptions, though European and Japanese researchers are rapidly developing increased capability in this important field. Progress is currently limited by the lack of basic scientific information; yet the major effort world-wide on biotechnology makes it certain scientific breakthroughs will occur within the next decade that will greatly change the agribusiness industry.

PB86-247095/XAB
Biotechnology: Analysis of Federally Funded Research
General Accounting Office, Washington, DC. Resources Community and Economic Development Div.
Corp. Source Codes: 010682026
Report No.: GAO/RCED-86-187; B-223522
Aug 86 41p Languages: English
NTIS Prices: PC A03/MF A01 Journal Announcement: GRAI8626
Country of Publication: United States
In August 1984 and again in April 1985, 11 federal agencies were surveyed about the nature of all biotechnology-related research they support. The report contains biotechnology research activity profiles for five of the agencies: the Department of Agriculture (USDA), the Environmental Protection Agency (EPA), the Food and Drug Administration (FDA), the National Institutes of Health (NIH), and the National Science Foundation (NSF). Each profile includes estimates of the fiscal year 1985 level of support, in terms of dollars obligated and number of projects funded, for agencywide activity for the conduct of research and development, biotechnology-related research, and biotechnology risk assessment research. The data for these estimates were compiled by contacting officials in agency budget offices and agency program offices, and from written responses surveys.

97-26356-5 2
New Developments in Biotechnology: Background Papers (Biotechology legal, ethical, and economic issues, series)
Office of Technology Assessment
GPO; for individual bibliographic data, see below
ITEM NO: 1070-M
Y3.T22/2:2B52/4/v.(nos.)
DOC TYPE: SERIES PUBLICATION
JOURNAL ANNOUNCEMENT: 8711
Series of reports on legal, ethical, and economic issues surrounding new developments in biotechnology.
Reports are described below in order of receipt.

85-2046-11.5
Biotechnology (Biotechnology industry (US) intl competitiveness, with selected operating data and listing of collaborative agreements, 1970s-83 and projected to 2000)
<July 1984. 217 p. C61.2:T22/6. LC 84-603710. MC 85-4201. S/N 003-009-00430-6. $7.00. ASI/MF/5>
Includes 19 tables showing:
a. Projections: world demand for biotechnology products by category; and projected sales of laboratory equipment by type; with some actual data.
b. Collaborative agreements: lists showing terms of research, marketing, and other agreements between individual Japanese and non-Japanese firms, small and large U.S. firms, U.S. firms and universities, and U.S. and

foreign firms.
c. R&D and patents: NIH and NSF R&D funding , by research area; and patents, by date granted, country, and owner (U.S. and foreign corporations, governments, and individuals).
d. Industry operations: share of shipments from top 4 and top 8 firms, by product; and foreign investment in U.S. firms, by investor and recipient.
Data are for 1970s-83, with projections to 2000.

86-26113-200
Biotechnology: The U.S. Department of Agriculture's Biotechnology Research Efforts (Biotechnology R&D projects of USDA, funding by State, environmental releases, and risk assessment, 1985 GAO rpt)
General Accounting Office
Oct. 1985 80 p. +
FICHE: 3 ITEM NO: 546-D
GA1.13:RCED-86-39BR REPORT NO: GAO/RCED-86-39 BR
DOC TYPE: SPECIAL SERIES
JOURNAL ANNOUNCEMENT: 8603
Report on biotechnology R&D projects conducted or sponsored by the USDA Agricultural Research Service (ARS), Office of Grants and Program Systems (OGPS), and Cooperative State Research Service (CSRS), FY84-85.
Data are from ARS research compendium; OGPS records; and a survey of State agricultural experiment stations and veterinary medicine colleges, funded by CSRS in FY84 and conducted by GAO and the National Assn of State Universities and Land Grant Colleges.
Survey covered biotechnology research projects, staff, expenditures by funding source (USDA, other Federal and State agencies, and industry), and funding needs; use of genetic engineering methods; expected environmental releases of genetically engineered organisms, and potential release problems and response efforts; and research risk assessment activities.
Includes text statistics and 8 tables showing number of USDA-funded biotechnology research projects, and USDA biotechnology and total agricultural research funding, by USDA funding agency; ARS planned biotechnology research expenditures, by research topic and region; and summary survey results; often by State.
Also includes facsimile survey form with tabulated responses; and lists of State agricultural experiment stations and veterinary colleges, with descriptions of biotechnology research accomplishments and projects expected to result in release of genetically engineered organisms, all arranged by State.

Special: Biotechnik.
Special Report on Biotechnology.
Wirtschaftswoche
June 21, 1985 no.26 pg.82-94
PUBLISHER: Gesellschaft fur Wirtschaftspublizistik G W P mbH and Company KG
Kasernenstrasse 67 P.O.B. 3734 Dusseldorf D-4000
West Germany
TELEPHONE: (01149521)559-0;TELEPHONE: (01149211)8388-0 TELEX: 932934 dehla

Space Business Research Center

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Consists of various articles dealing with markets for biotechnology products in the USA, Japan, and the FRG and profits and profits expectations of industries engaged in research on biotechnology and production or use of biotechnology products. Special reference is given to competition on national and international markets and competition for the introduction of new products and the exploitation of new research results in the field of biotechnology for food processing, bioelectronics, agriculture, energy, and chemical and pharmaceutical industries. Articles are supported by tables showing forecasts of dates for the industrial use of biotechnology research results in the USA (1985-2015) in different industries, government funding for research on biotechnology in the FRG (1974-85), estimates of the size of the world market for biotechnology products (1980-2000) by industry.

BIOTECHNOLOGY INDUSTRY
FEB 1987 26 P. $250 ONE-TIME
Publ: Research From Wall St, New York, NY 212-645-4500
Availability: PUBLISHER
Report No.: Q787
Document Type: MARKET/INDUSTRY STUDY
The two-part report focuses on new drug developments and industrywide competition. Part One offers highlights of the November 1986 annual American Heart Association meeting: potential use of Genentech's t-PA for unstable angina; Centocor's cardiac imaging products and antiplatelet monoclonal antibody; SOD use; and Eli-Lilly's t-PA product. Part Two profiles Amgen, Genentech, Centocor and Applied biosystems. Tables contrast industrywide therapeutic and animal health care/supply and diagnostic products and competition.

STATUS OF BIOTECHNOLOGY
JUL 1987 270 P. $995 ONE-TIME
Publ: Market Intelligence Research Co, Mountain View, CA 415-961-9000
Availability: PUBLISHER
Report No.: A231
Document Type: MARKET/INDUSTRY STUDY
Biotechnology in this report has been defined to include primarily the use of recombinant DNA, monoclonal antibodies, and advanced somatic cell techniques in the production of new pharmaceuticals, diagnostics, and agricultural products. Features of the study include a discussion of how the application of the new biotechnologies has affected the investment community, an overview of the science behind the new biotechnologies, major near-term applications, and a discussion of the theoretical potential for growth and development of the markets for each of the applications discussed.

88-9626-6.20
Biotechnology Research and Development Activities in Industry: 1984 and 1985 (Biotechnology R&D funding by industry by funding source, and employment, by field, 1984-85)
<May 1987. v+27 p. NSF 87-311.. NS1.22:B52/984-85. ITEM 834-T. ASI/MF/3>
Report on industrial biotechnology R&D spending and S/E employment, 1984-Jan. 1986. Based on a survey of 94 firms, representing approximately 56% of biotechnology R&D spending in 1985.
Includes 1 chart and 10 tables showing industrial biotechnology R&D spending, by source of funds and major application and technique, 1984-85; and S/E employment, by field and major technique, as of Jan. 1985-86.

Cell/tissue culture

87-26356-5.1
Ownership of Human Tissues and Cells Ownership of Human Tissues and Cells. New Developments in Biotechnology New Developments in Biotechnology: Ownership of Human Tissues and Cells (Biotechnology products sales and profits, by selected firm, 1985)
<Mar. 1987. vii+167 p. OTA-BA-337.. CIS Index (87) J952-14. Y3.T22/2:2B52/4/v.1. LC 87-619804. MC 87-10434. S/N 052-003-01060-7. 7.50. ASI/MF/4>
Report on economic, legal, and ethical rights of human sources of tissues and cells, and rights of physicians or researchers who obtain and develop these biological materials. Focuses on technologies related to tissue and cell cultures, hybrid cell lines, and recombinant DNA.
Includes 3 charts and 10 tables showing sales and profits of selected biotechnology companies, 1985.

Enzymology

ENZYME TECHNOLOGY FOR THE LIPIDS INDUSTRY: AN ENGINEERING OVERVIEW.
YAMANE T
LAB. BIOREACTION ENG., DEP. FOOD SCI. TECHNOL., SCH. AGRIC., NAGOYA UNIV., NAGOYA 464, JPN.
JOURNAL OF THE AMERICAN OIL CHEMISTS' SOCIETY, VOL.64, NO.12, P.1657-1662, 1987.
Language: ENGLISH

Fermentation

BIOENGINEERING ANALYSIS AND EVALUATION OF A CONTINUOUS FERMENTATION PROCESS.
RYCHTERA M; BURIANEC Z; NEDBAL F
INST. CHEMICAL TECHNOLOGY, PRAGUE.
FOLIA MICROBIOLOGICA, VOL.29, NO.5, P.397, 1984.
16th Annual Congress of the Czechoslovak Society for Microbiology, Banska Bystrica, Czechoslovakia, Oct. 21-23, 1983. FOLIA MICROBIOL
Language: ENGLISH

A SURVEY OF SEPARATION SYSTEMS FOR FERMENTATION ETHANOL RECOVERY. SERRA A; POCH M; SOLA C
UNITAT D'ENGINYERIA QUIMICA, DEP. DE QUIMICA, UNIV. AUTONOMA DE BARCELONA, BELLATERRA, SPAIN.
PROCESS BIOCHEMISTRY, VOL.22, NO.5, P.154-158, 1987.
Language: ENGLISH

Hybridoma/cell fusion

CELL CULTURE BIOTECHNOLOGY: EQUIPMENT REAGENTS AND CONSUMABLES
JAN 1986 300 P. $2250 ONE-TIME
Publ: Frost & Sullivan Inc, New York, NY 212-233-1080
Availability: PUBLISHER
Report No.: E771
Document Type: MARKET/INDUSTRY STUDY
1983+4 base years, 1985-90 forecasts: CO2 incubators, ultra-low temperature freezers, biohazard and laminar flow cabinets, cell analyzers (2 types), mass cell culture systems (6 products), consumables (3 groups, 7 components), and reagents (3 groups, 5 products) 1984-90 in each of 6 major EEC countries and rest of Europe. Market size and shares by product, by country, by manufacturer. New opportunities in this venture capital dominated development.

Large-scale purification

Partition of cell particles and macromolecules : separation and purification of biomolecules, cell organelles, membranes, and cells in aqueous polymer two-phase systems and their use in biochemical analysis and biotechnology
Albertsson, Per Ake.
3rd ed. New York : Wiley, c1986. 346 p. : ill. ; 24 cm.
Publication Date(s): 1986
ISBN: 0471828203 :
LC Call No.: QH324.9.S4A423 1986 Dewey Call No.: 574.1/92/028

Biotechnology: Separations Technology - The Production Hurdle.
November 1984 no.F528 22 pg. PRICE: $300.00
PUBLISHER: FIND / SVP, Research from Wall Street 500 Fifth Ave. New York NY 10110
United States of America
TELEPHONE: (800)223-2054;TELEPHONE: (212)354-2424
ATT: Van Velsor, Patty

Reports on the U.S. biotechnology market for separations technology equipment and disposables, 1984-1987. Examines new products, end uses, and manufacturers.

SEPARATION AND PURIFICATION EQUIPMENT MARKET IN U.S. BIOTECHNOLOGY APPLICATIONS
SEP 1986 241 P. $1900 ONE-TIME
Publ: Frost & Sullivan Inc, New York, NY 212-233-1080
Availability: PUBLISHER
Report No.: A1661
Document Type: MARKET/INDUSTRY STUDY
Covers forecasts through 1990 by five major market segments (pharmaceuticals, veterinary drugs, specialty chemicals, agricultural chemicals, foods and beverages) for filtration: ultrafitration (hollow fiber, plate and frame, spiral wound), microfiltration, reverse osmosis, traditional (filter press, rotary drum); chromatography: HPLC, ion exchange, gel filtration, affinity; centrifuges; disc, laboratory, solid bowl, tubular; electrophoresis; electrodialysis; cell disruption: homogenizers, bead mills. Provides 39 company profiles.

Process monitoring control

Mass spectrometry in biotechnological process analysis and control
edited by Elmar Heinzle and Matthias Reuss
Heinzle, Elmar.; Reuss, Matthias.
Corporate Source: Institut fur Umweltforschung.; International Federation of Automatic Control.; International Federation of Automatic Control.; Technical Committee on Applications.
New York : Plenum Press, c1987. xi, 241 p. : ill. ; 26 cm.
Publication Date(s): 1987
ISBN: 030642777X
LC Call No.: TP248.25.M38M37 1987 NLM Call No.: QC 454.M3 M41435 1986
Dewey Call No.: 660/.6

PROCESS INFORMATION AND CONTROL SYSTEMS: A TECHNOLOGY OVERVIEW.
FADUM O
FADUM ENTERPRISES INC., P.O. BOX 368, NORWOOD, MASS. 02062.
TAPPI (TECHNICAL ASSOCIATION OF THE PULP AND PAPER INDUSTRY) JOURNAL, VOL.70, NO.3, P.62-66, 1987. Language: ENGLISH

Environmental Assessment and Overview of Biotechnology Process Applications
(Final rept. Sep 83-Jun 84)
Stein, N. P. ; Hayes, B. J. ; Gates, N. S. ; Page, G. C.
Radian Corp., Austin, TX.
Corp. Source Codes: 029117000
Sponsor: Industrial Environmental Research Lab., Research Triangle Park, NC.
Report No.: EPA-600/7-84-081
Aug 84 125p
Languages: English
NTIS Prices: PC A06/MF A01 Journal Announcement: GRAI8421
Country of Publication: United States
Contract No.: EPA-68-02-3171
The report is an overview of industrial biotechnology processes, waste streams associated with these processes, and the effectiveness of current control technologies in treating process waste streams. (Biotechnology is defined here as processes that employ microbial cultures or enzymes to produce a product or effect a specific physical or chemical change.) Commercial applications are divided into contained product manufacturing processes (industrial fermentation) and uncontained/semicontained processes (metal extraction, energy production, and pollution control). Agricultural applications of biotechnology, the use of higher order organisms, and biological treatment of wastewaters are not considered in detail in this report. Acceptable levels of control for viable microorganisms are currently not well defined. Data on the effectiveness of technologies for control of viable microorganisms and certain chemical constituents of bioprocess wastes were found to be very limited.

Biotechnology Instrumentation in 1985
October 1985 150 pg. PRICE: $795.00
PUBLISHER: Theta Technology Corporation 462 Ridge Rd. Wethersfield CT 06109 United States of America
TELEPHONE: (203)563-9400

Examines the following biotechnology instruments: DNA synthesizers, UV/VIS spectrophometers, gel electrophoresis, robotics, HPLC columns, HPLC detectors, HPLC systems, computer-aided biotechnology, protein synthesizers and fermenters. Provides data for current market shares, projected shares for the next five years, funding for research, trends in instrument design and usage, and profiles of 32 companies involved in biotechnology research, 1985.

Recombinant DNA

THE USE OF RECOMBINANT DNA TECHNOLOGY IN DNA REPAIR STUDIES IN ESCHERICHIA COLI: A REVIEW.
SEDGWICK S G
GENETICS DIVISION, NATIONAL INSTITUTE MEDICAL RESEARCH, MILL HILL, LONDON NW7 1AA.
HEREDITY, VOL.53, NO.3, P.574, 1984.
200th Meeting of the Genetical Society held jointly with the United Kingdom Environmental Mutagenesis Society, Liverpool, England, Apr. 2-4, 1984.
HEREDITY
Language: ENGLISH

Sequencing

TECHNOLOGY EVALUATION OF SEQUENCING BATCH REACTORS.
ARORA M L; BARTH E F; UMPHRES M B
JAMES M. MONTGOMERY CONSULTING ENGINEERS INC., 250 NORTH MADISON AVE., PASADENA, CALIF. 91109-7009.
JOURNAL WATER POLLUTION CONTROL FEDERATION, VOL.57, NO.8, P.867-875, 1985.
Language: ENGLISH

Unclassifed - Chemicals

BIOTECHNOLOGY IN THE MANUFACTURE OF SPECIALTY AND COMMODITY CHEMICALS: TECHNOLOGY AND OPPORTUNITIES IN WESTERN EUROPE
MAR 1987 348 P. $3500 ONE-TIME
Publ: Business Communications Co, Inc, Norwalk, CT 203-853-4266
Availability: PUBLISHER
Report No.: 2H-105
Document Type: MARKET/INDUSTRY STUDY
This study assesses the impact of biotechnology on the manufacture of specialty and commodity chemicals into the 21st century. Special notice is taken of recent and anticipated advances in genetic engineering, fermenter design, biocatalysis, plant tissue cultue and related technologies deemed likely to make fermentation chemicals more cost competitive with established chemical synthetic routes. Projections are made for the chemical products under review, and the commercial prospects for Western European chemical and biotechnology companies are highlighted.

BIOTECHNOLOGY APPLICATIONS IN CHEMICALS
NOV 1984 108 P. $1800 ONE-TIME
Publ: Predicasts Inc, Commack, NY 516-462-5454
Availability: PUBLISHER
Report No.: 3532
Document Type: MARKET/INDUSTRY STUDY
This detailed technoeconomic study analyzes the impact of biotechnology of over 25 chemical products within the aliphatic organic (organic acids, alcohols and other aliphatics) amino acids, and enzyme segments. Current and potential applications for the fermentation process are also reviewed along with an assessment of diffusion for each individual case provided within a detailed analytical framework of analysis. A review of current company involvement is also provided.

84-9886-4.78
International Developments in Biotechnology and Their Possible Impact on Certain Sectors of the U.S. Chemical Industry International Developments in Biotechnology and Their Possible Impact on Certain Sectors of the U.S. Chemical Industry: Report on Investigation No. 332-174 Under Section 332(b) of the Tariff Act of 1930
(Biotechnology firms, patents, and trade by country, and effect of industry growth on US drug and chemical trade, selected years 1979-2000) <Oct. 1984. xxi+164 p. USITC Pub. 1589. ITC1.12:332-174. ASI/MF/4>
Report on the biotechnology industry, focusing on the potential impact of industry growth on trade in selected drugs and chemicals, selected years 1979-83 with some projections to 2000. Drugs and chemicals covered are antibiotics, biologicals, hormones, vitamins, amino acids, enzymes, ethyl and methyl alcohol, fertilizers, and pesticides.
Includes text statistics and 100 tables showing biotechnology firms;

patents held, by class (enzymes, mutation and genetic engineering, tissue culture); and imports and exports of each drug and chemical; all by country, selected years 1979-83 with U.S. consumption and trade projected to 2000.

International Developments in Biotechnology and Their Possible Impact on Certain Sectors of the U.S. Chemical Industry: Report on Investigation No.332-174 Under Section 332(b) of the Tariff Act of 1930.
Michels, David G.; Briggs, Tedford C.; Greenblatt, Jack
October 1984 USITC Pub.1589 Irregularly 185 pg. PRICE: $Free
PUBLISHER: U.S. International Trade Commission 701 E. St., NW Washington DC 20436
United States of America
TELEPHONE: (202)523-0173

Reports on international developments in biotechnology and their possible effect on the U.S. chemical industry. Tables, compiled from U.N., U.L., and foreign government and industry sources, indicate number of projects and government funding, product lines, licenses, and patents, 1979-1982; domestic production and shipments, exports, imports, and percent of ratios, 1979-1983; and capital expenditures, cost of operations, and raw materials costs, 1983.

Advances in Bioprocess Technology: Industrial / Specialty Chemicals via Biological Sources / Routes.
1985 PRICE: $700.00
PUBLISHER: Technical Insights, Inc. P.O. Box 1304, 158 Linwood Plaza Ft. Lee NJ 07024
United States of America
TELEPHONE: (212)233-1080;TELEPHONE: (201)944-6204

Analyzes the market for bioprocessing and biological raw materials, 1985. Examines research and development and new technology. Provides addresses and telephone numbers of leading research groups and companies.

Unclassified - Pharmaceuticals

NEW BIOTECHNOLOGY AND PHARMACEUTICAL MANUFACTURING
MAR 1984 $500 ONE-TIME
Publ: Creative Strategies Research International, Santa Clara, CA 408-245-4750
Availability: PUBLISHER
Document Type: MARKET/INDUSTRY STUDY
A comprehensive analysis of the application of advanced technology to the production of steroids, antibiotics, vitamins, and alkaloids. This study describes the emerging industry and the market in terms of intermediates and finished products with five-year revenue forecasts. The new technology is clearly explained and the competition identified in terms of market share and prominence in the market.

Unclassified - Japan

Japanese technology assessment : computer science, opto- and microelectronics, mechatronics, biotechnology
J. Albus ... [et al.] for Science Applications International Corporation
Albus, James Sacra.
Corporate Source: Science Applications International Corporation. Park Ridge, N.J., U.S.A. : Noyes Data Corporation, 1986. xviii, 597 p. : ill. ; 24 cm.
Publication Date(s): 1986
ISBN: 0815510969 :
LC Call No.: T27.J3J39 1986 Dewey Call No.: 338.4/76/0952

APPENDIX C

MAILING LIST OF COMPANIES

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EnBio, Inc.
Union Avenue, #408A
Fairfield, CA 94533 Sir or Madam

Mr. Roy A. Dempsey, CEO and Scientific Director
Endogen, Inc.
451 D Street
Boston, MA 02210 Mr. Dempsey
617-439-3250

VP/Research Director
Engenics, Inc.
2 Palo Alto Square, Suite 500
Palo Alto, CA 94304 Sir or Madam

VP/Research Director
Enzo Biochem, Inc.
325 Hudson Street
New York, NY 10013 Sir or Madam

Mr. Paul Mansfield, Marketing Director
Epitope, Inc.
13425 S.W. Koll Parkway
Beaverton, OR 97006 Mr. Mansfield
503-641-6115

VP/Research Director
FMC Corporation
2000 Market Street
Philadelphia, PA 19103 Sir or Madam

Mr. David Hurwitz, Marketing Director
Fisher Scientific
711 Forge Avenue
Pittsburgh, PA 15219 Mr. Hurwitz
412-562-8300

Dr. Petty Lever-Fischer, Research Director
Flow Laboratories, Inc.
7655 Old Springhouse Road
McLean, VA 22102 Dr. Lever-Fischer
703-893-5925

Mr. James M. Gower, Marketing Director
Genetech, Inc.
460 Point San Bruno Blvd.
South San Francisco, CA 94080 Mr. Gower

Dr. Phillip Berman
Genetech, Inc.
460 Point San Bruno Blvd.
South San Francisco, CA 94080 Dr. Berman
415-266-1000

VP/Research Director
Genetic Replication Technologies, Inc.
1533 Monrovia Avenue
Newport Beach, CA 92663 Sir or Madam

VP/Research Director
Genetic Systems Corp.
3005 First Avenue
Seattle, WA 98121 Sir or Madam

VP/Research Director
Genetics Diagnostics Corp.
160 Community Drive
Great Neck, NY 11021 Sir or Madam
516-487-4711

Barbara Deptula/Robert Kay Ph.D.
Genetics Institute
87 Cambridge Park Drive
Cambridge, MA 02114 Mr. Kay & Ms. Deptula
617-876-1170

VP/Research Director
Genetics International, Inc.
50 Milk Street, 15th Floor
Boston, MA 02109 Sir or Madam

Mr. Barry A. Soloman
VP Biomedical Research
W. R. Grace & Co.
25 Hortwell Avenue
Lexington, MA 02173 Mr. Solomon
617-861-9600 x 126

Dr. Craig McMullen, CEO
Hana Biologics, Inc.
626 Bancroft Way
Berkeley, CA 94710 Dr. McMullen

Mr. Ben Walthall, Director Technical Admin
Hana Biologics, Inc.
850 Marina Village Parkway
Alameda, CA 94501 Mr. Walthall
415-748-3000

Mr. Paul Kamitsuka, Marketing Director
Hazleton Research Products
13804 W 107th Street
Lenexa, KS 62215 Mr. Kamitsuka
913-469-5580

Mr. Richard H. Stevenson
Asst. Director-Exploratory Research
Hoffmann-La Roche, Inc.
340 Kingsland Street
Nutley, NJ 07110 Mr. Stevenson
201-235-4920

Dr. Cam L. Garner, Marketing Director
Hybritech Inc.
PO Box 269006
San Diego, CA 92126 Dr. Garner
619-455-6700

Mr. Steve Murdock, Marketing Director
Hyclone Laboratories Inc.
1725 S State Hwy 89-91
Logan, UT 84321 Mr. Murdock
801-753-4584

VP/Research Director
Hytech Biomedical, Inc.
1440 Fourth Street
Berkeley, CA 94710 Sir or Madam

VP/Research Director
IGI Biotechnology, Inc.
9110 Red Branch Road
Columbia, MD 21045 Sir or Madam

Dr. Huei-Hsiung Yang
Director Research & Engineering
Igene Biotechnology, Inc.
9110 Red Branch Road
Columbia, MD 21045 Dr. Yang
301-997-2599

Dr. Frank E. Ruch, Jr.
V.P. Research & Development
Immucell Corp.
966 Riverside Street
Portland, ME 04103 Dr. Ruch
207-797-8386

VP/Research Director
Immulok, Inc.
1019 Mark Avenue
Carpinteria, CA 93013 Sir or Madam

VP/Research Director
Immunex Corp.
51 University Building, Suite 600
Seattle, WA 98101 Sir or Madam
206-587-0430

Mr. H. Stewart Parker, Marketing Director
Immunex Corp.
51 University Street
Seattle, WA 98101 Mr. Parker

VP/Research Director
Immuno Modulators Laboratories, Inc.
10511 Corporate Drive
Stafford, TX 77477 Sir or Madam

Dr. Art Gottlieb, President
Imreg, Inc.
PO Box 56643
New Orleans, LA 70156 Dr. Gottlieb
504-523-2875

VP/Research Director
Interferon Sciences, Inc.
738 Jersey Avenue
New Brunswick, NJ 08901 Sir or Madam
201-240-3250

VP/Research Director
Integrated Genetics, Inc.
51 New York Avenue
Framingham, MA 01701 Sir or Madam
617-875-1336

VP/Research Director
International Genetic Engineering, Inc.
(INGENE)
1701 Colorado Avenue
Santa Monica, CA 90404 Sir or Madam

Mr. Stanley C. Erck, Marketing Director
Integrated Genetics, Inc.
31 New York Avenue
Framingham, MA 01701 Mr. Erck

Mr. Gary L. Snable, Marketing Director
Invitron Corp.
4649 Le Bourget Drive
St. Louis, MO 63134 Mr. Snable
314-426-5000

Mr. William B. Iaconelli, Marketing Director
Ionics, Inc.
65 Grove Street
Watertown, MA 02172 Mr. Iaconelli
617-926-2500

VP/Research Director
Lederle Laboratories
One Cyanamid Plaza
Wayne, NJ 07470 Sir or Madam

Mr. James A. Lee, Marketing Director
Life Sciences, Inc.
1818 Market Street
Philadelphia, PA 19103 Mr. Lee
215-299-8700

Dr. Robert M. Cohn, Research Director
The Liposome Co., Inc.
1 Research Way
Princeton Forrestal Center
Princeton, NJ 08540 Dr. Cohn
609-452-7060

VP/Research Director
The Liposome Co., Inc.
1 Research Way
Princeton Forrestal Center
Princeton, NJ 08540 Sir or Madam

VP/Research Director
Litton Bionetics
5516 Nicholson Lane
Kensington, MD 20895 Sir or Madam

Dr. Leon R. Lyle
Associate Director, Medical Products R&D
Mallinckrodt, Inc.
625 McDonnell Blvd. (PO Box 5840)
St. Louis, MO 63134 Dr. Lyle
314-895-2352

VP/Research Director
Meloy Laboratories, Inc.
6715 Electronic Drive
Springfield, VA 22151 Sir or Madam

Dr. Jackie Leszczak, Marketing Director
Memtek Corp.
28 Cook Street
Billerica, MA 01821 Dr. Leszczak
617-667-2828

Stanley J. Fidelman, Senior V.P./Planning & Development
Merck Sharp & Dohme Research Laboratories
Division of MERCK & Co., Inc.
PO Box 2000
Rahway, NJ 07065 Dr. Fidelman
201-574-5328

Dr. Ronald W. Ellis, Director & Head
Cellular and Molecular Biology
Merck Sharp & Dohme Research Laboratories
West Point, PA 19486
215-661-7545

VP/Research Director
Miles Laboratories, Inc.
1127 Myrtle Street
Elkhart, IN 46515 Sir or Madam
815-937-8270

Dr. Ken Widder, Chairman & CEO
Molecular Biosystems, Inc.
10030 Barnes Canyon Road
San Diego, CA 92121 Dr. Widden
619-452-0681

VP/Research Director
Molecular Diagnostics
400 Morgan Lane
West Haven, CT 06516 Sir or Madam
203-934-9229

Dr. David Reed, Research Director
Molecular Genetics, Inc.
10320 Bren Road, East
Minnetonka, MN 55343 Dr. Reed
612-935-7335

VP/Research Director
Monoclonal Antibodies, Inc.
2319 Charleston Road
Mountain View, CA 94043 Sir or Madam
415-960-1320

Dr. Ernest G. Jaworski
Director of Biological Sciences
Monsanto Company
700 Chesterfield Village Parkway
St. Louis, MO 63198 Dr. Jaworski
314-537-6829

Mr. Tom Defosse, Research Director
New Brunswick Scientific
44 Talmadge Road
Edison, NJ 08818 Mr. Defosse
201-287-1200

VP/Research Director
New England Biolabs
32 Tozer Road
Beverly, MA 01915 Sir or Madam
617-927-5054

VP/Research Director
Nuclear and Genetic Technology, Inc.
172 Brook Avenue
Deer Park, NY 11729 Sir or Madam

VP Research Director
Novo Laboratories, Inc.
59 Danbury Road
Wilton, CT 06897 Sir or Madam

Dr. Shiu-Lok Hu
Laboratory Director
Oncogen
3005 First Avenue
Seattle, WA 89121 Dr. Hu
206-728-4800

VP/Research Director
Oncogene Sciences Inc.
Nassau Hospital Professional Building
Suite 330
222 Station Plaza North
Mineola, NY 11501 Sir or Madam

Mr. W. Barry McDonald, Marketing Director
Oncogene Science, Inc.
350 Community Drive
Manhasset, NY 11030 Mr. McDonald
516-365-9300

VP/Research Director
Organon, Inc.
375 Mt. Pleasant Avenue
West Orange, NJ 11501 Sir or Madam

Mr. Seth Rudwick, V. P. Product Development
Ortho Biotech
Route 202 (PO Box 300)
Raritan, NJ 08869 Mr. Rudwick
201-218-7192

Mr. Michael Burgett, Director
Operations and Development
Ortho Diagnostic Systems, Inc.
1125 Mark Avenue
Carpinteria, CA 93013 Mr. Burgett
805-684-8717

Dr. Jim Gardner
Director of Corporate Strategic Planning
Pfizer, Inc.
235 East 42nd Street
New York, NY 10017 Dr. Gardner
212-573-3267

Dr. Robert M. Flora, VP-R&D
Pharmacia LKB Biotechnology, Inc.
800 Centennial Avenue
Piscataway, NJ 08854 Dr. Flora
201-457-8000

Dr. Stephen M. Coutts
VP Therapeutic Research
Quidel
11077 North Torrey Pines Rd.
La Jolla, CA 92037 Dr. Coutts
619-450-1533

Mr. E. Michael Egan, Marketing Director
Repligen Corp.
One Kendall Square, Building 700
Cambridge, MA 02139 Mr. Egan
617-225-6000

Dr. Jon A. RudBach
V. P. Research & Development
Ribi Immunochem Research, Inc.
PO Box 1409
Hamilton, MT 59840 Dr. RudBach
406-363-6214

VP/Research Director
Ribi Immunochem Research, Inc.
PO Box 1409
Hamilton, MT 59840 Sir or Madam

VP/Research Director
Sandoz, Inc.
Route No. 10
East Hanover, NJ 07936 Sir or Madam
201-386-7500

Dr. Joseph F. Lameudolce
Director of Pharmaceutical Research
Schering-Plough Corporation
2000 Galloping Hill Road
Kenilworth, NJ 07033 Dr. Lamendolce

VP/Research Director
G. D. Searle & Co
PO Box 1045
Skokie, IL 60076 Sir or Madam

VP/Research Director
Serono Laboratories, Inc.
280 Pond Street
Randolph, MA 02368 Sir or Madam

Dr. Ron Wolfe, Research Director
Sigma Chemical Co.
PO Box 14508
St. Louis, MO 63178 Dr. Wolfe
314-771-5765

Mr. John J. Dingerdissen
Scientific Coordinator/Biotechnology Research
Smith Kline & French Laboratories
PO Box 1539
King of Prussia, PA 19406-0939 Mr. Dingerdissen
215-270-7358

Dr. George Poste, Director of Research
SmithKline Beckman
PO Box 7929
Philadelphia, PA 19101 Dr. Poste
215-751-4000

Dr. Peter Sears
SmithKline Beckman
PO Box 7929
Philadelphia, PA 19101 Dr. Sears
215-751-4000

Dr. Edgar Haber, President
The Squibb Institute for Medical Research
PO Box 4000
Princeton, NJ 08540-4000 Dr. Haber
609-921-4487

VP/Research Director
Standard Oil Co. of California
225 Bush Street
San Francisco, CA 94104 Sir or Madam

A. K. Rao, Director of Technology,
Business Development
Stearns Catalytic Division,
United Engineers & Constructors
30 South 17th Street
Philadelphia, Pennsylvania 19101 Mr. Rao
215-422-4210

Ms. Patricia Pallares
Technical Services Director
Summa Medical Corp.
4272 Balloon Park Road, N.E.
Albuquerque, NM 87109 Sir or Madam
505-345-8891

VP/Research Director
Syncor International
12847 Arroyo Street
Sylmar, CA 91342 Sir or Madam

Dr. Claire T. Wake, Director
Technical Development
Synergen, Inc.
1885 33rd Street
Boulder, CO 80301 Dr. Hirsh
303-938-6270

Dr. Tony Allison
Syntex Research
c/o Syntex Corp.
3401 Hillview Avenue
Palo Alto, CA 94304 Dr. Allison

Dr. Arlen Nordhagen, Director,
Business Development
Synthetech, Inc.
2585 Central Avenue
Boulder, CO 80301 Dr. Nordhagen
303-444-9597

Dr. Thomas Gutshall
Syva Co.
900 Arastradero Road
Palo Alto, CA 94303 Dr. Gutshall

VP/Research Director
3M
3M Center
St. Paul, MN 55144 Sir or Madam

Mr. Oran W. Nicks
Director, Space Research Center
Texas A&M University
College Station, TX 77843-3118 Oran
409-845-5293

Mr. David L. Corbet, Marketing Director
T Cell Sciences, Inc.
840 Memorial Drive
Cambridge, MA 02139 Mr. Corbet
617-864-2160

VP/Research Director
Techniclone International Corp.
3301 South Harbor Blvd., Suite 104
Santa Ana, CA 92704 Sir or Madam

Terry Malone, Business Development Manager
Triton Biosciences Inc.
1501 Harbor Bay Parkway
Almeda, CA 94501 Mr. Malone
415-769-5370

VP/Research Director
Unigene Laboratories, Inc.
110 Little Falls Road
Fairfield, NJ 07006 Sir or Madam
201-882-0860

Mr. A. K. Rao
Director of Technology
United Engineers & Constructors
30 S. 17th Street
Philadelphia, PA 19101 Mr. Rao
215-422-4210

Dr. Curtis Miller
The Upjohn Company
7000 Portage Road
Kalamazoo, MI 49001 Dr. Miller

Mr. Barry Godowsky, Marketing Director
Ventrex Laboratories, Inc.
217 Read Street
Portland, ME 04104 Mr. Godowsky
207-773-7231

Dr. David Berry
Welcomme Research Laboratories
3030 Cornwallis Road
Research Triangle Park, NC 27709 Dr. Berry

VP/Research Director
Worne Biotechnology, Inc.
Medford Medical Builsing
Stokes Road, Box 458
Medford, NJ 08055 Sir or Madam
609-654-5065

Mr. James Burchall, Head
Microbiology Division
Burroughs Wellcome Co.
3030 Cornwallis Road
Research Triangle Park, NC Mr. Burchall

Mr. Steven C. Mendell, Marketing Director
Xoma Corp.
2910 Seventh Street
Berkeley, CA 94710 Mr. Mendell
415-644-1170

Melanie Call, Market Analyst
Zymogenetics
4225 Roosevelt Way NE
Seattle, WA 98105 Ms. Call
206-547-8080

VP/Research Director
Research and Development Laboratories
One River Road
Schenectady, NY 12345 Sir or Madam

APPENDIX D

SURVEYED BIOTECHNOLOGY COMPANY PROFILES

Dr. Dennis E. Vaccaro, VP-Marketing
Advanced Magnetics, Inc.
61 Mooney Street
Cambridge, MA 02138 Dr. Vaccaro_
617-497-2070

TECHNOLOGIES: Purification (lab-scale)
MAJOR PRODUCTS: BioMag magnetic affinity chromatography reagents, research RIA kits for prostaglandins, thromboxane, leukotrienes, cyclic nucleotides.

Mr. Allen J. Dines
Director Business Development
Agracetus
8520 University Green
Middletown, WI 53562 Mr. Dines_
608-836-7300

TECHNOLOGIES: Recombinant DNA, Fermentation, and Cell/tissue culture
MAJOR PRODUCTS: Genetically improved crops, animal health products, microbial crop treatments.
PRODUCTS UNDER DEVELOPMENT: Rhizobium, insect resistance crops, disease resistant crops, vaccine-adjuvants, corn yield enhancer microbe, vaccines, IL-2 as shipping fever preventative..

Dr. Philip L. McMahon
Director of R&D
Agritech Systems, Inc.
100 Fore Street
Portland, ME 04101 Mr. Shaw_
207-774-4334

TECHNOLOGIES: Recombinant DNA, Hybridoma/cell fusion, and Cell/tissue culture
MAJOR PRODUCTS: Diagnostics for animal and food applications

Dr. Richard L. Eichholz
Manager Strategic Planning
Amersham Corp.
2636 S. Clearbrook Drive
Arlington Heights, IL 60005 Mr. Dunbar_
312-593-6300 x 255

TECHNOLOGIES: Recombinant DNA, Purification (lab-scale), Hybridoma/cell fusion Synthesis, Sequencing, and Enzymology

Amersham Corp. (continued)

MAJOR PRODUCTS: P-32/S-35 nucleotides: cDNA synthesis and cloning kits; I-125; RAS image analysis system; biomedical research assays; sulpher-35 methionine for protein synthesis studies; sulpher-35 labelled nucleotides for sequencing nucleic acids; labelled lymphokines, growth factors and petides for new drug studies; monoclonal antibody detection systems.

Dr. W. Neal Burnette, Research Scientist
Amgen
1892 Oak Terrace Lane
Newbury Park, CA 91320 Dr. Burnette_
805-499-5725 x 3015

TECHNOLOGIES: Recombinant DNA, Fermentation, Purification (lab-scale), Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Synthesis, Sequencing, Enzymology

MAJOR PRODUCTS: Erythropoietin, granulocyte colony stimulating factor (G-CSF); consensus interferon, gamma interferon; interleukin-2; hepatitis B vaccine; porcine and bovine somatotropin; epidermal growth factor, platlet derived growth factor IGF-I, FGF, indigo; enzymes; vitamins.

Laura J. Crane
Director, R&D-Laboratory Products
J.T. Baker Inc.
222 Red School Lane
Phillipsburg, NJ 08865 Ms. Crane_
201-859-2151 x 9417

TECHNOLOGIES: Purification (lab-scale), Large-scale purification

MEJOR PRODUCTS: Chromatography media for protein, chiral and small molecule separation; high purity solvents for chromatography, DNA and protein synthesis, solid phase extraction columns for sample preparation; TLC plates; buffer salts; electrophoresis chemicals; dyes, salts and solvents for bioprocessing.

PRODUCTS UNDER DEVELOPMENT: New chromatography media high purity chemicals and solvents.

Mr. Deither J. Recktenwald, Senior Scientist
Becton Dickinson Immunocytometry Systems
2375 Garcia Avenue (PO Box 7375)
Mountain View, CA 94043 Mr. Recktenwald_
415-968-7744

TECHNOLOGIES: Hybridoma/cell fusion, Cell/tissue culture
MAJOR PRODUCTS: FACScan, FACStar, FACStar Plus, Leu monoclonal reagents, Simultest reagents, CAS Image Analysis System (flow cytometers, image analysis, monoclonal antibodies for cellular immunology).

Andrew P. Lesniak, Ph.D., Product Manager
Bellco Biotechnology
340 Edrudo Road (PO Box B)
Vineland, NJ 08360 Dr. Lesniak_
800-257-7043

TECHNOLOGIES: Recombinant DNA, Fermentation, Hybridoma/cell fusion, Cell/tissue culture
MAJOR PRODUCTS: Cell culture labware and equipment; bioreactor system utilizing immobilized cells.

Joanne T. Caha, Director/Personnel & Amin.
Biomatrix, Inc.
65 Railroad Avenue (P. O. Box 174)
Ridgefield, NJ 07657 Ms. Caha_
201-945-9550

TECHNOLOGIES: Purification (lab-scale), Bioprocess,Cell/tissue culture
MAJOR PRODUCTS: Biomatrix, Hyladern, BioCare, HA-24
PRODUCTS UNDER DEVELOPMENT: Advanced biological matrices with applications in orthopedics including arthroscopic surgery, opthalmology, wound care, cardiovascular surgery and drug delivery.

Dr. Keith C. Backman
Biotechnica International, Inc.
85 Bolton Street
Cambridge, MA 02140 Dr. Backman_
617-864-0040

TECHNOLOGIES: Recombinand DNA, Fermentation, Purification (lab-scale), Bioprocess, Cell/tissue culture, Process Monitoring Control, Synthesis, Enzymology
MAJOR PRODUCTS: DMD test for periodontitis, Endo H, chitinase, silage inoculants, improved rhizobial strains.
PRODUCTS UNDER DEVELOPMENT: Vaccines and therapeutic proteins, amino acids and vitamins, DNA probes, dental diagnostics and advanced dental products, crop agriculture, industrial yeasts, specialty enzymes.

Dr. John Lifter, Director
Viral Immunology
Cambridge Bioscience Corp.
365 Plantation Street
Worcester, MA 01605 Dr. Lifter_
617-797-5777

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Large-scale purification, Synthesis, Sequencing
MAJOR PRODUCTS:	Rotaclone rotavirus diagnostic, Adenoclone adenovirus diagnostic, Clin Ease Leukotest feline leukemia diagnostic, Recombigen AIDS diagnostic.
PRODUCTS UNDER DEVELOPMENT:	Feline leukemia vaccine, AIDS vaccine, infectious disease diagnostic.

Mr. John H. Wheeler, VP for Sales and Marketing
Charles River Biotechnical Services, Inc.
251 Ballardvale Street
Wilmington, MA 01887 Mr. Wheeler_
617-658-6000

TECHNOLOGIES:	Purification (lab-scale), Bioprocess, Cell/tissue culture, Large-scale purification, Process Monitoring Control
MAJOR PRODUCTS:	Opticell cell culture systems; Maxitap ascites production system.

Dr. Pablo Valenzuela, VP R&D
Chiron Corporation
4560 Horton Street, Suite 0214
Emeryville, CA 94608 Dr. Valenzuela_
415-655-8730

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab-scale), Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Sequencing
MAJOR PRODUCTS:	Hepatitis B vaccine, Recombivax RIBA 216 AIDS Diagnostic test
PRODUCTS UNDER DEVELOPMENT:	Vaccines; AIDS, herpes, malaria, FeLV, CMV; superoxide dismutase, epidermal growth factor, IFGs, FGFs, factor VIII, hepatitis and AIDS diagnostics.

C. F. Thompson, Director of Biotechnology
Dow Chemical Co.
1701 Building
Midland, MI 48674 Mr. Thompson_
517-636-1066

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab-scale), Hybridoma/cell fusion, Cell/Tissue Culture, Synthesis, Enzymology, Bioprocess, Large-scale purification, Process Monitoring Control,
MAJOR PRODUCTS:	NEN Research Products, Sorvall centrifuges, Coupler peptide synthesizer, Coder DNA synthesizer, Zorbax HPLC columns, cell culture products, Genesis 2000 DNA sequencer, AIDS research products.

Mr. P. R. Grisdale, Director
Exploratory Sciences Division/Life Sciences
Eastman Kodak Co.
1909 Lake Avenue
Rochester, NY 14617 Mr. Grisdale_
716-722-0190

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Process Monitoring Control, Synthesis, Sequencing, Enzymology
MAJOR PRODUCTS:	Snomax snow inducer; diagnostic enzymes; blood and body fluid analyzers.
PRODUCTS UNDER DEVELOPMENT:	Pharmaceuticals, pharmaceutical intermediates, food additives, food additives, fluid analyzers.

Dr. Mark P. Becker
Senior Biochemical Engineer
Eli Lilly and Co.
Lilly Corporate Center, KY409
Indianapolis, IN 46285 Mr. Step_
317-276-7665

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab scale), Bioprocess, Hybridoma/cell fusion, Large-scale purification, Synthesis, Sequencing
MAJOR PRODUCTS:	Ceclor, Humulin, Dobutrex, Darvon Keflex, Oncovin.
PRODUCTS UNDER DEVELOPMENT:	t-PA, APC, proinsulin, BST.

Mr. Roy A. Dempsey, CEO and Scientific Director
Endogen, Inc.
451 D Street
Boston, MA 02210 Mr. Dempsey_
617-439-3250

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Process Monitoring Control
MAJOR PRODUCTS:	Ultrapure IL-1, consensus IL-1, anti-TNF alpha, anti-lymphotoxin (TNF-beta), anti IL-1, anti IL-2, affinity purified, tumor necrosis factor/cachectin, interleukin-2, anti-IFN-gamma
PRODUCTS UNDER DEVELOPMENT:	Purified human lymphotoxin, anti-hIL-4, LIF, anti-LIF, anti-GM-CSF

Barbara Deptula/Robert Kay Ph.D.
Genetics Institute
87 Cambridge Park Drive
Cambridge, MA 02114 Mr. Kay & Ms. Deptula
617-876-1170

TECHNOLOGIES:	Recombinant DNA, Purification (lab-scale), Large-scale purification, Sequencing, Enzymology
PRODUCTS UNDER DEVELOPMENT:	M-CSF, IL-3, 2d generation TPA, bone growth factors.

Dr. Huei-Hsiung Yang
Director Research & Engineering
Igene Biotechnology, Inc.
9110 Red Branch Road
Columbia, MD 21045 Dr. Yang_
301-997-2599

TECHNOLOGIES:	Fermentation, Purification (lab-scale), Bioprocess, Large-scale purification, Enzymology
MAJOR PRODUCTS:	Macroin milk/eggwhite replacer, MinraLac calcium and milk minerals food supplement; ClandoSan nematicide-soil conditioners; butyric and propionic acids and esters for flavors and fragrances; LevaSan (Poly-LevyLan) polyfructose biogum; streptoccal lysins for clinical diagnostic tests

Dr. Frank E. Ruch, Jr.
V.P. Research & Development
Immucell Corp.
966 Riverside Street
Portland, ME 04103 Dr. Ruch_
207-797-8386

TECHNOLOGIES: Purification (lab-scale), Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification

MAJOR PRODUCTS: RPT (Rapid Progesterone Test)-cowside progesterone in milk assay; RMT (Rapid Mastitis Test); RJT (Rapid Johnes Test); group A streptococcal reagents and tests

Dr. Ken Widder, Chairman & CEO
Molecular Biosystems, Inc.
10030 Barnes Canyon Road
San Diego, CA 92121 Dr. Widden_
619-452-0681

TECHNOLOGIES: Purification (lab-scale), Synthesis, Sequencing, Emzymology

MAJOR PRODUCTS: SNAP non-radioactive DNA probes for infectious diseases; magnetic microspheres for cell sorting; DNA synthesis supports; The Extractor nucleic acid purification system; Albunex ultrasound contrast agent.

PRODUCTS UNDER DEVELOPMENT: Albunex ultrasound contrast agent; MRI contrast agent; ultrasensitive probe detection systems.

Mr. Seth Rudwick, V. P. Product Development
Ortho Biotech
Route 202 (PO Box 300)
Raritan, NJ 08869 Mr. Rudwick_
201-218-7192

TECHNOLOGIES: Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Process Monitoring Control, Synthesis, Sequencing

MAJOR PRODUCTS: OKT3 (Orthoclone OKT3), Timunox (thymopertin)

PRODUCTS UNDER DEVELOPMENT: r-Hu-EPO, IL-2, hepatitis B, EGF, cancer monoclonal antibodies

Dr. Robert M. Flora, VP-R&D
Pharmacia LKB Biotechnology, Inc.
800 Centennial Avenue
Piscataway, NJ 08854 Dr. Flora_
201-457-8000

TECHNOLOGIES: Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Process Monitoring Control, Synthesis, Sequencing, Enzymology

MAJOR PRODUCTS: FPLC and GTi chromatography systems and instrument components; PhastSystem and electrophoresis systems (Pulsaphor , Multiphor), Gene Assembler and Violynx synthesyzers; FPLCpure , restriction nucleasis; nucleic acids including vectors; chromatography media including Sephadex , Sepharose , Sephacryl , MonoBeads , Superose , ultrafiltration products; large-scale bioprocessing.

Dr. Stephen M. Coutts
VP Therapeutic Research
Quidel
11077 North Torrey Pines Rd.
La Jolla, CA 92037 Dr. Coutts_
619-450-1533

TECHNOLOGIES: Recombinant DNA, Purification (lab-scale), Hybridoma/cell fusion, Cell/tissue culture

MAJOR PRODUCTS: Quidel pregnancy test, Quidel ovulation test, Quidel Strep Group A test, Quidel allergy screen, Open Alert /Bovi-Pro 21 milk progesterone test (distributed by Santel S.A.) QTEST pregnancy and ovulation tests (distributed by Becton, Dickinson and Co.).

PRODUCTS UNDER DEVELOPMENT: D-GL, suppressive factor of allergy; diagnostic products; allergy, infectious disease assay technologies, drug testing (TDM and DOA).

Dr. Jon A. RudBach
V. P. Research & Development
Ribi Immunochem Research, Inc.
PO Box 1409
Hamilton, MT 59840 Dr. RudBach_
406-363-6214

TECHNOLOGIES: Fermentation, Purification (lab-scale), Cell/tissue culture, Large-scale purification, Synthesis

MAJOR PRODUCTS: Ribigen veterinary anti-tumor product; Detox , human anti-tumor, anti-viral product; Ovamid , human anti-tumor product; adjuvants (MPL, TDM); research products (adjuvants, lipopolysaccharides, mitogens, custom polyclonal sera).

PRODUCTS UNDER DEVELOPMENT: Detox , in Phase II human clinical trials for malignant melanoma, Kaposi's sarcoma, genital warts; Ovamid , in Phase I human clinical trials for ovarian cancer, human testing against colorectal cancer planned; adjuvants for non-specific resistance, malignant and infectious disease vaccine applications

Mr. John J. Dingerdissen
Scientific Coordinator/Biotechnology Research
Smith Kline & French Laboratories
PO Box 1539
King of Prussia, PA 19406-0939 Mr. Dingerdissen_
215-270-7358

TECHNOLOGIES: Recombinant DNA, Fermentation, Purification (lab-scale), Bioprocess, Hybridoma/cell fusion, Cell/tissue culture, Large-scale purification, Synthesis, Enzymology, Sequencing

MAJOR PRODUCTS: Tagamet, Dyazide.

PRODUCTS UNDER DEVELOPMENT: t-PA, rDNA malaria vaccine, leukotriene receptor antagonist.

Dr. Claire T. Wake, Director
Technical Development
Synergen, Inc.
1885 33rd Street
Boulder, CO 80301 Dr. Hirsh_
303-938-6270

TECHNOLOGIES: Recombinant DNA, Fermentation, Purification (lab-science), Bioprocess, Cell/tissue culture, Large-scale purification, Process Monitoring Control, Synthesis, Sequencing, Enzymology

PRODUCTS UNDER DEVELOPMENT: Protease inhibitors (elastase inhibitor, collagenase inhibitor), fibroblast growth factor (FGF), vaccines for livestock, feed additives, materials for tertiary oil recovery.

Terry Malone, Business Development Manager
Triton Biosciences Inc.
1501 Harbor Bay Parkway
Almeda, CA 94501 Mr. Malone_
415-769-5370

TECHNOLOGIES:	Recombinant DNA, Fermentation, Purification, Hybridoma/cell fusion, Cell/tissue culture, Synthesis, Sequencing
MAJOR PRODUCTS:	Anti-cytokeratin Mabs (MAK-6) , Ras-ha Abs. TGF-alpha Abs. Betaseron .
PRODUCTS UNDER DEVELOPMENT:	Recombinant beta-interferon (Betaseron), transforming factor-alpha, automated immunoassay system, HTLV-1 assay, cytokeratin assay, cancer markers.